Ololade Olatunji *Editor*

# Natural Polymers

## Industry Techniques and Applications

Springer

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ISBN 978-3-319-26412-7 ISBN 978-3-319-26414-1 (eBook)
DOI 10.1007/978-3-319-26414-1

Library of Congress Control Number: 2015955390

Springer Cham Heidelberg New York Dordrecht London


Printed on acid-free paper

Springer International Publishing AG Switzerland is part of Springer Science+Business Media (www.springer.com)

# Preface

The word polymer is derived from the Greek word "poly" meaning many and "meros" which means parts. Hence polymer refers to molecules made up of many parts. More specifically, polymers are defined as molecules made up of repeated units of smaller molecules. Although recent decades has seen a boost in the polymers in various industries from pharmaceutical to construction to fashion industries where designer shoes and bags made from synthetic and natural polymers from both plants and animals have become commonplace, polymers have been in existence since the very existence of life. DNA, cellulose, cotton, and rubber are all polymers occurring in nature since the beginning of the ages. Processing of natural polymers has been taking place since the early humans who have long woven and dyed fibers of silk, wool, and carbohydrates from flax and cotton. Natural rubber (*Hevea brasiliensis*) has been used by the early South American civilization for waterproofing and elastic materials (Seymour and Carraher 1992). Today processing techniques of natural and synthetic polymers have become more advanced with broader applications from scaffold in tissue engineering (Chap. 5) to films for packaging (Chap. 7). An account of the development of synthetic polymers over the years exists in the literature (Seymour and Carraher 1992) showing the development of polymers from mainly natural polymers such as wool, cotton, flax, leather cellulose, and silk in the early 1800s to the development of vulcanized rubber in 1839. Later developments led to development of bakelite, cellulose acetate, and cellulose nitrate between 1907 and 1923. Later in the 1930s–1940s as understanding of polymers gradually developed, more polymers such as poly(methyl methacrylates), polyvinyl acetate, and polystyrene were developed. Polycarbonate, polypropylene, high-density polyethylene, flurocarbones, silicones, and polyurethanes and a host of other polymers were developed between 1940 and the late 1950s, where polymer saw a huge development. Later years saw development of more polymers such as Kevlar and development of more varied forms of pre-existing polymers to improve properties such as electrical conductivity. Today biopolymers such as Polylactic acid and chitosan have gained increasing attention in industries in applications such as 3D printing and tissue engineering.

Polymers have for centuries been an attractive alternative to metals due to the rather unique properties they possess. These properties include their tendency to

be biocompatible, relative lighter weight, and ease of chemical modification compared to metals. Natural polymers herein refer to polymers obtained from natural sources with minimal or no alteration to their chemical structure. This book looks at their extraction, purification, modification, and processing for various industrial applications. Although a large portion of the organic chemistry industry is dedicated to producing systemic polymers, natural polymers play a significant role in many industries ranging from biomedical, pharmaceutical, to construction industries. These are discussed in this book.

Chapter 1 discusses the classification of natural polymers within the scope of the book. Natural polymers are classified based on their sources in nature as polysaccharides, proteins, polynucleotides, polyisoprenes, and polyesters. The chapter goes further to give descriptions and examples of natural polymers which fall within these classifications.

Chapter 2 discusses the processing and characterization techniques that are applicable to natural polymers of industrial relevance. For each processing and characterization technique discussed, example case studies of natural polymers which the techniques apply to are provided. The chapter discusses some recent works that present innovative approaches to processing of natural polymer-based materials. This includes techniques for production of polymer composites. Electrospinning, extrusion, film casting, and spin coating are some of the processes discussed. Characterization methods presented are mainly methods such as TEM, XRD, and NMR with some example results of their applications to natural polymer-based materials for various applications.

In Chap. 3 methods for extraction, purification, and modification of some natural polymers of industrial relevance are discussed. These include acid and alkali methods of extraction of gelatin from various sources, extraction of starch, chitin, and chitosan among others. In doing so the structure of the polymers are also discussed as well as the structural modifications that they undergo in the process of extraction and modification.

Chapter 4 discusses some biomedical applications of natural polymers. This includes applications in scaffolds, wound healing, and repair of skin and bones. The chapter gives examples of cases where natural polymers either alone or blended with other materials are used in such applications. Gelatin, chitosan, and cellulose have shown wide application in this particular industry.

Chapter 5 discusses applications of natural polymer in the food industry. This chapter does not greatly focus on food packaging as application of natural polymers in packaging is discussed in a separate chapter. The chapter looks at application of natural polymer-based microparticles, gels, and emulsions in the food industry with some example case studies.

Chapter 6 looks at the recent applications of natural polymers used in packaging, with particular focus on various polymer blends. This chapter takes the approach of pointing out some of the challenges in the packaging industry and the role natural polymers play in this. Here food packaging, both edible and nonedible, as well as pharmaceutical packaging are discussed as they cover a significant portion of the packaging industry.

Chapter 7 discusses the application of natural polymers in engineering with a large part focusing on drilling engineering. The first part of the chapter describes the role of natural polymers in the nonrenewable energy industry (drilling fluids). In doing so the problems of drilling fluid loss during its circulation in oil field wells and its solution by using natural polymers are also discussed. The second part deals with the role of natural polymers in the renewable energy industry, particularly as biomass; this part reviews the types of renewable energy produced from biomass. The third part focuses on the role of natural polymers in wastewater treatment technology.

The application of natural polymers in the cosmetics industry is discussed in Chap. 8, mainly polysaccharides and proteins obtained from vegetable, animal, and biotechnology origins. The use of cellulose derivatives which are widely used for their physicochemical properties and cosmetic benefits are also discussed. The versatile role of natural polymers as stabilizers, modifiers, or other additives is discussed. Examples of cosmetic formulations in the cosmetic industries are presented. Natural polymers are sometimes alone, but more often in combination with synthetic polymers to broaden their applicability in hair care, skin care, or toothpaste products.

In Chap. 9 the application of natural polymers in the pharmaceutical industry is discussed. This chapter covers a broad area which includes transdermal drug delivery, oral, topical, nasal, and ocular drug delivery, among others. Natural polymers as hydrogels, crosslinked with other natural and synthetic polymers in their various pharmaceutical applications are discussed.

The environmental impacts of natural polymers are discussed in Chap. 10. The use of natural polymers in place of synthetic polymers or in combination with synthetic polymers poses some advantages as well as disadvantages. Consideration should be given to the overall impact on the environment during extraction, purification, modification, and processing of natural polymers for various applications. Case studies in the case of lignocellulose-based natural polymers are considered alongside others.

Chapter 11 covers the economic impact of natural polymers. The chapter in a couple of pages highlights some natural polymers of economic importance. The chapter then looks at the global impacts of natural polymer in various economies mainly UK, US, Brazil, and some African regions.

In Chap. 12 some future prospects of natural polymers in specific industries are discussed. This includes some novel developments which point to the possible direction of natural polymer applications and processing in the various industries in the future. The future economic prospects of natural polymers are also discussed in this chapter with reference to some reported economic reports. This leads to the final chapter which gives some concluding remarks for the book.

## Reference

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# Chapter 1
# Classification of Natural Polymers

**Ololade Olatunji**

## 1.1 Introduction

Natural polymers by themselves are a class of polymers which refer to polymers sourced from nature (plants or animals). They include mainly carbohydrates and proteins which exist in plants and animals providing mainly structural support. Other polymers include thermoplastics, thermosets, elastomers, and rubbers. The focus of this book is primarily on natural polymers. This refers to polymers that are derived through extraction from their bulk form in nature, for example, cellulose or lignin extracted from wood. This also includes polymers produced by biological process such as bacteria synthesis or fermentation.

Like synthetic polymers, natural polymers can be grouped based on their formation method as addition and condensation polymers. Most natural polymers are condensation polymers which are formed as a result of monomer units combining to form a small molecule (usually water) as a by-product. Additional polymers are those formed by direct combination of the monomer units making up the polymer without any by-product. Polymers existing in nature can be grouped into six main classifications with respect to their sources: Proteins, polysaccharides polynucleotides, polyisoprenes, polyesters, and lignin (Atkins 1987). In Table 1.1, a list of polysaccharides from various sources is provided (Olatunji et al. 2014; Brostow 2010; Abdelfadeel 2012; Rinaudo 2005).

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O. Olatunji (ed.), *Natural Polymers*, DOI 10.1007/978-3-319-26414-1_1

**Table 1.1** List of some polysaccharides from various sources

| Source | Polymer |
|---|---|
| Cells walls of plants | Pectin |
| Seeds and roots | Galactomannans |
| Seaweeds | Carragenans, alginates, agar |
| Animal cell walls | Hyaluronan |
| Shells of aquatic animals | Chitin |
| Wood | Cellulose, lignin, hemicellulose |
| Skins and bones of animals and scales of fish | Gelatin |
| Bacteria | Xanthan, hyaluronan, gellan |
| Fungi | Cardlan, scleroglucan, schizophyllan |

## 1.2 Polysaccharides

These are homopolymers of glucose or amino sugars linked by acetic bonds. Polysaccharides are known to be by far the most abundant renewable resource in the world. Overall, the amount of polysaccharide produced from synthesis from plants by the sun exceeds that produced synthetically on an annual basis by several orders of magnitude (Dumitriu 2005).

Polysaccharides are of various types depending on their structure or function. In terms of function there are three main types; storage polysaccharides such as starch and glycogen, structural polysaccharides such as cellulose and chitin, and gel forming polysaccharides such as alginic acid and mucopolysaccharides (Yui 2005). They can also be branched or straight chained polymers, ionic or nonionic (cationic and anionic) polymers.

The major storage polysaccharides are starch (amylase and amylopectin) and glycogen (Yui 2005), while the most common structural ones are chitin and cellulose. Chitin being the structural polysaccharides in some animals such as crustaceans while cellulose is the main structural component of plants alongside hemicelluloses, pectin, and lignin. Hyaluronan is another structural polysaccharide found in human cells. Hyaluronic acid is also an anionic polysaccharide.

The overall physiological property of each polysaccharide depends on the monopolymers it contains as well as on their orientation within the polymer structure (Kajiwara 2005). Many polysaccharides show irregular properties unlike synthetic polymers which makes their classification and characterization somewhat challenging. An example is in the case of amylopectin, where due to its highly branched nature, by laws of polymer science should ideally be noncrystalline. Yet amylopectin takes a semicrystalline form (Burchard 2005). This has for many years kept many researchers inclined toward studying synthetic polymers rather than natural polymers, especially polysaccharides that show many irregularities in

their structure and properties. However, polysaccharides have become more attractive due to their biodegradable and biocompatibility tendencies.

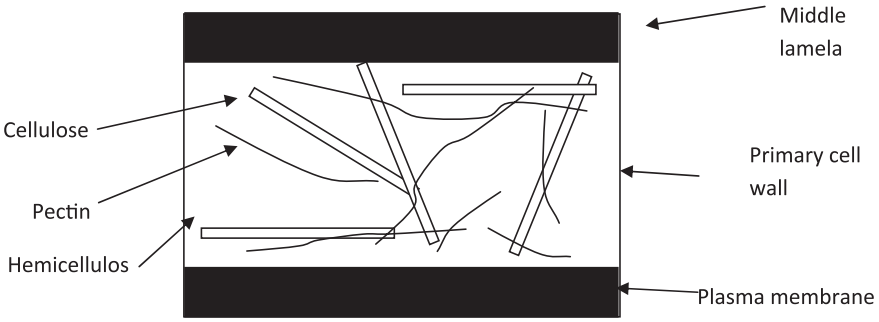
The following paragraphs summarize the structure and function of each of these polysaccharides.

### *1.2.1 Cellulose*

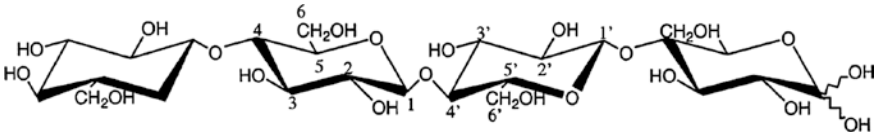
Cellulose as the principal component of plant cell wall makes up about half of the biomass of photosynthetic organisms, thus making cellulose possibly the most abundant molecule on earth. Alongside other components such as lignin, pectin, and hemicelluloses, it makes up the cell wall which is the distinguishing difference between animal and plant cells. The application of cellulose goes way back to the Chinese dynasties and Egyptian pharaohs where evidence exists of their use in writing materials and lingerie (Perez 2005). For many centuries cellulose has been abundantly sourced from wood, cotton, hemp, linen, jute, kenaf, sugar beet cereal straws, flax and is widely exploited for various industrial applications. Applications of cellulose range from clothing pulp and paper to food conferring huge economic relevance (Perez 2005). Other sources of cellulose include bacteria (e.g., Acetobacter), algae (e.g., Valonia and Microdicyon), and marine animals of the Ascite family. Cellulose cannot be digested by the human body, however, animals, in particular ruminants, can digest cellulose. It is also water insoluble. (Viahakha 2012).

The word cellulose was first coined by the French chemist, Anselme Payen in 1838, who also was the first to identify the molecule as a fibrous component of plant cell. Earlier works had made mention of acid hydrolysis of a component of plant cell (Viahakha 2012; Payen 1838). The fundamental formula of the cellulose structure was established by Willstatter and Zechmeister (1913) while further work (Irvine and Hirst 1923) resulted in the presently accepted concept of cellulose as macromolecular. By late 1931, following the numerous various work done on cellulose the primary structure had already been established as a linear homopolymer of glucose residues with D configuration linked by β-(1 → 4) glycosidic linkages (Perez 2005).

A healthy plant cell wall is defined by its rigidity and dynamic nature. These two requirements are met by a mixture of cellulose and protein within the plant cell walls with cellulose microfibrils providing the resistance against tensile strength and allowing for cell growth and extension (Jarvis 1984). Terminal complexes of cellulose synthase, 5c-diphosphate (UDP) glucose, and glucose molecules are important components of the formation and elongation of cellulose microfibrils (Malcom 2000; Perez 2005).




Schematic representation of plant cell wall showing the various polysaccharide components.



Schematic representation of cellulose chain.

### *1.2.2 Hemicelluloses*

Another major component of plant cells is hemicelluloses which form a matrix for the cellulose microfibrils. Hemicelluloses are made up of a variety of molecules such as xyloglucans, xylans, mannans, and β(1-3)-β(1-4)-glucans (Chanzy 1990; Viahakha 2012; Perez 2005) forming a matrix around the cellulose microfibrils. They are usually molecularly bonded to the cellulose microfibrils via forces such as hydrogen bonds, van der Waals forces, and other molecular interactions. Hemicelluloses also serve other functions such as cell signaling or acting as reserves for metabolism.

While cellulose is strong and relatively chemically stable straight chain crystalline polysaccharide, hemicelluloses have an amorphous branched structure and little mechanical strength. They also have a more random nature with shorter chain. Hemicelluloses make up about 20–30 % of dry plant biomass. The industrial significance of hemicelluloses lies in their potential to be hydrolyzed into fermentable sugars for applications such as ethanol production. However, a limitation in

this application is that other than glucose hemicelluloses typically consist of four other sugars which include arabinose, galactose, xylose, and mannose. In addition to this it also contains other molecules such as acetic, glucuronic, and ferulic acids. This poses a limitation because fermentation of such a wide range of substances is relatively more complex than fermentation of, for example, cellulose (Wyman 2005).

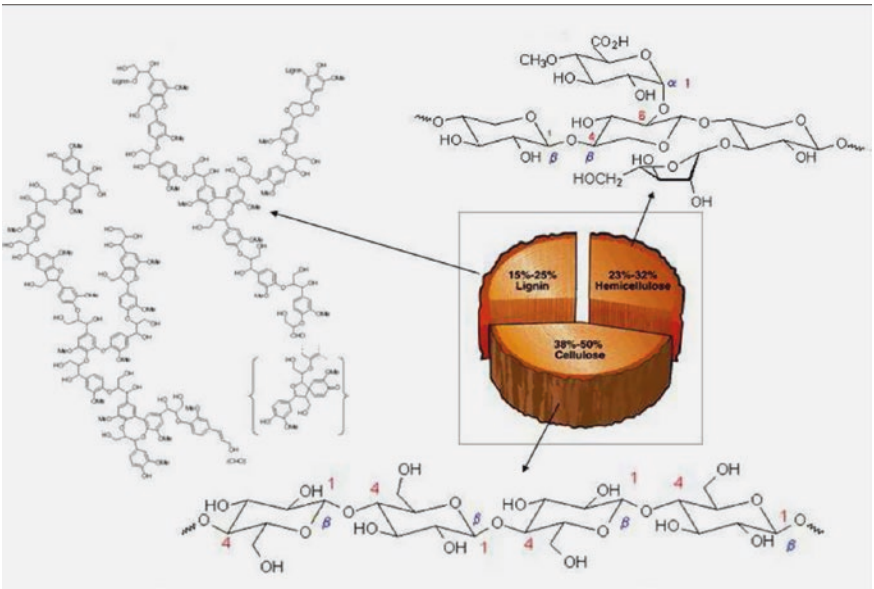
### *1.2.3 Lignin*

While cellulose is regarded as the most widely abundant natural polymer and indeed the most abundant natural resource, lignin is the most abundant aromatic polymer in nature and the next most abundant polymer. Lignin comes from the Latin word lignum, meaning wood. Lignin was first referred to as a constituent of wood by Ansleme Payen in 1838 as the carbon substance acting as the matrix in wood composite embedding cellulose in wood. Later in 1865 this matrix was identified as lignin by Schulze.

Synthesis of lignin is as a result of the free radical polymerization of alcohols of para-hydroxy cinamic acid (Perez 2005). Like cellulose it also plays a role in the cell structure of mainly vascular plants. Lignins are heteropolymers with rather complex structures. These hydrophobic polymers exist in plant cell walls providing the matrix that binds the cellulose microfibrils and other components of the cell walls, thus providing biomechanical strength and rigidity. They are responsible for the upright growth of plants (Wainwright 1982; Ralph 2004). Some studies have also discovered presence of lignin in other nonvascular plants (Martone 2009). It is believed that when plants evolved from aquatic to terrestrial habitat about 475 million years ago, the formation of lignified cell walls was a major structural evolution (Martone 2009; Kendrick 1997; Peter 2007; Boyce 2004).

Lignin is formed within the spaces existing around the cellulose microfibrils in the final stage of cell differentiation in plant cell walls, thus forming a lignocelluloses matrix which contributes to the strength of the plant (Perez 2005).

Lignin is generally viewed as a waste material from industrial processes such as pulp and paper production and ethanol production from lignocelluloses biomass. It makes up about 20–305 % of cellulosic biomass. It is considered as non-fermentable, however, it is useful as a boiling fuel (Wyman 2005). On average, between 40 and 50 million tons of lignin is produced as a waste by-product from the pulp and paper industry (Sakakibara 1991; Cotana 2014).




Structure of lignin and other wood constituents (Sourced from Adler (1977) with permission license number 3633070804725).

Lignin makes up between 18 and 25 % of wood with the remaining constituents being cellulose and hemicelluloses forming a matrix within the xylem (Brostow 2010). Lignin is present in the plant cell wall, the extracellular matrix that surrounds the plant cell providing rigidity and support characteristics of plants (Brostow 2010).

To date the precise structure of native lignin is yet to be known and the structure of a particular lignin varies with source and extraction method. However, it is known that it contains mainly methoxyl groups, phenolic hydroxyl groups, and a few thermal aldehyde groups approximately in the following proportions: carbonyl 10–15 %, benzyl alcohol 15–20 %, phenolic hydroxyl 15–30 %, and methoxyl 92–96 % (Froass et al. 1996; Adler 1977).

Other than its structural role, lignin is also significant for water and nutrient transportation within the plant and prevents the penetration of destructive enzymes thereby preventing degradation (Sarkanen 1971; Sjöström 1993).

## 1.3 *Pectin*

Pectin refers to a complex group of molecules with a framework of mainly α-D-(1-4_ galacturonan with intermittent units of α-L-(1-2)rhamnose. It belongs to the class of gel forming polysaccharides alongside others such as agar and mucopolysaccharides. Pectin is present in the primary cell wall of plants alongside other components such as cellulose, hemicelluloses, and lignin. It makes up to 35 % of

the dry weight of the cell walls of dicotyledon higher plants. It constitutes less proportion and is of different forms in monocotyledon plants. Pectin acts as a structural and developmental polysaccharide in plants and also contributes its ion exchange capacity, thus regulating the movement of ions and the pH of the plant cell wall (Perez 2005; Jarvis 1984).

### *1.3.1 Starch (Amylose and Amylopectin)*

Starch in its pure form is an odorless, tasteless white powder. It is a polysaccharide that consists of two types of molecules; amylose and amylopectin. The concentration of each varies with the source and type of starch, however, it is usually around 20–25 % w/w amylose and 75–80 % amylopectin.

Starch is generally insoluble in water and alcohol; however, in the presence of heat and water it can be irreversibly dissolved in water by the process known as gelatinization. Starch is used in a variety of industrial applications, mainly adhesives, paper, and clothing. The application of starch for various purposes dates as far back as 700 A.D. when it was applied as cosmetic creams, food thickener, and in paper production.

Amylose is a water soluble polysaccharide made up of (1-4)-α-D linked polyglucan in a wobbled helix configuration (Kajiwara 2005), while amylopectin takes a branched form with branching occurring after every 28–30 glucose unit. The branched configuration of amylopectin relative to amylase makes it more susceptible to hydrolysis and degradation as it has more regions exposed.

Despite the variation in the composition of amylase and amylopectin for different types and sources of starch, the observed microstructure of starch granules is almost identical for all types of starch (Burchard 2005).

### *1.3.2 Glycogen*

Glycogen is another type of storage polysaccharide. It is similarly highly branched and compact like other storage polysaccharides such as amylopectin (Yui 2005) except with more branching and compactness. Glycogen exists in the cytoplasm of animal cells where it serves as the main storage form for glucose. Albeit very significant for body metabolism, glycogen has no industrial application and is only mentioned here for completeness.

### *1.3.3 Chitin*

Chitin is a highly hydrophobic linear polysaccharide of animal origin containing amino and acetyl groups within its unit. It is insoluble in water and other organic

solvent, it is however soluble in specialized solvents such as chloroalcohols in conjugation with aqueous solutions of mineral acids, hexafluoro-isopropanol, and dimethylacetamide containing 5 % lithium chloride. It is another abundantly available structural polysaccharide in nature, present in the exoskeleton of invertebrates such as insects, crustaceans, and other organisms including in the mycelia and spore of fungi (Kokate 2003; Viahakha 2012). Chitin is similar in structure to cellulose except for the hydroxyl groups contained within the cellulose chain that are substituted with an acetamido group (Viahakha 2012).

Unlike most natural polymers that are either neutral or acid in nature, chitin (as well as chitosan) is alkali in nature. This gives it some desirable properties for various applications such as film and gel forming ability, chelation of metal ions, and formation of polyoxysalts (Sharma et al. 2011). Chitin is especially applied in biotechnology in the modified form of chitosan which is obtained from the deacetylation of chitin. Chitosan is widely applied in transdermal drug delivery, particularly for its mucoadhesive, reactive, and mechanical property, for its tendency to be insoluble in neutral and alkali environment, and its solubility in acidic environment which makes it attractive in controlled delivery (Sharma et al. 2011; Kajiwara 2005).

### *1.3.4 Hyaluronic Acid*

Hyaluronic acid is an example of a glycoprotein, also known as mucopolysaccharides or mucins. It is also one of the few polysaccharides found in the tissue of vertebrates and more abundantly in young embryo; another example of such is heparin. These are polysaccharides bound to proteins in a covalent bond. Other types include proteoglycans. Hyaluronic acid or hyaluronan that plays a significant role in tissue development and cell proliferation (Guizzardi et al. 2013) is a straight chain polysaccharide with a molecular mass of about $7 \times 10^6$ g/mol, usually strongly attached to proteins in a hydrogen bond similar to that of water, thus making its extraction and isolation rather onerous. Nonetheless, pure hyaluronic acid has been isolated from sources such as cord bovine vitreous humor and rooster combs and bacteria streptococcus zooepidemicus (Burchard 2005). It is useful for certain biomedical applications; for instance, in combination with alginate it is used in surgical applications for wound healing (Taravel et al. 2005; Oerther et al. 1999).

### *1.3.5 Alginate*

Alginate is a long chain hydrophilic polymer sourced from seaweeds, where it exists within the cell walls providing flexibility and strength. It has been in use as food as far back as 600 B.C. However, it was not until 1896 that the purified form

of alginate was extracted from seaweed by Akrefting. By 1929 alginate became a commercialized product with the company Kelco being the first to commercialize it as a stabilizing agent in ice cream (Sabra and Deckwer 2005).

It usually exists in association with other cations, mainly sodium and calcium as sodium alginate and calcium alginate. The cations attached to the alginate have an effect on its properties. The properties of the alginate also depend on the species of algae, which is mainly *Laminaria hyperborean, Macrocystis pyrifera, Laminaria digitat, and Ascophyllum nodosum.* Bacteria of the species Pseudomonas and Azotobacter also produce alginate-like polymeric materials. (Sabra and Deckwer 2005) Alginic acid serves diverse biological functions and has various industrial applications as a stabilizing agent, drug carrier, voscosifier, and as binding agent (Sharma et al. 2011; Sabra and Deckwer 2005). It is also used in combination with other polymers such as chitosan and hyaluronic acid to serve more varied functions (Taravel et al. 2005; Oerther et al. 1999).

Further details on the structures and functions of various polysaccharides can be found in (Dumitriu 2005). Details provided here are to provide sufficient understanding of the various types of polysaccharides. Further chapter looks at their applications in various industries.

## 1.4 Proteins

The previous sections have summarized the important roles that polysaccharides play in plants. Proteins are also an integral part of the plant cell wall serving both structural and functional molecules. They determine the functionality and specificity of an organism (Perez 2005).

Proteins are made up of amino acid groups and sometimes other groups joined together by amide bonds, also known as peptide bonds. Proteins can be classified with regard to their shape, size, solubility, composition, and function.

Globular and fibrous proteins are the two types of proteins based on shape and size. Globular proteins are water soluble types which are rather fragile in nature. Antibodies, enzymes, and hormones are typical examples of globular proteins. Fibrous proteins are tougher water insoluble proteins. These are usually proteins found in structural tissues such as hair, nails, and skin.

Proteins can also be classified based on their solubility as simple, compound, and derived proteins. Simple proteins are those which when hydrolyzed produce amino acids only. These protein also have subcategories, which are albumins, globins prolamins, glutelins, histones, prolamins, and abuminoids. Compound proteins, also known as conjugate proteins, are a combination of simple proteins and prosthetic groups. Conjugate proteins are of various types depending on the prosthetic group attached. These could be nucleoproteins lipoproteins, glycoproteins, mucoproteins, phosphoproteins, metalloproteins, or chromoproteins.

Derived proteins are those derived from complete or partial acidic alkali or enzymatic hydrolysis of simple or conjugate proteins. These derived proteins

could be either primary or secondary derived proteins. Primary derived proteins are proteans, metaproteins, and coagulated proteins derived from partial hydrolysis of the protein molecule where very little or no peptide bonds are broken. Secondary proteins are a result of more pronounced cleavage of the peptide bonds through hydrolysis. The main types are proteoses, peptones, and peptides. Proteins are also classified based on their functions as catalytic, protective regulatory, storage, transport, toxic, exotic, contractile, secretary, and structural proteins. Catalytic, regulatory, and protective proteins are enzymes, hormones, and antibodies respectively.

The following sections describe a few common proteins that are commonly applied in industries. These include silk fibroin, silk sericin, zein, collagen, gelatine, casein, wheat gluten, and soy protein.

### *1.4.1 Silk Fibroin*

Silk fibroin is a **fibrous** protein found in silkworms, particularly the bombyx mori, a domestic insect of the Bombycide family. It is semicrystalline in nature with its main amino acid contents being tyrosine, glycine serine, and alanine. Silk fibroin makes up about 75–83 % of silk fibers with the rest of the silk fiber being made up of sericin, wax, and other components such as hydrocarbons. Like other silks, the silk fibroin is attractive for biomedical application due to its nontoxic, biodegradable, and biocompatible nature. In addition, the silk fibroin shows desirable mechanical and chemical properties making it an excellent fiber for a variety of applications such as food additives, cosmetics, matrix for transdermal drug delivery, scaffolds, and fibers (Prasong and Yaowalak 2009; Sharma et al. 2011; Taddei 2006; Min 2004). The silk fibroin is very versatile and can be prepared into various forms such as gels, films, fiber, and powder (Park 2004). The amount of silk fibroin obtained from a particular insect is affected by the nutritional intake and environmental conditions such that these insects can be cultivated for the purpose of producing the desired quantity and quality of silk fibroin.

### *1.4.2 Silk Sericin*

Silk sericin is a **globular**, gumming protein present in the silkworm bombyx mori alongside silk fibroin where it makes up about 17–25 % of the silk fiber. Silk sericin is insoluble in cold water but will easily disperse in hot water (Kaewkorn 2013). Although it is most often discarded as a waste by-product of silk fibroin production, silk sericin has found potential application in biomedicine due to its gel forming property and its role in films and scaffolds for cosmetics and pharmaceutical applications. It is particularly attractive for biological application due to the fact that it does not cause any immunological responses (Aramwit et al. 2012).

Treatment of colon cancer and anti-aging agent in cosmetics are some of the potential applications of silk sericin in industry (Kaewkorn 2013; Kitisin 2013).

### *1.4.3 Zein*

A by-product of corn processing, zein is a hydrophobic **prolamin** protein with thermoplastic property. It is soluble in alcohol and has good film forming properties albeit forming rather brittle films; the film property can be improved through use of other additives and by maintaining the right operating conditions (Guo 2012). It has potential for application as films and coatings in food and pharmaceuticals (Sharma et al. 2011; Elisangela 2007).

### *1.4.4 Wheat Gluten*

Gluten is a by-product from processing of starch present in wheat flour (Tanada-Palmu 2003). It contains two **prolamin** proteins, gliadin a monomeric polypeptide soluble in dilute salt and glutenin a polymer complex soluble in acidic solutions (Waga 2004). Although in the wheat plant these proteins serve mainly as **storage protein**, gluten has unique viscoelastic properties which make it commercially attractive in structural applications such as film forming and bread making. Wheat gluten also contains other proteins, such as albumins and globulins, which serve mainly biological purposes as catalysts and regulators (Waga 2004). The film forming ability of wheat gluten can be modified through addition of plasticizer such as glycerol (Tanada-palmu 2000) or varying the pH (Herald 1995).

### *1.4.5 Collagen*

Collagen is the most abundant protein in mammals making up about 25 % of the dry mass. It is a **structural protein** made of three polypeptide chains folded into a triple helix structure usually produced by fibroblast cells. Due to its biodegradability, biocompatibility, availability, and versatility, collagen is widely applied in biomedicine, pharmaceutics, and cosmetics. It is found in tissues such as muscles, skin, and bone where it provides strength and flexibility. Its industrial application includes use as scaffold and injectable (Parenteau-Bareil 2010). Collagen type varies from source to source and also within sources, with the most common type used in industries being type 1 collagen. Other types are listed in Table 1.2.

**Table 1.2** Collagen type, forms, and distribution

| | Type | Molecular formula | Polymerized form | Tissue distribution |
|---|---|---|---|---|
| Fibril—forming (fibrillar) | I | $[\alpha I(I)]_2\alpha 2(I)$ | Fibril | Bone, skin, tendons, ligaments, cornea (represent 90 % of total collagen of the hitman body) |
| | II | $[\alpha I(n)]_3$ | Fibril | Cartilage, intervertebrate disk, notochord, vitreous humor in the eye |
| | III | $[\alpha I(III)]_3$ | Fibril | Skin, blood vessels |
| | V | $[\alpha I(V)]_2\alpha 2(V)$ and $\alpha I(V)\alpha 2(V)\alpha 3(V)$ | Fibril (assemble with type I) | *Idem* as type I |
| | XI | $\alpha I(XI)\alpha 2(XI)\alpha 3(XI)$ | Fibril (assemble with type II) | *Idem* as type II |
| Fibril—associated | IX | $\alpha 1(IX)\alpha 2(IX)$ $\alpha 3(IX)$ | Lateral association with type II fibril | Cartilage |
| | XII | $[\alpha I(XII)]_3$ | Lateral association with type I fibril | Tendons, ligaments |
| Network—forming | IV | $[\alpha I(IV)]_2\alpha 2(IV)$ | Sheet-like network | Basal lamina |
| | VII | $[\alpha I(VII)]_3$ | Anchoring fibrils | Beneath stratified squamous epithelia |

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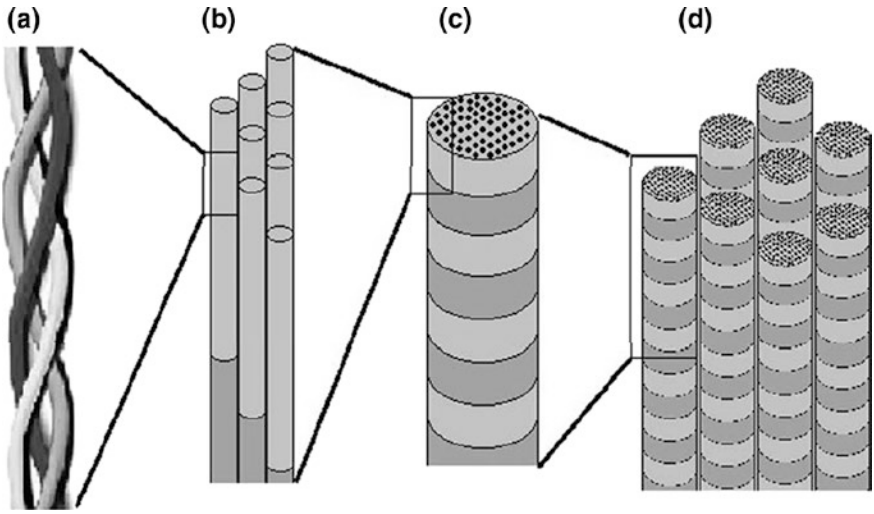


Schematics representing (a) a segment of a triple helix collagen chain, (b) collagen molecules, (c) collagen fibril made up of collagen molecules, (d) Collagen fibril aggregates forming collagen fiber. (Reproduced from Parenteau-Bareil (2010) under creative commons attribution license.)

### *1.4.6 Gelatine*

Gelatine is a derived protein; it is the partially hydrolyzed form of collagen extracted from tissues such as bones and skins of animals through thermal hydrolysis using either an acid or alkali (Zhang 2011). There is also growing interest in extraction of gelatine from the scales of fish (Olatunji et al. 2014) and insects (Mariod and Adam 2013) as potential preferred alternatives to mammalian sourced gelatin. It is a mixture of polypeptides and proteins formed as a result of irreversible hydrolysis of collagen, which results in the unfolding of the α triple helix structure by partially breaking some of the hydrogen bonds between the inter wound polypeptide chains. Gelatin is of two types, type A which is gelatine obtained through acid hydrolysis and type B obtained through basic (alkali) hydrolysis (Mariod and Adam 2013). The properties of gelatine depend on the source and extraction method; for instance, studies have shown that gelatine from insects have properties that are different from commercial gelatine (Abdelfadeel 2012). Studies also show that gelatine from different fishes and their parts also differ (Koli et al. 2012). Gelatin is widely applied in foods, pharmaceutics, and cosmetics for its viscoelastic properties to act as gelling agent, thickener, or stabilizer.

## 1.5 Polyester

The main known polyesters in nature are cutin, suberin, and polyhydroxyalkanoates.

### *1.5.1 Cutin*

It is a complex combination of nonpolar lipids which form part of the waxy layer that envelopes the plant on the outermost layer, protecting it against water loss to the environment. This plant outermost layer is referred to as cuticle; it is the structure thought to be a major enabler of plant evolution from water to dry land due to the enhanced water retention capacity it provides. The discovery of natural polyester from plant cuticle came later than that of polysaccharides and proteins (Holloway 1982).

### *1.5.2 Suberin*

Suberin is synthesized within the extracellular matrix of mainly the root tissue. It plays a similar role as cutin of protecting the root tissue against water loss. It is commonly used industrially as the main constituent of cork.

### *1.5.3 Polyhydroxyalkanoates*

Polyhydroxyalkanoates are complexes found in bacteria, however, efforts are being made to synthesize it in plants, particulary in the leaves (Nawrath and Poirier 2008).

## 1.6 Polynucleotides

Polynucleotides are mainly ribonucleic acid (RNA) and deoxyribonucleic acid (DNA) which serve as the building blocks of life that make up the instructions necessary for a cell to perform its function. Polynucleotides in industry serve biomedical purposes such as gene therapy and DNA sequencing (Manavbasi and Suleymanoglu 2007; Templeton 2002; Ulrich 2002). Polynucleotide structure consists of 13 or more nucleotide monomers joined together to form a chain. DNA for example is made up of two chains of polynucleotides folded in a double helix. The sequence of the nucleotides determines the instruction for the particular cell.

## 1.7 Polyisoprenes

Polyisoprenes are natural rubbers with thermosetting properties (Tanaka 2001). Polyisoprenes are classified into two types, *cis* and *trans,* also known as Z-polyisoprene and E-polyisoprene. The type of polyisoprene formed is determined by the isoprene unit present and the two forms have different properties. The *cis*-polyisoprene is more widely available as it is produced in over 200 latex producing higher plants, particularly the rubber tree (hevea brasiliensis), which serves as the main commercial source of polyisoprene due to the high polyisoprene yield and the desired mechanical properties of the product. Albeit much fewer in existence, plants producing the *trans* polyisoprene include balata (Minusops balata) and Gutta percha (Palaquium gutta and Eucommia ulmoides (Bamba et al. 2002; Backhaus 1985; Hendricks et al. 1946). The desired properties of *trans* isoprene include rigidity, insulation properties, extremely low coefficient of thermal expansion/contraction, and alkali and acid resistance (Asawatreratanakul et al. 2003).

## 1.8 Conclusion

Some natural polymers have been replicated in the laboratory. This is done in some cases to reduce the chances of impurities or undesired components that might be difficult to separate while extracting the desired polymer from its bulk

form. For example, use of synthetic polyisoprene in place of natural polyisoprene is more common in industry today as the polyisoprene produced by plants such as rubber plant is *cis*-polyisoprene, whereas *trans* polyisoprene has more desirable properties for commercial application (Chen et al. 2012).

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# Chapter 2
# Processing and Characterization of Natural Polymers

**Ololade Olatunji and Olsson Richard**

## 2.1 Introduction

Polymer processing involves two main aspects, processing of polymers into forms for further processing as powders and pellets and processing of polymers into finished products of desired geometry such as scaffolds, microneedles, and films for food packaging. The former involves techniques such as extrusion and blending, while the latter could involve processes such as injection molding or film casting. Such will be discussed in this chapter. Furthermore to determine the usefulness and for quality assurance and safety, it is necessary to characterize polymers to determine properties such as mechanical strength, thermal conductivity, microstructure, and density. For such purpose techniques such as Fourier transform infrared spectroscopy, transmission electron microscopy, differential scanning calorimetry, and thermogravimetry analysis have been developed and are widely applied in characterization of polymers.

Many processing techniques applied for the industrial synthetic polymers are applicable to natural polymers, however, in several cases certain limitations exist which limit the applicability of some of the conventional polymer processing techniques to natural polymers. Measures have been taken by researchers to address such limitations and/or modify the polymer processing technique to suit natural polymers. For example, starch is plasticized to form thermoplastic starch (Nafchi et al. 2013) which can be processed using extrusion molding, a process typically applied to thermoplastics.

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O. Olatunji (ed.), *Natural Polymers*, DOI 10.1007/978-3-319-26414-1_2

Proper characterization aids in the selection of polymers for specific application such that the best suited polymer or combination of polymers can be selected. It is desired that the typical processes used in industry for processing of synthetic polymers to be adoptable for natural polymers in order to save costs and for convenience. In this chapter we also look at processing of natural polymers into composites and blend. This extends to combination of natural and synthetic polymers. We look at the role of natural polymers in composites containing either natural or synthetic polymers as matrices. Typical characterization methods which are applied in industry and how they are applied for characterization of natural polymers are discussed.

## 2.2 Blends and Composites

Blends and composites are a good means of obtaining broader usability from polymers either as matrix or fillers. Composites have been defined as a combination of two or more elements with distinct identity and properties bonded to form a multiphase multicomponent system, while the component elements maintain their physical and chemical identities. A composite is made up of a polymer as a matrix and a filler, where the filler could be a fiber, flake, or a woven fabric which could be a ceramic, metal, or polymer element. Polymers can therefore play the role of a filler or matrix in composites. The need for such systems is in the desire for physical and/or physicochemical parameters which cannot be met by other simple mono-component synthetic or natural materials (Cazacu and Popa 2005).

Composites can be made up of both synthetic and natural polymers. The blending of both natural and synthetic polymers yields a new breed of materials with more varied properties for broader applications. Composites based on natural polymers have gained increasing attention as over the years largely due to the fact that the production of synthetic polymers, albeit involving advantages such as consistency of product and ease of production, have raised environmental concerns due to their nonbiodegradability and potential toxicity.

Blends are formed when two or more polymers are physically mixed either in the molten state or dissolved in appropriate solvent. Polymer blends obtained from mixing of polymers can be of various forms such as miscible one phase, miscible separated phase, compatible, incompatible, alloys, interpenetrating and semi-interpenetration polymer networks, or molecular composites. The two main classifications of polymer blends are either as compatible or incompatible blends.

Incompatible blends are immiscible blends where the separate phases are well defined. These blends generally have poor mechanical properties. Compatible blends are those blends which form a single phase where different components cannot be separately identified morphologically. These types of polymer blends are more likely to attain superior mechanical properties than the component polymers. Incompatible blends are more common than compatible polymer blends.

Composites exist in nature in the form of wood and bones. Wood, for example, is a good representation of polymer composite. The hemicellulose and lignin act as the polymer matrix component, while the cellulose fibers act as the filler components (Freudenberg 1932; Lee et al. 2014). The interactions between the hydrophobic lignin and hydrophilic cellulose components are thought to be due to one ester and one ether linkage forming a lignin cellulose complex (LCC) (Rozmarin 1984), which acts as a compatibilization agent thought to be responsible for the peculiar structural stability of wood (Takase et al. 1989). Understanding of naturally existing composites has contributed to the development of novel composites with improved properties.

Man-made composites have been in existence since 500 BC where pitch was used by the middle easterners as binders, papyrus, and reeds in building boats. The Europeans, Asians, and Americans are also reported to have used laminated wood veneers as decorations as far back as first century AD. Shellac resin-based laminates have also been used by the Indians for over 300 years, while evidence of laminated wood is seen in Thebes dating as far back as 1500 BC (Cazacu and Popa 2005; Lee 1989).

Methods employed in formation of blends and composites include hand lay-up, low-pressure injection molding, compression, molding, extrusion, centrifugal casting, spray-up, reinforced reaction injection rolling, filament winding and pultrusion methods (Cazacu and Popa 2005; Kulshreshtha 2002).

### *2.2.1 Compatibilization*

The compatibility of polymer blends can be significantly improved by the presence of specific interactions such as hydrogen bonding (Cao et al. 1989) electron-donor and electron-acceptor complexation (Simmons and Eisenberg 1986) and ion–ion pairing (Simmons and Eisenberg 1986; Cazacu and Popa 2005). The properties of a polymer blend are dependent of the properties of individual components. These properties can be improved by modifying the interfacial and superficial properties of the components. This process is referred to as compatibilization.

Compatibilization can be achieved by the use of additives known as compatibilizing agents. Compatibilization is also done by using a graft copolymer of the natural polymer which is miscible with each of the components of the polymer blend. This is reactive compatibilization and is chemically formed during mixing. Chemically modifying the natural or synthetic polymers such that certain functional groups are formed on the polymers, thus improving interactions between the components of the polymer blends. Copolymerization, i.e., forming polymers from more than one monomer unit, is also a method of compatibilization as the different monomer units result in interactions which may improve miscibility.

Silanes such as amino silanes, aminopropyltriethoxysilane, glycidoxypropyltrimethoxysilane (Tran et al. 2014) and methacrylopropyltrimethoxysilane (Salon et al. 2005), and isocyanates can also be used alongside or in place of MAPP.

The mechanism of compatibilization involves a silanol group (Si–OH) forming between the silane and the water molecule on the cellulose. This then forms a covalent or hydrogen bond with the cellulose (Xie et al. 2010). Silane has also been used as compatibilizer in cellulose/low-density polyethylene (LDPE) composites. Pre-impregnated cellulose fibers in LDPE dissolved in xylene solution yielded composites which show up to 50 % increase in mechanical strength (Herrera-Franco and Agular-Vega 1997).

In one innovative approach degraded LDPE is used as a compatibilizer for LDPE–wood composites (Ndlovu et al. 2013). As the LDPE degrade they form functional groups which make them applicable as compatibilizers. Although the degraded LDPE does not increase the thermal stability, significant improvement in the mechanical and viscoelastic properties of the LDPE–wood composite can be achieved using the degraded LDPE as compatibilizer. Such processing techniques allow for utilization of partially degraded LDPE which could be in the form of recycled LDPE contributing toward waste recycling. Some detailed examples of compatibilizers used for producing composites of synthetic and natural polymers can be found in (Cazacu and Popa 2005). Some of which are listed in Table 2.1.

### *2.2.2 Blending of Natural Polymers with Synthetic Polymers*

The mixing of natural and synthetic polymers allows for the combination of the desirable high-performance mechanical properties, consistency, and water resistance property of synthetic properties with the low cost, biodegradability, multifunctionality, and biocompatibility of natural polymers. This leads to achieving new materials with more varied physical and physicochemical properties for broader applications. The main aims of mixing natural and synthetic polymers are either to reduce cost, improve performance, or tune specific properties such as biodegradability.

Blending of polymers allows the possibility of mixing inexpensive and relatively abundant polymers with expensive ones using low-cost mixing methods, thus reducing the cost of the polymer while still attaining high performance required. The presence of natural polymers within synthetic polymer systems also speed up the process of biodegradation. The degradation of the blend or composite begins with the degradation of the natural polymer component within the material which results in increasing the surface area available for water, photo, chemical, and microbial action. This is due to the degradation of the natural polymer within the material leaving behind spaces between the fragments of the material making it more susceptible to degradation (Cazacu and Popa 2005). Figure 2.1 shows a sketch of possible route for degradation of natural polymer composites.

Lignocellulose-based biomass is used in combination with synthetic polymers as they are widely available. Lignocellulose deposited to the biosphere annually is reported to be about 200 billion tons. This includes lignocellulose from wood waste, e.g., furniture and construction industry, agro wastes of plants, waste from

**Table 2.1** Natural/synthetic composites and compatibilizers

| Synthetic polymer | Natural polymer | Compatibilizer | Processing technique | Reference |
|---|---|---|---|---|
| Polypropylene | Sawdust | Maleic anhydride | Extrusion | Cazacu and Popa (2005) |
| Polypropylene | Wood fibers | Ethylene–propylene or ethylene–propylidene copolymer Maleate polypropylene Calcium stearate | Injection forming | Cazacu and Popa (2005) |
| Low density polyethylene | Lignocellulosic fibers Sawdust | Ionomer polyethylene Maleate polypropylene Low molecular weight polypropylnene Maleic anhydride | Extrusion Injection | Cazacu and Popa (2005) |
| Polyurethane | Mechanical pulp | Isocyanates | Pressing | Cazacu and Popa (2005) |
| Phenol formaldehyde | Lignocellulose | Chemical modified fibers | Pressing | Cazacu and Popa (2005) |
| Polyester + PE + PP | Wood fibers | Phenol resins | Pressing | Cazacu and Popa (2005) |
| Carboxylated Nitrile Rubber | Natural Rubber | Maleic anhydride grafted polyisoprene epoxy resin | Roll milling | Onyeagoro (2013) |
| Chlorinated Polyethylene | Natural Rubber | Maleic anhydrided grafted ethylene propylene diene rubber EPDM-g-MA | Thermal mixing followed by roll milling | Sirisinha et al. (2004) |
| Carboxylated nitrile rubber | Natural rubber | Bis(disopropyl) thiophosphoryl polysulphides | Thermal mixing followed by roll milling | Naskar et al. (2001) |
| Poly(lactic acid) | Natural rubber | Poly(lactic acid)-natural rubber tri block copolymer | | Chumeka et al. (2014) |

pulp and paper industries (Cazacu and Popa 2005). This is even more than the quantity of synthetic polymers produced every year which is estimated at 150 million tons per year.

The main challenges in blending natural polymers such as lignocellulose with synthetic polymers lie in the hydrophilic nature of natural polymers such as polysaccharides and the hydrophobic nature of synthetic polymers such as

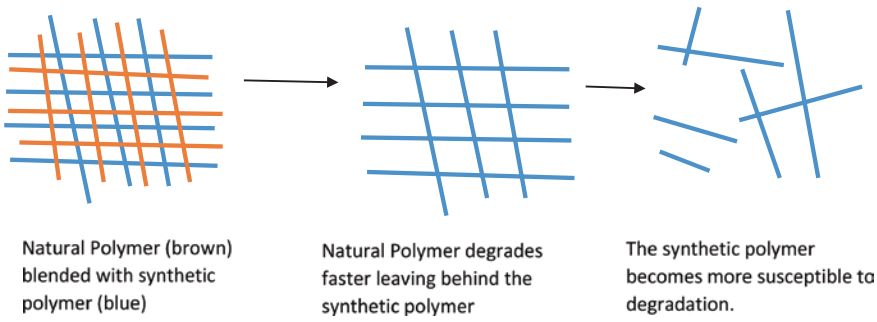


**Fig. 2.1** Degradation of natural and synthetic polymers

polyethylene. The polarity leading to intermolecular attraction between the natural polymer but poor adhesion between the natural polymer and the synthetic polymer leading to poor wettability and dispersion. An advantage of natural polymers is the presence of many functional groups such as hydroxyl, ester, and carbonyl groups (Rozmarin 1984). This makes it possible for them to be modified for desired functionality and to improve compatibility with synthetic polymers, thus forming blends and composites of high performance.

Natural polymers can be blended with synthetic polymers either as fillers, reinforcement fibers, mixing components, or grafted copolymers for compatibility. Figure 2.2 shows some materials obtainable from mixing of natural and synthetic polymers and some example applications summarized from various texts (Yeh 1995; Garg and Jana 2007; Cazacu and Popa 2005).

Incorporation of natural polymers within synthetic polymer matrices can be done through impregnation of the natural polymer component within the monomer units such as styrene, vinyl chloride or methyl acrylate, resins such as epoxy or polystyrene or within polymer–monomer systems such as styrene–polyester resin or methyl methacrylate–polyester resin–styrene systems, followed by polymerization. This impregnation allows for strong interaction between the functional groups and components of the natural polymer and the impregnation agent.

Another means of incorporating natural polymers with synthetic polymers is through compounding. This involves mechanical mixing of the natural polymer with the synthetic polymer either in the melt state followed by extrusion and thermoforming or at room temperature. Polypropylene, polystyrene, and polyethylene are the most common synthetic polymers blended with natural polymers.

TPS blended with LDPE and linear low-density polyethylene (LLDPE) are formed in at twin screw extruder using PE-grafted maleic anhydride as compatibilizer. Despite the reduction in tensile strength and elongation from 18 to 10.5 MPa and 340–200 % as the TPS content increased from 5 to 20 % (Sabetzadeh et al. 2015), the composites had sufficient thermoplastic property to be processed into films using the conventional blowing process used for commonly used polymers in industry. The films also had the required standard mechanical properties suitable for packaging application according to ASTM standards.

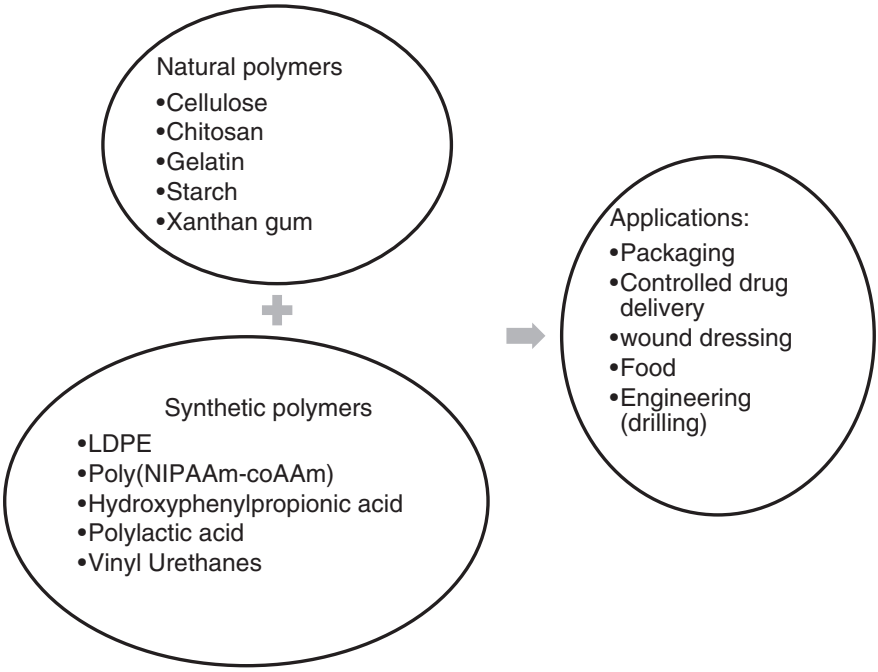


**Fig. 2.2** Blends of natural and synthetic polymers with example applications (arranged in order of correspondence)

It is important to be able to process biopolymers using the common industrial processes as this makes them more adoptable industrially without the need for specialized equipment which could increase cost of production. It must therefore be considered that a trade-off between the optimum performance property of the material and the environmental friendliness should be carefully considered, while selecting natural- and synthetic-based polymers for any industrial application.

Natural polymers are also blended with other natural polymers. This allows a combination of their properties to obtain a fully biodegradable material with improved properties. For example, a combination of chitosan with cellulose combines the film-forming properties of chitosan with the structural strength of cellulose. Such blends of natural polymers tend to be more compatible due to the similarity in structure and hydrophilic nature.

Energy of mixing for blends and composites

It is not enough to simply mix components to obtain a composite with the expectation that it would result in a new material with desired properties. It is important to study the particular properties of each component, the interactions between the component, compatibility or incompatibility of the components, and the long-term stability of the produced composite. The structural and molecular characterization of the composites is therefore of importance.

Detailed understanding of the structural and morphological properties of components makes it possible to pre-evaluate the miscibility of components to form composites thus making for easier selection processes. Such did not become possible until 1995 (Cazacu and Popa 2005). It is established that the miscibility of two or more polymers is dependent on the free energy of mixing ($\Delta G_{\text{mix}}$).

$$\Delta G_{\text{mix}} = \Delta H_{\text{mix}} - T\Delta S_{\text{mix}} < 0 \tag{2.1}$$

$\Delta H_{\text{mix}}$ and $\Delta S_{\text{mix}}$ are the enthalpy and entropy variations and $T$ is temperature. To form a miscible blend, the $\Delta G_{\text{mix}}$ must be negative (Cazacu and Popa 2005).

### *2.2.3 Natural Polymers as Matrix in Composites*

Natural polymers are used as matrices for composites either alone or in combination with synthetic or other natural polymers. Natural polymers such as rubber, starch, cellulose, chitosan, and gelatin are used as composite matrix in various applications such as construction and biomedical. This could be either in their modified form, refined form, partially isolated form, or in their raw complex form. Although natural polymers have disadvantages such as poor consistency, high moisture absorbance, low resistance to UV, chemical and microbial activity, they possess advantages such as low cost, biodegradability, lightweight, versatility (due to the fact that they can be modified into different forms based on their functional groups) and availability, for example, lignocellulose-based waste estimated to up to 200 billion tons annually).

Starch is a good candidate for polymer matrix, however, starch is prone to destruction and polymerization during processing into the melt state (Bergthaller et al. 1999). This challenge is addressed by adopting the right processing conditions, using a twin screw extruder or a corotating twin screw extruder. The application of plasticizers such as glycerol, sorbitol, urea, polyethylene glycol, poly vinyl alcohol, and sucrose also improves the processibility of starch (Roper and Koch 1990). This results in a thermoplastic, flexible, biodegradable, hydrophilic starch form referred to as thermoplastic starch (TPS). TPS has better thermoplasticity, film forming, and molding properties (Cazacu and Popa 2005).

TPS starch composites incorporating natural and synthetic polymers can be formed using industrial thermoforming methods such as extrusion and injection molding. In particular, example compounding TPS from cassava source with synthetic polymer, LDPE significantly improves the thermal and mechanical properties of TPS. Further improvement in the mechanical properties is observed by modification into composites using cotton fibers as reinforcement and carrageenan as gelling agent. The composite was processed using an internal melt mixer followed by injection molding without damaging effects on the TPS (Prachayawarakorn and Pombage 2014).

Composites of glycerol-plasticized TPS from rice starch with either cotton or LDPE as reinforcing agents show improved tensile strength and Young's modulus

with the incorporation of cotton or LDPE compared to TPS only. The compatibility between TPS and LDPE is improved using either maleic anhydride polyethylene or vinyltrimethoxysilane as compatibilizing agents. The water absorption property which is important in maintaining the stability of the material is reduced by the inclusion of cotton and LDPE in the TPS matrix (Prachayawarakorn et al. 2010). In this case the synthetic polymer is also acting as a filler rather than a matrix in the composite, while the natural polymer TPS acts as the matrix component.

### *2.2.4 Natural Polymers as Fillers and Reinforcements*

Natural polymers in their modified, refined, or complex raw form can also be incorporated into natural or synthetic polymer matrixes. In Table 2.2 we summarize some natural polymers used as filler in composites of natural and synthetic polymers. Most of the natural fibers used as reinforcement in polymer composites are cellulose, lignocellulose, or pectin based. They derived from sources such as wood, cereal straw, bagasse, cotton bark, rice husks, pulp, and vegetables such as jute, flax, sisal, hemp, and ramie (Cerqueira et al. 2011).

Cellulose is commonly used as reinforcement or fillers in natural and synthetic polymer matrices as fibers, viscose, and powders or in modified forms as esters, ethers, or grafted onto the polymer. Other than being the most abundant polymer in nature, it offers advantages such as low cost, low density, mechanical strength, ease of processing and biodegradability (Cazacu and Popa 2005). Cellulose also tends to form better bonds with polymers, a property thought to be due to the interaction between the –OH groups in cellulose's anhydroglucose unit

**Table 2.2** Natural polymer as matrices in composites

| Natural polymer matrix | Filler/ reinforcement | Compatibilizer | Processing method | Reference |
|---|---|---|---|---|
| Natural rubber | Jute fiber | – | Roll milling followed by hot compression | Pantamanatsopa et al. (2014) |
| Wheat starch | Cotton fiber | – | Hand layup | Komuraiah et al. (2013) |
| Natural rubber | Organophilic layered clay (organoclay) | Epoxidized natural rubber | Internal mixer followed by vulcanization using conventional sulphuric system | Teh et al. (2004) |
| Natural rubber/LLDPE blend | White rice husk ash | Poly(propylene–ethylene–acrylic acid) (PPEAA) | Internal mixer | Ismail et al. (2001) |
| Rice starch | Cotton fiber | – | Hand layup | Komuraiah et al. (2013) |

and the functional groups present in the synthetic polymers. Cellulose has three –OH groups which have different polarity and regioselectivity which attribute to the peculiar physical properties of cellulose and its ability to form various derivatives. The versatility of cellulose makes it possible to modify for various composite systems.

The poor solubility in organic solvent, low thermal stability, hydrophillicity, and polarity of cellulose poses some challenges in application as fillers in composites. This leads to poor dispersion in melted polymer, weak interaction between the cellulose fiber and matrix and difficulty in thermal processing. These challenges can, however, be met by using a compatibilizer, chemical modification of the cellulose, or by dissolving cellulose in a suitable solvent prior to dispersing in non-solvent for better dispersion (Cazacu and Popa 2005).

As an example we look at natural fiber jute reinforced natural rubber. In this case natural polymers are being used as matrix and reinforcement. Compatibilization is achieved through coating of the jute fiber with natural rubber using immersion technique. The fibers are treated with sulphuric acid to delignify prior to coating. The impact of treatment of the jute fiber is compared with untreated jute fibers and natural rubber in Fig. 2.3. In Table 2.2 we list some composite systems which use natural polymers as matrices. While Table 2.3 gives some examples of natural polymers as fillers in synthetic and natural matrices.

Polypropylene is one of the common synthetic polymers for producing cellulose-reinforced composites. For this purpose maleic anhydride-grafted polypropylene (MAPP) is the preferred compatibilizing agent. MAPP can be bonded covalently through esterification to the cellulose functional groups. The effectiveness of the bonding depends on the PP chain length in the MAPP. Where short

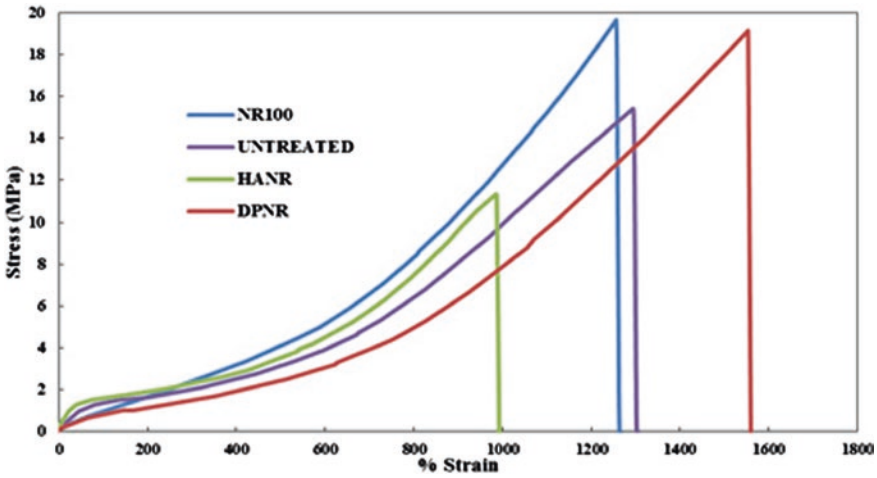


**Fig. 2.3** Stress–strain graph of HANR and DPNR-treated jute composite compared with untreated jute composite and natural rubber (Pantamanatsopa et al. 2014) (creative commons license)

**Table 2.3** Some examples of natural polymer fillers in synthetic and natural matrices

| Natural polymer filler | Polymer matrix | Compatibilizer | Processing method | Reference |
|---|---|---|---|---|
| Cotton fiber | Rice starch<br>Wheat starch<br>Urea formal dehyde<br>Plaster of paris | | Hand layup | Komuraiah et al. (2013) |
| Sugarcane bagasse fiber | Polypropylene | | 10 % Sulfuric acid, delignification and compounding in a thermokinetic mixer | Cerqueira et al. (2011) |
| Sisal fiber | Polylactide (PLLA) | Bacteria nanocellulose coating | Solvent casting followed by injection molding | Lee et al. (2012) |
| Cellulose | Fish gelatin | – | Solvent casting | Santos et al. (2014) |

chains facilitate coupling between polar groups on cellulose and nonpolar groups of the synthetic plastic. While longer PP chains cause steric hinderance which limits the attraction between the cellulose and polymer to the superficial layer (Felix and Gatenholm 1991; Cazacu and Popa 2005).

Composites of natural polymer blends can be produced by dissolving the fiber and matrix material, mixing the dissolved form followed by film casting and drying. This can be achieved by either dissolving the fiber and matrix in the same solvent, coagulating in a nonsolvent or coagulation in a vinyl solvent prior to polymerization of the resulting gel (Nishio 1994; Cazacu and Popa 2005).

## 2.3 Processing Techniques

The method of processing of polymer composites depends on the factors such as the nature of the polymer and fiber, the targeted application which could be biomedical applications such as wound healing and scaffold or for construction or producing vehicle car parts. In this section we will look at some specific examples where natural polymer has been processed into composites for various applications. In so doing we will discuss the processing techniques used to produce the natural polymer being discussed. The processing techniques discussed here vary from those used for engineering applications such as composites used for aircrafts to those used in biomedical applications such as scaffolds for tissue replacement and transdermal films for wound healing.

### 2.3.1 Extrusion Molding

Extrusion molding is generally used for polymers with thermoplastic properties. The process involves melting polymers under heat and shear to achieve uniformity of the polymer with or without other polymers and additives to form blends or composites. Processing of polymers as matrixes for applications such as pharmaceutical or engineering often require processing the polymer in its melt state to attain uniformity and desired shape. Extrusion molding is mostly based on flow of a molten polymer in a screw, while injection molding in addition to this involves flow of the molten polymer into a cavity and cooling of the polymer within the cavity. The polymer is usually introduced into the system through the hoper in the pellet or granular form, this then forced through a screw and barrel which melts and mixes it and then through a die where it forms into desired shape. There usually exists a breaker plate and screen between the barrel and die to filter out unwanted particles and achieve uniformity. This is followed by sizing and cooling where the extruded polymer is formed into final size and cooled. The conditions (such as temperature, pressure, speed, time) in an injection or extrusion molding system depend on the type of polymer and other constituents of the blends (fillers, additives, etc.). Extrusion is a very versatile process of much industrial relevance. Typically, extrusion process is used widely in plastics industries to achieve end products such as pipes, tubing, straws, and films for packaging. Further reading on extrusion can be found in Seymour and Carraher (1992) and Ebewele (2000). Figure 2.4 is a representative sketch of an extruder.

This method has been applied in various industries such as pharmaceutical (Vervaet et al. 2008). In the pharmaceutical application, for example, where the incorporation of drug within a polymer is required as a matrix carrier for drug component and other additives. A hot melt extrusion process is used to achieve a uniform blend of the drug formulation. In such applications there are usually temperature restriction to prevent denaturing of the active drug ingredient such that hot melt extrusion of pharmaceutical agents employ polymers which can be thermoformed at relatively low temperature which will not damage the drug ingredient. Hot melt extrusion is often preferred over other methods such as compression molding of casting due to its continuity which makes automation more possible as all processes (mixing, melting, and shaping) can be completed in a single equipment (Repka et al. 2007; Crowley et al. 2007).

Hot melt extrusion is also preferred due to the homogeneity attainable from the process. Examples of natural polymers which can be processed using hot melt

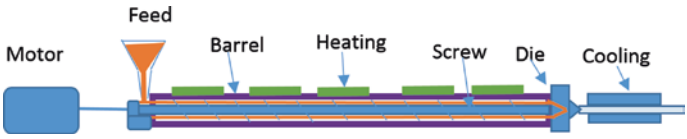


**Fig. 2.4** Illustrative sketch of an extruder

process include gelatin (Andreuccetti et al. 2012), starch, waxes, lipids, and derivatives of cellulose such as ethyl cellulose (Vervaet et al. 2008). Often plasticizers are used to improve the thermoplastic properties of the polymer for better thermal processing.

Here we use an example of the preparation of gelatin-based films containing Yucca schidigera extract using glycerol as plasticizer where extrusion molding is applied in preparing the films (Andreuccetti et al. 2012). Glycerol concentration varies between 0.25 and 8.75 g per 100 g of protein. When extrusion, blown extrusion and casting method are compared, the processing technique does affect the properties of final film formed. The films produced by extrusion showed higher flexibility than the blown or casted films. While the solubility of the films is not affected by the processing method, the extrusion blown films had lower water permeability. It is also necessary to add water up to a moisture content of 35 % to the gelatin-based film to further aid the extrusion process. Prior to extrusion the samples are allowed to equilibrate at 5 C and 60 % humidity for 24 h. The temperature in the feeding zone of the extruder was 65, 100 C in the intermediate zone and 75 C at the die while the screw rotated at a speed of 47.2 rpm.

In one novel approach, conditions in an extrusion process provided the right conditions (temperature and pressure) for wood to exhibit flow properties which results in more compatible blending with engineering plastics to form better wood plastic composites. Here the wood was first modified using phenol formaldehyde. Under these conditions the polymers in wood, mainly lignin and carbohydrate serve as plasticizers and binders, to give wood its thermoplastic properties making it possible for wood to be heat extruded like other engineering plastics (Miki et al. 2014).

Multilayer extrusion is also possible. This is of particular importance for moisture-sensitive polymers such as starch and proteins. In this case a layer of water-resistant polymer or other material can be coated unto the moisture-sensitive polymer forming multiple layers of controlled thickness (Yu et al. 2006; Martin et al. 2001; Van Tuil et al. 2000; Wang et al. 2000).

### *2.3.2 Injection Molding*

Injection molding is also a fairly versatile process of industrial significance. It involves conversion of thermoplastic and thermosetting polymers in the molten or viscous state into solid finished materials. It is typically used for achieving finished products such as forks, spoons, and parts for electronics. The process generally involves heating of the polymer which is introduced in the form of pellets of powder, followed by injection within a heated barrel and screw and then injecting into a mold cavity and cooled under pressure to minimize shrinkage. The resulting cooled polymer is then ejected from the unit.

Injection molding has been shown to be applicable in the biomedical area for producing, for instance, 3D scaffolds. Scaffolds developed from cornstarch-based polymers have been introduced using hydroxyapatite as reinforcement and

carboxylic acid-based blowing agent (Gomes et al. 2001). It is possible to achieve 3D scaffolds with complex structures and porosity, while maintaining significant mechanical strength. Producing scaffolds using conventional injection molding offers the possibility of achieving a reproducible method for producing biodegradable polymer-based scaffolds for load-bearing tissues. A review of injection molding and its applications in drug delivery contains some natural polymer-based polymer products of injection molding (Zema et al. 2012).

A biocomposite consisting or crayfish powder with 60 % protein and polycaprolactone has been used to prepare biocomposite using injection molding (Felix et al. 2015). The plasticity of the protein was enhanced using glycerol as plasticizer. The injection molding conditions such as temperature and speed were optimized by rheometry and thermal analysis. The mechanical properties of the crayfish powder protein were significantly enhanced to yield a composite material with suitable mechanical properties for injection molding.

### *2.3.3 Solvent Casting*

This is a processing method commonly used for forming polymer films. The ability of polymers to form films is important for various applications such as packaging, transdermal drug delivery, and wound healing. Films may also be used as coatings. Uniformity is key characteristics of films for any application. To achieve consistency in film formation either from neat polymers or blends certain procedures are followed. Methods for film forming include self-absorption of monolayers (SAM), spin coating, thermal spraying, solvent casting, floating technique, and Langmuir–Blodgett film forming. Most common techniques being solvent casting and spin coating.

Here we take a case study of nanocellulose as a reinforcement in polymer composite focusing on the processing techniques applied in developing such composite. Gelatin from fish skin is acting as the polymer matrix, while cellulose whiskers from cotton linter are used as the reinforcement component (Santos et al. 2014).

First water at 24 °C was used to hydrate the gelatin and glycerol using 25 wt% glycerol concentration. The suspension was heated to 50 °C and stirred for 15 min at this temperature. This was followed by slowly adding the cellulose whiskers, while homogenizing at 10,000 rpm for 10 min. After the first 2 min the cellulose was completely added. The homogenization is a mechanical method of preventing aggregation of the cellulose in the gelatin mixture. To eliminate gas bubbles, some of which might have been formed during the homogenizing, the gelatin/cellulose mixture was vacuum degassed using a V-700 vacuum pump at 30 mbar for an hour. The films were formed by pouring on a glass plate and allowed to dry at room temperature for 24 h, after which dry films are formed. The films are detached from the glass plate and can be stored in a desiccator to maintain a constant humidity (Santos et al. 2014).

### 2.3.4 Spin Coating

Spin coating is a well-established technique widely used in polymer industry to produce thin films on substrates. The typical setup includes a dispenser unit and a spinning unit as illustrated in Fig. 2.5. The dispenser deposits a small amount of the material which could be in the form of a neat polymer, a polymer composite or a resin, onto the center of the substrate attached to the spinning unit. The spinning unit then spins at a set speed which is usually between 1500 and 6000 rpm depending on the requirement. This spinning motion induces a centripetal force, which results in the material spreading to form a thin film. Excess film is spun off the substrate. A film in the micrometer range is classified as a thin film.

The film thickness can be controlled by varying parameters such as spinning speed, spinning time, and the fluid viscosity. This process has been employed for coating thin films of natural polymers such as chitosan (Mironenko et al. 2014), hyaluronic acid (Ding et al. 2012), and cellulose (Da Roz et al. 2010) for various applications. An example is the coating of thin films of chitosan in application as planar optical waveguides (Mironenko et al. 2014).

### 2.3.5 Self-assemble of Monolayers (SAM)

Although more applied to synthetic polymers, the SAM method has been used to process cellulose into biofunctional interfaces (Yokota et al. 2008). The cellulose maintained its biological functionality after processing by the SAM method. This was evident by good cell proliferation and adhesion. This method involves modifying the surface of a material in order to impose certain functionalities to improve properties such as adhesion, biosensing, friction, and wetting (Chaudhury 1995). The mechanical properties of the material such as stiffness and flexibility may be

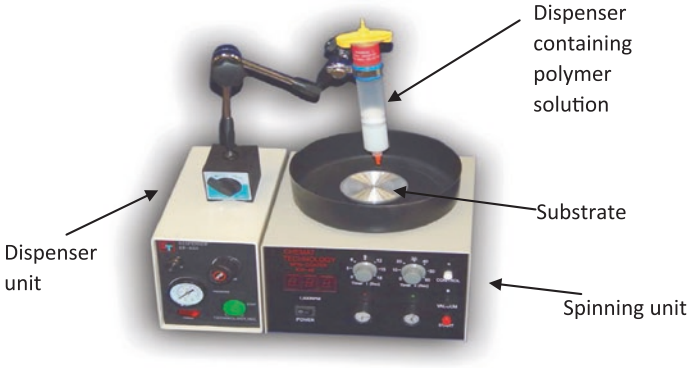


**Fig. 2.5** A commercially available spin coater Chemat precision spin from Sigma Aldrich (image publicly available at www.sigmaaldrich.com)

desired, however, the surface properties might limit its applicability for particular functions. Self-assembly of monolayers is applied to alter the surface properties, while retaining the mechanical properties of the material. For instance in applications for scaffold, a polymer material may possess the required mechanical properties, however, the surface properties could limit cell adhesion and proliferation.

### *2.3.6 Natural Polymer Microneedles*

The field of micromanufacturing has been fast expanding in the past decades. The ability to make omicron-sized devices with precision and mass reproducible techniques is of much industrial significance. This is key to designing more effective tools for applications in biomedical, engineering, and pharmaceutical industries for example. Natural polymers are particularly attractive for micromanufacturing due to their relative low cost and ease of processing. In this section particular focus is placed on microneedle production as example of micromanufacturing-based devices used in biomedical applications for drug and vaccine delivery.

Microfabrication of microneedles from natural polymer generally requires obtaining the dissolved form of the polymer such that the polymer is molded using centrifugal micromolding followed by drying to allow the solvent evaporate leaving behind a polymer which takes the shape of the mold. Silk fibroins from the Bombyx mori silkworm have been used to fabricate fast-dissolving microneedles using the centrifuge casting method (Kaplan et al. 2013; You et al. 2011). In a typical process the silk is extracted from the Bombyx mori silkworm by boiling for 30 min in aqueous solution of sodium carbonate ($Na_2CO_3$) followed by thorough rinsing with deionized water to extract the sticky sericin proteins. This was followed by overnight drying of the extracted fibroin. Dissolving the dried fibroin in 9.3 M Lithium Bromide (LiBr) solution at room temperature yielded a 20 wt% solution. The LiBr was then removed from the solution through the dialysis process in water for 48 h. To remove particulates and contaminants the silk fibroin was centrifugated and microfilters yielding 8–10 wt% fibroin. Dry fibroin is obtained through evaporation to remove water. Microneedles are fabricated from the silk fibroin using the typical micromolding process as illustrated in Fig. 2.6, similar methods for polymer microneedle production have been presented in other studies (Olatunji et al. 2014). The polymer in the dissolved form is poured over a PDMS (Polydimethyl siloxane) mold which has been prepared by either reverse micromolding or laser drilling, under applied centrifugal force of about 2500 rpm for 15 min, the polymer takes the shape on the PDMS as illustrated in Fig. 2.6. The polymer is then left to dry in the mold, after which it is separated from the mold.

Likewise fish scale biopolymers have been microfabricated into microneedles using centrifuge molding (Olatunji et al. 2014). Biopolymer was extracted from fish scale using thermal hydrolysis. The polymer was then used to produce microneedles which were shown to have sufficient strength to penetrate into the

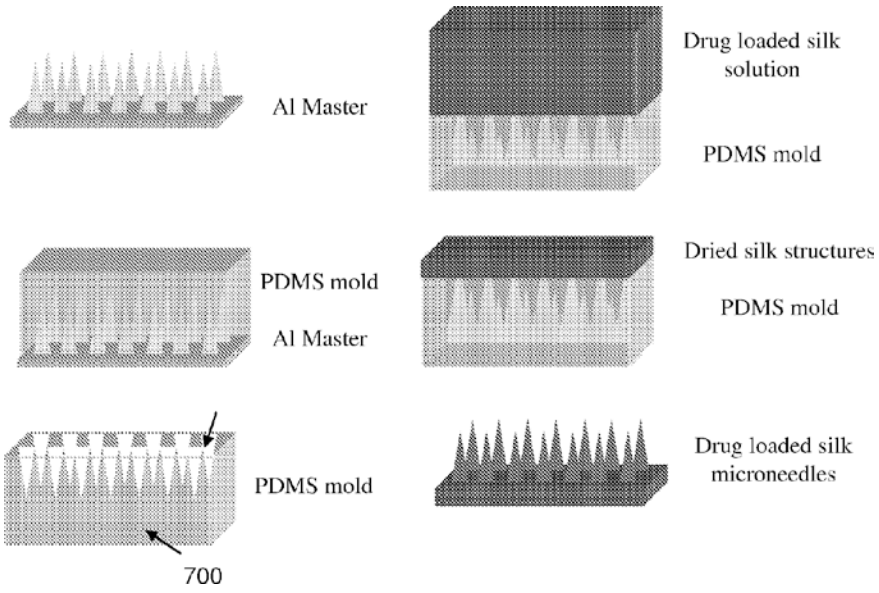


**Fig. 2.6** Schematics of micromolding process for silk fibroin microneedles (Kaplan et al. 2013). Reproduced with permission License number 3623650472538

skin. Figure 2.7 shows the microneedle gradually dissolving in the skin. Such microneedles take advantage of the fact that when in the dry form these polymers form hard glassy material but when in contact with moisture in the skin they dissolve to release the active ingredients embedded within the structure.

More recently, compression molding at low temperature of about 50 °C has been introduced for micromolding of fish scale polymer-based microneedles with cellulose nanocomposites. The study showed that the compression molding method can be used to obtain microneedles with sharp tip by optimizing the operating conditions for particular fish scale/nanocellulose compositions. As the polymer films of fish scale/nanocellulose blend do not easily redissolve in water,

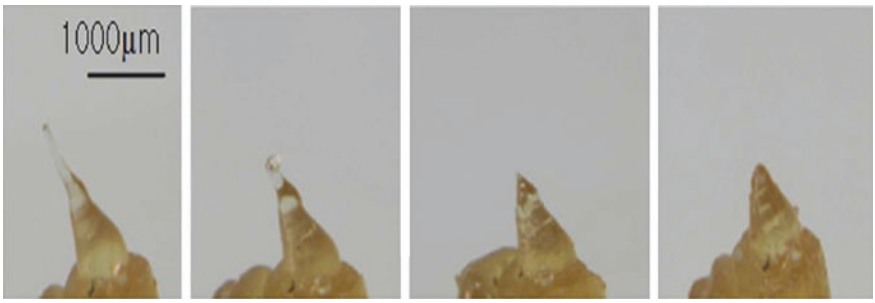


**Fig. 2.7** Fish scale microneedles gradually dissolving in the skin (Olatunji et al. 2014)

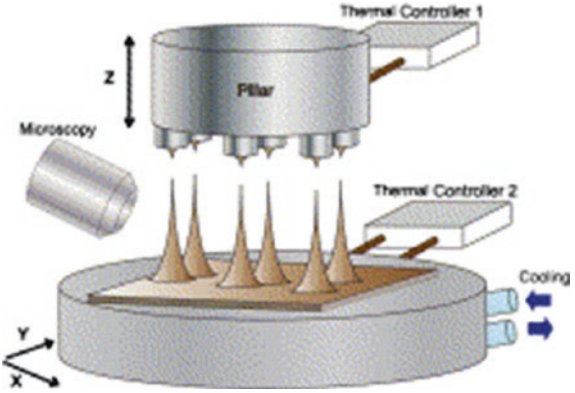


**Fig. 2.8** Spatially discrete thermal drawing of biodegradable polymer microneedles (Choi et al. 2013) with permission from Elsevier License number 3632190774292

this method offers a more ideal microfabrication to achieve microneedles from the fish scale nanocellulose blends and similarly for other polymer blends which do not easily dissolve in water but have limited thermoplasticity. Other novel methods for processing biodegradable polymer microneedles make use of spatially discrete thermal drawing (Choi et al. 2013). In this process the polymer is dispensed on a tray followed by application of another tray such that the polymer lies between the two plates. The plates are heated to a certain temperature depending on the melting and transition point of the polymer. The upper plate is then moved upward such that the polymer is pooled at a controlled speed while cooling this is illustrated in Fig. 2.8. The pulling results in formation of microneedles with sharp tips. Microneedles produced from glass albeit limited to experimental applications are produced using thermal drawing of glass micropipettes over Bunsen burner or using a pipette puller to form glass microneedles (Olatunji et al. 2014).

### *2.3.7 Cellulose Nanoparticles*

Reduction of particle size to the micro or nano scale could improve the functionality of the polymer significantly. Many research efforts are currently being placed on nanocellulose for production of high-performance composites. Nanocellulose is sourced from the bottom-up approach through biosynthesis by some bacteria such as bacteria of the Acetobacter species. Alternatively, they can be sourced from plants through the top-down approach by disintegration of the plant matter (Turbak et al. 1983; Herrick et al. 1983). Nanocellulose is also sourced from Algae (Preston and Nicolai 1948) and tunicate (Belton et al. 1989; Lee et al. 2014). Figures 2.9 and 2.10 show example of a plant and bacterial cellulose.

Magnetic decoration of cellulose nanoparticles have been used to achieve tough membranes suitable for application in speakers' production. Using the magnetic decoration method, well-dispersed nanomagnets in cellulose fiber network can be achieved leading to tough structures. Figure 2.11 shows steps in the preparation of

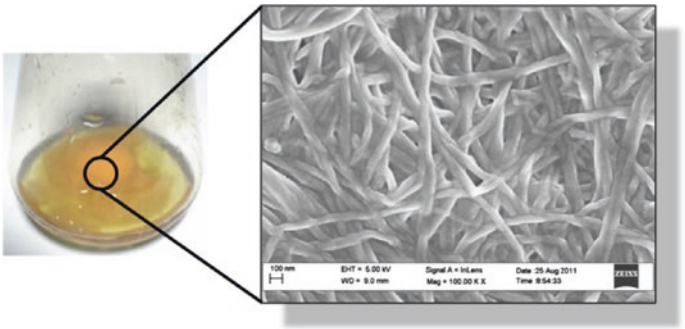

**Fig. 2.9** Image showing a 3-day-old culture of Acetobacter xylinum. The gel-like pellicle can be seen in the culture. Under SEM, the pellicle appears to be made of a nanofibrillar network of cellulose. Obtained from Lee et al. (2014). Reproduced under creative commons license

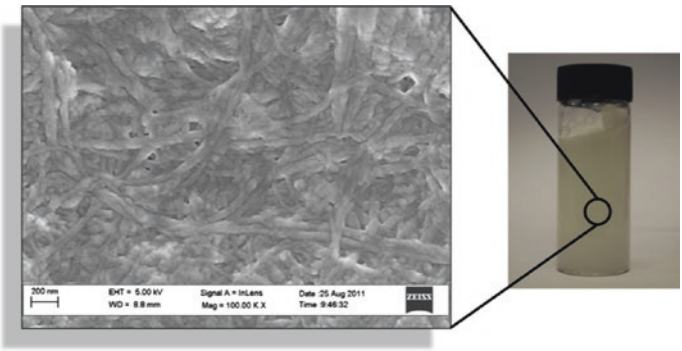

**Fig. 2.10** Image showing the nanometre scale of a 1 wt% NFC suspension in water (Lee et al. 2014). Figures taken from Lee et al. (2012a, b). Reproduced under creative commons license

magnetic nanocomposites from decorated cellulose nanofibrils (NFC). (a) shows structure of a softwood tissue; this is processed using high shear microfluidization to obtain nanofibrils from the cell wall; AFM image of the cellulose nanofibrils. (b) Magnetic decorated nanofibrils are obtained by in situ precipitation of magnetic ferrite nanoparticles onto the nanofibrils from metal salt solutions; SEM image of a decorated nanofibril. (c) Further drying results in formation of magnetic nanocomposite hydrogel, overnight drying, and rotation on a Teflon surface resulted in formation of hard permanently magnetized spherical beads—this is followed by vacuum filtration of the magnetic decorated nanofibril suspension to obtain large magnetic membranes (20 cm diameter); the image next to it shows adaption of hybrid magnetic membranes in a thin prototype loudspeaker without external magnet. The consecutive processing steps are indicated by the numbering in Fig. 2.11.

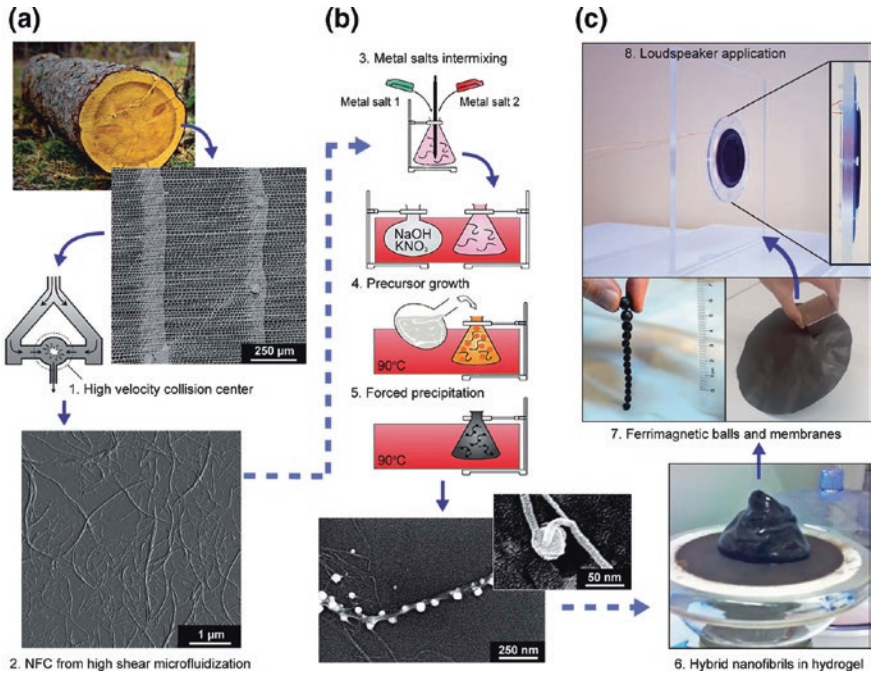


**Fig. 2.11** It shows steps in the preparation of magnetic nanocomposites from decorated cellulose nanofibrils (NFC). **a** Shows structure of a softwood tissue; AFM image of the cellulose nanofibrils. **b** Magnetic decorated nanofibril; SEM image of a decorated nanofibril. **c** Magnetic nanocomposite hydrogel, hard permanently magnetized spherical beads—large magnetic membranes (20 cm diameter); adaption of hybrid magnetic membranes in a thin prototype loudspeaker without external magnet. Reproduced under creative commons attributed license

### *2.3.8 Electrospinning, Melt Spinning, and Wet Spinning*

Production of microfibers from composite materials with good dispersion and mechanical properties in a reproducible manner can be achieved using electrospinning, melt spinning, and wet spinning. Figure 2.12 is a schematics of the working principles of electrospinning and melt spinning.

A typical electrospinning process consists of a syringe attached to a syringe pump with a pump controller, a high voltage supply, and a collector plate. The metallic tip of the needle of the syringe is connected to the high voltage supply. The pump pushes the polymer out of the syringe while the high voltage causes a spinning of the polymer resulting in fibers in the nano or micro range forming on the collector plate. The nature of the electrospun fiber obtained depends on operating conditions such as voltage, fluid properties of the polymer, nature of collector plate, flow rate, distance from collector plate, and dimensions of the needle tip (Rojas et al. 2009). Here we use an example of electrospun nanowhiskers with

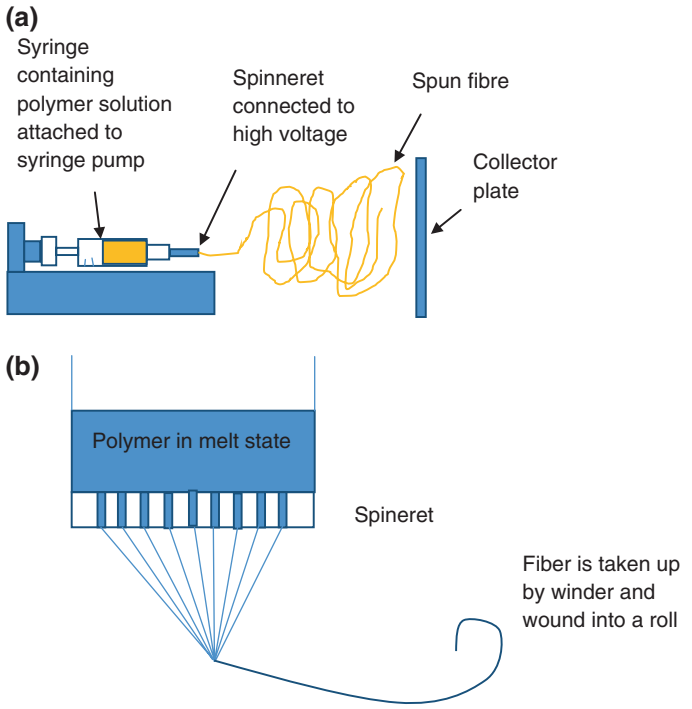


**Fig. 2.12** Schematics of **a** electrospinning process, **b** melt spinning process

polystyrene shown in Fig. 2.13. Electrospinning has been applied for processing of natural polymers such as silk fibroin (Cho et al. 2012), Chitosan (Wan et al. 2008).

Melt spinning process generally involves passing a polymer in the melt state through multiple spinnerettes and into a series of rolls and finally winder where it is wound up into fiber bundles (Fig. 2.12b). The main challenge in this process for application in the processing of natural polymers lies in the thermal sensitivity of natural polymers compared to synthetic thermoplastic polymers. Nonetheless melt spinning has been applied to a variety of natural polymer-based materials. For example, smooth defect-free nanocomposite fibers based on cellulose nanocrystals have been achieved using melt spinning process with the inclusion of cellulose acetate butyrate and triethylacetate. The spinning was done with a twin screw micro-compounder and it was observed that increasing the cellulose nanocrystal volume in the composite resulted in a fiber with better mechanical properties (Hooshmand et al. 2014).

Additionally, shell-core structured carbon fibers containing pyrolyzed fuel oil and natural polymer, lignin from wood have achieved using melt spinning. The blend was spun into fibers following dissolving in tetrahydrofuran as solvent. The blends were spun at 280 °C. The fibers showed both crystalline and amorphous regions due to the presence of lignin, however, they possessed good mechanical properties (modulus = 100 GPa) (Kim et al. 2015). In other studies PLA/bacteria

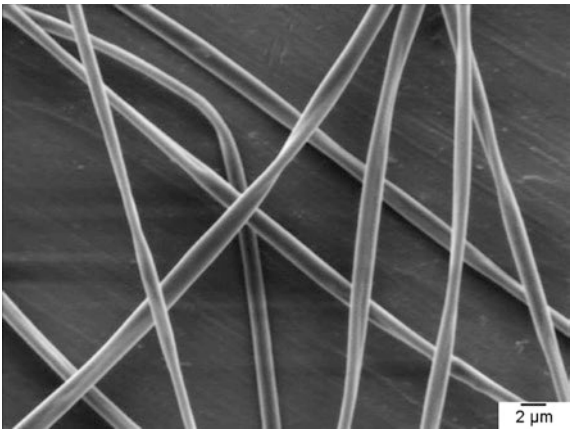


**Fig. 2.13** SEM of electrospun PS microfibers filled with 6 % cellulose nanowhiskers in the presence of nonionic surfactant (PS:CNW:S ratio of 94:6:6) showing ribbon-shaped structures. The operating conditions were 20 % PS in THF, Q = 0.2 mL/min, 40 kV, distance = 16 cm. Reproduced with permission from Rojas et al. (2009). License number 3632200995714. Original Publisher John Wiley and Sons

cellulose blends reinforced with PDLLA (poly(D, L) lactide were achieved using melt spinning (Blaker et al. 2015).

The wet spinning process similarly involves passing molten polymer through a spinnerette using a pump. The exiting fiber from the spinnerette in this case is passed toa spin bath containing solvent which allows coagulation to occur. This is then followed by further stretching, washing and drying, all in continuous stages on a series of rolls. The fiber is finally passed into a winder where it is wound up into a bundle. Collagen fibers have been processed using the wet spinning process and showed better mechanical properties than thermally spun collagen (Meyer et al. 2010).

## 2.4 Characterization

The structural characterization to determine the conformation of polymers such as polysaccharides is based on understanding the characteristic energy release for specific types of linkages which is measured by the angle of rotation about the linkage. This is particularly effective for compounds with well-established conformations such as polysaccharides and oligosaccharides. For instance by having information on the dihedral angles of rotation about the monosaccharide linkages in a polysaccharide or oligosaccharide chain, a detailed geometry of compound can be obtained (Kijawara and Miyamoto 2007). A random conformation is assumed, for example, for a polysaccharide showing independent rotations at each

monosaccharide link. Interactions between and within chains limit the likelihood of a random conformation as this allows less room for independent rotation.

Conformation is important in the functionality of the polymer. Taking a case of cellulose and amylose, polysaccharides both made up of the same monomer units and are both poly-D-glucans with (1→4)-α-D-Linkages. However, that of amylose results in a wobbled helix while cellulose has a stretched zig-zag chain conformation. This difference in conformation results in edible and soluble amylose while cellulose is inedible and water insoluble. Characterization of polymers also help determine the crystalline or amorphous nature of a polymer. Crystalline compounds tend to form much stronger structure. Polysaccharides rarely form crystal structures while proteins maintain their crystal structures even in solution (Kijawara and Miyamoto 2007).

In this section techniques such as small-angle X-ray scattering, X-ray diffraction, Fourier transform infrared spectrometry and magnetic resonance are employed.

### *2.4.1 Small-Angle X-ray Scattering (SAXS)*

This is an X-ray-based method that is characterized by a small angle. SAXS can produce rapid analysis of polymers such as proteins (Putnam et al. 2014) and polysaccharides (Kijawara and Miyamotos 2007) in solution. This process is based on the principles of reciprocal law which relates the distance r in a real space with the scattering vector $q$ in a scattering space also known as the Fourier space (Kijawara and Miyamotos 2007).

As presented by Glatter and Kratky, the electron density distribution within the object can be determined from the scattering intensity $I(q)$. This is done by expressing $I(q)$ as the Fourier transformation of the scattering angle (Eq. 2.2) (Glatter and Kratky 1982).

$$I(q) = V = \int_0^\infty 4\pi r^2 \gamma(r) \cdot \exp(-iq \cdot r)\mathrm{d}r \tag{2.2}$$

where $y(r)$ represents averaged product of two electron density fluctuations as a distance $r$. The scattering vector is expressed as a function of the wavelength $\theta$ and the scattering angle λ given as:

$$V = (4\pi/\lambda)\sin(\theta/2) \tag{2.3}$$

The shape of the scattering object $p(r)$ is characterized by the distance distribution which is defined as:

$$p(r) = Vr^2 \cdot \gamma(r) \tag{2.4}$$

The number of electrons in the object is represented by the scattered intensity. Maximum scattered intensity is at zero scattering angle and relates to the number

of electrons in the object. The set of relationships can then be solved by various mathematical models presented in literature (Putnam et al. 2014; Kijawara and Miyamoto 2007; Takeda et al. 1977). The data are then matched with existing models of conformations to establish the true conformation of the polymer being analyzed.

SAXS provides rapid but low-resolution structural characterization of polymers; it is also used in combination with other methods. As the properties of the X-ray being used is known, the other parameters can be calculated from the various mathematical models that exist for SAXS profile (Putnam et al. 2014). As an advantage SAXS is not limited to crystallized samples only and can be used to study macromolecules in solution. This is of particular advantage for natural polymers which do not easily crystallize. The reader is referred to other texts (Burchard and Meuser 1993; Glatter and Kratky 1982; Kijawara and Miyamoto 2007; Putnam et al. 2014) for more details on SAXS method.

### *2.4.2 Nuclear Magnetic Resonance (NMR)*

The assignment of specific protons or carbons to specific linkages and determination of conformation of these linkages provides more detailed information about a material. This can be done using NMR. This is a noninvasive spectroscopic method used for the structural analysis and conformational dynamics of polymers. A NMR spectrometer typically consists of a magnet, a radio frequency (RF) transmitter (Oscillator), and an RF detector. A sample placed between the magnets is subjected to an RF at s known frequency. The material absorbs the RF and detector picks up the absorption of the RF at a particular frequency and the magnetic field strength. The absorption of the RF is called resonance. A plot of the oscillator frequency against the magnetic strength at the particular frequency provides information on the chemical property of the material (Roberts 1959).

Despite its limitation to polymers which are mostly noncrystalline, it is relatively robust as it can be used to obtain data on the conformation, stereoregularity, primary and secondary structure of proteins, polysaccharides and synthetic polymers in liquid, solid, or gel forms. NMR spectroscopy is specific, the analysis can be directed at functional groups, main chain and side chains at specific sites. Information on the time-dependent structure of the polymer as well as molecular motion can be obtained. When compared to other methods such as X-ray scattering, NMR has a better sensitivity to microscopic structure within a short-range order, however, on a long-range and higher order information is not well retained and may be lost. NMR does not accurately determine spatial position of atomic groups. NMR also takes a considerable amount of time to run compared to other more rapid methods such as SAXS (Kijawara and Miyamoto 2007). A number of NMR techniques exist, these include one-dimensional pulse NMR which can be used for determining relaxation times and primary structures of carbohydrates and sugars in solution, solid-state high-resolution NMR is applied to determine the

structure of polymers in viscose solution, gel and solid forms while two-dimensional and tree-dimensional NMR techniques provide information on the primary and secondary structures and conformation of polymers (Kijawara and Miyamoto 2007). The technique chose therefore depends on the nature of the polymer to be analyzed and the information required.

Analysis of polymers using the NMR technique is based on the chemical shifts and relaxation times recorded from an NMR spectrometer. Reading of $^{1}$HNMR signal peaks at specific regions of the spectrum between 2 and 6 ppm provides information of the polymer being analyzed such that proper translation of the presence of particular peaks at certain points of the NMR spectra provides information on the presence of certain structures in the object being analyzed. Table 2.4 summarizes $^{1}$H NMR chemical shifts for identifying monomer units of polysaccharides.

The relaxation time relates to the local tumbling motion and conformational changes of polymers under NMR. The time-dependent structure and dynamics of a polymer such as hydration structure, helix–coil transition, amorphous and crystalline structures, sol–gel transition, and the structure-dependent molecular motion

**Table 2.4** Chemical shifts (ppm) of monosaccharides from acetone at 2.225 ppm in $D_2$ at 22.27 °C (Kijawara and Miyamoto 2007)

| Monosaccharide[a] | Protons | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | $H_1$ | $H_2$ | $H_3$ | $H_4$ | $H_5$ | $H_6$ | $H_7$ | $CH_3$ | $NA_c$ |
| α-D-Glc-(1→ | 5.1 | 3.56 | 3.72 | 3.42 | 3.77 | 3.77 | 3.87 | – | – |
| B-D-Glc-(1→ | 4.4 | 3.31 | 3.51 | 3.41 | 3.45 | 3.74 | 3.92 | – | – |
| α-D-Man-(1 | 1.9 | 3.98 | 3.83 | 3.70 | 3.70 | 3.78 | 3.89 | – | – |
| β-D-Man-(1 | 4.7 | 4.04 | 3.63 | 3.58 | 3.37 | 3.76 | 3.93 | – | – |
| α-D-Gal-(1→ | 5.2 | 3.84 | 3.90 | 4.02 | 4.34 | 3.69 | 3.71 | – | – |
| β-D-Gal-(1→ | 4.5 | 3.52 | 3.67 | 3.92 | 3.71 | 3.78 | 3.75 | – | – |
| β-D-GlcNAc-(1→ | 4.7 | 3.75 | 3.56 | 3.48 | 3.45 | 3.90 | 3.67 | – | 2.04 |
| α-D-GalNAc-(1→ | 5.2 | 4.24 | 3.92 | 4.00 | 4.07 | 3.79 | 3.68 | – | 2.04 |
| β-D-GalNAc-(1→ | 4.7 | 3.96 | 3.87 | 3.92 | 3.65 | 3.80 | 3.75 | 1.23 | 2.01 |
| α-L-Fuc-(1→ | 5.1 | 3.69 | 3.90 | 3.79 | 4.1–4.9[b] | – | – | 1.28 | – |
| α-L-Rha-(1→ | 4.9 | 4.06 | 3.80 | 3.46 | 3.74 | – | – | – | – |
| β-D-Xyl-(1→ | 4.5 | 3.27 | 3.43 | 3.61 | [c] | – | – | 1.32 | – |
| 3-θ-Me-α-L-Fuc-(1→ | 4.8 | 3.70 | 3.40 | – | 3.89 | – | – | 1.32 | – |
| 3-θ-Me-α-L-Rha-(1→ | 5.0 | 4.24 | 3.59 | 3.52 | 3.77 | – | – | 1.32 | – |
| 2,3-di-θ-Me-α-L-Rha-(1→ | 5.1 | 3.94 | 3.52 | 3.41 | 3.73 | – | – | – | – |
| 3,6-di-θ-Me-β-D-Glc-(1→ | 4.7 | 3.34 | 3.31 | 3.51 | 3.51 | 3.66 | 3.78 | | – |

[a]These are average values for nonreducing terminal sugars linked by a glycosidic linkage to the adjacent monosaccharides. Signals for protons at the ring carbons are shifted downfield when linked by another monosaccharide at the hydroxyl group of that carbon

[b]These are signals which are considerably vary more than other signals due to conformational features

[c]H5ax 3.29; H5eq 3.93

can be obtained from the relaxation times. This involves the spin–lattice relaxation time ($T_1$) and the spin–spin relaxation time ($T_2$).

$T_1$ can be measured using repeated pulse sequence of $\pi$–$\tau$–$2/\pi$ radio frequency through the inversion recovery method using the following equation:

$$\ln(A_\infty - A_\tau) = \ln 2A_\infty - \tau/T_1 \tag{2.5}$$

$A_\tau$ and $A_\infty$ represent the magnitude of the recovering vector of magnetization evolved the pulse at time $t = \infty$ and $t = \tau$. A plot of $\ln(A_\infty - A_\tau))$ against $\tau$. $T_1$ also relates to viscosity $\eta$ and temperature $T$ (Bovey 1972).

$$\frac{1}{T_1} = \left(\frac{128\pi^3}{h^2}\right)\left(\frac{\mu^4 a^3}{r^6}\right)\left(\frac{\eta}{kT}\right) \tag{2.6}$$

where $\mu$ denotes a nuclear moment, a is the effective radius of a spherical molecule, and $r$ is the distance from the observed nucleus to its magnetic neighbor. $T_1$ decreases in proportion to $\eta/T$ and $a^3$ increases with $r^6$. The effective volume $a^3$ is replaced with the molar volume in the case of oligosaccharides and polysaccharides in solution. $T_1$ as a function of the correlation time indicated the degree of molecular motion, and $T_1$ takes a minimum at the temperature when the relaxation occurs according to the dipole–dipole interaction,

The correlation time is given by:

$$\tau_c = 4\pi^3 a^3 \eta / 3kT \tag{2.7}$$

The spin–spin relaxation time $T_2$ is used in extreme situations of low viscosity and fast motion. $T_2$ is derived using the Carr-Purcell method or the Meiboom Gill (CPMG) method (Carr and Purcell 1954; Meiboom and Gill 1958). In the case of spin–spin relaxation time pulse sequence $(\pi/2)-\tau-\pi\gamma-2\tau-\pi\gamma-2\tau-\pi\gamma-\rho\ldots$ at $\tau$ pulse intervals.

### *2.4.3 X-ray Diffraction*

The extent of crystallinity, crystalline microstructure, occurrence of amorphous structure and the phases present in a polymeric material can be determined using X-ray diffraction. The working principles of X-ray diffraction are based on the diffraction and interference of X-ray beams as they leave a crystal. XRD can also provide other information about a material such as the orientation of the filler within the polymer or the orientation of the polymer itself. Example, biaxially orientated polypropylene properties vary significantly from that of polypropylene with other orientations.

The crystallization of a polymer sample can also be measured in situ while the process is ongoing. This can allow for controlling parameters during processing.

Sample for XRD must be well crystallized and well oriented in order to achieve good quality readings. There are a variety of methods for preparing samples for

XRD analysis, for example, starch powders and films can be pretreated bzxy drying and conditioning in a desiccator prior to XRD analysis (Detduangchan et al. 2014).

For a diffraction to occur Bragg's law must be obeyed

$$n\lambda = 2d \sin\theta \tag{2.8}$$

where $n = 1, 2, 3,\ldots$, $d$ is the spacing between adjacent plane, $\lambda$ is the wavelength of the X-ray, and the diffraction angle is $2\theta$ kl.

Here we look at some XRD processing methods that have been used for natural polymers (Polnaya et al. 2013). The starch sample was dried into powdered form and tightly packed in a sample holder of the X-ray diffractometer. X-ray beam at 30 kV and 30 mA was passed through the sample scanning at a diffraction angle of $2\theta = 5°$ to $5°$ at 0.40 intervals with a rotary speed of 30 $\text{min}^{-1}$ and a count time of 1 s. The degree of crystallinity was obtained by identifying an amorphous region and a crystalline region by plotting a smooth curve on the diffractogram. This is illustrated in Fig. 2.14.

Crystallinity is calculated using the following equation:

$$\text{Crystallinity } (\%) - A_c/(A_c + A_m) \times 100 \tag{2.9}$$

where $A_c$ and $A_m$ are the area of the crystalline and amorphous regions respectively.

Figure 2.15 shows the X-ray diffraction curves, which is a plot of X-ray intensity against diffraction angle, for native sago starch (NSS) (a) and sago starch

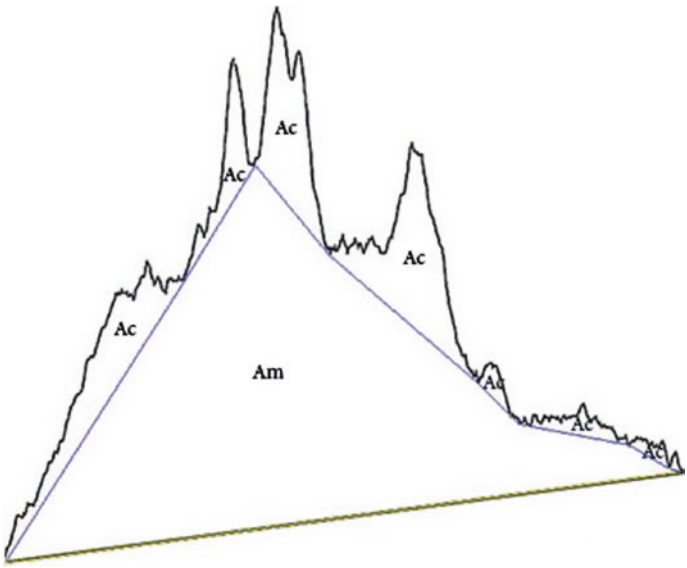


**Fig. 2.14** Smooth curve on diffractogram showing amorphous and crystalline portions of a starch sample. Reproduced from Polnaya et al. (2013) under IFRJ open access stated terms

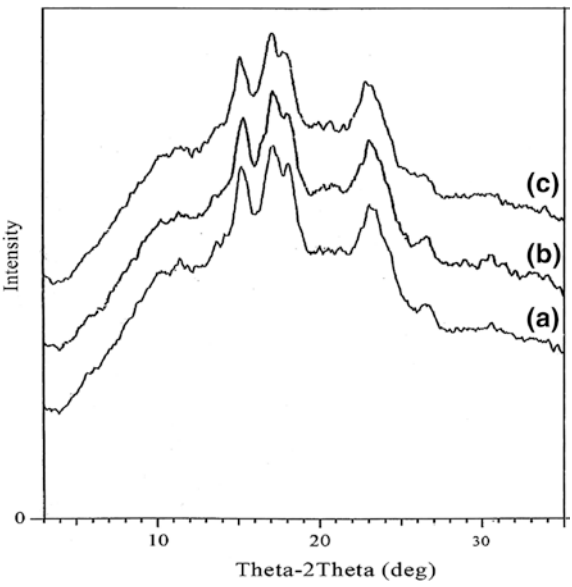


**Fig. 2.15** Intensities for native sago starch (**a**) and sago starch treated by phosphorylation with 5 % sodium tripolyphosphate STPP (**b**) and cross-linking with 4 % phosphorous oxychloride (POCl3) (cN) (Polnaya et al. 2013). Reproduced from Polnaya et al. (2013) under IFRJ open access stated terms

treated by phosphorylation with 5 % sodium tripolyphosphate STPP (b) and cross-linking with 4 % phosphorous oxychloride (POCl3) (c).

The plot shows that native starch shows a C-type crystalline pattern which is suggested by the weak diffraction pattern at a diffraction angle of 5.67° and broad peaks at 15.3°, 17.12°, 18.08°, and 23.46°. These crystalline patterns are typical of native sago starch as it has been observed in other studies on native sago starch where similar peaks were exhibited (Leong et al. 2007). The nature of crystallinity shown by the material, in this case starch is indicative of the composition. In this case starch with relatively high amylose content is reported to display such XRD peaks (Polnaya et al. 2013; Ahmad et al. 1999). Further study of the X-ray diffraction graphs shows that the phosphorylation and the cross-linking had no effect on the crystallinity of the starch. Although the peaks at 18° disappeared and new peaks were formed at 17.88° and 17.84° for cross-linked and phosphorylated sago starch, the degree of crystallinity was not much affected.

### *2.4.4 Thermogravimetry*

Thermal characterization of polymers to determine the behavior of the polymer under different temperature conditions is usually carried out using DSC or TGA. Thermogravimetry analysis involves monitoring the changes in the mass of a substance with respect to temperature over a given time under controlled atmospheric conditions. The setup typically consists of a sensitive weighing balance, a pan connected to the weighing balance, and a high temperature furnace with an inlet and purge for inert gas (which could be helium, nitrogen, or argon). The change in

mass over the duration of heating is indicative of the degradation property of the material at different temperatures.

### 2.4.5 *Differential Scanning Calorimetry*

The differential scanning calorimeter typically consists of two heating pans connected to heating plates and a temperature reader connected to a computer. This is illustrated in Fig. 2.16. The process involves placing the polymer sample on one of the heating pans while the other pan acts as a reference pan. Heat is then applied at a constant heat flow rate. The temperature readings of both pans are recorded at different times and heat flow.

Here we look at examples where the thermal properties of nanocellulose-coated sisal fiber-reinforced PLLA is obtained using DSC (Lee et al. 2012a, b). 20 mg of the nanocomposite sample is placed on the heating pan. This particular process involves a heating period where the sample was heated at a rate of 10 °C $min^{-1}$, followed by a cooling period where the sample is cooled at a rate of 50 °C $min^{-1}$, and then another heating period where the sample is reheated at a rate of 10 °C $min^{-1}$ to a temperature of 210 °C. The heating curves are then plotted for each heating and cooling cycle. The crystallinity of the composite after thermal processing is calculated from the Eq. 2.10. The properties obtained for each sample are shown in Table 2.5.

$$x_c = \frac{\Delta H_m - \Delta H_c}{(1-f)\Delta H_m^0} \times 100\,\% \tag{2.10}$$

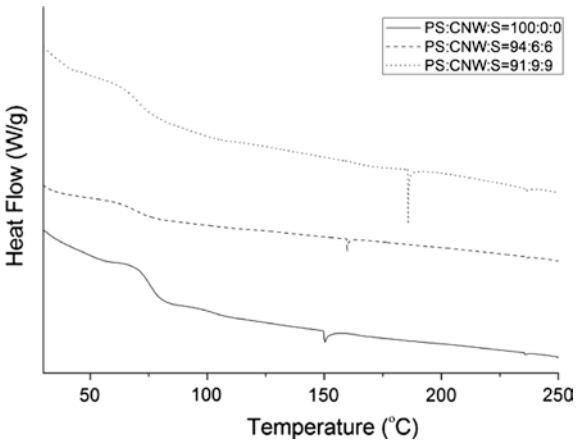


**Fig. 2.16** DSC thermograms of electrospun polystyrene microfibers showing neat polystyrene PS (100:0:0) and polystyrene loaded with 6 and 9 % cellulose whiskers (CNW) using an equivalent amount of nonionic surfactant (S). Reproduced with permission from Rojas et al. (2009). License number 3632200995714. Original Publisher John Wiley and Sons

**Table 2.5** Crystallization and melt behavior of neat PLLA and its fiber/BC reinforced hierarchical composites $T_g$, $T_c$, $T_m$ and $x_c$ are glass transition temperature, crystallization, temperature, melt temperature and crystallinity of the composites based on the 1st heating curve, respectively (Lee et al. 2012b)

| Sample | Heating | $T_g$ (°C) | $T_c$ (°C) | $T_m$ (°C) | $X_c$ (%) |
|---|---|---|---|---|---|
| PLLA | 1st | 63 | 113 | 171 | 18 ± 2 |
| | 2nd | 61 | 110 | 169 | |
| PLLA–sisal | 1st | 57 | 100 | 168 | 21 ± 3 |
| | 2nd | 59 | 103 | 168 | |
| PLLA–DCNS | 1st | 57 | 88 | 168 | 20 ± 3 |
| | 2nd | 62 | 93 | 169 | |
| PLLA–HNSF | 1st | 57 | 94 | 166 | 18 ± 2 |
| | 2nd | 57 | 94 | 166 | |
| PLLA–sisal–BC | 1st | 55 | 83 | 165 | 23 ± 4 |
| | 2nd | – | – | 168 | |
| PLLA–DCNS–BC | 1st | 56 | 85 | 163 | 18 ± 3 |
| | 2nd | – | – | 166 | |
| PLLA–HNSF–BC | 1st | 54 | 81 | 165 | 24 ± 4 |
| | 2nd | – | – | 167 | |

where $x_c$ is the crystallinity of the composite $H_m$, $H_c$, $f$, and $H_m^0$ are the melting enthalpy and cold crystallization enthalpy determined from DSC curves, weight fraction of the reinforcing phase (20 wt%) and the melting enthalpy of pure crystalline PLLA (75.57 $Jg^{-1}$) respectively.

The transition temperature can also be obtained from dynamic mechanical analysis, this is discussed in the next subsection. Differential scanning calorimetry for thermal characterization of natural polymer-based materials include electrospun polystyrene cellulose nanofibers (Rojas et al. 2009). In this case the glass transmission temperature for electrospun polystyrene with varying amount of cellulose nanowhiskers were compared (Fig. 2.16). The said fibers were electrospun at 20 % PS in THF, Q ¼ 0.2 mL/min, 40 kV, distance ¼ 16 cm. Electrospun microfibers of cellulose nanowhiskers showed lower glass transition temperature of 78 °C compared to film casted polystyrene films with the same amount of cellulose nanowhiskers which had a glass transition temperature of 93 °C (Rojas et al. 2009). This is attributed to high voltage used in the electrospinning process causing some structural modifications in the polystyrene nanocellulose fiber. The difference in glass transition temperature of electrospun fibers compared to film casted fibers with the same contents indicated that the processing method has an effect on the structural properties of the material.

### *2.4.6 Mechanical Characterization*

*Tensile Strength Test*

The tensile test is most commonly applied to polymer materials to establish the amount of work input required to cause the material to yield or fail. Properties such as stress at break, elongation at break, Young's modulus, and work of failure can be obtained from a static strength test on a polymer material. The standard

procedure for natural polymer materials is the same for other synthetic materials. This generally involves placing a strip of known dimension, i.e., width thickness and length, between two grips of a tensile testing machine. At a set speed the strip is pulled apart as the force applied varies with the displacement/elongation of the polymer strip (Singh et al. 2009).

A typical tensile testing machine consists of a station and a static crosshead, grips, load sensor, and a monitor or computer which records and displays the force displacement profile for the test.

The tensile properties can be calculated from the following equations (Belton et al. 1989):

$$t = \frac{L\text{max}}{A_i} \tag{2.11}$$

$$\varepsilon = \frac{\Delta l_b}{li} \times 100 \tag{2.12}$$

$$YM = \mathrm{d}L/\mathrm{d}m/A_i \tag{2.13}$$

$$w = \text{AUC} \times \frac{\delta}{A_i} \tag{2.14}$$

where $L_{\text{max}}$ is the maximum load, $A_i$ is the initial cross-sectional area of the sample, $li$ is the initial gauge length, $\Delta l_b$ is the increase in the length at the breaking point, d$L$/d$m$ is the slope of the linear portion of the elastic deformation, $w$ is a function of the work done in the breaking of a film specimen and representative of film toughness. AUC refers to the area under the curve (Singh et al. 2009). The results obtained are dependent on humidity and temperature, therefore these parameters should be noted and kept constant as much as possible.

The tensile properties of biopolymers derived from fish (Olatunji et al. 2014; Santos et al. 2014), jute/natural rubber composite (Pantamanatsopa et al. 2014) have been reported. Table 2.6 lists Young's modulus, elongation at break and stress at peak for some natural polymer-based materials.

*Dynamic Mechanical Analysis* (*DMA*)

Dynamic mechanical analysis refers to the study of a material's behavior under sinusoidal applied force applied at a frequency f Hz and an angular frequency of ω. A phase lag $\delta$ usually exists between the stress and strain of a viscoelastic body. Such that the dynamic stress $\sigma$ and strain $\varepsilon$ can be expressed as:

$$\varepsilon = \varepsilon_o \sin(\omega t) \tag{2.13}$$

$$\sigma = \sigma_o \sin(\omega t + \delta) \tag{2.14}$$

**Table 2.6** Mechanical properties of some natural polymer materials

| Material | Elongation (%) | Stress at break ($N/mm^2$) | Young modulus ($N/mm^2$) | Reference |
|---|---|---|---|---|
| Fish scale biopolymer | 393.45 | 1.8105 | 0.2324 | Olatunji et al. (2014) |
| Gelatin + glycerol | 71.66 | 1.040 | 1.452 | Jadhav et al. (2010) |
| Wheat starch + cotton | 0.94 | 15.2175 | 154.27 | Komuraiah et al. (2013) |
| Rice starch + cotton | 1.28 | 12.828 | 119.57 | Komuraiah et al. (2013) |
| Fish gelatin + nano-cellulose | 18 | 17 | 650 | Santos et al. (2014) |

The stress can be divided into real and imaginary parts. The real part refers to the ability of the material to store energy and release this energy when deformed while the imaginary part represents the energy lost as heat during deformation. Including the in-phase and out-of-phase components the stress can be expressed as:

$$\sigma = \sigma_o \sin(\omega t)\cos\delta + \sigma_o \cos(\omega t)\sin\delta \tag{2.15}$$

where $(\sigma_o \cos\delta)$ is the in-phase component and $(\sigma_o \sin\delta)$ is the out-of-phase component. These define the real and imaginary moduli $E'$ and $E''$ respectively as follows:

$$\sigma = \varepsilon_o E' \sin(\omega t) + \varepsilon_o E'' \cos(\omega t) \tag{2.16}$$

$$E' = \frac{\sigma_o}{\varepsilon_o}\cos\delta \tag{2.17}$$

$$E'' = \frac{\sigma_o}{\varepsilon_o}\sin\delta \tag{2.18}$$

$$\varepsilon = \varepsilon_o \exp(i\omega t) \tag{2.19}$$

$$\sigma = \sigma_o \exp(\omega t + \delta)i \tag{2.20}$$

$$E^* = \frac{\sigma}{\varepsilon} = \frac{\sigma_o}{\varepsilon_o}e^{i\delta} = \frac{\sigma_o}{\varepsilon_o}(\cos\delta + i\sin\delta) = E' + iE'' \tag{2.21}$$

Such a relationship between the shear modulus $G^*$ and storage modulus $G'$ and the loss modulus $G''$ can be expressed as:

$$G^* = G' + iG'' \tag{2.22}$$

Or in terms of phase angle as:

$$\tan\delta = \frac{G''}{G'} \tag{2.23}$$

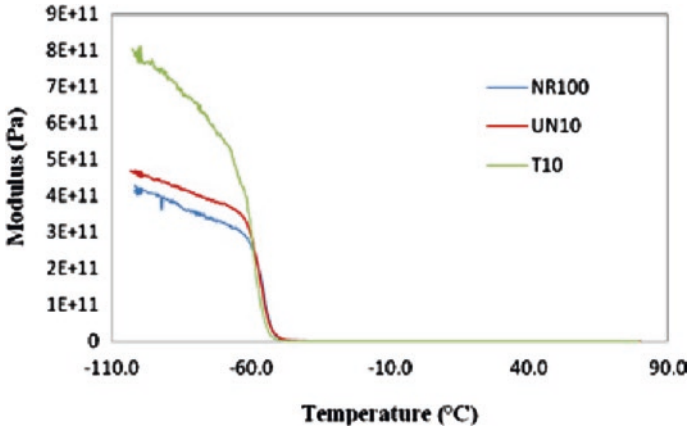


**Fig. 2.17** Modulus of elasticity for natural neat natural rubber (NR), unmodified jute fiber in natural rubber matrix (UN) and treated jute fiber with natural polymer matrix (Pantamanatsopa et al. 2014)

While the storage modulus relates to the stiffness of the material or Young's modulus, the loss modulus relates to the internal friction of the material. Factors such as motions at the molecular level, transitions, relaxation, and morphology affect the loss modulus.

The glass transition temperature is also obtainable from dynamic mechanical analysis. The glass transition temperature of −60 °C was obtained for natural rubber matrix using the DMA (Pantamanatsopa et al. 2014). As shown in Fig. 2.17, the sharp drop in the modulus beyond 60 °C corresponds to a glass transition state of the material. Where NR100 indicates a neat natural rubber polymer, UN10 indicates a natural rubber polymer matrix with untreated jute fiber reinforcement and T10 indicates natural rubber matrix containing treated jute fiber as reinforcement.

### *2.4.7 Microscopy*

Most commonly used microscopy method for characterization of natural polymers is scanning electron microscope (SEM) and transmission electron microscope (TEM). Scanning electron microscopy is often used to obtain microphotographs of fibers and composites in the micro- and nanoscale in order to study the morphology of the material. In an example the morphology of electrospun cellulose nanowhiskers were obtained using a Hitachi S-3200N variable pressure SEM (Fig. 2.13). The process required collecting of the electrospun nanowhiskers on aluminum foils, shadowing with an approximately 150 Å thick layer of gold–palladium. The prepared sample was observed at a working distance of 3 and 60 mm and accelerating voltage of between 0.3 and 30 kV. Scanning electron microscopy gives good information about the dispersion of the fiber within the composite and compatibility between the polymers. It has been widely applied in studying natural

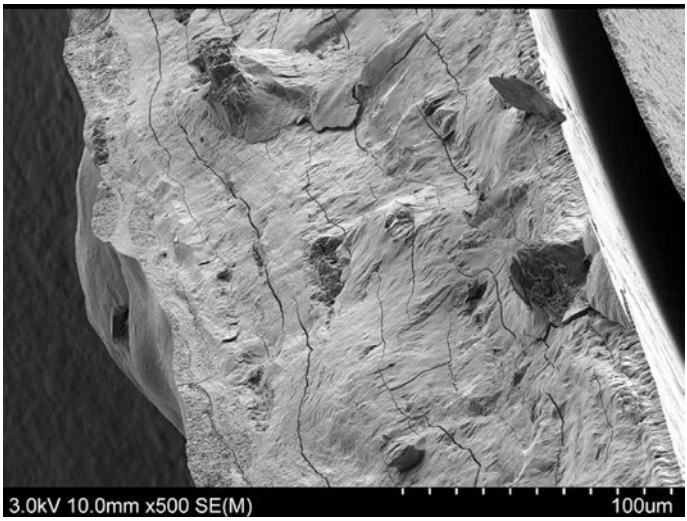


**Fig. 2.18** TEM images of fish scale gelatin with cellulose nanocrystals as reinforcement (Olatunji and Olsson 2015)

polymers used as fillers, fibers, or matrix in films and composite. Figure 2.18 shows scanning electron micrographs of fish scale gelatin with cellulose nanocrystals from wood (Olatunji and Olsson 2015).

Through the micrographs issues such as aggregation or beading can be observed. For example, Rojas et al. (2009) observed using SEM that the beading in electrospun polystyrene–cellulose nanowhiskers was significantly reduced with the use of nonionic surfactant by comparing micrographs of the electrospun fibers with and without surfactant. The diameters of the fibers formed were also observed using SEM.

TEM is often used for more detailed analysis of polymer morphology. Figure 2.19 shows the TEM images of electrospun polystyrene–cellulose nanowhiskers. For this purpose a Hitachi HF-2000 TEM using a cold field emission electron source at a 200 kV voltage was employed. TEM grids which are made up of 3-mm copper mesh were placed on the collector plate during electrospinnig to collect the electrospun samples on the TEM grids. Figure 2.18a shows TEM of neat electrospun polystyrene films without cellulose nanowhiskers, these had smoother surface while those of electrospun polystyrene with cellulose nanowhiskers shown in Fig. 2.18b were rougher and darker. Figure 2.18c shows the cellulose containing fibers at a higher magnification to show the surface roughness.

### *2.4.8 Fourier Transform Infrared (FTIR) Spectrometry*

FTIR is commonly used to analyze polymers with the aim of identifying the chemical bonds which exist within a sample. FTIR could also be a measure of

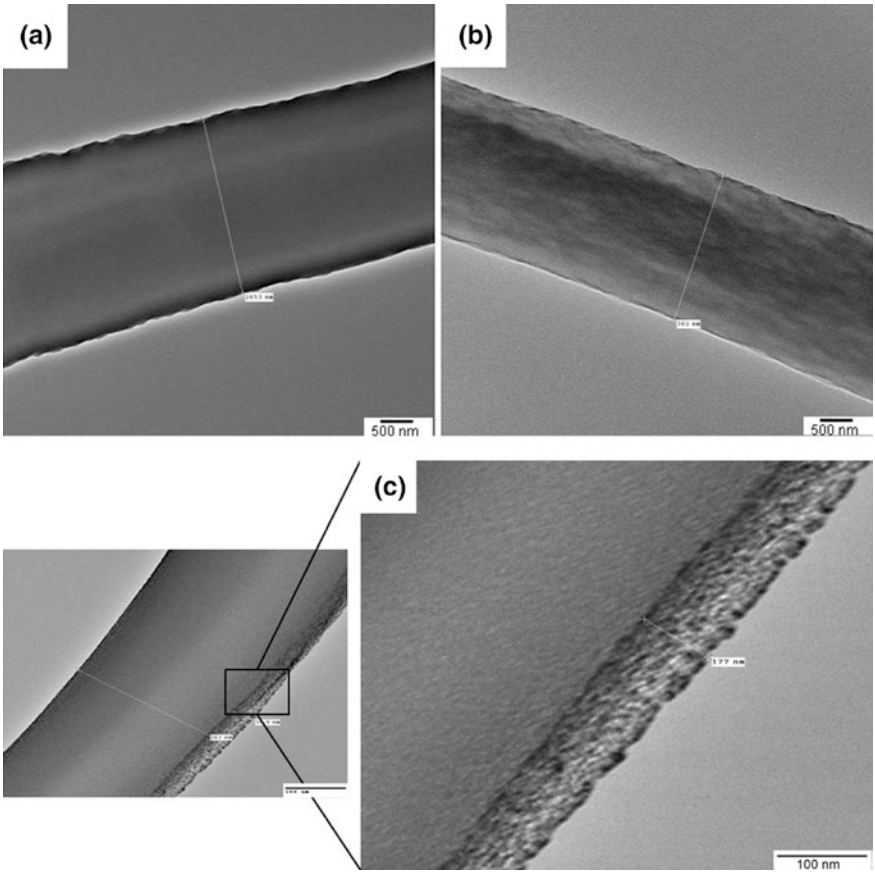


**Fig. 2.19** TEM of electrospun microfibers from neat polystyrene (**a**) and from polystyrene filled with 9 % cellulose nanowhiskers in the presence of equivalent amount of nonionic surfactant (**b**, **c**). Operating conditions: 20 % PS in THF. Q = 0.2 mL/min, 40 kV, distance = 16 cm. Reproduced with permission from Rojas et al. (2009). License number 3632200995714. Original Publisher John Wiley and Sons

compatibility between polymers. Figure 2.20 shows FTIR of lignin, cellulose, and hemicellulose obtained from biomass.

The main functional groups represented by the peaks in Fig. 2.20 for the three components, lignin, cellulose, and hemicellulose are shown in Table 2.7. Using FTIR the observation of the peaks translate to the presence of specific bonds which can be used to determine the chemical components of a sample. In the particular study by Yan et al. (2007), the FTIR was used to identify the components of biomass from plants prior to pyrolysis. The pyrolysis of biomass is of importance in the industries for energy generation from biomass from waste plant product as an alternative to fossil fuel which is fast depleting (Yan et al. 2007).

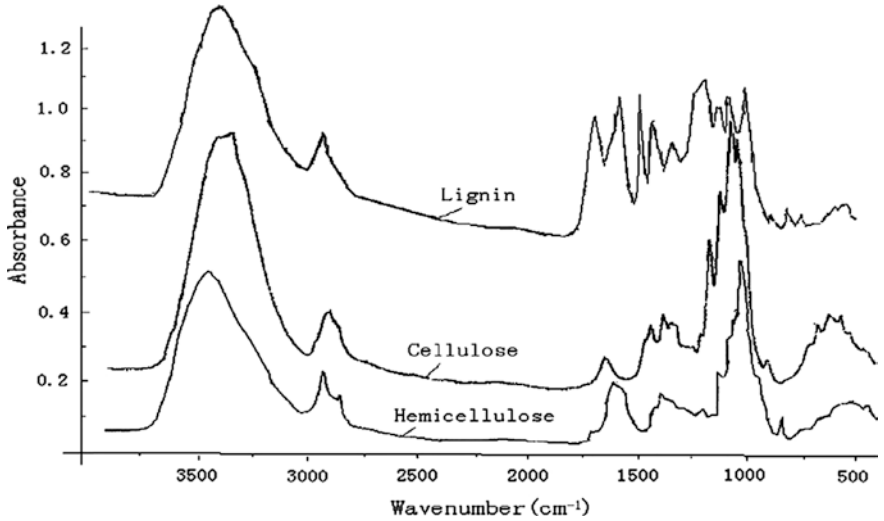


**Fig. 2.20** FTIR of lignin, cellulose, and hemicellulose (image obtained from Yan et al. 2007 with permission from Elsevier, license number 3633510294045)

**Table 2.7** The main functional groups in lignin, cellulose, and hemicellulose from FTIR

| Wave number ($cm^{-1}$)[a] | Functional groups | Compounds |
|---|---|---|
| 3600–3000 (s) | OH stretching | Acid, methanol |
| 2860–2970 (m) | C–$H_n$ stretching | Alkyl, aliphatic, aromatic |
| 1700–1730 (m), 1510–1560 (m) | C=O stretching | Ketone and carbonyl |
| 1632 (m) | C=C | Benzene stretching ring |
| 1613 (w), 1450 (w) | C=C stretching | Aromatic skeletal mode |
| 1470–1430 (s) | O–$CH_3$ | Methoxyl–O–$CH_3$ |
| 1440–1400 (s) | OH bending | Acid |
| 1402 (m) | CH bending | |
| 1232 (s) | C–O–C stretching | Aryl–alkyl ether linkage |
| 1215 (s) | C–O stretching | Phenol |
| 1170 (s), 1082 (s) | C–O–C stretching vibration | Pyranose ring skeletal |
| 1108 (m) | OH association | C–OH |
| 1060 (m) | C–O stretching and C–O deformation | C–OH (ethanol) |
| 700–900 (m) | C–H | Aromatic hydrogen |
| 700–400 (w) | C–C stretching | |

[a]*s* strong, *m* middle, *w* weak

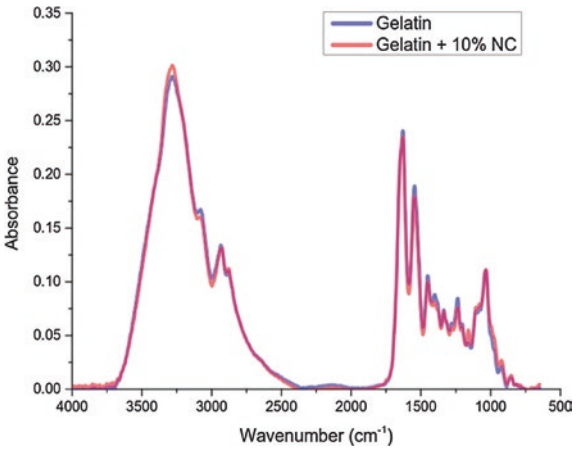


**Fig. 2.21** FTIR of fish gelatin with and without cellulose nanowhiskers (obtained from Santos et al. 2014 with permission from Elsevier, License number 3633491129379)

In another example Santos et al. (2014) obtained the FTIR analysis of gelatin with and without nanocellulose blended (Fig. 2.21). This was carried out using a Varian 660-IR spectrophotometer equipped with an attenuated total reflectance (ATR) sampling accessory scanning at a wavelength between 4000 and 6500 $cm^{-1}$. The samples showed similar peaks for both samples with a slight increase in intensity at 3280 $cm^{-1}$, representative of the amide A functional group, for the nanocellulose-blended sample (Gelatine + 10 %NC). There is also a decreased intensity at the amide I, II, and III group seen at 1361, 1542, and 1238 $cm^{-1}$ wavelength respectively. These are attributed to the protein dilution effect and/or the cellulose gelatin interactions (Santos et al. 2014).

More recent approach to FTIR makes use of nondestructive methods in which the samples require no pretreatment. As a further example the FTIR analysis of nanocellulose is carried out and shown in Fig. 2.22. To obtain FTIR peaks for the

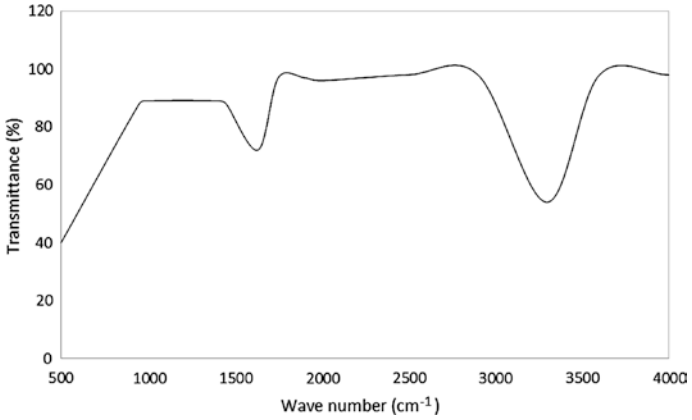


**Fig. 2.22** FTIR of nanocellulose extracted from wood

nanocellulose gel, a diamond ATR spectrometer accessory attached to the Agilent Cary 630 FTIR using a diamond crystal at a wavelength ranging between 63,000 and 350 $cm^{-1}$ is employed. The sample of nanocellulose gel is placed on the sample window and the press closed to allow contact. The sample is then scanned to obtain the absorbance plot (Fig. 2.22). The main peaks obtained occur at about 3600 $cm^{-1}$ which is indicative of the presence of OH group due to intramolecular hydrogen bonding. The other major peak occurs at about 1600, which is indicative of absorbed water. Similar peaks for nanocellulose have been reported by (Zain et al. 2014) using a Perkin Elmer type FTIR.

## 2.5 Conclusion

Processing of natural polymers into blends and composites consisting of natural polymers as fillers or as matrices in combination with other polymers can significantly alter the properties and applicability of the polymer. Further processing techniques common to industry such as extrusion, electrospinning, and microneedle production can be used to form products from natural polymers for different applications. Natural polymers can be characterized using methods such as XRD, TEM, DMA, and TGA. Although a variety of other methods exist and others are yet to emerge the techniques discussed here are those with known applications in natural polymers. In each case, examples of reported applications of these processing and characterization techniques to natural polymers are provided. Some characterization techniques presently applicable to synthetic polymers are not applicable to natural polymers due to limitations in their physical or mechanical properties. Modifications of these properties have extended some of the methods previously limited to only synthetic materials to natural polymers.

**Acknowledgment** This research was supported by the international Foundation for Science, Stockholm Sweden through a grant to Ololade Olatunji.

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# Chapter 3
# Extraction, Purification, and Modification of Natural Polymers

**Abdalbasit Adam Mariod**

## 3.1 Introduction

"Polymer" signifies "numerous parts" (from the Greek poly, signifying "numerous," and meros, signifying "parts"). Polymers are large molecules with molar masses extending from thousands to millions. About 80 % of the organic chemical industry is committed to the generation of manufactured polymers, for example, plastics, material filaments, and engineered rubbers. A polymer is incorporated by synthetically joining together numerous small molecules into one big molecule. The small molecules used to synthesize polymers are called monomers. Manufactured polymers can be called expansion polymers, structured from monomer units specifically joined together, or build up polymers, framed from monomer units joining such that a small molecule, ordinarily water, is delivered amid every response. Polymers are broadly found in nature. The human body, plants, and animals contain numerous natural polymers, for example, proteins, cellulose, gelatine, starch, chitin, and chitosan (Joesten and Wood 1996). These polymers can be extracted, purified, and modified for improved functionality in various applications.

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O. Olatunji (ed.), *Natural Polymers*, DOI 10.1007/978-3-319-26414-1_3

## 3.2 Extraction, Purification, and Modification of Gelatin

**Gelatin** or **gelatin** (from Latin: *gelatos* meaning "stiff," "frozen") is a translucent, dismal, weak (when dry), flavorless polymer, obtained from collagen acquired from different animal by-products. It is generally utilized as a gelling agent in food, pharmaceuticals, photography, and cosmetic manufacturing. Substances containing gelatin or working in a comparative manner are called gelatinous. Gelatin is an irreversibly hydrolyzed type of collagen. Gelatin is a mixture of peptides and proteins delivered by incomplete hydrolysis of collagen separated from the skin, bones, and connective tissues of animals, for example, cattles, chicken, pigs, and fish. Gelatin is derived from collagen by partial thermal hydrolysis. It is an important functional biopolymer that has a very broad application for food, material, pharmacy, and photography industries (Hao et al. 2009).

Despite the fact that gelatins from beef and pork have been broadly considered, less work has been published on extraction techniques and utilitarian properties of gelatin from cold-blooded animals, for example, fish (Cho et al. 2005; Gudmundsson 2002a, b), recently insect was used as a new gelatine source (Mariod et al. 2011a). Since it is acquired by the corruption of a bigger structure, it brings about a wide-mixed variety of peptide chain species. This degradative methodology is totally arbitrary, therefore most gelatin arrangements are not homogenous resulting in variation in molecular weight or weight distribution (Gomez-Guillen et al. 2002). Due to the acid obligation of cross-connecting in fish skin collagen, gentle treatment with acid ought to be sufficient to influence solubilisation (Norland 1990). Such treatment prompts a sort A gelatin with an isoelectric point between pH 6 and 9, which conveys a net positive charge in most food uses (Stainsby 1987). Various studies on collagen from diverse species have concentrated on acid extractions (Montero and Gomez-Guillen 2000). On the other hand, for the assembling of food grade gelatin from fish, citric acid is widely utilized as it does not impart objectionable color or odor to the gelatin (Gudmundsson and Hafsteinsson 1997). The sort of acid used, the ionic strength, and the pH emphatically impact swelling properties and solubilization of collagen. Expanding hydrogen ions supports the entrance of water to the collagen filaments, and this water is held in by electrostatic powers between charged polar gatherings (electrostatic swelling) or by hydrogen holding between uncharged polar groups and negative atoms (lyotropic hydration) (Gómez-Guillén and Montero 2001).

### *3.2.1 Primary Structure of Gelatin*

The essential structure and composition of gelatin resembles the parent collagen. This likeness has been substantiated for a few tissues and animal varieties (Fernandez-Diaz et al. 2001). Slight contrasts are because of the wellspring of crude material in mix with the pretreatment and extraction methodology utilized. The functional group of gelatin, for example, –NH2, –SH, and –COOH endow

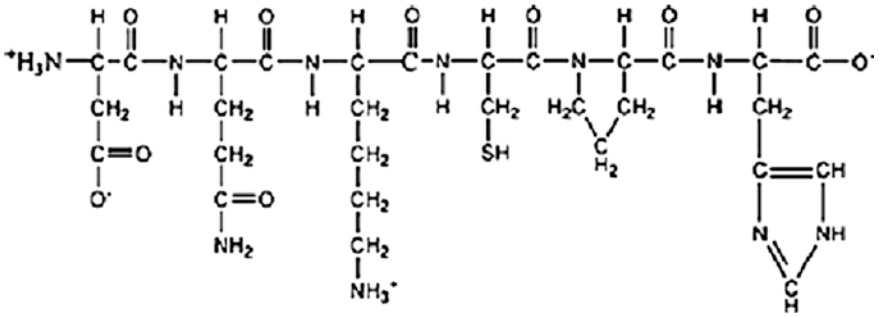

**Fig. 3.1** A typical structure of gelatin polypeptide (*Source* Liu et al. 2011)

it as lessening and stabilizing agent to diminish Au(III) to structure a gold colloid. As shown in Fig. 3.1, decently scattered gelatin stabilized gold nanoparticles. Gelatin polypeptide chains with predominately loop compliance are unreservedly soluble in water at raised temperature (>35 °C). Nonetheless, gelatin particles connected together to structure aggregates when gelatin solution and gelatin-AuNPs colloid were gradually cooled to room temperature.

### *3.2.2 Secondary Structure of Gelatin*

Different aspects of gelatin behavior in solution and gels have been disclosed in connection to its molecular weight. Gelatin is not polydispersed totally, yet has a distinct molecular weight dissemination design, which relates to the α-chain and its oligomers (Buice et al. 1995). One to eight oligomers may be discovered or distinguished in solution, however the likelihood of higher numbers being available cannot be precluded. Oligomers of three α-chains will exist primarily as in triple helices while a certain extent will exist as augmented α-polymers bonded arbitrarily by end-to-end or side-to-side bonds. The vicinity of oligomers with expanding quantities of α-chains becomes more complex and hard to peruse (Buice et al. 1995). Polyacrylamide gel electrophoresis (PAGE) is utilized to acquire profoundly precise molecular weight spectra of both commercial and laboratory gelatins, giving quantitative separation (Buice et al. 1995).

### *3.2.3 Denaturation of Collagen to Obtain Gelatin*

The least complex approach to change collagen to gelatin is to denature soluble collagen. It includes hydrolysis catalyzed by enzyme, acid, or soluble base. Thermal denaturation happens in gentle conditions by warming the collagen in neutral or somewhat acidic conditions to around 40 °C (Gimenez et al. 2005). At the point

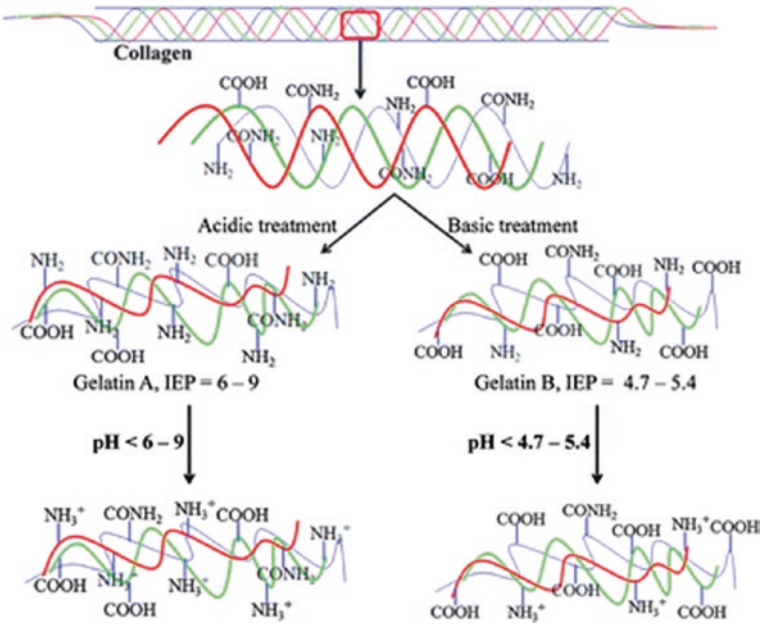


**Fig. 3.2** Denaturation of collagen to obtain gelatin (Reproduced from Samal et al. (2012), with permission from Royal Society of Chemistry, License number 3634181495264)

when collagen is warmed for amplified periods of time, the triple helix atomic structure unfolds at a certain temperature, and the collagen breaks down into irregular peptide chains in arrangement. Collagen that is denaturated by heat and gets dissolved in water is alluded to as gelatin (Fig. 3.2). The move is sharp and complete within a couple of minutes over a little temperature interim. The activation energy for denaturation is pretty nearly 81 kcal (Jusila 2004). By then just the hydrogen bonds and hydrophobic bonds that assistance to settle the collagen helix are broken, creating the filaments and fibrils of collagen to separate into tropocollagen units. The following venture, in the hydrolysis of collagen comprises in breaking the intramolecular bonds between the three chains of the helix (Nishimoto et al. 2005).

### *3.2.4 Extraction of Gelatin*

Two systems are typically used to produce gelatine from mammalians: the acid and the basic methods. The gelatin arranged by the acid methodology is called type A gelatin, while that arranged by the alkaline procedure is called type B gelatin (Schrieber and Gareis 2007). In spite of the fact that the property of collagen in fish skin is not the same as that of well-evolved mammals and avian species, the fish gelatin extraction techniques may in any case be isolated into two classes: an acid methodology and an alkali procedure. Amid fish gelatin extraction, the

acid procedure alludes to the extraction that is done in an acid medium (Gómez-Guillén and Montero 2001), and at times acid pretreatment before extraction is applied. The alkaline procedure alludes to a pretreatment of fish skin with alkaline solution, as a rule taken after by balance with an acid arrangement, hence the extraction may be done in an alkaline, neutral, or acid medium (Montero and Gómez-Guillén 2000; Jamilah and Harvinder 2002; Zhou and Regenstein 2004).

The acid methodologies are primarily utilized with pig skin and fish skin and sometimes bone crude materials. It is essentially one in which the collagen is acidified to about pH 4 and later heated stepwise from 50 °C to boiling to denature and to solubilize the collagen. From that point the denatured collagen or gelatin solution must be defatted, separated to high clarity, thought by vacuum evaporation or film ultrafiltration treatment, to a sensibly high fixation for gelation and afterward drying by passing dry air over the gel. The last process is one of the crushing and mixing to consumer prerequisites and packaging. The subsequent gelatin has an isoionic purpose of 7–9 in light of the seriousness and term of the acid handling of the collagen which causes constrained hydrolysis of the asparagine and glutamine amino acid side chains (Cole 2000).

The alkali method is utilized in bovine hide and collagen sources where the animals are generally old at slaughter. The procedure is one in which collagen is submitted to a caustic soda or extensive liming methodology preceding extraction. The alkali hydrolyses the asparagine and glutamine side chains to glutamic and aspartic acids rapidly, with the outcome that the gelatin has a customary isoionic point of 4.8–5.2, then again, with shortened (7 days or less) alkali treatment, isoionic points as high as 6 are delivered. After the alkali processing, the collagen is washed free of alkali and treated with acid to the desired extraction pH (which has a stamped impact on the gel quality to the thickness degree of the last item). The collagen is then denatured and changed over to gelatin by heating, as with the acid method. In view of the alkali treatment, it is regularly important to demineralise the gelatin solution to remove excessive amounts of salts utilizing ion exchange or ultrafiltration. From there on the procedure is the same for all the acid extraction methods—vacuum vanishing, filtration, gelation, drying, crushing, and mixing (Cole and Roberts 1996).

### *3.2.5 Extraction of Fish Gelatin*

Gelatin can be acquired from the skin and bones of animals as well as from fish. The waste from fish handling in the wake of fileting can represent as much as 75 % of the total catch weight (Shahidi et al. 1995). Around 30 % of such waste comprises of skin and bones with high collagen content that can be utilized to produce fish gelatin (Gomez-Guillen et al. 2002). Extraction of gelatins from fish skins and edible insects (sorghum and melon bugs) may provide an option to meet requirements for Halal items and serve as an option for business sectors worried about bovine spongiform encephalopathy (BSE). The yield and nature of gelatin

are impacted not just by the species or tissue from which it is separated, but additionally by the extraction process, which may rely on pH, temperature, and time during both pretreatment and extraction (Montero and Gómez-Guillén 2000; Mariod et al. 2011a). Hence, an optimization of the extraction method ought to enhance the extraction of fish gelatin. It is conceivable to acquire a light colored, dry collagen separate from megrim skins by solubilizing collagen with consistent moderate mixing overnight and uprooting the leftover, not solubilised, dim skin. The dried collagen transforms into a soluble gelatin when dissolved in warm water. Swelling limit of collagen, pH of extraction, and ionic strength, which shifts relying upon the kind of acid utilized, are important for the utilitarian viability of the extraction. Acetic acid and propionic acid delivered the most elevated swelling limit and pH of extraction, prompting the most noteworthy viscoelastic and gelling properties, particularly, when skins were pretreated with diluted NaOH and the pH was adjusted to 4.5–5 (Gómez-Guillén and Montero 2001).

### *3.2.6 Insects Gelatin*

Some insect species can be utilized to concentrate gelatine for sustenance purposes, e.g., Aspongubus viduatus and Agonoscelis pubescens; the powdered adults of these bugs demonstrated 27.0–28.2 % crude protein, respectively. The two bugs' proteins contained 16 known amino acids, including the majority of the essential amino acids. Compared with the amino acid profile prescribed by FAO/WHO, the bug protein was of mid-range quality because of its medium substance of fundamental amino acids (Mariod et al. 2011a). Gelatin was extracted from melon bug and sorghum bug utilizing boiling hot water, gentle acid, and distilled water extraction techniques.

The extraction of gelatin from melon bug utilizing hot water extraction gave high return of 150 mg/g representing 3.0 % after gentle acid extraction and distilled water extraction at 125–33.0 mg/g representing 2.5–0.6 %, respectively. While the extraction of gelatin from sorghum bug demonstrate similarly as hot water extraction was high trailed by gentle acid and distilled water extraction with the yield of 152, 66, and 134 mg/g. Amid insect gelatin extraction, basic and acid pretreatments demonstrated impacts on removing noncollagenous proteins with least collagen loss, and alkaline pretreatment followed by hot point water extraction demonstrated a superior impact than acid pretreatment,which was far superior to soluble pretreatment followed by distilled water extraction.

SDS-PAGE pattern demonstrated low molecular weight chains, and the two insect's gelatin contained protein with molecular weight of 40 kDa as a fundamental part. The differential scanning calorimetry thermograms results affirm no difference between extraction methods concerning the separated gelatin quality. FTIR spectra of melon and sorghum bug gelatins were comparative and the absorption bands were situated in more than 6 bands in melon bug gelatin and just 6 bands in sorghum bug gelatine (Fig. 3.3). Amide II bands of gelatins from both

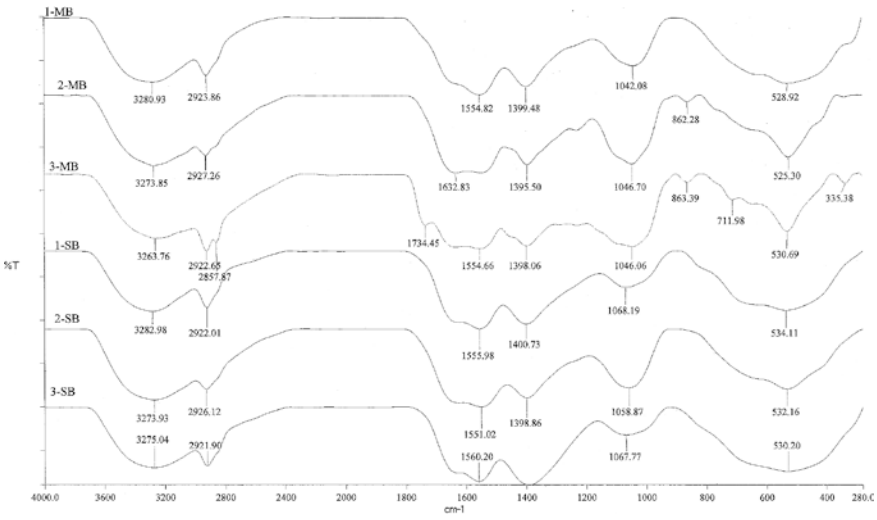


**Fig. 3.3** FTIR spectra (3282–3263, 2927–2921, 1400–1395, 1068–1042 $cm^{-1}$) of melon bug (MB 1, 2, 3) and sorghum bug (SB 1, 2, 3) gelatin extracted using three methods (*Source* Mariod et al. 2011b)

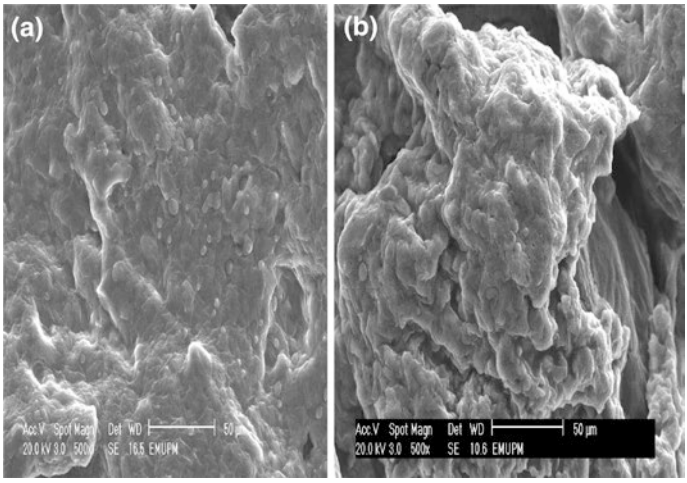


**Fig. 3.4** Scanning Electron Microscopy (SEM) micrographs for gelatine from melon bug (**a**) and sorghum bug (**b**)

melon and sorghum bugs showed up at around 1554 $cm^{-1}$, while Amide I bands (1734–1632 $cm^{-1}$) seemed just in melon bug.

Microstructures of the insect gelatin examined with the scanning electron microscope (Fig. 3.4) showed that melon bug exhibited the finest gelatin network with very small voids. Melon bug gelatin showed finer structure with smaller protein strands and voids than sorghum bug gelatin (Mariod et al. 2011b).

## 3.3 Extraction, Purification, and Modification of Chitin

After cellulose, chitin is the most far reaching biopolymer in nature. Chitin and its subsidiaries have awesome monetary worth on account of their biological activities and their industrial and biomedical applications. It can be obtained from three sources, to be specific shellfish, insects, and microorganisms. However, the principle commercial sources of chitin are shells of shrimps, crabs, lobsters, and krill that are supplied in huge amounts by the shellfish handling commercial enterprises. Extraction of chitin includes two stages, demineralization and deproteinisation, which can be directed by two techniques, chemical or biological. The chemical method obliges the utilization of acids and bases, while the biological method includes microorganisms. Although lactic acid bacteria are mostly applied, other microbial species, including proteolytic bacteria have additionally been effectively executed, and blended cultures including lactic acid-producing bacteria and proteolytic microorganisms (Arbia et al. 2013).

The structure of chitin is indistinguishable to that of cellulose, with the exception of the substitution of the OH group on the C-2 carbon of each of the glucose units with a $–NHCOCH_3$ group. In industrial processing, chitin is removed from crustaceans by acid treatment to break down calcium carbonate took after by alkaline extraction to solubilize proteins. Furthermore, a decolorization step is regularly added to evacuate extra pigments and acquire a colorless material. These treatments must be adjusted to every chitin source, owing to contrasts in the ultrastructure of the introductory materials. The subsequent chitin needs to be evaluated as far as purity and color since residual protein and pigment can result in issues for further use, particularly for biomedical items. By fractional deacetylation under alkaline conditions, one acquires chitosan, which is the most imperative chitin derivative regarding applications (Rinaudo 2006).

Of late, chitin acquired by extraction from fungi mycelia is gaining significance. Fungi mycelia can be developed during the time by fermentation under submerged culture which is quick and synchronized and can be performed in bioreactors with all robotized and controlled conditions; along these lines, mycelial biomass delivered in every batch is homogeneous, in quality and quantity (Zapata et al. 2012).

Álvarez et al. (2014) isolated chitin from the Ganoderma lucidum submerged cultures mycelium. In the said study, the extraction of chitin was carried out through five separate measures which included basically three stages: pulverization of the mushroom, deproteinization of the mycelia with NaOH solution, and a process of decolorization with potassium permanganate and oxalic acid. The five assays for the chitin isolation were made as follows: for the first three assays, the dried fungi biomass was pulverized and was subjected to alkaline treatments with sodium hydroxide solution (NaOH) at a ratio of 1:30 (w/v). For each assay, molar concentrations, temperature, and reaction time were varied; for A1 assay: 1 M NaOH 1:30 (w/v), 40 °C for 2 h; for A2 assay: 1 and 2 M NaOH 1:30 (w/v), 90 °C for 2 h; and finally for A3 assay: 2 and 4 M NaOH 1:30 (w/v), 90 °C for 2 h.

In A3 assay, a decolorization process was added; the crude chitin was treated with 10 $g L^{-1}$ potassium permanganate for 1 h and then reacted with 10 $g L^{-1}$ oxalic acid for 1 h. Assays A4 and A5 had different processes. In A4 assay, the dried fungi biomass was pulverized and a part of it was subjected to extraction twice with hot water for removing some unwanted polysaccharides. The residue was collected and dried in an oven at 40 °C. Deproteinization was performed using alkaline treatment with different molar concentrations of NaOH (2, 4, 6, and 8 M) in 1:20 (solid:alkali) ratio, at 100 °C for 3 h. The suspension was centrifuged and washed with deionized water until reaching neutrality. Decolorization process was similar to the one carried out in A3 assay.

In A5 assay, the dried fungi biomass was pounded and blended with deionized water, and afterward the mixture was subjected to a sonication process for 40 min and afterward centrifuged. The powder was washed with ethanol for 24 h. Deproteinization was performed utilizing alkaline treatment with 4 M NaOH at the ratio of 1:20 (w/v), at 100 °C for 2 h. This treatment was repeated three times. The suspension was centrifuged and washed with deionized water until reaching neutrality. Decolorization procedure was similar to the one carried out in A3 assay. At the end of the processes of each assay, each suspension was centrifuged and washed with deionized water until reaching neutrality and dried at 50 °C until reaching a constant weight. Finally, the amount of chitin obtained by each method was separated by drying weight method. Álvarez et al. (2014) reported that the amount of chitin produced was between 78 and 413 mg $g^{-1}$ in different assays (milligrams of chitin for grams of dry biomass). A1 and A2 show the highest amounts of chitin production. A difference between A1 and A2, with A3, A4, and A5 was the decolorization treatment with potassium permanganate ($KMnO_4$) and oxalic acid ($C_2H_2O_4$); A3, A4, and A5, showed a low chitin yield likely due to the strong oxidant nature of potassium permanganate. It is possible that the treatment has not only removed pigments but also chitin (Álvarez et al. 2014).

Alkali chitin was prepared by dissolving chitin at low temperature in NaOH solution. The chitin is first dispersed in concentrated NaOH and allowed to stand at 25 °C for 3 h or more; the alkali chitin obtained is dissolved in crushed ice around 0 °C (Einbu et al. 2004). The resulting chitin is amorphous and, under some conditions, it can be dissolved in water, while chitosan with a lower degree of acetylation (DA) and ordinary chitin are insoluble. This phenomenon might be related to the decrease of molecular weight under alkaline conditions and to some deacetylation; and to get water solubility, the DA has to be around 50 % and, probably, that the acetyl groups must be regularly dispersed along the chain to prevent packing of chains resulting from the disruption of the secondary structure in the strong alkaline medium (Kubota and Eguchi 1997).

Recently, Arguelles-Monal et al. (2003) used interesting techniques for chitin extraction, such as rheology, turbidimetry, and fluorescence; they found that alkali chitin solubilized in cold (~0 °C) aqueous NaOH (16 % w/w) forms an LCST solution with a critical temperature around 30 °C. A chitin gel, obtained from the solution by washing to extract NaOH, was found to be temperature- and pH-sensitive. A volume phase transition at ~21 °C was observed as the

result of the influence of temperature on polymer–polymer and polymer–water interactions such as hydrogen bonding and hydrophobic interactions. This transition is observed only within a narrow range of pH (7.3–7.6) and modifies the mechanical shear modulus as a function of oscillating variation in temperature (Rinaudo 2006).

## 3.4 Extraction, Purification, and Modification of Chitosan

**Chitosan** is a linear polysaccharide composed of randomly distributed β-(1-4)-linked D-glucosamine (deacetylated unit) and *N*-acetyl-D-glucosamine (acetylated unit). It is made by treating shrimp and other crustacean shells with the alkali sodium hydroxide (Fig. 3.5).

Chitosan is an assumed nontoxic and hydrophilic polysaccharide acquired from shellfish sources, for example, crabs and shrimps. Bioapplications of chitosan were presumably more advanced in the most recent 25 years; chitosan is as of now better known to be a dietary supplement to people in general than its other biomedical applications due to its ease, large-scale accessibility, antimicrobial activity, and in addition biodegradation and biocompatibility (Wenjuan et al. 2012).

### *3.4.1 Extraction and Isolation of Chitosan*

Paul et al. (2014) separated and secluded chitosan from the prawn waste (shell). In the first place, they removed the exoskeletons independently and washed thrice with tap water and after that twice with distilled water. At that point they dried in a hot air oven for around 24 h at 55 °C. The sample obtained was soaked in boiling 4 % sodium hydroxide utilizing 1000 mL beaker for 60 min. The example was evacuated and after that permitted to cool at room temperature for 30 min. They were then crushed further into little pieces of around 0.5–5.0 mm. The specimen acquired was demineralized utilizing 1 % hydrogen chloride with four times its amount. They were then soaked for 24 h to remove minerals. The above examples were treated with 50 ml of 2 % sodium hydroxide for 60 min. The remaining parts

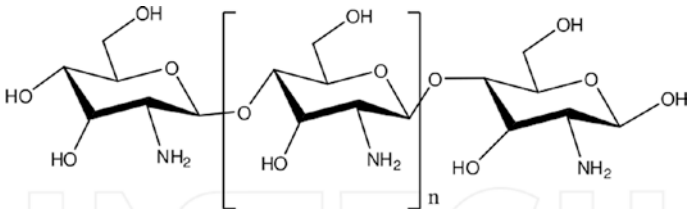


**Fig. 3.5** Chemical structure of chitosan (Wang and Uchiyama 2013)

of the specimen were washed with deionized water and after that drained off. The deacetylation methodology was then done by adding half sodium hydroxide to the obtained test on a hot plate and bubbling it for 2 h at 100 °C. The example was then permitted to cool at room temperature for 30 min. At that point they were washed consistently with half sodium hydroxide. The test acquired is filtered (chitosan is obtained). The sample was left revealed, and oven dried for 6 h at 110 °C. The acquired chitosan was cleaned to make it suitable for utilization. The purifying procedure was outlined in three stages—evacuation of insoluble with filtration, precipitation of chitosan with 1 N sodium hydroxide, and demetallization of recovered chitosan (Paul et al. 2014).

Paul et al. (2014) reported that the molecular weight of their prepared chitosan was variable due to high temperature, alkali concentration, time of reaction, chitin concentration, dissolved oxygen deliberation, shear stress, etc., and the determined molecular weight is 159,653 g/mol. They checked the solubility of the obtained chitosan with five different solvents that is water, ethanol, NaOH, acetic acid, and lactic acid. They found that their chitosan was not soluble in alkaline or neutral solution, but was soluble in acidic condition, whereas compared with lactic acid; it was more soluble in acetic 90–95 % solubility. The pH value of chitosan also varies from the range 6.2–8.0. Paul et al. (2014) study shows that the production of chitosan from sea prawn waste (shell) would successfully reduce the environmental pollution.

A common method for the synthesis of chitosan is the deacetylation of chitin using sodium hydroxide in excess as a reagent and water as a solvent. This reaction pathway, when allowed to go to completion (complete deacetylation) yields up to 98 % product. The degree of deacetylation (%DD) can be determined by NMR spectroscopy, and the %DD in commercial chitosan ranges from 60 to 100 %. On average, the molecular weight of commercially produced chitosan is between 3800 and 20,000 Da. The amino group in chitosan has a pKa value of ~6.5, which leads to a protonation in acidic to neutral solution with a charge density dependent on pH and the %DA value. This makes chitosan water soluble and a bioadhesive which readily binds to negatively charged surfaces such as mucosal membranes (Shahidi and Jozef 1991; Thomas et al. 2005).

When the degree of deacetylation of chitin reaches about 50 %, it becomes soluble in aqueous acidic media and is called chitosan. The solubilization occurs by protonation of the $–NH_2$ function on the C-2 position of the D-glucosamine repeat unit, whereby the polysaccharide is converted to a polyelectrolyte in acidic media. Chitosan is the only pseudonatural cationic polymer and thus, it finds many applications that follow from its unique character (flocculants for protein recovery, depollution, etc.). Being soluble in aqueous solutions, it is largely used in different applications as solutions, gels, or films and fibers. The first step in characterizing chitosan is to purify the sample: it is dissolved in excess acid and filtered on porous membranes (with different pore diameters down to 0.45 mm). Adjusting the pH of the solution to ca. 7.5 by adding NaOH or $NH_4OH$ causes flocculation due to deprotonation and the insolubility of the polymer at neutral pH. The polymer is then washed with water and dried.

Recently, Chenite et al. (2001) obtained a water-soluble form of chitosan at neutral pH in the presence of glycerol 2-phosphate. They obtained stable solutions at pH 7–7.1 and room temperature, but a gel formed on heating to about 40 °C. They noticed that the sol–gel transition was partially reversible and the gelation temperature depended slightly upon experimental conditions.

Puvvada et al. (2012) synthesized chitosan through various chemical steps, they prepared the chitin from the crude shells exoskeleton of shrimp that initiate chitosan synthesis with the removal of the proteins in the shells followed by demineralization for the removal of the carbon and other salts present in the crude form which will be preceded by the deacetylation of the chitin that would result in chitosan. They obtained regular chitosan but a polymer of pharmaceutical grade has to fall in the region of its predetermined quality aspects and usually commercial chitins are prepared by a first step of deproteinisation followed by a second step of demineralization.

Chatterjee et al. (2005) used the cell wall of fungi as an alternative source of chitosan, they manipulated the fungal culture media and fermentation condition and they provided a chitosan of more consistent physicochemical properties compared to that derived chemically from chitin. They isolated chitosan from *Mucor rouxii* cultured in three different media, viz., molasses salt medium (MSM), potato dextrose broth (PDB), and yeast extract peptone glucose (YPG) medium under submerged condition and their yield has been found to be almost the same. These authors found production of chitosan to be influenced by the composition of the growth medium, as the highest amount was obtained with MSM. Chitosan from MSM was less polydispersed and more crystalline compared to those from YPG and PDB.

Chitosan is not soluble in water, which limits its wide application, particularly in the medicine and food industry. Water-soluble chitosan (WSC) can be prepared by hydrolyzing chitosan using hydrogen peroxide $H_2O_2$ under the catalysis of phosphotungstic acid in homogeneous phase under optimum conditions of $H_2O_2$ 2 % (v/v), phosphotungstic acid 0.1 % (w/v), 65 °C, and 40 min, affording the maximum DE. The average degree of polymerization (DP) of chitooligosaccharides was approximately 7. The WSC content in the product and the WSC yield were 94.7 and 92.3 % (w/w), respectively. All products were white powders and soluble in water (Xia et al. 2013).

Song et al. (2013) extracted the chitosan from the blowfly larvae by a series of steps: deproteinization with sodium hydroxide, decolorization with sodium hypochlorite, decalcification with oxalic acid, and deacetylation with concentrated sodium hydroxide solution. These authors reported that the recovery rate of chitosan from the blowfly was 26.2 %, the molecular weight of the blowfly chitosan (501 kDa) was lower than that of the commercial chitosan (989 kDa), and its degree of deacetylation (DDA) (87.9–89.6 %) was also higher than that of the commercial chitosan (83.8–85.8 %).

Wu et al. (2011) obtained Chitosan oligomers (COS) by enzymatic hydrolysis and $H_2O_2$ oxidative treatment, and then they separated it into different fractions using ultrafiltration membranes. Each $COS_M$ fraction prepared using enzymatic

hydrolysis retained its structure, especially the reduced end residue ($–NH_2$ group), and had a peak for molecular weight. On the other hand, each $COS_H$ fraction prepared by oxidative treatment had partly damaged $–NH_2$ groups and two peaks for molecular weight. These results indicate that the same COS fractions prepared by the two methods differ in their amino groups and in their molecular weights, though they can both pass through the same size ultrafiltration membrane. The differences in molecular weights due to ultrafiltration separation can be observed for all fractions.

## 3.5 Extraction, Purification, and Modification of Cellulose

### *3.5.1 Cellulose Extraction*

Cellulose is a long polysaccharide chain that does not translocate within a tree or exchange carbon with the atmosphere following its formation. Radiocarbon dates performed on cellulose alone are therefore thought to be a good measure of past atmospheric 14 °C. A study by Gaudinski et al. (2005) indicated that the Jayme-Wise method produces extracts that are most chemically similar to pure cellulose as compared to other cellulose extraction methods. A batch processing protocol for Jayme-Wise cellulose extraction, developed by Leavitt and Danzer (1993) and commonly used for stable isotope measurements, involves three steps to isolate alpha-cellulose, each step followed by multiple water washes:

1. *Cleaning*: treatment in a Soxhlet system with toluene and ethanol to remove waxes, fats, oils, resins, and other compounds soluble in organic solvents.
2. *Isolation of holocellulose*: bleaching with a mixture of sodium chlorite and acetic acid to remove lignins.
3. *Isolation of alpha-cellulose*: treatment with strong base followed by a neutralizing acetic acid wash.

Cellulose consists of β-glucopyranosyl residues joined by 1 → 4 linkages. Cellulose crystallizes as monoclinic, rodlike crystals. The chains are oriented parallel to the fiber direction and form the long b-axis of the unit cell (Fig. 3.6). The chains are probably somewhat pleated to allow intrachain hydrogen bridge formation between O-4 and O-6, and between O-3 and O-5. Intermolecular hydrogen bridges (stabilizing the parallel chains) are present in the direction of the a-axis while hydrophobic interactions exist in the c-axis direction. The crystalline sections comprise an average of 60 % of native cellulose. These sections are interrupted by amorphous gel regions, which can become crystalline when moisture is removed. The acid- or alkali-labile bonds also apparently occur in these regions. Microcrystalline cellulose is formed when these bonds are hydrolyzed. This partially depolymerized cellulose product with a molecular weight of 30–50 kD, is still water insoluble, but does not have a fibrose structure (Belitz et al. 2009).

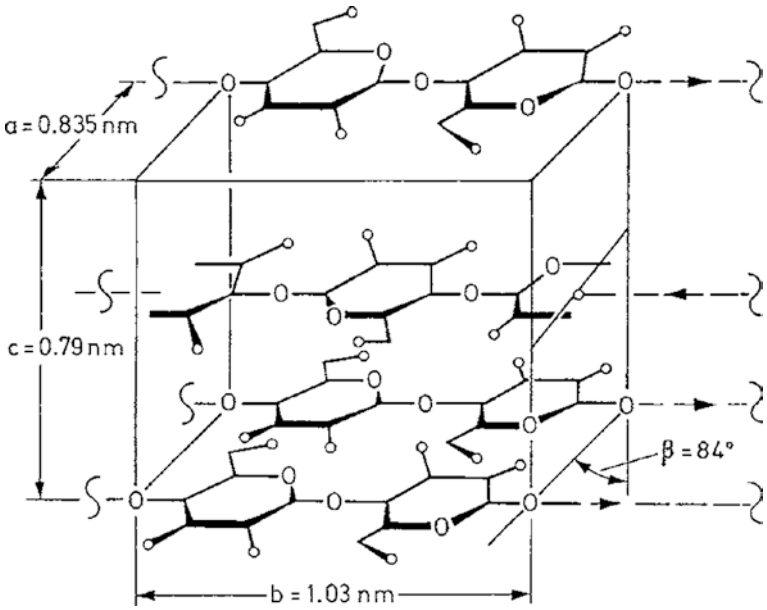


**Fig. 3.6** Unit cell of cellulose (*Source* Belitz et al. 2009)

### *3.5.2 Extraction of Alpha-Cellulose*

A protocol (Fig. 3.7) is described to isolate small quantities of highly purified cellulose for isotopic analysis of 10–100 mg samples of secondary (*Pinus sylvestris* L.) and primary (*Rubus idaeus* L.) plant cell wall material. Elemental analysis of 350 cellulose samples isolated from pine wood samples estimated the relative carbon content to be ca. 43.7–1.2 %. This value indicates that the cellulose quality is high and that the protocol is highly reproducible. High-performance anion exchange chromatography with pulsed amperometric detection of hydrolysis products quantified the purity of the cellulose as ca. 99 % of wood cellulose and primary cell wall cellulose. DRIFT spectroscopy corroborated this purity and found no evidence of cellulose degradation. Carbon isotopic composition of the purified cellulose using mass spectrometry was measured with an accuracy of 0.11 % (standard deviation). The method is rapid (56 samples may be routinely processed within 8 h) and requires only standard laboratory equipment and chemicals.

Samples (10–100 mg, routinely 50 mg) were weighed into 10 mL Pyrex2 tubes and the combined weight was measured on a balance capable of recording to 10 μg. Subsequently, 2.0 mL of acetic acid (80 %; v/v) and 0.2 mL of concentrated nitric acid (69 %; v/v) were added. In order to minimize losses, it was essential that the tube walls remained free of sample material at all stages of the protocol. Any sample left adhering to the inner wall of the test tube was washed

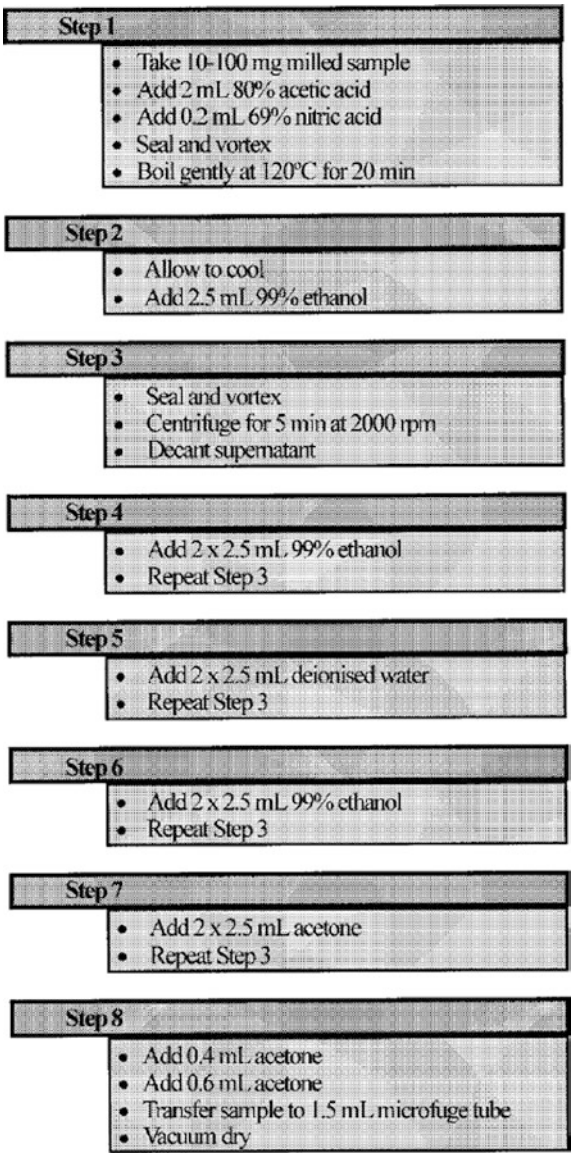


**Fig. 3.7** The protocol for purification of cellulose from micro samples of plant cell wall material using acetic acid:nitric acid for simultaneous delignification and removal of noncellulose polysaccharides. Obtained with permission from Brendel et al. (2000) License number 3622470298990

downward to aid complete extraction: this was achieved by adding liquid extraction reagent in two parts, the first to suspend the sample and the second to rinse the tube wall. Samples were then suspended by careful vortexing.

The tubes were sealed using screw caps fitted with Teflon liners and placed into a heating block preheated to 120 °C for 20 min (extraction). Once cooled, 2.5 mL of ethanol (99 %; v/v; AnalaR1 quality) was added and the samples were

centrifuged (5 min at 2000 rpm). The supernatant was then carefully decanted and the pellets were washed sequentially as follows: (1) with 2–2.5 mL ethanol, to remove extraction breakdown products; (2) with 2–2.5 mL deionized water, to remove traces of nitric acid (omission of this water wash resulted in samples with increased nitrogen content); (3) with 2–2.5 mL ethanol; and (4) with 2–2.5 mL acetone (general purpose grade). Steps (3) and (4) allowed more thorough washing and sample dehydration. Between each wash, samples were pelleted by centrifugation and the supernatant was discarded. In order to free the sample tubes for further extractions, it was necessary to transfer the purified cellulose into 1.5 mL microfuge tubes using 0.4 mL of acetone. Subsequently, the inner walls of the sample tubes were rinsed with a further 0.6 mL of acetone and the washings were transferred to the microfuge tubes. The 1 mL sample was then centrifuged for 10 min in a vacuum evaporator and the remaining acetone was decanted. Samples were recentrifuged in the vacuum evaporator until no further weight loss could be recorded. Samples were kept in sealed bags containing anhydrous silica gel. For quantitative analysis the samples can be dried to constant weight in the Pyrex test tubes.

### *3.5.3 Modification of Cellulose*

Cellulose macro- and nanofibers have gained increasing attention due to the high strength and stiffness, biodegradability and renewability, and their production and application in development of composites. Application of cellulose nanofibers for the development of composites is a relatively new research area. Cellulose macro- and nanofibers can be used as reinforcement in composite materials because of enhanced mechanical, thermal, and biodegradation properties of composites. Cellulose fibers are hydrophilic in nature, so it becomes necessary to increase their surface roughness for the development of composites with enhanced properties. In the present article, we have reviewed the surface modification of cellulose fibers by various methods. Processing methods, properties, and various applications of nanocellulose and cellulosic composites are also discussed in this article.

## 3.6 Extraction, Purification, and Modification of Starch

### *3.6.1 Starch Methods of Extraction*

Starch is widely distributed in various plant organs as a storage carbohydrate. As an ingredient of many foods, it is also the most important carbohydrate source in human nutrition. In addition, starch and its derivatives are important industrially, for example, in the paper and textile industries. Starch is isolated mainly from the sources. Starch obtained from corn, potatoes, cassava, and wheat in the native and

modified form accounted for 99 % of the world production. Some other starches are also available commercially. Recently, starches obtained from legumes (peas, lentils) have become more interesting because they have properties which appear to make them a suitable substitute for chemically modified starches in a series of products. Starches of various origins have individual, characteristic properties which go back to the shape, size, size distribution, composition, and crystallinity of the granules. The existing connections are not yet completely understood (Belitz et al. 2009).

Starch production is an isolation of starch from plant sources. It takes place in starch plants. Starch industry is a part of food processing which is using starch as a starting material for production of starch derivatives, hydrolysates, dextrins. At first, the raw material for the preparation of the starch was wheat. Currently, main starch sources are:

- maize (in America)—70 %,
- potatoes (in Europe)—12 %,
- wheat—8 %,
- tapioca—9 %,
- rice, sorghum, and others—1 %.

### *3.6.2 Corn Starch Production*

Alkaline cooking, which is referred to as nixtamalization, is an important process used in the preparation of tortillas, com chips, taco shells, tamales, and other Mexican-style foods. During nixtamalization, com is first cooked in the presence of lime, steeped, and then washed to produce nixtamal. Nixtamal is stone-ground to form a soft, moist dough that is called masa (Gomez et al. 1987; Serna-Saldivar et al. 1990). Although nixtamalization is widely used in the food industry, a comprehensive, fundamental understanding of starch functionality and its thermal behavior in masa is still lacking.

The starch gelatinization process during masa preparation has not been studied in detail, and only few reports are available on the effect of masa components on starch functionality (Bryant and Hamaker 1997; Campus-BaypoJi et al. 1999). Starch in masa has been characterized without extracting starch in purified form (Gomez et al. 1991, 1992), although studies of them are helpful in identifying changes in starch granules during masa.

### *3.6.3 Starch Extraction from Masa*

Starch from masa was extracted using two different methods. For Method 1, freeze-dried masa was ground into flour using a cyclone sample mill. Masa (10 g) was dispersed in 500 mL of distilled water by stirring using a magnetic stirrer for

6 h. The mixture was passed through a loose cotton wool plug in a funnel and then it was filtered using a 60 μm polyester mesh screen under suction to remove coarse particles. The filtrate containing starch was collected and washed with distilled water containing 1 % (w/v) sodium hydroxide four times and then washed with distilled water several times. The recovered starch was dispersed in 500 mL of distilled water and filtered using 10-μm nylon mesh under suction to remove fine contaminants. Starch was recovered and freeze-dried at −55 °C and 200 mTorr pressure for 36 h. Samples were stored in sealed polypropylene containers until used.

For Method 2, dried masa was ground into flour using a cyclone sample mill. Starch in masa was extracted by the protease. Dry masa flour (5 g) was mixed with 330 units of thermolysin in the presence of 5 mM calcium chloride in 100 mL of aqueous solution in a screw cap Erlemmeyer flask. The mixture was kept in a 60 °C water bath for 4 h and gently hand-mixed at 30-min intervals. The enzyme action was terminated by adding 0.03 g of EDTA to the reaction mixture. After cooling to room temperature, the mixture was filtered through a loose cotton wool plug in a funnel to remove coarse particles and washed five times with distilled water to remove residual proteins. Starch was recovered by centrifuging the suspension at $1300 \times g$ for 7 min after each washing step. Recovered starch was redispersed in 500 mL of distilled water and filtered using a 60-μm polyester mesh screen under suction to remove coarse particles. The filtrate containing starch was collected and washed with distilled water containing 1 % (w/v) sodium hydroxide four times and then washed with distilled water several times. Recovered starch was dispersed in 500 mL of distilled water and filtered using a 10-μm nylon mesh screen under suction to remove fine contaminants and freeze-dried using a freeze dryer at −50 °C and 100 m Torr vacuum pressure for 36 h. Samples were stored in sealed polypropylene containers until used.

Han et al. (2005) reported that thermolysin (the proteolytic enzyme) can be successfully used to remove proteins associated with starch granules. Accordingly, thermolysin digestion was used to remove starch granules from protein matrices in masa. Starch isolated by enzyme digestion gave starch with significantly ($P < 0.05$) less protein compared with starches isolated by water washing.

According to these results, 57.7 % of protein in masa can be removed by water washing method, and the rest of the starch granule bound proteins (35.6 %) are removed by thermolysin action method. A very small amount (6.5 %) of total protein in masa is left with purified starch granules after thermolysin treatment. In SEM images (Figs. 3.7 and 3.8), protein and endosperm remnants were clearly visible among starch granules isolated by washing water method, whereas digesting protein with thermolysin method resulted in relatively "uncontaminated" starch granules. The starch yield of thermolysin extraction (weight of granules extracted from masa) was 60.0 % (w/w, SD 2 %). The starch extraction efficiency of the method was 74 % (w/w, db) based on the amount of starch in masa (Ratnayake et al. 2007).

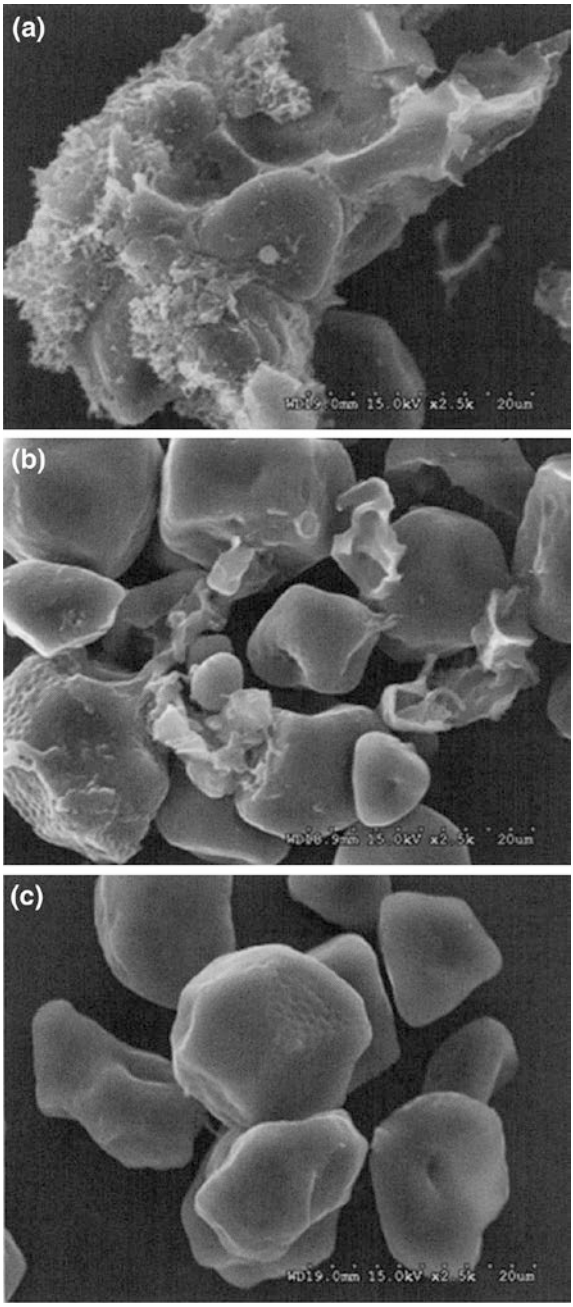


**Fig. 3.8** Scanning electron microscopic images of masa (**a**), starch isolated by Method 1 (**b**), and starch isolated by Method 2 (**c**). Magnification 2500×. *Source* Ratnayake et al. (2007)

### 3.6.4 Potato Starch Production

The production of potato starch comprises the steps such as delivery and unloading potatoes, cleaning, rasping of tubers, potato juice separation, starch extraction, starch milk rafination, dewatering of refined starch milk, and starch drying.

### 3.6.5 Starch Extraction

After separation of potato juice the pulp is directed to the washing starch station, to isolate the starch. The most used are stream-oriented washers. In these machines pulp diluted with water is washed with a strong stream of water to flush out the milk starch. The mash smuggling with water is a waste product—dewatered potato pulp. Starch milk is contaminated by small fiber particles (potato tissue fragments) and the remaining components of the potato juice—that is why it is called raw starch milk.

### 3.6.6 Starch Milk Raffination

Raw starch, milk is purified in the refining process. This involves the removal of small fibers from the starch milk and then the removal of juice water and starch milk condensation. For this purpose, the screens and hydrocyclones are commonly used. Hydrocyclones due to the low output (approximately 0.3 $m^3$/h) are connected in parallel and works as multihydrocyclones. For the starch milk desanding bihydrocyclones are used. In order to prevent enzymatic darkening of potato juice the chemical refining of starch is carried out using sulfurous acid. Refined starch milk has a density of about 22° Be, which is about 38 % of starch.

### 3.6.7 Dewatering of Refined Starch Milk and Starch Drying

It is a suspension of starch in water, which needs dewatering up to 20 % of moisture. This is equivalent to the moisture content of a commercial starch when stored. High temperature cannot be used in this process because of the danger of starch gelatinization which destroys granular structure. It may result in significant changes of the functional starch properties. Therefore, removal of excess water from milk shall be done only under conditions that prevent the gelatinization of starch.

Dewatering of refined starch milk is carried out in two stages. In the first stage, the excess water is removed by means of a rotary vacuum filter. Second, moist

starch is dried, without starch pasting. For this purpose a pneumatic drier is used. In this device moist starch (with water content 36–40 %) is floating in strong and hot (160 °C) air flow and then dried during 2–3 s. Then, the starch is separated from hot air in cyclones. Due to the short time of high temperature drying and intensive water evaporation from the starch granules, its surface is heated only to 40 °C (Pałasiński 2005).

### *3.6.8 Rice Starch Extraction*

Rice starch is used as an additive in various food and industrial products. With the inherent merits of small and uniform size distribution of rice starch and its white color and clean odor, deserts and bakery products are some of the favorable applications among processed foods. Rice protein in the endosperm, however, tightly associates on the surface of starch granules and the difficulty in removing the protein makes the starch isolation more costly compared to other starches. To isolate rice starch, alkaline solvents, surfactants, or protein hydrolyzing enzymes could be used to remove rice protein from rice flour (Maningat and Juliano 1979). Alkaline solvents such as NaOH and surfactants such as dodecylbenzene sulfonate (DoBS) and sodium lauryl sulfate (SLS) are commonly used in the protein extraction for starch isolation. These solvents destruct the oligomeric protein structures and transform them to the soluble forms. An aqueous 1.2 % DoBS solution containing 0.12 % sodium sulfite was more effective than 0.2 % NaOH or 1.2 % SLS containing 0.12 % sodium sulfite for the protein removal to isolate rice starch. The protein removal efficiency could be further increased by repeating short extraction steps (1–2 h) with fresh solution. Raising the extraction temperature was not recommendable because the protein extractability increase was minor, but starch loss became significant. Pasting characteristics of rice starch were highly dependent on the residual protein content, and protein removal imparts to the paste a viscosity increase and a pasting temperature decrease (Lim et al. 1999).

### *3.6.9 Modification of Starches*

Starch properties and those of amylose and amylopectin can be improved or "tailored" by physical and chemical methods to fit or adjust the properties to a particular application or food product. When starch granules are damaged by grinding or by application of pressure at various water contents, the amorphous portion is increased, resulting in improved dispersibility and swellability in cold water, a decrease in the gelatinization temperature by 5–10 °C, and an increase in enzymatic vulnerability. In bread dough made from flour containing damaged starch, for instance, the uptake of water is faster and higher and amylase degradation is greater. Extruded starches are easily dispersible, better soluble, and have

a lower viscosity. The partial degradation of appropriately heated amylase shows that chemical changes also occur at temperatures of 185–200 °C. Apart from maltose, isomaltose, gentiobiose, sophorose, and 1,6-anhydroglucopyranose appeared (Belitz et al. 2009).

## 3.7 Extraction, Purification, and Modification of Pectin

Pectin is a polysaccharide consisting mostly of two moieties. These are homogalacturonan, (1-4) linked, a-D-galacturonic acid and its methyl ester; and rhamnogalacturonan I, (1-2) repeating linked, a-L-rhamnose-(1-4) a-D-galacturonic acid disaccharide. Rhamnogalacturonan II contains arabinan, galactan, and arabinogalactan side chains. These monosaccharide units comprise most of sugar units found in pectin. Natural polymer like pectin is easy to isolate and purify, it is nontoxic and biocompatible (Khule et al. 2012).

Pectin is widely distributed in plants. It is produced commercially from the peels of citrus fruits and from apple pomace (crushed and pressed residue). It is 20–40 % of the dry matter content in citrus fruit peel and 10–20 % in apple pomace. Extraction is achieved at pH 1.5–3 at 60–100 °C. The process is carefully controlled to avoid hydrolysis of glycosidic and ester linkages. The extract is concentrated to a liquid pectin product or is dried by spray or drum drying into a powdered product. Purified preparations are obtained by precipitation of pectin with ions which form insoluble pectin salts (e.g., $Al_{3+}$, followed by washing with acidified alcohol to remove the added ions, or by alcoholic precipitation using isopropanol and ethanol (Belitz et al. 2009).

### *3.7.1 Extraction and Isolation of Pectin*

Extraction of pectin most commonly occurs using a dilute mineral acid, usually hydrochloric, sulfuric, or nitric acids. Commercial pectin extraction is as the follows. A factory receives previously washed and dried apple pomace or citrus peel from a number of sources. The material is added to hot water and a dilute mineral acid is added for extraction. Sufficient time elapses to allow the extraction to occur and then the solids are separated from the pectin containing liquid through filtration or centrifugation. The remaining solution is concentrated and mixed with an alcohol for pectin precipitation. The precipitated pectin is separated and washed with alcohol to remove impurities. The pectin is dried, ground to a powder, and blended with other additives, if necessary (IPPA 2001).

Many authors extracted and isolated pectin from different plant materials, Khule et al. (2012) extracted and isolated pectin from dried citrus fruit peel powder, where they blended 50 g of the powder with 300 ml distilled water. The water to be used for extraction was acidified using 40 % citric acid and pH was

maintained at 1.2–2. The acidified mixture of blended peel powder was then heated at 60 °C for around 120 min. After the heating period was over, the mixture was passed through the twofold muslin cloth and was cooled to room temperature. They isolated the pectin using ethyl alcohol as precipitating agent. Following that, concentrated pectin extracts were precipitated in 95 % ethanol. One volume of extracts was added in various volumes of ethanol. The orange fruit extracts and ethanol ratios (ER) were 1:0.5, 1:1, 1:1.5 and continuous stirring was done in 15 min. Then the mixture was kept aside for 2 h without stirring. Pectin was filtered through four-layered muslin cloth. The precipitate was washed 2–3 times by ethyl alcohol, to further remove any remaining impurity. Finally, the precipitate was kept for drying at 35–40 °C in hot air oven and percentage yield was found to be around 18.21 %. It was then stored in desiccators until further use. Pectin was extracted by water-based extraction technique and 9.1 g of pectin was obtained from 50 g of dried citrus fruit peel. The highest pectin yield was obtained at pH 2, the yield was peaked at the ER of 1:1. The yield ranged from 5.29 to 18.21 % (Khule et al. 2012). The effects of temperature, time, and pH on pectin yield for orange pectin using nitric acid extraction were investigated by Aravantinos-Zafiris and Oreopoulou (1991). Optimal extraction conditions of pH 1.6, 84 °C, and 64 min resulted in yields up to nearly 26 % of the dried peel weight. Galacturonic acid content, methoxyl content, and ash were reported to be independent of the extraction variables. Optimal extraction conditions found through varying extraction time, pH, and temperature for pectin extraction from sugar beet pulp were reported as the use of hydrochloric acid to adjust pH to 1.5 extracted for 4 h at 80 °C (Phatak et al. 1988). The resulting pectin yield was 19.53 % dry basis at these extraction conditions.

Campbell (2006) successfully extracted pectin from watermelon rind using acid and enzyme as comparative extraction methods. Pectin yields for the two extraction methods were increased through the optimization of extraction parameters. Extraction using nitric acid and precipitation using isopropanol appeared to be the best acid/alcohol combination. Further experimentation indicated that there was not a difference in pectin yield due to solid-to-liquid ratio. No significant difference in pectin yield occurred with increasing temperature, although the trend showed higher yields with increased temperature. An extraction temperature of 95 °C was chosen for further extractions. The use of *Trichoderma viride* cellulase for watermelon rind pectin extraction resulted in a minimal amount of pectin. Enzyme loading did not result in a significant difference in pectin yield for Cellupract (Campbell 2006).

## 3.8 Extraction, Purification, and Modification of Lignin

Lignin is a natural, highly branched and amorphous, polymer of high molar mass, acting as the essential glue that gives plants their structural integrity, and representing the second most abundant natural polymer on earth. As an integral part of

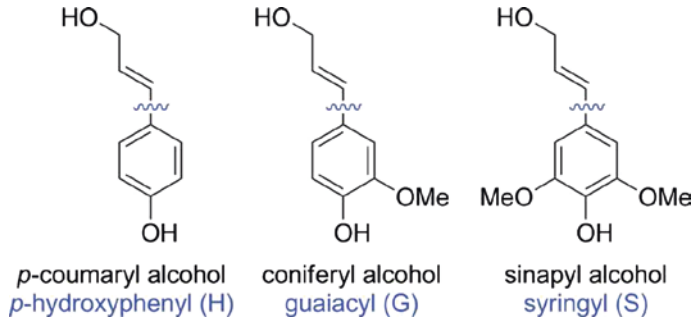


**Fig. 3.9** Three fundamental monolignols (and their respective phenylpropanoids): *p*-coumaryl alcohol (*p*-hydroxyphenyl), coniferyl alcohol (guaiacyl), and sinapyl alcohol (syringyl) (Reproduced with permission from Pinkert et al. (2011) License number 3622560015292)

the secondary cell wall of plants, and due to its hydrophobic character, it plays an important role in transporting water in plant stems. Lignin lacks a clearly defined secondary or tertiary order and its variable composition depends on the plant source. In a simplified way, lignin can be regarded as the polymerized product of three fundamental phenylpropane units, commonly known as monolignols: *p*-coumaryl alcohol, coniferyl alcohol, and sinapyl alcohol. In the ligninmacromolecule, these monolignols are incorporated in the form of phenylpropanoids: *p*-hydroxyphenyl (H), guaiacyl (G), and syringyl (S) (Figs. 3.7 and 3.8) (Pinkert et al. 2011).

### *3.8.1 Lignin Extraction with Ionic Liquids*

To date, it is still impossible to study naturally occurring lignin in its unaltered form, because all known isolation procedures result in chemical modification of its three-dimensional network (Kilpelainen et al. 2007). After the first report in 2002 that some ILs can dissolve cellulose, wood scientists were gradually becoming aware of the immense potential of ILs for their research. In 2007, Kilpelainen et al. (2007) reported the complete dissolution of wood in ILs. The possibility to dissolve lignin in ILs triggered investigations on both the nature and the chemical behavior of IL-derived lignin (Zoia et al. 2011) and also includes studies on the depolymerisation of the IL-dissolved biopolymer. Pu et al. (2007) investigated a range of imidazolium ILs for their ability to dissolve kraft lignin. In their study, up to 0.2 mass fraction of lignin could be dissolved in ILs containing triflate or methylsulfate anions, and it was suggested that the IL anion dominates the dissolution behavior. Imidazolium chlorides and bromides were less potent to dissolve kraft lignin, compared to sulfur containing anions, and both tetrafluoroborates and hexafluorophosphates did not dissolve the polymer (Pu et al. 2007). However, the chemical nature of kraft lignin—containing sulfur residues from the pulping process—cannot be compared with that of native wood lignin, and caution is required when interpreting

these observations. Most ILs with cellulose-dissolving ability do also dissolve lignin to a certain degree. This behavior is exploited to reduce the recalcitrance of lignocellulosic biomass toward enzymatic hydrolysis. Especially, the IL 1-ethyl-3-methylimidazolium acetate ([EMIM]Ac) has been used to reduce both the lignin content and the crystallinity of biomass prior to its hydrolysis (Kilpelainen et al. 2007).

Imidazolium acesulfamate ILs have the ability to dissolve wood lignin without dissolving cellulose. In particular, 1-ethyl-3-methylimidazolium acesulfamate exhibits physical properties that are desirable in industrial processing. The extracted lignins possess both a larger average molar mass and a more uniform molar mass distribution compared to lignin obtained from the kraft process, which is the dominant process for the extraction of lignin in the pulp and paper industry. These results represent a significant progress toward the development of superior methods for the environmentally benign extraction of wood lignin that still allows exploiting the desirable mechanical properties of crystalline cellulose for the production of advanced biocomposites. Viewed from a different perspective, it allows to transform native wood into a lignin-deficient material with an increased cellulose content, but without compromising its crystallinity. IL lignin removal has numerous advantages compared to prevailing methods, representing an opportunity for future biorefineries producing renewable feedstock material for aromatic biochemicals and cellulosic biocomposites with the potential to transform current industries such as the pulp and paper industry. In conclusion, IL extraction of wood lignin holds promising potential for being a low-cost and environmental benign method to obtain both uniform lignins and cellulosic-rich wood residues with a high degree of crystallinity, which can be used for the manufacturing of biocomposites with superior mechanical properties. However, it is equally important to acknowledge the current limits and drawbacks of the studied IL lignin extractions. Although the incorporation of the IL anion into the extracted lignin was only observed at elevated extraction temperatures or with increased extraction times, this does not imply a nonreactive IL anion in general. Both the wood load and the wood particle size, used in the experiments, are far below the requirements of the wood industry, and the results obtained cannot quite simply be compared to those of large scale processes. Moreover, the wood samples were extensively dried prior to use in the IL extraction experiments. Although it has been shown that small amounts of residual water do not negatively impact the lignin extraction efficiency, it is very likely that the water content of natural biomass material exceeds this tolerance. In addition, both the high price and the environmental footprint of imidazolium-based ILs require successful recycling for more than 100 times to compare in the biomass arena (Pinkert et al. 2011).

Currently, the main industrial methods used for extracting lignin from woody or nonwoody lignocellulosic feedstocks are the kraft, soda, sulfite, and organosolv processes (Pye and Lora 1991). Most of these methods require high temperatures and high pressure. The high temperatures requested are usually reached by conductive heating from an external heat source, which implies reaction times of several hours. These long reaction times are not desirable because of high energy consumption and multiple unwanted side reactions (Monteil-Rivera et al. 2012).

Monteil-Rivera et al. (2012) used microwaves to isolate lignin from agricultural residues, they used a central composite design (CCD) to optimize the processing conditions for the microwave (MW)-assisted extraction of lignin from triticale straw. They found that the maximal lignin yield (91 %) was found when using 92 % EtOH, 0.64 N $H_2SO_4$, and 148 °C. They compared the yield and chemical structure of MW-extracted lignin to those of lignin extracted with conventional heating. They reported that, under similar conditions, MW irradiation led to higher lignin yields, lignins of lower sugar content, and lignins of smaller molecular weights. Except for these differences the lignins resulting from both types of heating exhibited comparable chemical structures. Their present findings should provide a clean source of lignin for potential testing in manufacturing of biomaterials.

## 3.9 Conclusion

In recent years, there is a progressive shift in the field of natural polymers. The improved interest is mainly due to the environmental concerns, which have surfaced recently and also due to the low cost involved in obtaining these polymers, which is an ideal substitute for synthetic ones, which might be toxic. Natural polymers from natural sources had its own advantages, such as no seasonal limit on accessibility to raw materials, low inorganic salt content, and no regional limit on industrial production. Some of these natural polymers are used as a possible food ingredient or in the pharmaceutical industry. This review provided information on the conditions suitable for the extraction, purification, and modification of natural polymers (gelatin, chitosan, pectin, starch, and lignin). Extraction techniques showed rapid progress using most advancements easy to apply and give pure bioactives.

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# Chapter 4
# Biomedical Application of Natural Polymers

**Ololade Olatunji**

## 4.1 Introduction

The main areas of biomedicine where biopolymers find applicability include tissue engineering, bone repair/replacement, dental repair/replacement, controlled drug delivery and skin repair. The applicability of biopolymers in biomedical science is largely due to their versatility which meets the wide variety of design and functional requirements of the different tissue types. Biopolymers selected for biomedical applications are selected based on the criteria which include material chemistry, molecular weight, shape structure, hydrophobicity/hydrophilicity, lubricating property, surface energy, degradation rate, water absorption, erosion mechanism and solubility. Polymers are particularly attractive in biomedical application as they possess these preferred criteria, particularly biocompatibility, porosity, can undergo a diverse range of chemical and physical modification for specific tissue regeneration requirement and they possess biological properties which are desirable for biomedical applications (Dhandayuthapani et al. 2011; Hutmacher 2001). Biomedical application of natural polymers is often dominated by combination of polymers with natural and synthetic bioactive particles towards attaining required mechanical and biological performance (Roether et al. 2002).

Scaffold can be produced from combination of natural polymers with other natural or synthetic polymers. Nanocomposite of silk fibroin, a natural protein from the silk worm and sodium alginate also a natural polymer sourced from sea weed, were made into fibrous scaffolds for tissue engineering (Zhang et al. 2015). Such composites can be produced by methods such as electrospinning (Pu et al. 2015; Rajzer et al. 2014),

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O. Olatunji (ed.), *Natural Polymers*, DOI 10.1007/978-3-319-26414-1_4

freeze drying (Lima et al. 2013), thermally induced phase separation (Zhang et al. 2015) and melt spinning (Cui et al. 2015) for use as various types of scaffolds.

## 4.2 Scaffolds for Tissue Engineering

The three main aspects of tissue engineering include seed cell proliferation–which involves implanting of specialized cells into the organism, cell growth–which involves introduction of growth factors which encourage tissue formation and the third is scaffolding which involves inducing tissue formation or repair using the supporting three-dimensional biomaterials known as scaffolds (Li et al. 2014a, b; Dhandayuthapani et al. 2011; Langer et al. 1993) with the general goal of restoration, maintenance or improvement of tissue functions.

A scaffold should be able to perform the following functions (Dhandayuthapani et al. 2011):

(1) Promotion of interaction between the cell and biomaterial adhesion and deposition
(2) Regulate transfer of essential substances such as nutrients, gases and regulatory factors necessary for cell growth, division and survival
(3) Controlled biodegradation rate synchronized with tissue regeneration rate
(4) Induce minimal inflammation and toxicity

Scaffolds serve as supportive structures for regeneration and restoring, and function to the tissue by acting as a temporary matrix for the cell to grow and multiply into the desired tissue structure. Tissues such as skin, bones, ligaments, cartilage, muscles, neural and vascular tissues can be regenerated using scaffolds. Scaffolds are also used for controlled delivery of bioactive compounds such as drugs, proteins and DNA. The advancement in tissue engineering in the past decade can be attributed to advancement in the major research areas pertaining to tissue engineering which includes material science, imaging, cell biology and cell material interactions, and surface characterization, thus leading to more promising prospects for treating a wider range of diseases and today there is a potential for regenerating every tissue in the body (Dhandayuthapani et al. 2011).

Scaffolds can be either biological, i.e. sourced from human or animal tissues; they can also be synthetic, i.e. made from mainly synthetic polymers. Biopolymers are widely used for scaffold production due to their biodegradability, biocompatibility, microstructure, morphology, modifiable mechanical properties and versatility. Research work into development of biologically active scaffold was first presented in 1974 (Yannas et al. 1975) and later patented in 1977 (Yannas et al. 1977). There has since been gradual development in this area as this was followed by studies to establish the principles for synthesizing a biologically active scaffold, scaffold-induced tissue regeneration in skin, peripheral nerve and conjunctiva (Yannas and Burke 1980; Yannas et al. 1981, 1982, 1985; Burke et al. 1981; Hsu et al. 2000).

Biomaterials which are inert with modifiable structural and mechanical properties are proffered for use as scaffolds. Typically, porous scaffolds are made from metals (e.g. steel and titanium), polymers (e.g. PLA and PGA), ceramics or composites. Natural polymers commonly used in scaffold production include collagen, fibrin, fibrinogen, platelet rich plasma, alginate, gelatin, albumin and hyaluronan (Mazaki et al. 2014). A major advantage of scaffolds from natural polymers is that these natural materials are more likely to encourage cell growth. Newer approaches to producing scaffold for biomedical use is the hybrid systems, where the scaffold incorporates both natural and synthetic materials thus combining the advantage of both natural and synthetic (Webber et al. 2014).

Design requirement for scaffolds are those which enable uniform cell distribution, nutrients transfer and organized cellular structure development. These requirements are met and tailored to specific cell by careful selection of polymer formulations and fabrication techniques. Polymers which have been used in production of scaffolds include chitosan, collagen (Catalina et al. 2013) elastin (Wu et al. 2014), hydrogel foams (Vlierberghe et al. 2014), fibrin and fibrinogen (Rajangam and An 2013) and other materials (Gong et al. 2005). Most recent approaches include use of polymer as matrix for carbon nanotube-based scaffolds (Serrano et al. 2014) and the use of polymers as coatings for Bioglass-based scaffold materials to improve the mechanical properties (Li et al. 2014a, b, c; Roether et al. 2002).

There are various types of scaffold depending on their structure and function. These include: porous, hydrogel, fibrous, acellular, microsphere and polymer-bioceramic scaffolds. The following sections describe some of these scaffolds and applications of natural polymers in productions of these scaffolds.

### *4.2.1 Hydrogel Scaffolds*

Hydrogels refer to covalently or non-covalently crosslinked polymer chains forming a highly hydrophilic network with similar structural properties to macromolecular components of tissues and biochemically similar to highly hydrated GAG components of connective tissues. They can hold up to 99 % of water making them applicable in promotion of high water contents in tissues. Hydrogels could be polysaccharide-based, alginate, Ethylene-vinyl alcohol or polyelectrolyte or thermo responsive hydrogels. Although synthetic polymer-based hydrogels can be synthesized to precision and have less batch variation, hydrogels from natural polymers have the advantage of being potentially biocompatible, attaining cell-controlled degradability and processing intrinsic cellular interaction.

In addition to the general physical requirements for biomaterials used in tissue engineering, hydrogels must show good biological properties such as good cell adhesion to be applicable as tissue scaffolds. Hydrogels can be designed such that the degradation rate is well controlled by, for e.g. varying the concentration of crosslinker or plasticizer (Singth et al. 2009).

Applications of biocompatible hydrogel scaffolds include bone regeneration, cartilage wound healing and wound dress. They are also used for drug delivery or incorporate growth factors to directly act on the newly regenerated tissue to support cell development and differentiation. Hydrogels are often preferred for scaffold application due to their promotion of cell migration, high water content, rapid nutrient diffusion and angiogenesis (Dhandayuthapani et al. 2011). Natural polymers such as collagen, fibrin, alginate, gelatine, fibrin, chitosan and hyaluronic acid are examples of natural polymers used for producing hydrogels. In a particular example, hybrid hydrogel scaffolds for application in cartilage replacement can be produced using chitosan/gelatin hydrogels. This was done using a technique involving a spinner flask with custom framework for effective nutrients and oxygen transfer (Song et al. 2015).

### *4.2.2 Fibrous Scaffolds*

These are scaffolds made of nanofiber materials. Manipulating polymers at nanoscale using methods such as electrospinning, self-assembly or phase separation tends to achieve fibrous scaffolds which closely mimic the target tissue. Fibrous scaffolds are particularly preferred due to their high surface-area-to-volume ratio; a property common to nanostructures, as well as their microporous orientation. This property encourages good cell migration, proliferation adhesion and differentiation. Applications of fibrous scaffolds include tissue engineering of skin, vascular neural and musculoskeletal tissues. They are also applied as drug delivery systems for controlled delivery of proteins, DNA and drugs. Silk fibroin (Mou et al. 2013), chitosan, collagen, gelatine and hyaluronic acid are examples of natural polymers used for fibrous scaffolds. As other nanostructures, nanofibres need to be surface modified using methods such as blending, coating or surface grafting to prevent agglomeration due to the high surface attraction between the nanoparticles. Another method in the production of fibrous scaffold is to mix active ingredients to be delivered such as growth factors, drugs and genes into the polymer prior to production of the nanofibers such that the nanofibers/scaffold can also act as a delivery vehicle.

A novel approach is to apply a combination of hydrogel and fibrous systems by coating the fibrous scaffolds with hydrogels. In a particular work, fibrous scaffolds made of electrospun polycaprolactone micro- and nanofibers where coated with chitosan/hyaluronan hydrogel (Deepthi et al. 2015). The scaffold is applied for rapid regeneration of torn ligaments which is common in young athletes. The PCL fibres were prepared as either random or aligned fibres via dual electrospinning method shown in Fig. 4.1.

The use of random and aligned fibre was for the purpose of comparing the effect of fibre alignment on the effectiveness of the scaffold. The electrospun fibres were then coated with prepared chitosan/hyaluronic acid hydrogel as outlined in Fig. 4.2.

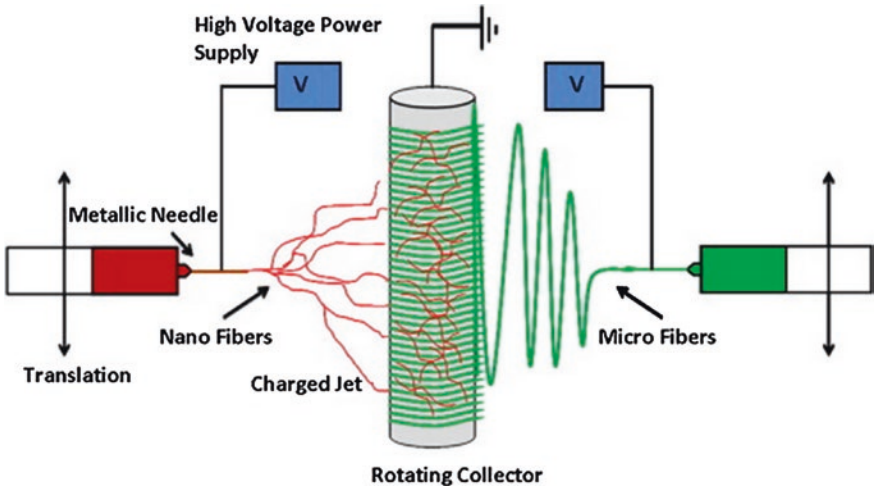


**Fig. 4.1** Dual electrospinning of PCL fibres. Obtained with permission from Deepthi et al. (2015) licence number 3637631134426

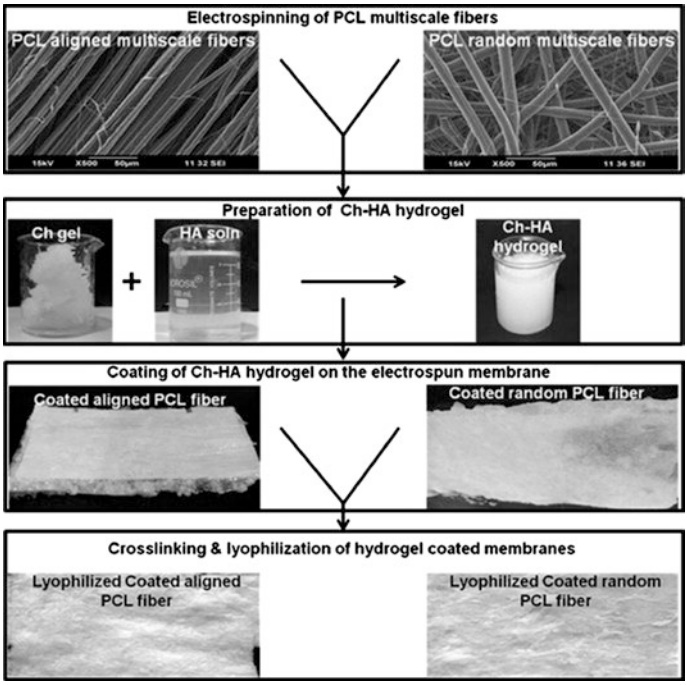


**Fig. 4.2** Flow chart for production of Hydrogel coated fibrous scaffolds. Obtained with permission from Deepthi et al. (2015) licence number 3637631134426

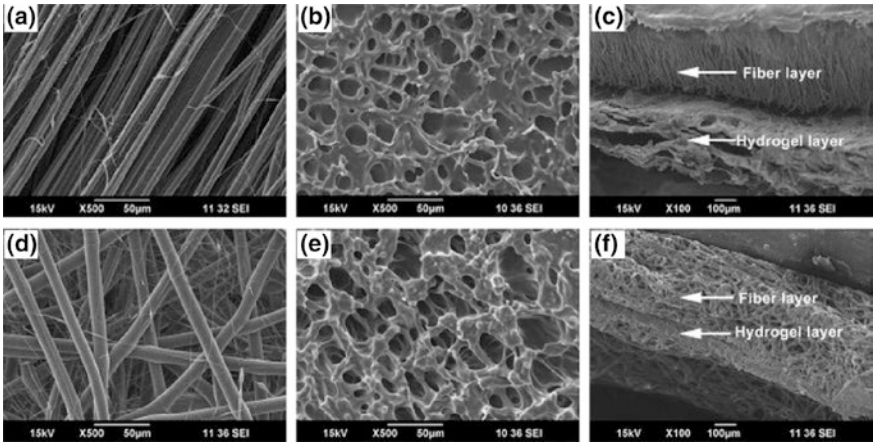


**Fig. 4.3** **a** PCL aligned multiscale fibres. **b** *Top view* CH-HA hydrogel on PCL aligned multiscale fibres. **c** *Cross-section view* CH-HA hydrogel on PCL aligned multiscale fibres. **d** PCL random multiscale fibres. **e** *Top view* CH-HA hydrogel on PCL random multiscale fibres. **f** *Cross-section view* CH-HA hydrogel on PCL random multiscale fibres. Obtained with permission form Deepthi et al. (2015) licence number 3637631134426

When compared, the hydrogel coated scaffolds showed enhanced protein adsorption compared to the uncoated PCL scaffolds leading to improved cell viability. In addition to this, the cell growth pattern encouraged alignment of cells along the direction of force to make the scaffold function as effectively as the native ligament. The hydrogel coating on the scaffolds led to better cell attachment and proliferation. Furthermore, despite the reduced mechanical strength of the random PCL fibres compared to the aligned fibres, the random PCL fibres showed better cell attachment and proliferation; this is attributed to the increased porosity (Fig. 4.3).

### *4.2.3 Porous Scaffolds*

These are either sponge or foam porous scaffolds made up of evenly distributed pores often used in tissue engineering applications such as bone regrowth, development of vasculature in organs and host tissue growth. They are chosen for these functions due to their porous nature which mimic ECM (extracllular matrix) architecture thus promoting cell growth by allowing for cell attraction, proliferation and differentiation. Polymers which have been used in production of porous scaffolds include elastin (Wu et al. 2014), hydrogel foams (Vlierberghe et al. 2014) and other materials (Gong et al. 2005). Advantages of porous scaffolds include the ECM mimicking porous structure which encourages cell interaction with the environment thus providing a framework over which the cells can develop their own ECM, inhibits the development of adherent contact-inhibit cells and allowing

good nutrition distribution in the centre of the structure and limits the formation of clusters which may lead to cell necrosis; this is by virtue of its pore size which limits the size of clusters. Foam type porous scaffolds can have either random or organized patterns which can be determined by the solvent type and separation conditions (Ma and Zhang 2001). Different cells and tissues have varying requirements. Recent research focus on porous scaffold is directed towards developing more controlled pore size, porosity, orientation, surface-area-to-volume ratio and crystallinity towards developing more sophisticated and specified tissue scaffolds (Ma and Zhang 2001; Freiberg and Zhu 2005; Mooney et al. 1994; Wei and Ma 2004; Ouriemchi and Vergnaud 2000).

As an example of porous scaffold production from natural polymers, we take an example of preparation of silk fibroin/collagen/hydroxyapatite composite scaffolds as an example. The process of particulate leaching was employed to create the silk fibroin/collagen/hydroxyapatite composite scaffolds. The composite combined the sinterability and enhanced densification property of hydroxyapatite hence it's good mechanical properties, with collagen's ability to form a good ECM and enhance cell adhesion and migration together with the low cost, biocompatibility, water vapour permeability, biodegradability and minimal inflammatory reaction of silk fibroin. Thus, making up a composite material with desirable properties for biomedical application—in particular scaffold production (Mou et al. 2013).

The particulate leaching method used in this particular example employs a one-step fabrication method which is relatively simpler than conventional particulate leaching processes which have been used for scaffold production. The method as illustrated in Fig. 4.4 is as follows. Sodium Chloride particles were mixed with hydroxyapatite particles with a dimension of 150 nm by 20 nm needle-like structures at 99 % purity. This was closely packed into a 20 mL plastic syringe followed by adding a mixture consisting of 6 % v/v solution of silk fibroin and

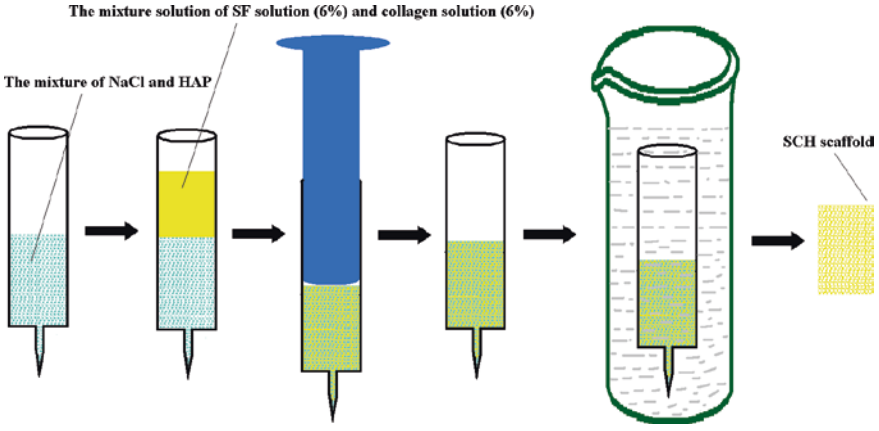


**Fig. 4.4** Illustration of stages for production of scaffolds by particulate leaching process. Image obtained with permission from Mou et al. (2013) licence number 3637080927038 original publisher, Elsevier

6 % w/v collagen. The mixture was then pressed down with the syringe piston and in the process excess materials consisting of water, excess protein solution air were released from the syringe tip. The material left in the syringe tip, which is a composite of silk fibroin, collagen, hydroxyapatite and sodium chloride was left at room temperature for 24 h after which it was removed and crystalized using ethanol (70 % v/v) for 30 min after which it becomes insoluble in water. The remaining salt and excess unbounded hydroxyapatite was removed by repeated washing in ultra water. The porous scaffold is thereby formed.

The composites formed showed good blending and uniform distribution of the silk fibroin, collagen and hydroxyapatite. A uniform scaffold was formed with good three-dimensional structure and controllable pore size (decreased sodium chloride concentration resulted in decreased pore diameter) and interconnected porosity. The scaffold significantly promoted Human Osteosarcoma MG-63 cells proliferation as shown in the confocal laser scanning microscope (CLSM) shown in Fig. 4.5 and taking a count of viable cells on the scaffolds following incubation period of 0, 1 and 3 days. The properties of the scaffold such as porosity, shape of pores and water uptake was affected by the sodium chloride particle size and the content of the collagen, silk fibroin and hydroxyapatite. As such, this method for producing porous scaffold can achieve scaffolds with controllable pore size and interconnected porosity as well as good cell proliferation (Mou et al. 2013).

Porous scaffolds have also been prepared from natural polymers using other methods such as freeze drying. For example, porous scaffold produced from a blend of chitosan, silk fibroin and hydroxyapatite. The mixture was stirred by a magnetic stirrer for a day followed by sonication for 10 min. The suspended mixture was then poured into a 40 mm by 90 mm mould made of polytetraflouroethylene and frozen to −20 °C for 24 h. This was followed by lyophylization for another 24 h after which the dried samples were separated from the mould and then neutralized in sodium hydroxide aqueous ethanolic solution 8:2 vol.% for 3 h. This was followed by washing in ultra pure water and crosslinking with 2.5 % sodium tripolyphosphate solution for 3 h to further stabilize the chitosan. 3D scaffolds

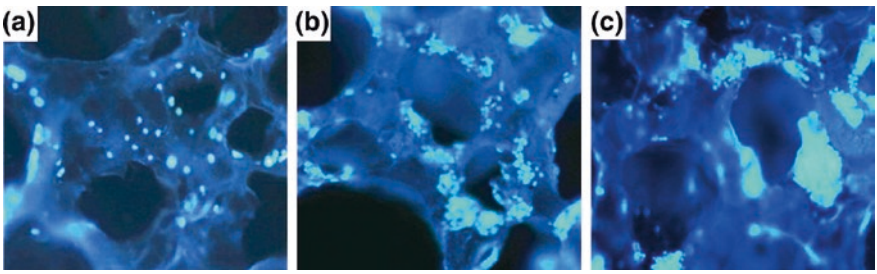


**Fig. 4.5** CLSM photographs showing MG-C6 cell growth of the silk fibroin/collagen/hydroxyapatite scaffolds after culturing at **a** day 0, **b** day 1, **c** day 3. Image obtained with permission from Mou et al. (2013) licence number 3637080927038 original publisher, Elsevier

were eventually obtained following an additional cycle of freeze drying and lyophilisation (Lima et al. 2013). The scaffolds achieved using this method showed good biocompatibility without any cytotoxic effect, they also allowed good cell growth and differentiation.

### *4.2.4 Acellular Scaffolds*

These are produced by decellularizing a tissue, i.e. removing all cellular components of the tissue, leaving behind a collagen-rich matrix which will act as the structural frame of the newly growing tissue. The removal can be either by chemical or mechanical processing but without causing damage to the ECM of the original tissue. This is then followed by cell implantation; the decelularized matrix then gradually degrades and is replaced by the new cells. Naturally derived polymers can also be used for acellular scaffolds. This is done by coating the decellularized scaffold with the naturally derived materials such as a biopolymer to give mechanical strength and the decelularization process achieves a matrix which is a physiological replica of the naturally existing tissue. The advantage of this approach to scaffold production includes; decellularizing achieves a tissue matrix structure which is a replica of the original tissue, retention of the cell adhesion ligands and architecture or the native ECM, reduced tenencies of an immune response as decellularization process has removed cellular components and the decellularized tissue has similar biomechanical properties of the native tissue (de Blacam et al. 2011).

Some acellular scaffolds approved for human application as scaffolds include those from accellularized heart valves, small intestine submucosa and urinary bladder. Human collagen-based scaffolds can also be achieved from acellular adipose matrix (Sano et al. 2014).

### *4.2.5 Gelatin-Based Scaffolds*

Scaffolds from various forms of gelatine have been reported in recent years. Gelatin is particularly attractive in tissue engineering due to its ability to keep cells in a gel state at low temperature, amidst its other attributes such as ease of modification, cost effectiveness and biocompatibility as it naturally occurs in the ECM. Gelatin however has a major limitation posed by its relative mechanical weakness. The mechanical, morphological and bioactive properties of gelatin can be controlled by crosslinking and/or including particulate carriers incorporating either drugs or growth factor which are necessary to encourage the growth of tissue (Nazeer and Sri Suganya 2014; Zhang et al. 2011; Nandagiri et al. 2011; Wu et al. 2010). The possibility of tuning the pore size and distribution makes gelatine-based porous scaffolds applicable in a variety of applications.

Gelatin scaffolds can achieve pore sizes of between 50 and 750 μm with recent studies revealing potential for achieving smaller pore sizes of between 30 and 350 μm with improved interconnectivity by crosslinking with zeolite using formaldehyde (Ninan et al. 2013). Crosslinking with other polymers such as hyaluronic acid (Zhang et al. 2011), starch and chitosan have been shown to lead to improved mechanical properties on the scaffolds and incorporation of nanoparticules such as PLGA (Nandagiri et al. 2011) and hydroxyapatite (Sundaram et al. 2008) have resulted in biocomposite **porous scaffolds** with enhanced mechanical properties. Gelatin–chitosan porous scaffold are examples used in porous scaffold for bone tissue regeneration, combining the flexible gel property of gelatine with the cell adhesion, reinforcement and ionic property of chitosan to produce a porous scaffold with sufficient physiochemical and biomechanical properties. Gelatin–chitosan porous scaffolds incorporating PLGA nanoparticles showed decreased pore size, scaffold dissolution rate, water uptake while compression modulus was increased and biocompatibility was unaffected (Nandagiri et al. 2011). Hyaluronic acid has also been crosslinked with gelatine showing tendency to produce porous scaffolds with tuneable properties such as mechanical strength, porosity, swelling and degradation rate by varying the concentration of the hyaluronic acid.

A network composite of hydroxyapatite/chitosan–gelatin have been used to produce three-dimensional porous scaffolds with uniform pores in the microscale with good biomimetic properties. The scaffold formed showed cell adhesion, proliferation and induced expression of new osteoblast cells (Hule and Pochan 2007). Porous gelatine scaffolds produced by freeze drying and mineralized by coating with hydroxyapatite to further control degradation rate have been shown to be effective scaffolds for protecting encapsulated drugs or growth factors in tissue engineering. Biological studies showed the mineralized porous gelatine scaffold to demonstrate good cell proliferation and differentiation of osteoblast cells which is suitable for tissue engineering (He et al. 2012). More recent techniques employ a blend of chitosan—collagen–gelatin in a multistep process involving freeze drying and use of genipin as a stabilizer in producing porous tissue engineering scaffolds (Gorczyca et al. 2014).

The mechanical properties and morphology of porous gelatine scaffold can also be controlled by varying the fabrication conditions. Example of such approach is the introduction of cryogenic conditions to improve the mechanical property of nano-hydroxyapatite–gelatin porous scaffold (Swain and Sarkar 2013). Photo chemically modified gelatine scaffolds have also been applied in corneal tissue regeneration.

Recent years have seen developments in chemical modification of gelatine scaffolds using visible light. This has led to improvement of biomechanical properties as well as specificity and minimizing invasiveness of scaffold application. Gelatin incorporated with furfuryl isocyanate and furfurylamine using photo-cross-linking with Rose Bengal to produce **hydrogel scaffolds** used for applications such as cartilage replacement. An area of tissue engineering where such hydrogel gelatine scaffolds have become applicable is in the scaffold healing of injured knee (Mazaki et al. 2014). This type of injury poses a challenge as it is an osteochondral injury which results in damage to both the articular cartilage which has limited healing capabilities and the underlying subchondral bone which without

protection of the articular cartilage continues to degenerate. Since the articular cartilage provides cushioning to protect the underlying subchondral bone, failure to regrow the articular cartilage will further wear the underlying bone which potentially results in more serious medical problems such as osteoarthritis and osteoarthrosis. A treatment approach is to use a scaffold to regrow new articular tissue at the location thus preventing further damage to the subchondral bone. Natural polymers such as gelatin have had some applications here.

### *4.2.6 Natural Polymers in Carbon Nanotube-Based Scaffolds*

Carbon nanotubes (CNTs) have demonstrated properties which make them very applicable in biomedical applications such as production of scaffolds. Natural polymers play significant role in production of 3D scaffolds incorporating CNTs. Although CNTs are attractive options for scaffold production due to their exceptional properties such as thermal stability, mechanical properties, electrical conductivity, versatile structure and ease of mass production amongst other properties (Serrano et al. 2014) which make them applicable in scaffold production. Natural polymers play a significant role in production of CNT-based scaffolds with improved since despite their favourable properties, scaffolds based solely on CNTs face limitations which are mainly in the area of biocompatibility and mechanical properties. Combination with natural polymers tend to biocompatibility and introduce more desirable mechanical properties (Pandey and Thostenson 2012; Sahoo et al. 2010).

In such approach, CNTs are generally used as reinforcements in natural polymer-based composites from which scaffolds are then fabricated using methods such as freeze casting, electrospinning and gel forming. Natural polymers used fro such include gelatin, chitosan, alginate, silk and collagen (Shin et al. 2012; Olivas-Armendariz et al. 2010; Yildirim et al. 2008; Ayutsede et al. 2006; Hirata et al. 2011). These have achieved scaffolds with controllable and interconnecting pore dimensions.

In a particular example multiwalled CNTs reinforced chitosan at 89 % wt CNT were used to produce scaffolds with evenly distributed interconnecting porosity using the ice segregation-induced self-assembly (ISISA) method (Serrano et al. 2014). This method achieves macroporous, well-aligned microchannels with well-patterned morphology. It involves dipping the composite in a liquid nitrogen bath at constant rate to achieve unidirectional freezing. Such scaffolds are applicable for bone tissue regeneration as they show good conductivity as a result of good CNT interconnection. For instance when recombinant human morphogenetic protein 2 (rhBMP-2) were implanted in mice, ectopic bone formation was observed (Abarrategi et al. 2008). In other cases regeneration of osteoblast cells was encouraged when implanted into scaffold made from chitosan incorporating CNTs (Nardecchia et al. 2012).

Similar approach has been used to fabricate scaffolds from CNT reinforced scaffolds of gelatine combined with chondroitin sulphate, chitosan combined with hydroxyapatite and hyaluronic acid hydrogels. These formed scaffolds with good

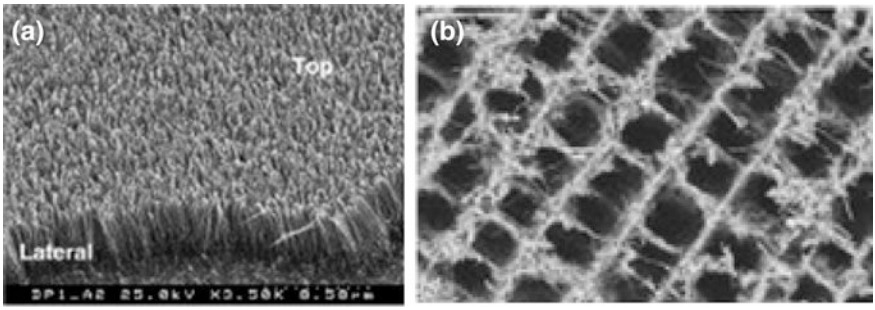


**Fig. 4.6** **a** MWCNT films by CVD. **b** Porous 3D chitosan/MWCNT scaffolds by ISISA process (Serrano et al. 2014). Reproduced with permission from Elsevier, licence number 3640171060983

pore characteristics and mechanical properties as well as promotion of cell growth. Figure 4.6 shows images of CNTs produced by Chemical Vapour deposition and CNT reinforced chitosan produced by ISISA. Electrospun CNT-based scaffolds incorporated into natural polymers are also produced from natural polymers such as silk fibroin, agarose, zein and cellulose acetate (Serrano et al. 2014).

## 4.3 Wound Healing

There are occurrences of sever wounds and burns which pose some challenges in clinical care. Wound healing products are required to protect the injury during the four stages of healing (haemostasis, inflammation, proliferation and maturation) (Lee et al. 2015), from infection and physical contact which may lead to further damage of the injured area or cause pain to the patient. The wound healing material also enhances healing and repairs of the injured tissue. Natural polymer such as collagen, gelatin, chitin, chitosan, heparin, alginates and silk fibroin are widely used in wound healing application as they possess desirable properties to this effect (Dreifke et al. 2015). An effective wound healing material should provide a conducive environment for cell proliferation, migration and differentiation and encourage re-epithelialization (Mogosanu and Grumezescu 2014). The ultimate target in wound healing is for the injured area to be completely returned to its native form without visible scars or pain.

Materials used in wound healing applications must meet certain requirements. For example, tissue adhesives used for wound closure following surgical or hemostatic procedures are required to be cost effective, biocompatible, biodegradable, possess good binding strength, allow simple application and cause no toxic effect on the patient (Lee et al. 2015; Thirupathi et al. 2013; Hadba et al. 2011). Natural polymers find good applicability in wound healing as tissue adhesives, membrane fibres or gels for wound healing. They are used either solely or in combination with other synthetic or natural polymers.

Chitin and chitosan have shown good prospects in wound healing application (Minami et al. 2014; Antunes et al. 2015). More recently nanofibrils of chitosan and chitin have been applied in wound healing (Muzzarelli et al. 2014; Izumi et al. 2015), although showing varying effectiveness. Talymed® is an example of commercially available wound healing product which uses the chitosan nanofibril technology. It is applied in the healing of venous leg ulcers showing improved healing effect compared to standard treatments (Kelechi et al. 2012). Other reports show nanofibers of chitosan affected the antibacterial activity and cell attachment and proliferation in murine fibroblasts in vitro (Cai et al. 2010).

In a novel approach (Izumi et al. 2015), superficially deacetylated chitin are used. Unlike chitosan of chitin nanofibrils, SDACNFs tend to induce better re-epithelium and fibroblast and collagen proliferation in the skin tissue. As shown in Fig. 4.7, the wound healing was much more advanced on day 8 for SDACNF group than the other groups (NT-non treated, Water treated, Chitin treated, CNF—Chitin nanofibrils, CSNF—Chitosan nanofibrils).

Furthermore the SDACNF group was the only group which showed re-epithelization at day 4 in the histographs shown in Fig. 4.8. SDACNFs have the surfaces of the chitin nanofibrils deacetylated to form chitosan while the cores remain as chitin crystals (Fan et al. 2010; Izumi et al. 2015).

Another polymer that has been recently explored in novel approach to wound healing application is poly lactic acid which is commonly derived from the natural polymer, starch. To achieve a wound healing material with improved biocompatibility and reduced toxicity, polylactic acid is blended with allyl 2-cyanoacrylate which is a synthetic polymer commonly used as tissue adhesive (Lee et al. 2015).

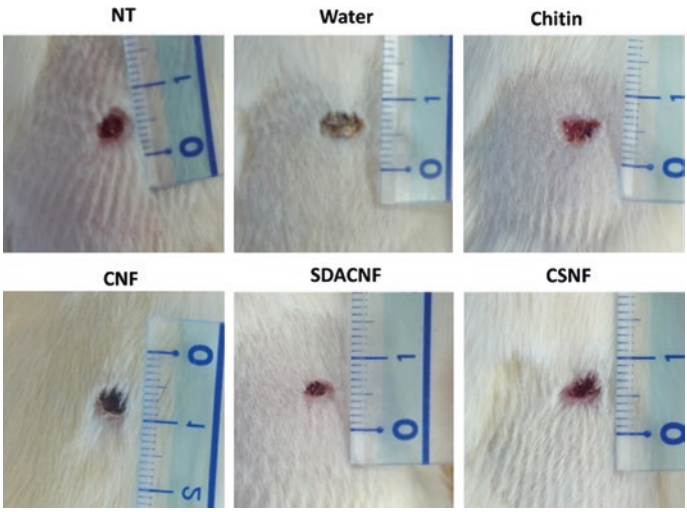


**Fig. 4.7** Healing of circular excision wound model on mice after day 8 for each group. Image obtained from Izumi et al. (2015) with permission from Elsevier licence number 3641300131392

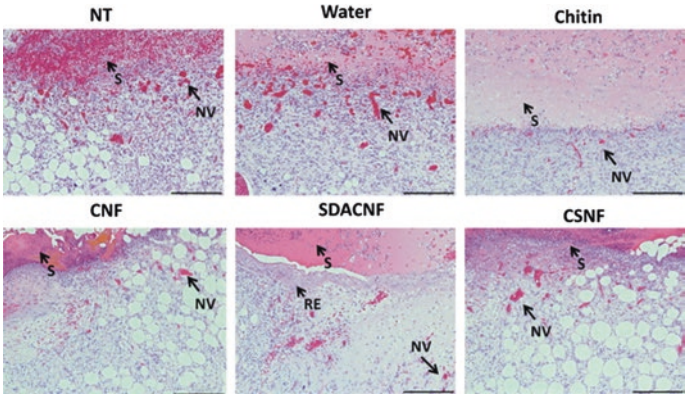


**Fig. 4.8** Histographical images showing the various sections in the skin wound healing of mice with the circular excision wound model after day 4, for different samples showing sections of scab(s), re-epithelization (RE) and neovascularization (NV). Image obtained from Izumi et al. (2015) with permission from Elsevier licence number 3641300131392

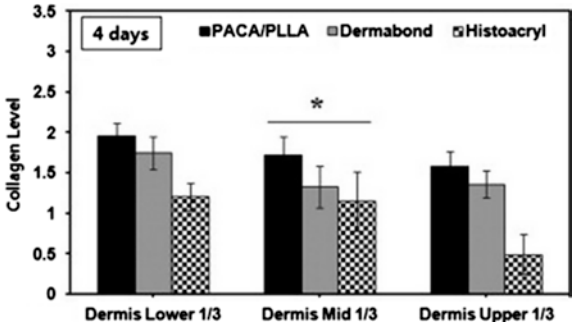


**Fig. 4.9** Comparison of Collagen content for tissue treated with different tissue adhesives for wound healing. Image obtained from Lee et al. (2015) with permission from Elsevier. License number 3641351146064

Tissues treated with tissue adhesives with PACA/PLLA showed better tensile properties indicating better collagen formation hence wound healing when compared to two other commercial wound healing tissue adhesives, Dermabond® and Histoacryl®. PACA/PLLA tissue adhesives showed higher collagen formation at day 4 compared as shown in Fig. 4.9. In addition to this it demonstrated better biocompatibility.

Wafers of lyophilized composite of sodium alginate SA/GE with 1 % silver sulfadiazine drug loading (0.1 % w/w) can also be applied in healing of chronic wounds (Boateng et al. 2015). At a 75/25 % sodium alginate/gelatin composition, such wafers showed good mechanical properties, uniformity, mucoadhesiveness, hydration and good drug release kinetics which makes them applicable in

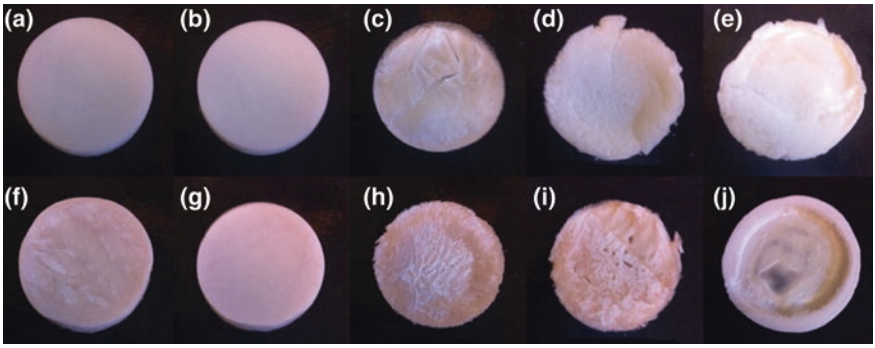


**Fig. 4.10** Digital photographs of BL SA/GE wafers **a** 100/0, **b** 75/25, **c** 50/50, **d** 25/75, **e** 0/100 and SSD loaded SA/GE wafers **f** 100/0, **g** 75/25, **h** 50/50, **i** 25/75, **j** 0/100. Image obtained from Boateng et al. (2015) with permission from Elsevier, Licence number 3641440617065

wound healing. Although alginates have been widely applied in wound healing (Mogosanu and Grumezescu 2014), this is a novel approach which is aimed at improving the hydration induced gel dehydration of alginate-based wound dressing by blending with gelatin. Figure 4.10 shows the wafers formed at varying composition of sodium alginate and gelatin.

## 4.4 Natural Polymer Implants

Implants are often a preferred option for controlled delivery of active pharmaceutical ingredients (APIs) into the body as a means to avoid the limitations and adverse effects which may occur in other forms of drug delivery such as first pass metabolism leading to low bioavailability in oral and discomfort and pain associated with intravenous injections as well as generally increase risk of side effects associated with bolus systemic delivery.

Applications of natural polymer in implants are of much interest for similar reasons as in every other biomedical application (Ivanova et al. 2014). Since these are materials which remain embedded in the body for long periods, it is important that they are biocompatible and remain functional throughout the duration they will remain embedded in the body until they are removed or are to degrade into the body rerelease not toxic, biocompatible degradation products which can be harmlessly eliminated from the body.

Drug eluting implants are implants which are loaded with APIs should meet the requirement of allowing drug loading to desired concentration and release the drug when implanted at controlled rate (Guzman-Aranguez et al. 2013; Siepmann et al. 2012). Polymer-based drug eluting implants can be fabricated using methods such as hot melt extrusion, solvent casting, coating or soaking of the polymer in the API (Loxley 2012; Iqbal et al. 2013; Zurite et al. 2006).

Recent method of loading API unto polymeric drug eluting implants is the supercritical $CO_2$ assisted impregnation process (Champeau et al. 2015). This method is introduced as a measure to address the drawbacks of the other aforementioned methods of producing drug loaded polymeric implants. These drawbacks are mainly high processing temperature requirement which could potentially damage temperature sensitive drugs such as protein-based drugs, and need for organic solvents which then necessitate numerous purification stages.

The supercritical $CO_2$ impregnation technic has been applied in loading of various natural polymer-based implants which are produced from natural polymers such as chitosan, agarose, cellulose, collagen and polylactic acid. The process is based on the unique properties of $CO_2$ at its supercritical state which enhances the solubility of APIs in manufactures polymers. The supercritical $CO_2$ causes the polymer to swell thereby increasing its permeability; it also dissolves many APIs making them diffuse better into the polymer matrix. The process can be carried out at relatively low temperature (31 °C and 73.8 bar) and does not require additional process for solvent removal as non is used (Champeau et al. 2015; Kikic and Vecchione 2003). Table 4.1 lists some natural polymers which have been applied as implants and the API which was loaded on the implant.

Natural polymers can be applied as coatings on implant for purposes such as improving biocompatibility, modifying the release profiles of the implant (Green et al. 2009) or improving the stability, bioactivity and resistance to corrosion (Ahmed et al. 2013) while retaining the properties of the main implant material.

In an example implants produced with nanoscope polyelectrolyte multilayers (PEMs) of hyaluronic acid/chitosan blends for delivery of chitosan imidazole binded siRNA (Small interfering RNA) nanoplexes (Hartmann et al. 2013). The assembly is illustrated in Fig. 4.11.

Small Interfering RNAs are bioactive molecules which play important role in therapeutic mediation of enzymatic cleavage of mRNA of targeted cells such as

**Table 4.1** Examples of natural polymers used in implants

| Polymer | API/implant | References |
|---|---|---|
| Chitosan | Flurbiprofen<br>Timolol maleaic<br>Tymol<br>Quercetin<br>Dexamethason<br>Vycomycin | Braga et al. (2008)<br>Braga et al. (2008)<br>Dias et al. (2011)<br>Dias et al. (2011)<br>Duarte et al. (2009)<br>Yang et al. (2013) |
| Hyaluronic acid/chitosan multilayer coating | Chitosan Imidazole/siRNA nanoplexex | Hartmann et al. (2013) |
| Chitosan/carbonnanotube | Titanium implant | Ahmed et al. (2013) |
| Collagen/cellulose | Juca extract | Dias et al. (2013) |
| Agrose | Thymolol<br>Querecetin | Dias et al. (2011) |
| Poly (Lactic acid) | Ibuprofen<br>Acetylsalicylic acid | Ma et al. (2010) |

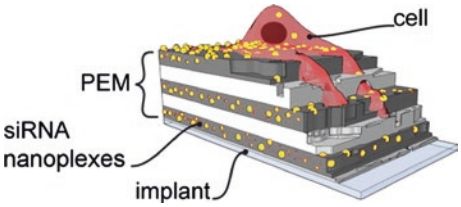


**Fig. 4.11** Structure of Hyaluronic acid/chitosan coated implant for delivery of siRNA nanoplexes Obtained from Hartmann et al. (2013), with permission from Elsevier, licence number 3642361195751

cancer cells (Meister and Tuschl 2004; Fire et al. 1998). This is a technique being investigated for biomedical applications such as cancer therapy and viral infections (Brower 2010). The aim of siRNA implant is to release siRNA from the implant, attach the siRNA to target cells to allow cell destruction through enzymatic cleavage of mRNA. The implant should therefore effectively incorporate the siRNA nanoplexe, maintain its integrity and deliver it to target cells.

Chitosan is particularly of interest in this application due to its electrostatic attraction to nucleic acids allowing it to form stable chitosan siRNA nanoplexes (Hartmann et al. 2013). Furthermore, combination with hyaluronic acid a polyanion to obtain a polyelectrolyte multilayer system using layer by layer assembly techniques which allow alternative adsorption of positive and negative charged polyelectrolytes to form a multilayer with diverse functionality which is essential in such biomedical application.

The use of chitosan and hyaluronic acid composite as drug release coatings on the implant material which could be made from another polymer material such as polydiocanone (Ribeiro-Resende et al. 2009) it to mitigate against the tendency of the nanoplexe to affect the stability of the implant and also to improve cell adhesion and uptake of nanoplexes by the cell. While other polyelectrolytes such as poly (sodium-4-Styrene-Sulfonate) and poly (L-glutamic acid) cause destabilization of nanoplexes Chitosan Polyelectrolyte PEM does not (Hartmann et al. 2013).

Chitosan coatings can also be applied for surface modification of titanium implants to address the issue of corrosion and biocompatibility which is sometimes seen in titanium implants. Although other surface modifications exists such as thermal oxidation and hydrothermal synthesis and ion implantation as well as use of other bioactive coating such as hexamethyldisilazane and calcium phosphate, chitosan provides a potential alternative as it has been widely used in various biomedical applications. In a recent approach chitosan reinforced with carbon nanotubes showed enhanced toxicity resistance and passivation compared to other coatings (Ahmed et al. 2013).

Cardiovascular devices such as stents (Iqbal et al. 2013) and heart valves are implanted into the heart for controlled drug delivery targeted at the cardiovascular systems or to play functional role such as controlling the heartbeat or sending out signals in case of potential or occurring cardiovascular emergencies (Venkatraman et al. 2008).

## 4.5 Conclusion

In this chapter, we have explored how natural polymer-based materials are applied in various aspects of biomedical industry. Example cases of natural polymers which play prominent roles such as chitosan, hyaluronic acid, silk fibroin and gelatin are discussed. Innovative approaches to producing natural polymer-based biomedical moieties are also discussed. These include supercritical $CO_2$ impregnation of implants, particulate leaching to produce porous scaffolds and superficial deacetylation of chitin to produce nanofibrils for wound healing are discussed. We also look at the role natural polymers play in advancing the particular biomedical application by, for e.g. improving biocompatibility, bioactivity and reducing toxicity. Natural polymers generally show good applicability in present and future biomedical industry.

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# Chapter 5
# Application of Natural Polymers in Food

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## 5.1 Introduction

In this chapter, the application of natural polymers is considered in the context of formulated foods. Basically, all food contains macromolecules, and almost all of these macromolecules are polymers of some kind. Polymer molecules in their simplest form are linear chains of covalent bonded monomers. The number of times these monomers are repeated along the polymer chain is the degree of polymerization. Most polymers vary in degree of polymerization and thus molar mass. If several monomers are involved then the structure can be more complicated. Moreover, polymers can be branched, and the individual monomers can also possess different attributes, such as charge (i.e., polyelectrolytes) and hydrophobicity (amphipathic polymers), further adding to the complexity. These higher order structures are what often give polymers their function in food (Walstra 2003).

Most foods are made up of the three main types of naturally occurring polymers, primarily polysaccharides (i.e., starches, celluloses) and polyamides (proteins), as well as small amounts of polynucleotides (DNA, RNA) found in cellular material.

*Polynucleotides* (or nucleic acids), i.e., DNA (deoxyribonucleic acid) and RNA (ribonucleic acid) are linear heteropolyelectrolytes containing four types of monomers. Each monomer unit within the polymer chain has three components: a sugar

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O. Olatunji (ed.), *Natural Polymers*, DOI 10.1007/978-3-319-26414-1_5

(either deoxyribose in DNA or ribose in RNA), a phosphate, and a base. The backbone is constant in DNA and RNA, however, the bases vary between four possible. Adenine (A), guanine (G), cytosine (C), and thymine (T) in DNA, and A, G, C, and uracil (U) for RNA (Berg et al. 2002). This sequence of bases uniquely characterizes a nucleic acid and represents a form of linear biological information. Although DNA and RNA are present in all cells and thus in many foods materials based on meat and plant tissues, their concentrations are far too small to affect the food's physicochemical properties and will not be discussed further in this chapter.

*Proteins* are complex linear heteropolyelectrolytes containing a unique sequence of up of 20 different amino acids monomers, having highly diverse configurations and reactivity with respect to charge, hydrophobicity, and aromatic structure. Proteins typically have a degree of polymerization of around $10^3$ and have numerous biological functions in living cells and organisms. As a food ingredient, in addition to a source of amino acids for our own metabolism, proteins provide both structure and function. They can create gels, increase viscosity and water holding capacity, as well as generating and stabilizing emulsions and foams. Despite their functionality, the higher price of proteins compared to other natural biopolymers (especially with respect to starches and celluloses) has limited their technical application (VâniaReginaNicoletti 2012). Major protein ingredients include: gelatin, milk proteins, egg proteins, and plant proteins.

*Polysaccharides* are heteropolymers of sugars and derived components. They can be linear or branched, and several of them are polyelectrolytes. The degree of polymerization of polysaccharides is generally $10^3$–$10^4$. The main biological functions are ''nutritional'' as energy stores for metabolism (primarily starch in plants, glycogen in animals) and ''building material'' (such as cellulose in plants and chitin component of the cell walls of fungi and in the exoskeletons of arthropods such as crustaceans). The latter are called structural polysaccharides, which occur in a great variety of types and mostly form mixed and highly complex structures.

In the scientific and trade literature, proteins and polysaccharides are also often referred to as "hydrocolloids." There are a number of different natural sources of commercially important hydrocolloids as given in Table 5.1.

**Table 5.1** Sources of commercially important hydrocolloids used in the food industry (Williams and Phillips 2009)

| | | |
|---|---|---|
| Botanical | Plants | Starch, pectin, cellulose |
| | Trees | Cellulose |
| | Tree gum exudates | Gum arabic (acasia), gum tragacanth, karaya gum |
| | Seeds | Guar gum, tara gum, locust bean gum, fenugreek gum |
| | Tubers | Konjac mannan (glucomannan), potato starch |
| Algal | Red seaweed | Agar, carrageenan |
| | Brown seaweed | Alginate |
| Microbial | | Xanthan gum, dextran, gellan gum, cellulose |
| Animal | | Gelatin, caseinate, whey protein, chitosan |

Protein and starch are major component of foods in general, and as such important sources of macro nutrients. However, in this chapter, the focus will be on natural polymers as food additives and ingredients in food formulations having a specific function beyond basic nutritional value. These specific functions of natural polymers added to foods can be classified into two main categories:

- *The creation and stabilization of food microstructures*: e.g., gelling, thickening, stabilization of emulsions, and foams, as well as processing aids, such as cyroprotectants to improve freeze thaw stability, drying aids, and encapsulating material.
- *Additional physiological and biological functions:* e.g., functional foods with specific health claims such has reducing blood cholesterol levels, increasing satiety, and improved bioavailability, as well as antioxidative and antimicrobial activity for preservation purposes.

This chapter will discuss the various types of natural polymers in food primarily from the perspective of their function in a food product formulation, rather than discussing the separate polymers by chemical structure or origin. Details on classification, processing, and extraction methods are provided in dedicated chapters in this book (Chaps. 2, 3, and 4, respectively). In addition to function and use of natural polymers in food, this chapter will also touch on regulatory and market aspects of these additives and ingredients in food products.

## 5.2 Creation and Stabilization of Food Microstructures

If we consider the creation and stabilization of food microstructures from the perspective of the functional roles natural polymers play in these systems, we can roughly classify them into three groups: (i) emulsion stabilizers, (ii) thickeners, and (iii) gelling agents. Although, it is also good to note that a given natural polymer may in fact be providing several of these functions concurrently (Giannou et al. 2014). An overview of the structure and function of some key natural polymers in generating and stabilizing food microstructures are presented briefly in Table 5.2 and applications of these natural polymers by product types are presented in Table 5.3.

The main role that natural polymers play when used in formulated food is to create and maintain texture and microstructure (Aguilera et al. 2000). Further quality improvements of existing foods and the creation and formulation of new products to satisfy the expanding consumers' demands in the near future will be based largely on interventions at the microstructure level. This is because the majority of factors that critically participate in transport properties, physical and rheological behavior, textural and sensorial traits of foods are elements and phenomena that are occurring on a scale below 100 μm (Aguilera 2005). These microstructural elements are often based on natural polymers and their function in formulations. Typically, they are dispersed in water creating viscous solutions,

**Table 5.2** Some key natural polymers in generating and stabilizing food microstructures

| Type | $M^1$ (Da) | Functions | Comments |
|---|---|---|---|
| Starch amylose<br>Starch amylopectin<br>Modified starches<br>*Chemical:* crosslinked, substitution (example acetate, phosphate and sodium octenyl succinate), dextrinization, oxidation and thinning<br>*Physical:* pre-gelatinized, granular and agglomerated | $2 \times 10^5$–$10^7$ | • Stabilizer (freeze/thaw, heat, acid, shear)<br>• Thickener<br>• Moisture control<br>• Texturizer<br>• For particle suspension<br>• Emulsifier (modified starch) | Starch gelatinization, the ordered crystalline regions undergo melting, permitting granule swelling and gel formation, this can be followed by recrystallization and formation of helix structures. Modifications can make the starch cold swelling or non-swelling. Different ratios of amylose and amylopectin affects the product characteristics. Thermally irreversible, opaque gels formed on cooling (modified starch). |
| Methylcellulose<br>Carboxymethylcellulose (CMC)<br>Hydroxypropylmethylcellulose (HPMC) | $2 \times 10^4$–$4 \times 10^5$<br>$10^5$–$10^6$ | • Stabilizer<br>• Thickener<br>• Water retention | Semi-soluble polymer with a wide range of viscosities. Viscosity increases with temperature (gelation may occur). The molecules associate on heating due to hydrophobic interaction of methyl groups. Methylcellulose form strong gels at elevated temperature while HPMC forms weak gels, the gels are reversible and not influenced by the addition of electrolytes or pH. CMC gives high viscosity but it is reduced by the addition of electrolyte and low pH. |
| Pectins<br>High Methoxyl (HM)<br>Low Methoxyl (LM) | $4 \times 10^4$–$10^5$ | • Stabilizer<br>• Thickener<br>• Gelation<br>• Protein protector | HM pectin forms gels at low pH (2.5–3.5) in the presence of high sugar concentration (>55 %). This combination reduces electrostatic repulsions between chains. Chain association is also encouraged by reduced water activity. LM pectin forms gels in the presence of divalent cations, notably calcium at low pH (3–4.5). The molecules are crosslinked by the cations. Sugar beet pectin is non-gelling—emulsification. |

(continued)

**Table 5.2** (continued)

| Type | M[1] (Da) | Functions | Comments |
|---|---|---|---|
| Gum Arabic (Acacia) | $4 \times 10^6$–$10^7$ | • Stabilizer<br>• Thickener<br>• Emulsifier<br>• Encapsulating agent<br>• Texturizer<br>• Coating agent | Newtonian behavior with low viscosity at concentrations <40 %, pseudoplastic at higher concentrations.<br>Cold and hot water soluble for concentrations <50 %.<br>Shear thinning at low shear rates (<10/s).<br>Near Newtonian behavior above 100/s of shear rate.<br>Rheology strongly affected by pH and electrolyte.<br>Temperature and high shear stable. |
| Gum Tragacanth | $8.4 \times 10^5$ | • Stabilizer<br>• Thickener<br>• Emulsifier | Swells rapidly in cold or hot water to form highly viscous dispersions, up to 4000 mPas at 1 % solids.<br>Pseudoplastic behavior.<br>Acid resistant and viscosity stable at pH 2–10. |
| Karaya gum | $16 \times 10^6$ | • Stabilizer<br>• Thickener<br>• Emulsifier | Producing a viscous colloidal sol when dispersed in water due to that it adsorb water and swell to more than 60 times the original volume. The swelling behavior is caused by the presence of acetyl groups in its structure.<br>Viscosities are higher when the gum is dispersed in cold water than in hot water. |
| Galactomannans<br>(Galactose: Mannose ratios)<br>Locust bean gum 1:4<br>Tara gum 1:3<br>Guar gum 1:2<br>Fenugreek gum 1:1 | | • Stabilizer<br>• Thickener<br>• Texturizer<br>• Water retention | Very high low shear viscosity and strongly shear thinning.<br>Not influenced by the presence of electrolyte but can degrade and lose viscosity at high and low pH and when subjected to high temperatures.<br>Locust bean gum: Gels formed after freezing.<br>Galactose deficient regions associate.<br>Tara gum is soluble in cold water and is often mixed with other hydrocolloids. |

(continued)

**Table 5.2** (continued)

| Type | M[1] (Da) | Functions | Comments |
|---|---|---|---|
| Konjac mannan/glucomannan | $2 \times 10^5$–$2 \times 10^6$ | • Thickener<br>• Gelation<br>• Dietary fiber<br>• Water binder<br>• Texturizer | Cold swelling.<br>Forms highly viscous dispersions which are not influenced by addition of salts.<br>Forms thermally irreversible gels with alkali. Alkali removes acetyl groups along the polymer chain and chain association occurs. |
| Agar | | • Stabilizer<br>• Thickener<br>• Gelation | Heat reversible gel formed on cooling. Molecules undergo a coil-helix transition followed by aggregation of helices.<br>Gives a firm and brittle gel to body/mouthfeel.<br>pH stability 2.5–10. |
| Carrageenans<br>Kappa<br>Iota<br>Lambda | $10^4$–$10^6$ | • Stabilizer<br>• Thickener<br>• Gelation | Forms reversible gels on cooling in the presence of salts in an aqueous environment. The presence of salt reduces electrostatic repulsions between chains promoting aggregation.<br>Gelling ability is seen for carrageenan that forms helical structures.<br>pH stability 4–10.<br>Kappa Carrageenan gives firm, brittle structure and syneresis.<br>Iota Carrageenan gives elastic and soft structure without syneresis.<br>Lambda-Carrageenan: no gelation, thickening, gives body. |
| Alginate<br>High M<br>High G | | • Stabilizer<br>• Thickener<br>• Gelation<br>• Emulsifier | Cold soluble and gelling.<br>Heat stable and shear reversible firm gel, pH stability 4–10.<br>Gels formed with the addition of polyvalent cations notably calcium or at low pH (<4). Molecules crosslinked by the polyvalent ions.<br>Propylene Glycol Alginate (PGA): surface active ingredient, cold soluble, non-gelling, pH stability 3.5–10. |

(continued)

**Table 5.2** (continued)

| Type | M[1] (Da) | Functions | Comments |
|---|---|---|---|
| Xanthan gum | $3 \times 10^5$–$10^7$ | • Stabilizer<br>• Thickener | Solutions have a thixotropic behavior.<br>Gels are formed at high concentration or in the presence of plant galactomannans such as locust bean gum on cooling. Xanthan and the polymannan chains associate following the xanthan coil-helix transition. For locust bean gum the galactose deficient regions are involved in the association.<br>Very high low shear viscosity (yield stress), highly shear thinning, maintains viscosity in the presence of electrolyte, over a broad pH range and at high temperatures. |
| Gellan gum<br>Low Acyl<br>High Acyl | $1 \times 10^6$ | • Protein protector<br>• Suspender | Gels formed on cooling in the presence of salts. Molecules undergo a coil-helix transition followed by aggregation of helices. Salts reduce electrostatic repulsions between chains and promote aggregation. Multivalent ions can act by crosslinking chains.<br>Low acyl gellan gels are thermoreversible at low salt concentrations but non-thermoreversible at higher salt contents (>100 mM) particularly in the presence of divalent cations. |
| Gelatin | $3 \times 10^4$–$10^6$ | • Stabilizer<br>• Thickener<br>• Gelation | Produces transparent gels with the highly desirable ability to melt in the mouth. Gel formed on cooling. Molecules undergo a coil-helix transition followed by aggregation of helices. |
| Chitosan | $4 \times 10^4$–$2 \times 10^5$ | • Emulsifier<br>• Rheology modifier<br>• Preservative | Positively charged partly hydrophobized polymer that can gel dependent on pH and presence of multivalent negative ions. |

[1]M Molecular Mass, Data from Dziezak (1991), Goldberg and Williams (1991), Le Cerf et al. (1990), Manners (1989), Saha and Bhattacharya (2010), Stephen et al. (2006), Verbeken et al. (2003), Walstra (2003), Williams and Phillips (2003, 2009)

**Table 5.3** Application areas, E/INS numbers and main functions of various commercial natural food polymer additives and ingredients

| | Starches | Carboxymethyl-cellulose | Methylcellulose/ Hydroxypropyl-methylcellulose | Pectin | Gum arabic | Gum Tragacanth | Karaya gum | Locust bean gum | Tara gum | Guar Gum | Konjac mannan | Agar | Carr-ageenan | Alginates | Xanthan Gum | Gellan Gum | Gelatin |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| *E-number /INS number* | *E14XX* | *E466* | *E461 E464* | *E440* | *E414* | *E413* | *E416* | *E410* | *E417* | *E412* | *E425* | *E406* | *E407* | *E401* | *E415* | *E418* | *N/A* |
| *Main functions* | *S,T* | *S,T* | *S,T,G* | *S,T,G* | *S,T* | *S,T* | *S,T,G* | *S,T* | *S,T,G* | *S,T* | *T,G* | *S,G* | *T,G,S* | *T,G* | *T,S* | *G,S* | *G* |
| *Applications* | | | | | | | | | | | | | | | | | |
| Bakery Products | ● | ● | ○ | ● | ● | ● | ● | ○ | ● | ● | ● | ● | | ● | ● | ○ | ● |
| Beverages | ○ | ● | ○ | ● | ● | ● | | | ● | ○ | | ○ | ○ | ● | ○ | ● | |
| Confectionary | ● | | | ● | ● | ○ | ● | | | | | ● | | | | ○ | ● |
| Sauces, dressings, soups | ● | ○ | ○ | ● | ○ | ● | ● | ○ | ● | ● | ● | | ○ | ● | ● | | |
| Dairy, acidified/ fermented drinks, desserts | ● | ● | | ● | ○ | | ○ | ○ | | | | ● | ○ | | | | ● |
| Dairy, sweet drinks, desserts | ● | ○ | | | ○ | | ● | ○ | ● | ○ | ○ | | ● | ○ | ○ | ○ | ● |
| Flavor emulsions | ○ | ○ | ○ | ○ | ● | ○ | | ○ | | ○ | | | | | | ○ | |
| Fruit preparations, jams, marmalades | | ○ | ○ | ● | | | | ○ | ● | ○ | | ● | ○ | ● | ○ | ○ | ○ |
| Ice cream | | ● | | ○ | ● | | | ● | ● | ○ | | | ○ | ○ | ○ | | |
| Meat and poultry processing | ● | ● | ● | | | | | | | ○ | ● | ● | ● | ● | ○ | | ● |
| Vegetable, potato preparations | | ● | ● | | | | | | | | | | | ○ | ○ | | ○ |

*S* Stabilizer, *T* Thickener, *G* Gelling agent, ○ application areas, ● most common application areas

dispersions, and gels, as well as functioning as stabilizers of emulsion oil droplets and gas bubbles in foams, etc. (Aguilera 2005).

### 5.2.1 Emulsifiers and Stabilizers

Many of the foods we enjoy are formulated products based on emulsions and foams. Emulsifiers are added in certain food products in order to establish a uniform dispersion or stabilize an emulsion or foam by increasing its' kinetic stability. Emulsifiers are used to prevent baked goods from becoming stale, to prevent cream sauces and mayonnaise from separating, to keep flavors suspended, and to stabilize ice cream. To make an emulsion or foam four basic ingredients are required: a continuous phase (1) into which a dispersed phase (2) is dispersed in the form of small droplets or bubble, by creating an interface between the two phases. The creation of this interface requires mechanical energy (3) from an emulsifying device and finally some sort of emulsifier (4) that assists in lowering the interfacial tension between the two phases assisting in the emulsification process and/or a stabilizer that preserves the newly formed interface. Emulsions may consist of oil droplets-in-water (O/W) or water droplets-in-oil (W/O), whereas foams are dispersions of air-in-water (A/W), but in all cases, droplets or bubbles need to be stabilized as this extra interface is for thermodynamic reasons inherently unstable. Emulsifiers typically consist of a lipophilic or hydrophobic part with good solubility in a nonaqueous phase (such as an oil or fat) and a polar or hydrophilic part, soluble in water. Surfactants and small molecular weight surfactants typically have a hydrophilic head and a lipophilic tail (Fig. 5.1d—bottom left). In the case of natural polymer-based emulsifiers, such as polysaccharides and proteins the affinity for the hydrophobic phase is achieved by either modification by lipophilic side groups (as is the case with modified starch, Fig. 5.1e—bottom center) or by the degree of hydrophobicity of the amino acid residues as in proteins (Fig. 5.1—top row).

Proteins are typically relatively small molecules (10–50 kDa) that rapidly adsorb to the surfaces of emulsion droplets and form thin electrically charged interfacial layers (Bouyer et al. 2012). These charges create electrostatic repulsion between emulsion droplets and can be an important stabilizing force for food emulsions. Both proteins and polysaccharides can be charged, depending on the pH, and thus, when adsorbed at the droplet interface gives rise to electrostatic repulsion. Emulsions stabilized by electrostatic repulsions are salt sensitive and in many cases sensitive to changes in pH. Proteins may adopt various interfacial conformations depending on their molecular structures and interactions (Singh 2011). Flexible proteins, such as caseins, readily undergo conformational changes, so that the hydrophilic groups protrude into water and the hydrophobic groups protrude into oil adsorbing as loop-train and tail train configurations (Fig. 5.1a). Rigid globular proteins, such as β-lactoglobulin in whey (as well as some of types of egg, soy, or pea proteins), may partially unfold exposing interior hydrophobic regions

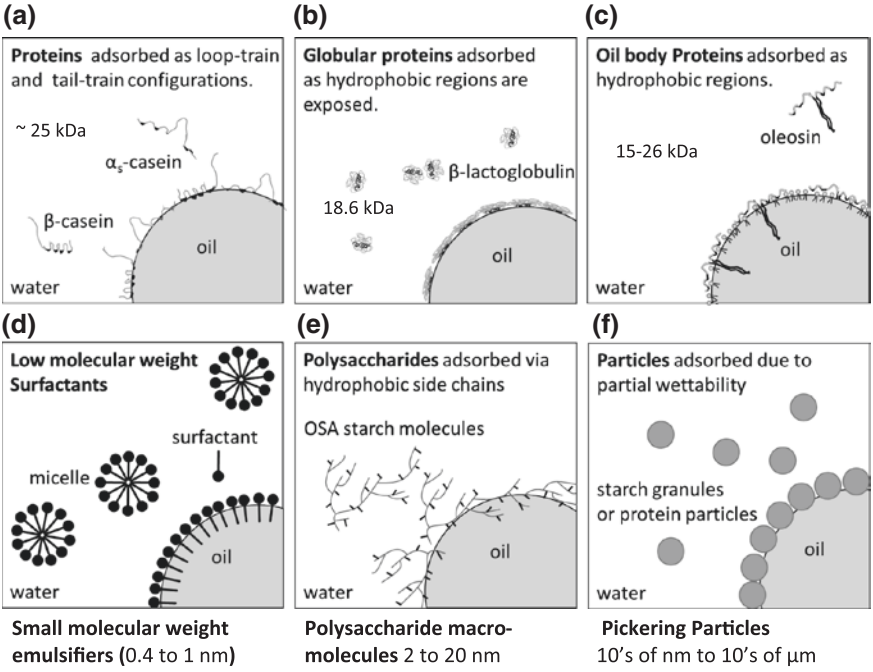



**Fig. 5.1** Schematic illustration of various types of emulsifiers and stabilizers, note scales differ

during adsorption, forming cohesive viscoelastic layers around the oil droplets (Fig. 5.1b) (Ozturk and McClements 2016). Proteins with a large hydrophobic domain such as oleosin (extracted from oil seeds), having 72 residues in a predominately α-helical structure (Maurer et al. 2013; Nikiforidis et al. 2013; Roberts et al. 2008), have been reported to irreversibly bind to the oil–water interface in a similar manner to apolipoproteins (Nikiforidis et al. 2013). Furthermore, the combination of oleosins' compact central hydrophobic pin (Fig. 5.1c) and its relatively small overall size of (15–26 kDa) explains its good emulsifying properties, and thus is an interesting plant-based alternative to protein emulsifiers isolated from dairy and eggs, which has been receiving a lot of research interest (Rayner 2015). In terms of market volumes, most natural polymer-based emulsifiers are proteins, the ones that are sold on the largest commercial scale being dairy proteins (whey and caseinate), various egg proteins, and soya proteins—however, other nonanimal-based protein emulsifiers that are gaining attention are zein and oleosin (see Table 5.4).

Polysaccharides are generally relatively large molecules (100–1000 kDa) that adsorb relatively slowly to droplet surfaces and form thick hydrophilic interfacial layers (Bouyer et al. 2012). In many cases, they have been hydrophobically modified, for example, through esterification with octenyl succinic anhydride (OSA) by incorporating hydrophobic alkenyl groups from OSA into the hydrophilic starch molecule (Simsek et al. 2015). The large size of polysaccharide molecules means

**Table 5.4** Common commercial protein based emulsifiers and examples of their specific key proteins

| Emulsifier | Key proteins | Molecular weight (kDa) |
|---|---|---|
| Whey protein[a] | β-lactoglobulin | 18.6 |
| | α-lactoalbumin | 14.2 |
| | Bovine serum albumin | 66 |
| Caseins[b] | $\alpha_1$-Casein | 23 |
| | $\alpha_2$-Casein | 25 |
| | β-Casein | 24 |
| | κ-Casein | 19 |
| Egg white[c] | Ovalbumin | 45 |
| | Ovotransferrin | 77.7 |
| | Ovomucoid | 28 |
| | Lysozyme | 14.3 |
| Egg yolk[c] | Phosvitin | 160–190 |
| | Low-density lipoproteins | 16–35 |
| | Cobalamin-binding proteins | 39 |
| | Riboflavin-binding; proteins | 37 |
| | Biotin binding proteins | 72 |
| | α,β Lipovitellins | 400 |
| Soya protein[d] | α-Conglycinin | 18–33 |
| | β-Conglycinin | 104 |
| | σ-Conglycinin | 141–171 |
| | Glycinin | 317–360 |
| Canola protein (rapeseed)[e] | Oleosin | 15–26 |
| Zein protein from corn | α-zein | 21–25 |

[a]Kinsella and Whitehead (1989)
[b]Swaisgood (1993)
[c]Awade (1996)
[d]Clarke and Wiseman (2000)
[e] Wijesundera (2014)

that they also tend to have higher surface loads than proteins, so more emulsifier is required to cover the droplet surfaces to achieve the same level of stabilization (Ozturk and McClements 2016). Due to their size, they can also give rise to both depletion attraction (leading to flocculation/aggregation) and steric repulsion (helping with droplet stabilization) depending if they are adsorbed at the interface or dispersed in the continuous phase. Depletion attraction is due to the fact that macromolecules (proteins, polymers, and colloidal particles) having no affinity for the interface, will be excluded in the space between two approaching emulsion drops, this will lead to an osmotic pressure gradient which then favors aggregation (Wahlgren et al. 2015). Depletion attraction is typically observed in emulsions containing dissolved neutral polysaccharides. Thus, addition of polysaccharides to alter rheology or form complex with emulsifying agents may cause depletion

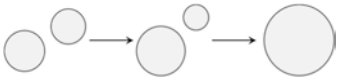
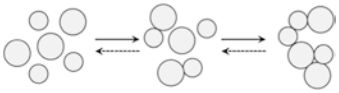
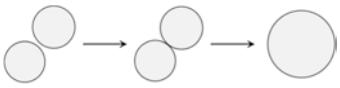
aggregation (Magnusson and Nilsson 2011). On the other hand, steric repulsion is induced by macromolecules adsorbed at the interface; this is mainly due to excluded volume effect as adsorbed molecules come close together (Israelachvili 1985). Steric repulsion thus requires affinity of the macromolecule to the interface but also high solubility of the macromolecule in the continuous phase. The latter allows parts of the adsorbed macromolecule to protrude into the continuous phase, giving rise to steric hindrance between approaching droplets. These systems are less sensitive to salt and pH than electrostatically stabilized emulsions. For a more detailed treatment of the emulsifying and emulsion stabilizing capacity of various natural polymers the interested reader is directed to the comprehensive reviews (and reference therein) on the topics of proteins as emulsifiers (Dickinson 2009, 2014; Lam and Nickerson 2013) and polysaccharides as emulsifiers (Dickinson 2009, 2014; George 2006; Kokubun et al. 2015).

In some cases, natural polymers are not used in the molecular form to stabilize emulsions, but rather as colloidal particles in the size range of tens of nanometers to tens of micrometers, as so-called Pickering emulsions. These particles are not amphiphilic but rather possess a dual wettability for both phases (Fig. 5.1f, bottom-right). Although adsorbed particles do not decrease the interfacial tension, and strictly speaking are stabilizers rather than emulsifiers, they do accumulate at the oil–water interface in an analogous way to molecular emulsifiers. However, the key difference is that particles once located at the oil–water interface are essentially irreversibility adsorbed due to their large size and exceptionally high free energy of detachment (Rayner et al. 2014). They stabilize by a kind of steric hinder or volume exclusion due to their large size physically separating droplets. Many of the recent works on particle stabilized emulsion have used natural polymers to generate Pickering type particles, including starch, cellulose, chitin, soy, and zein proteins, as well as soft microgel particles based on whey, gelatin, pectin, or starch (Berton-Carabin and Schroën 2015; Rayner 2015; Rayner et al. 2014; Shewan and Stokes 2013).

Stabilizers, are used to maintain a uniform dispersion of two or more components. Although, they are not classified as emulsifiers, nor particularly surface active, they assist in stabilizing food emulsions and foams. They are used in food formulations in order to provide a firmer and more stable texture profile and prevent the evaporation of volatile flavor components. Stabilizers are used both in dry and liquid products. They include several natural gums, such as carrageenan, xanthan, or locust bean gum, as well as natural and modified starches (Giannou et al. 2014). Typical products in which they are commonly used include jams, dairy products, ice cream, baked goods, infant formulas, salad dressings, and soups.

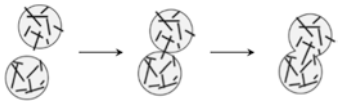
During the production, processing, storage, transportation, and use of food formulations based on emulsions, there are a number of destabilization processes that can occur. The main ones which can be affected by the use of emulsifiers and stabilizers, and natural polymers in particular include: creaming/sedimentation, coalescence, and aggregation/flocculation. These and other common destabilization mechanisms of emulsions and foams are illustrated in Table 5.5 and discussed briefly below.

**Table 5.5** Main mechanisms of destabilization in food emulsions, foams and dispersions

| Mechanism (types of dispersed phase) | | Description, driving force, and role of natural polymers as stabilizers (if applicable) |
|---|---|---|
| I | Growth/dissolution (solids, liquids, gases)  | The driving force is the difference in the chemical potential between the substance making up the dispersed phase and the same substance dissolved in the continuous phase. If the solution is unsaturated the particles or bubbles will dissolve, and if it is super saturated they can grow (i.e., growth of crystals). |
| II | Ostwald ripening (liquids, gases)  | Larger droplets of dispersed phase grow at the expense of smaller ones when there is sufficient solubility of the dispersed phase in the continuous phase. The driving force is the difference in the chemical potential of the material between droplets of differing surface curvature. This is partially reduced by decreasing interfacial tension. |
| III | Aggregation/flocculation (solids, liquids)  | Droplets of disperse phase stick together either reversibility as flocculation or irreversibility as aggregation. Main cause is often van der Walls attraction or depletion interaction where the driving force is the increase in mixing entropy of polymers molecules present in the solution. Polymers can both prevent and cause this type of instability depending on conditions. |
| IV | (a) Sedimentation (solids, liquids)  | Driving force is the difference in density between the dispersed phase and continuous phase causing either sedimentation (i.e., a denser disperse phase is sinking) or creaming (i.e., a less-dense dispersed phase is buoyant). This process can be greatly slowed or arrested by thickening and/or gelling agents by the process of increasing the continuous phase viscosity, or generating a gel with a yield value that needs to be overcome before movement of dispersed phase droplets can occur. Smaller droplets also settle/cream much slower, thus effective emulsifiers also help prevent this. |
| | (b) Creaming (solids, liquids, gases)  | |
| V | (a) Coalescence (liquids and gases)  | Caused by the rupture of the interfacial film between two droplets or foam bubbles. Driving force is the reduction of free energy of the system as the total interfacial area decreases as bubbles/droplets merge. Close contact between droplets is a prerequisite and thus (III or IV) is often a precursor. As coalescence progresses a total phase separation or collapse can occur. Stabilizing polymers can stabilize the interfacial film thus preventing coalescence. This together with lowering the interfacial tension is the main function of emulsifiers and emulsions stabilizers. |
| | (b) Phase separation/collapse  | |

(continued)

**Table 5.5** (continued)

| Mechanism (types of dispersed phase) | | Description, driving force, and role of natural polymers as stabilizers (if applicable) |
|---|---|---|
| VI | Partial coalescence (liquids with particles/crystals)  | A complicated phenomenon that can occur when lipid crystals form in a cooled emulsion and penetrate neighboring droplets creating an oil-bridge between them. Upon re-heating coalescence and phase separation can occur. Natural polymers can help improve freeze thaw stability by creating a strong interfacial film preventing crystal penetration, as well as ice crystal propagation. |

Inset figures redrawn from Walstra (2003). Dotted arrows indicate possible irreversibility

***Creaming/sedimentation*** occurs in emulsions and dispersions due to the density difference between the two phases. The rate of creaming and sedimentation can be reduced by decreasing the size of the dispersed phase droplet (or bubble), increasing the viscosity of the continuous phase, or by decreasing the difference in densities between the two phases. The rate at which a single spherical droplet, bubble, or particle will cream (or settle) in a Newtonian fluid can be predicted by the Stokes velocity, $\upsilon_{\text{Stokes}}$:

$$\upsilon_{\text{Stokes}} = -\frac{2gR^2(\rho_2 - \rho_1)}{9\eta_1}$$

where $g$ is acceleration due to gravity, $R$ is the radius of the creaming/settling entity, $\rho_1$ and $\rho_2$ are the densities of the continuous phase and the dispersed phase respectively, and $\eta_1$ is the continuous phase viscosity. Stokes equation is somewhat idealized, as in reality droplets are not all the same size and will be interacting during creaming or settling. Natural polymers (such as modified starches and gums) are often added to food emulsions to modify their flow behavior, which often results in a non-Newtonian rheology of continuous phase. Many of these natural polymer solutions exhibit pronounced shear thinning behavior, having a high viscosity at low shear rates that decreases dramatically over a certain range as the shear rate is increased (see Sect. 5.2). This property is important because it means that the droplets are prevented from creaming during storage, yet the food emulsion still flows easily when poured from a container as the shear rate increases. Since creaming usually occurs when an emulsion is at rest, it is therefore important to know the apparent viscosity that a droplet experiences as it moves through the continuous phase under these conditions. The shear stress, $\tau_{\text{gravity}}$ acting on a droplet undergoing gravitational separation is: $\tau_{\text{gravity}} = 2(\rho_2 - \rho_1)gR$. Which is typically between $10^{-4}$ and $10^{-2}$ Pa for food emulsions based on typical droplet sizes and phase densities (McClements 2005, 2007; Walstra 2003). Solutions of natural polymers used as thickening agents have extremely high apparent shear viscosities at low shear stresses, and hence, the creaming of droplets will be greatly reduced. Some polymer solutions have a yield stress, $\tau_{\text{yield}}$, below which the solution acts

like an elastic solid, and above which it acts like a viscous fluid (Walstra 2003). In these systems, droplet creaming is effectively arrested when the yield stress of the continuous phase is larger than the stress exerted by a droplet due to gravity, i.e., $\tau_{yield} > |2(\rho_2 - \rho_1)gR|$. Typically, a yield value of about 10 mPa is required to prevent emulsion droplets of a few micrometers from creaming, which is often exceeded in practice (Walstra 2003). The above discussion highlights the importance of carefully defining the rheological properties of the continuous phase and understanding the action of natural polymers that may improve emulsion stability by the action of thickening and gelling (discussed more in Sects. 5.2 and 5.2.3 respectively) (Dickinson 2009; Dickinson and Walstra 1993).

***Coalescence*** occurs to minimize the oil–water interface and hence the free energy. It leads to larger dispersed phase droplets and can eventually lead to complete phase separation of the emulsion. It can mainly be controlled by the adsorption of emulsifiers, such as proteins and modified starches, or stabilizing particles to the oil–water interface. They prevent coalescence either through a steric barrier or electrostatic repulsion which hinders drop–drop contact and thus the process of coalescence. Increased viscosity of the continuous phase can also decrease the rate of coalescence as creaming is often as precursor to coalescence.

***Flocculation*** is the aggregation of droplets. Flocculated systems may have desired properties for the formulation such as beneficial rheology, but extensive flocculation leads to increasing creaming and thus may lead to coalescence. Changes in the degree of flocculation can also affect the rheology of the emulsions changing properties such as mouth feel (Wahlgren et al. 2015).

The colloidal stability of the emulsion will be governed by the repulsive/attractive forces between individual droplets of dispersed phase (as described above), as well as the energy and rate of droplet collisions allowing for flocs or aggregates to arise. The choice of emulsifier could influence all of these, and a proper choice of viscosity modifier (such as thickeners and gelling agents discussed below) will influence all kinetic factors such as collision of droplets and diffusion of dissolved molecules.

***Freeze/thaw stability*** is an important industrial property, as many foods are stored and transported at low temperature. When a food emulsion is being cooled and eventually frozen, a variety of physicochemical processes may occur including fat crystallization, ice formation, interfacial phase transitions, and other conformational changes (Walstra 2003). When O/W emulsions are cooled to temperatures where only the oil phase becomes partially crystallized, a phenomenon known as partial coalescence is likely to happen due to penetration of oil crystals from one droplet into the liquid region of another partially crystalline oil droplet. Upon increasing the temperature again, it is often seen that emulsions subjected to partial coalescence undergo phase separation or that the emulsion becomes grainy and watery. On the other hand, when O/W emulsions are cooled to the temperature where the water phase also crystallizes, a number of additional physicochemical processes are likely to happen including: formation of ice crystals which force oil droplets to close proximity, the disruption of emulsifiers at droplet surfaces, freeze concentration of solutes in the unfrozen aqueous phase which may alter the electrostatic repulsion

between the droplets, and the possible penetration of ice crystals into the interfacial membranes making droplets prone to destabilization upon thawing, and the possibility for emulsifiers may lose their functionality (Thanasukarn et al. 2004). Although in general, the main factors that affect the freeze thaw stability of emulsions are related to the physical properties of the oil phase and the oil content (Magnusson et al. 2011), use of some additives can increase the freeze thaw stability of emulsions. For example, the freeze thaw stability of emulsions can be increased by the addition of cryoprotectants, such as polyols (sucrose, glucose, fructose, trehalose, maltose), antifreeze proteins, gelatin, and some carbohydrates (Degner et al. 2014). These alter the crystallization of water and the morphology of the ice crystals but some of them can also function by increasing viscosity and thus decreasing the number of oil droplet collisions leading to coalescence. The addition of polysaccharides has also been seen to improve freeze–thaw stability. This could be due to several factors, but increased viscosity of the nonfrozen phase and the capability of some polysaccharides to form protective layers around the dispersed phase hindering coalescence play a major role (Degner et al. 2014). The emulsifier is critical when it comes to destabilization due to increased concentration but can also be important for lipid crystallization induced freeze thaw instabilities. Emulsifiers that are able to stabilize droplets having a thick interfacial layer, at high oil concentrations, have also been reported to improve the freeze–thaw stability of emulsions. Examples include Pickering emulsions using quinoa starch granules or egg yolk granules as stabilizing particles (Marefati et al. 2013; Rayner et al. 2014), proteins, such as caseins, protein–polysaccharide complexes, and hydrophobic starches (Degner et al. 2014).

***Process stability during drying of emulsions***, like freeze–thaw stability, the ability of an emulsion formulation to be dried has a great deal of practical application in foods. Dehydration of emulsion systems have been used to increase shelf life, improve their use, and facilitate transportation (Adelmann et al. 2012; Bhandari et al. 1993; McClements 2004). However, dehydration may alter the interfacial properties and lead to disruption and collapse of emulsions during drying (Cerdeira et al. 2005; Fäldt and Bergenståhl 1995; Rosenberg et al. 1990). There are several approaches to maintain the stability of emulsions during drying and subsequent storage. A common way is to add a solid hydrophilic carrier to the aqueous phase in amounts ranging between 30 and 80 % of the total weight of the final powder (Gu et al. 2004; Jayasundera et al. 2009). Examples of such carrier compounds include sugars, such as lactose, glucose, as well as polysaccharides such as maltodextrin, and cellulose (Adelmann et al. 2012; Mezzenga and Ulrich 2010). As an alternative and to avoid carrier compounds, multiple, or layer-by-layer (LBL) deposition of polyelectrolytes that crosslink on the droplet surface, crosslinking of protein-stabilized interfaces, and protein–polysaccharide conjugates have also been applied (Kellerby et al. 2006; Moreau et al. 2003; Mun et al. 2008). Recent work in the area of particle stabilized emulsions has also eliminate the need for additional hydrophilic carriers, making it possible to produce emulsion powders with high oil content (up to 80 %) based on stabilizing oil droplets using starch granules (Marefati et al. 2013, 2015) or cellulose nanocrystals (Adelmann et al. 2012; Aveyard et al. 2003; Tasset et al. 2014).

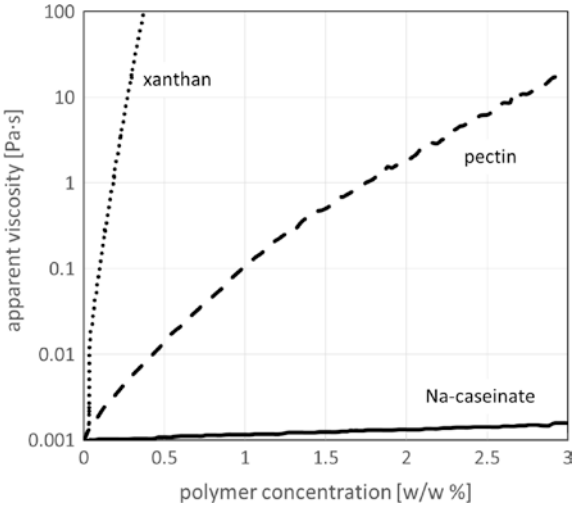



**Fig. 5.2** Effect of polymer concentration on apparent viscosity of various polymer types

### *5.2.2 Thickeners*

Natural polymers are widely used to thicken food systems, and unlike emulsifiers and stabilizers, which are used in food formulations to produce and stabilize emulsions droplets and foams, thickeners are added to increase the viscosity of the food without necessarily modifying other product properties. Thickeners increase the consistency to prevent multicomponent products from separating (for example, reducing the rate of creaming as described in Sect. 5.1). Examples of natural polymers commonly used as thickeners are presented in Table 5.2. The resulting viscosity of natural polymer solutions is highly dependent on the polymers' type and concentration. Figure 5.2 illustrates the effect of polymer concentration on apparent viscosity for three polymers, caseinate, pectin, and xanthan. Both the concentration and relative polymer size play a major role. Pectin and xanthan are 2–5 and 10–50 times larger than caseinate, respectively (Walstra 2003). Size, degree of polymerization, and branching also contribute to thickening characteristics. The process of thickening involves the nonspecific entanglement of conformationally disordered polymer chains.

The viscosity of polymer solutions and dispersions in general, shows a marked increase at a critical polymer concentration, commonly referred to as $C^*$ (Williams and Phillips 2003). This concentration indicates the transition from the "dilute-region" to the "semi-dilute" overlap region (see Fig. 5.3). In the dilute-region at concentrations well below $C^*$ polymer molecules are free to move independently in solution without touching. As concentration approaches $C^*$ molecules begin to be crowded which gives rise to overlap and entanglements as segments or polymer chains and loops begin to interpenetrate. In Fig. 5.3 the zero shear viscosity is plotted as a function of polymer concentration (log–log scale). The line has a

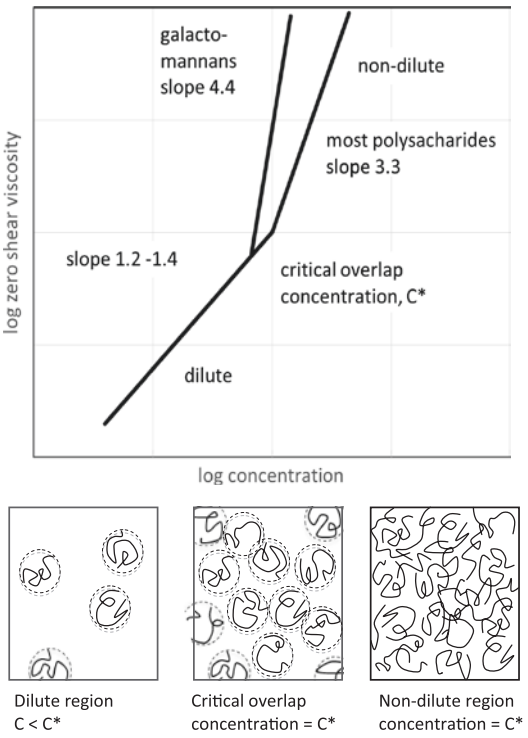



**Fig. 5.3** Effect of polymer concentration on viscosity and the concept of critical overlap concentration

linear slope that changes typically from a value within the range of 1.2–1.4 for concentrations below $C^*$ to a value of approximately 3.3 above the $C^*$. However, glactomannas (i.e., guar and locust bean gum) have a somewhat higher slope of 4.4 above the $C^*$, which is thought to arise due to specific attractive interactions between side groups on their polymer chains (Walstra 2003). Table 5.6 shows some examples of $C^*$ and slope of the lines in the non-dilute region for common polymer thickeners.

It is important to note that the relationships in Fig. 5.3 and Table 5.6 only applies for extremely low shear rates, as the viscosity of polymer dispersions approaching or above $C^*$ have a significant shear rate dependence. At concentrations well below $C^*$ polymer dispersions exhibit Newtonian behavior, i.e., the

**Table 5.6** The critical concentration $C^*$ for polymer chain overlap and slope of the relation: $\log(\eta)_0$ versus $C$ for $C > C^*$. Data from Walstra (2003)

| Polymer | $C^*$ g/100 mL | Slope |
|---|---|---|
| Dextran (linear) | 2.5 | 3.3 |
| Guar gum | 0.25 | 4.4 |
| Na-alginate | 0.2 | 3.3 |
| Lambda-carrageenan | 0.4 | 3.3 |
| Locust bean gum | 0.2 | 4.4 |
| Pectin | 0.3 | 3.3 |
| Xanthan | 0.1 | 3.9 |

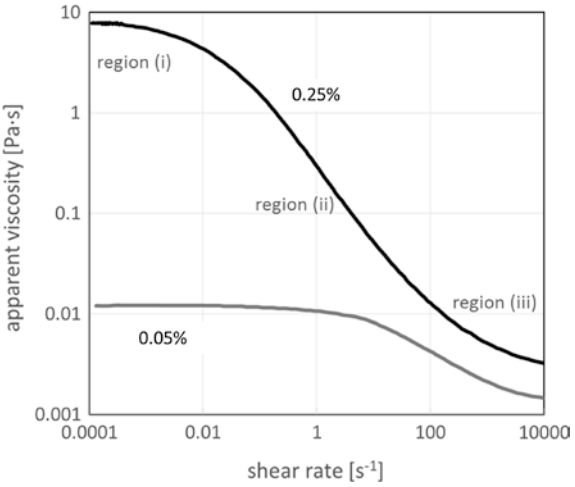



**Fig. 5.4** Effect of shear rate on the apparent viscosity of xanthan solutions at 0.05 and 0.25 ww% (data redrawn from Walstra (2003) based on various sources)

viscosity is independent of shear rate, however, above $C^*$ non-Newtonian behavior is generally observed for polymer dispersions (Williams and Phillips 2003, 2009) and is strongly shear thinning over a given shear range (Walstra 2003). This phenomenon is illustrated in Fig. 5.4 showing the change in apparent viscosity of xanthan dispersions, at polymer concentrations both below (0.05 %) and above (0.25 %), $C^*$ (being approximately 0.1 %), as a function of shear rate. Here, the apparent viscosity decreases by over three orders of magnitude over the range of shear rates applied for concentrations above $C^*$.

The curves in Fig. 5.4 also display three distinct regions as the shear rate increases: (i) an initial high viscosity low shear Newtonian plateau, (ii) a shear thinning region, and (iii) a high shear low viscosity plateau (if extended to even higher shear rates). The molecular-microstructural explanation of this phenomenon is as follows: in region (i) at very low shear rates, as many new entanglements between polymer molecules form as are disentangled per unit time, the viscosity is Newtonian and remains high. In this case, due to the polymer concentration exceeding the critical overlap concentration, polymers chains readily develop entanglements. The higher the polymer concentration, the greater the number of such entanglements per unit volume, and disentangling them requires a relatively larger amount of energy, thus, the much higher apparent viscosity low shear rates (region (i) in Fig. 5.4). When applying a shear rate to the polymer solutions/dispersions, the shearing stress provides the energy causing disentangling. However, Brownian motion of the polymer chains allows new entanglements to form. The time available for the formation of new entanglements during shearing is roughly on the order of the reciprocal of the shear rate. The apparent viscosity under a given shear rate is thus a balance between the number or entanglements possible based on the concentration and the relative time of entanglement and disentanglement processes. As the shear increases beyond the point that the Brownian-driven re-entanglements cannot keep up with the shear-driven disentanglements, the

apparent viscosity drops (region (ii) in Fig. 5.4). If the polymer molecules become fully disentangled the viscosity will be significantly lower and no longer a function of shear rate, as seen in region (iii) in Fig. 5.4. At very high shear rates, the time available for entanglements relative to the rate they are being pulled apart by the shear is short, thus, the polymer molecules are basically fully disentangled, yielding a relatively low and constant viscosity. Here, disentanglement dominates and viscosity drops to a minimum plateau at infinite shear rate (Williams and Phillips 2009). The relationship between the apparent viscosity at a given shear rate depends on the polymer type, size morphology, and solvent quality (Walstra 2003). Linear stiff molecules have larger hydrodynamic size than highly branched flexible polymers of the same molecular mass, and hence higher viscosity, assuming that other conditions are constant. Viscosity shear rate dependency increases with increasing molecular mass, and the shear rate at which shear thinning occurs [i.e., onset of region (ii)] shifts to lower values (Williams and Phillips 2009). For more details on the rheological properties of specific polymers the interested reader is recommended the Handbook of Food Hydrocolloids (Williams and Phillips 2009), as well as comprehensive reviewers on thickeners and references within (Chronakis and Kasapis 1995; Gibinski et al. 2006; Marcotte et al. 2001; Saha and Bhattacharya 2010; Sheldrake 2003; Sopade et al. 2008; Tolstoguzov 2008; VâniaReginaNicoletti 2012).

### *5.2.3 Gelling Agents*

Although all hydrocolloids thicken and increase the viscosity of aqueous dispersions, a few natural polymers have an additional key property of being able to form gels. Example of common natural polymers used as gelling agents and some of their properties are presented in Table 5.2. Gel formation arises from the association or crosslinking of polymer chains, thereby creating a three-dimensional network trapping water within it to form a semi-rigid structure being resistant to flow. Natural polymer-based gels are generally viscoelastic exhibiting characteristics of both liquids and solids depending on the applied deformation stress. Viscoelastic behavior is often characterized using a rheometer that measures the mechanical reaction of a material undergoing deformation at controlled rate (frequency) or controlled stresses. As the name implies, viscoelastic materials have both viscous and elastic properties being characterized by the magnitude and frequency dependence of the storage, $G'$ and loss modulus, $G''$. In dilute systems, where the polymer concentration is $<C^*$ and molecule entanglements do not occur, most polymers have a loss modulus (i.e., viscous dissipation of the applied stress at a given rate) greater that the storage modulus (the ability of an elastic body to store energy). As the concentration increases, intramolecular entanglements occur and if these are more enduring then a three-dimensional network structure can form creating a gel. The critical minimum concentration at which gelling occurs is often denoted $C_0$, and is specific for each natural polymer, and can vary greatly. Agarose, for

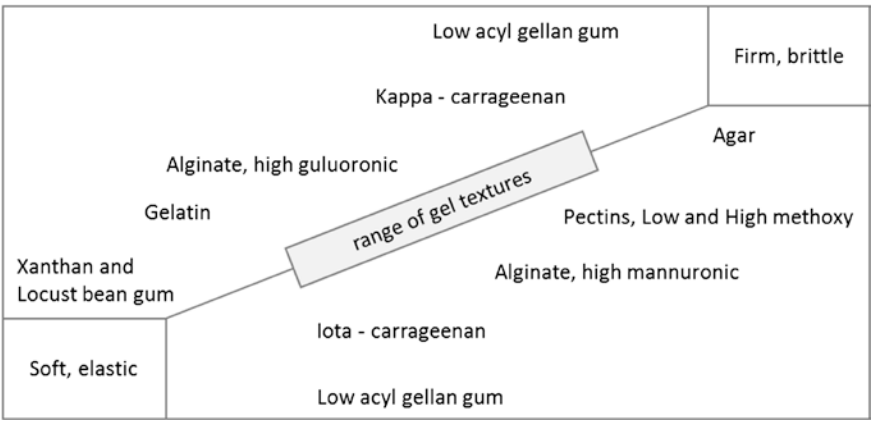



**Fig. 5.5** Qualitative comparison of gel textures produced by different natural polymers. Redrawn based on Williams and Phillips (2009)

example, gels with as little as 0.2 % while for acid thinned starch a concentration of up to 15 % is required before gels are formed. In general, for most natural polymers $C_0$ is in the range of up to 1 % (Williams and Phillips 2009) (note $C_0$ is not the same as $C^*$ presented above). Once formed, the specific textural properties (such as being elastic or brittle, chewy, or creamy, etc.) and other sensory properties (such as opacity, mouth feel, and taste) generated depend on the type and concentration of the gel forming polymers added in the formulation (Saha and Bhattacharya 2010).

A qualitative comparison of the textures of gels produced by various types of natural polymers commonly used in foods is illustrated in Fig. 5.5. Natural polymer gels also vary considerable in strength and elasticity owing to differences in the number and nature of the physical bond that join the polymers together, as well as the degree of aggregation between chains (Williams and Phillips 2003).

Proteins and polysaccharides are able to form gels by physical association of their polymer chains by a number of mechanisms: hydrogen bonding, hydrophobic association, and cation-mediated crosslinking. In some cases, natural polymer gels undergo covalent crosslinking, however, this is more uncommon. These zones of interaction that give rise to gel network formation are called gel junctions and are illustrated in Fig. 5.6. In most polymer gels, the junctions contain a substantial proportion of the polymer material, up to 30 % (Walstra 2003). Within food there are two main types of gels—polymer gels and particle gels, with polymer gels being the most common.

Polymer gels are made up of long polymer molecules that are crosslinked at some places. These crosslinks are rarely chemical bonds, with the exception of sulfide bridges (–S–S–) between protein molecules in, for example, whey gels (Fig. 5.6a), but rather junction zones comprising of a large number of relatively weak physical bonds. These bonds are often microcrystallites, i.e., straightened

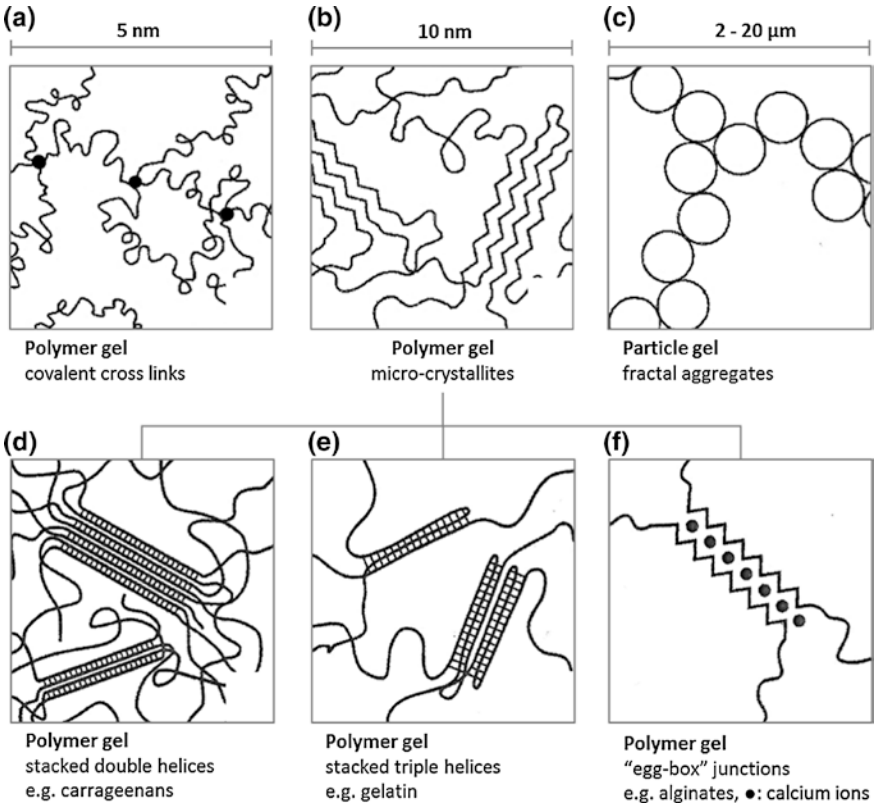



**Fig. 5.6** Types and scales of gel structures, showing various types of gel junctions. Redrawn from Walstra (2003)

polymer sections (Fig. 5.6b), or stacks of helices (Fig. 5.6d and e). Polymer gels with microcrystallites: here the gel structure is made up of junctions that are created by a large number of weak physical bonds in regions of micro-crystallinity, rather than covalent chemical bonds. These weak physical bonds arise from Van der Waals attraction, hydrophobic interaction, and hydrogen bonding. In the case of charged polymers, ionic bonds can also be involved. Most gels with microcrystallite junctions are thermoreversible—they melt upon heating and (re-) form upon cooling. The other types of junctions that can be formed are "egg-box" junctions (Fig. 5.6f) in the presence of calcium ions, as in the case of anionic polymers like alginates. Gels based on "egg-box" junctions do not generally melt at high temperature and are considered thermoirreversible. In case of protein gels, the gelation of proteins requires a driving force to unfold the native protein structure (often heat), followed by an aggregation process giving a three-dimensional organized network of aggregates or strands of molecules crosslinked by non-covalent bonds, and in some cases by covalent bonds (Totosaus et al. 2002). Among natural polymer protein ingredients, gelatin has a preponderant role in formulated foods due to

its unique functional properties. Gelatin produces transparent gels with the highly desirable ability to melt in the mouth, which is unparalleled by other gelation agents.

Particle gels are generally formed by the fractal aggregation of particles (Fig. 5.6c), where the particles are made up of natural polymers, for example, polysaccharide microcrystals or casein micelles. Here, the gel structure is determined by the volume fraction of the particle material, their size, and the fractal dimension of the aggregates. A typical food example of fractal particle gels is gelled casein micelles that are driven to aggregate by the action of acidification or rennet (Walstra 2003). In this context, the junction zone of a particle gel could be considered as the particle–particle interaction points.

Microgels are soft, colloidal particles made of highly swollen crosslinked polymers, which have recently been receiving significant research interest (Schmitt and Ravaine 2013). They are distinct particles that are made of a gelled material, and thus, microgels themselves can create a fractal particle gel, or even be used as a type of soft particle in stabilizing emulsions and foams. Food grade microgels have been generated from polysaccharides such as inulin (Sahiner et al. 2014), crosslinked starch, by the partial gelatinization of starch granules (Dickinson 2015; Rayner et al. 2014; Sjöö et al. 2015), proteins (Destribats et al. 2014; Phan-Xuan et al. 2014; Schmitt et al. 2014, 2010; Tan et al. 2014), and protein–pectin mixtures (Zimmerer and Jones 2014). They are generally generated through covalent crosslinking of proteins through a complex process of denaturation, aggregation, electrostatic interactions, and the formation of di-sulfide bonds (Schmitt et al. 2010). In the case of whey protein microgels, this is achieved by a combination of fast heat treatment in a plate heat exchanger, high shear, microfiltration, and in some cases a final spray drying step is performed producing a whey protein microgel powder that is readily re-dispersible (Destribats et al. 2014; Schmitt et al. 2010; Dissanayake et al. 2012). The resulting whey protein microgels are very efficient in the stabilization of emulsions and foams and will likely see greater industrial use in the near future.

The formation of all types of gels depends on a number of physicochemical phenomena that leads to the creation of junction zones. These "gelation reactions" can be roughly classified as either physically induced (heat, pressure) or chemically induced (acid, ionic, enzymatic) and are described briefly below.

***Temperature***: Heat-induced gelation is probably the most important and common method to obtain gels (Aguilera and Rademacher 2004). Gelation is a two-step process; an unfolding or dissociation of the molecules due to that the energy input takes place in the beginning to expose reactive sites. The second step is the association and aggregation of unfolded molecules to form complexes of higher molecular weight. The first step may be reversible while the second one is usually an irreversible process (Banerjee and Bhattacharya 2011).

***Pressure***: High pressure offers an additional option in creating gels during processing by modifying functional properties of molecules. In this case, high pressure can be applied as a single process or in combination with others (i.e., heating or chemically induced gelling described below). In general, high pressure favors

reactions, as it causes water to dissociate and the pH of solution becomes more acidic (Banerjee and Bhattacharya 2011).

***Ionic Strength***: Monovalent and divalent cations such as sodium and calcium can increase the ionic strength of polymer solutions causing the reduction of the electrostatic repulsive forces between the molecules and gelation can occur (Banerjee and Bhattacharya 2011). Ionic-induced gelation has been reported for pre-denatured whey proteins, however, in industrial applications, ionic-induced gelation is much more common in polysaccharide gels such as alginate, pectin, and carrageenan.

***pH***: Changes in pH, for example, by the addition of acids or microbial fermentation, changes the net charge of polymer molecules, and thus, the attractive and repulsive forces between molecules and hydration properties. In addition, the solubility of salts changes with pH which may contribute to gel formation (Banerjee and Bhattacharya 2011). Changes in pH can also cause aggregation of particles in fractal particle gels such as those based on casein micelle in acidified dairy products (Walstra 2003).

***Enzymatic activity***: Enzyme-induced gelation is based on the introduction of artificial covalent crosslinks into food proteins. For example, protein crosslinking reactions catalyzed by trans-glutaminase (TG), peroxidase, and polyphenol oxidase (Lauber et al. 2003). Another common enzymatic action causing the formation of particle gels is the action of rennet on casein micelles allowing for aggregation (Walstra 2003).

***Solvent quality***: The nature and presence of solvent markedly influences gel formation, for example, concentrated sugar solutions is a poor solvent for pectin, and thus assists in the gelling of jams and jellies. Here, hydrogen bonds in the junction zones can only be formed in concentrated sugar solution, and hence, gelation takes place only with the addition of a certain amount of sugar.

### *5.2.4 Characterization of Natural Polymer Formulations*

From a consumers' viewpoint, apart from taste, the two most important food product properties are physical appearance (phase separation, creaming, sedimentation, graininess, etc.) and texture (mouth feel, viscosity, etc.), and these are closely related to the stability of emulsion droplets, as well as the rheology of the resulting dispersion or gel. For this reason, the microstructure and particle size distribution of emulsions and/or the texture and rheology of the system is often studied in the development and evaluation of new natural polymer based formulations.

On a microstructural level, emulsion droplet size distribution is perhaps the most central quantifying measure in emulsion science, as emulsion characteristics and performance are to a large extent determined by their droplet sizes (Wahlgren et al. 2015). There are numerous methods to assess particle size distributions in emulsions, including direct droplet measurement by microscopy (light, confocal, electron, etc.), automated particle counters (i.e., Coulter counter), light scattering

(i.e., Malvern Mastersizer), dynamic light scattering, diffusional wave spectroscopy, NMR, and sedimentation or centrifugation (Walstra 2005). These techniques vary with respect to size ranges covered, measurement principles, degree of sample preparation, and dilution, as well as physical limitations. The interested reader is directed to comprehensive and critical reviews and references therein on emulsion characterization techniques for more details (Dalgleish 2003; Dickinson 2013; McClements 2005, 2007; Sherman 1995; Walstra 2005).

As pointed out previous, the action of natural polymers dispersions and gels in modifying product rheology is important to developing texture and mouth feel as well as emulsion stability (with respect to creaming and coalescence) (Le Révérend et al. 2010; Tadros 2004). Texture can be evaluated using techniques such as by oscillatory rheometers and texture analyzers. While texture analyzers can give quick information for comparison of systems they are empirical, while the data obtained by oscillating rheology gives more fundamental information. The modern development of controlled stress rheometers has allowed for characterization to be carried out at small strains and stresses, thus measurements do not destroy the structure of the samples. In this type of measurement, the sample is subjected to a sinusoidal shear deformation and the resultant stress response is measured. The frequency and the strain/stress on the sample can normally be varied and the response is divided into a viscous component G″ (loss module) and an elastic component G′ (storage module). Such measurements can give information of the viscoelastic character of the material over a wide range of stress and strain rates. Typically in strain tests, the strain is increased until the structure of the material is broken and the gel starts to flow shown as a rapid decease of elastic modulus G′. As mentioned in Sect. 5.1, even a weak gel can arrest the creaming of emulsions and thus, gelling polymers will only have to withstand the stress asserted by the droplet. Therefore any measurement to predict if the system is resistance to creaming will have to be evaluated at low stress, which can be obtained by constant stress or creep measurements. Oscillating measurements can also be used to follow the build-up of a gel during heating or cooling.

In addition to texture analyzers and controlled stress oscillatory rheometers there are several additional methods that evaluate texture properties of natural polymer dispersions and gels. For example, the RVA is a rotational viscometer which records the viscosity of a sample continuously during a preset controlled temperature profile. From the samples' viscosity profile, several parameters can be obtained, see Fig. 5.7 (Crosbie and Ross 2007). RVA type measurement have been used extensively in characterizing native starches with respect to gelatinization and pasting properties, as well as the ratio between the constituent amylose and amylopectin molecules. Properties of modified starches studied by the temperature cycling action of the RVA includes: studying how crosslinking starch increases its' stability to heat, shear, and acid, and how ethers or esters substitution improves freeze–thaw stability. Beyond starch applications, information and properties of different non-starch hydrocolloids have been obtained with the RVA. In most cases the cooling curve reveals the information. This is, therefore, also applicable when hydrocolloids are mixed with starch, since the pasting of the starch has

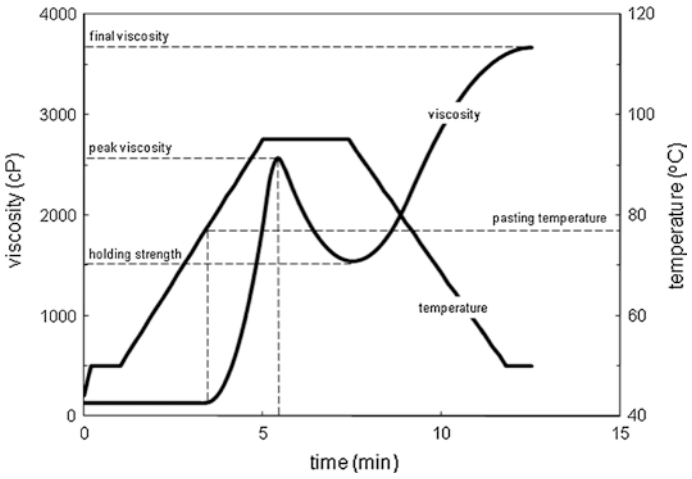



**Fig. 5.7** Typical RVA heating and cooling curve, showing the main parameters

already occurred before the cooling begins. Hydrocolloids such as carrageenan, guar gum, locust bean gum, xanthan, and konjac mannan all give specific cooling profiles (curve shapes) that can be associated with specific product properties (Young 2007). In this section only a short overview of characterization methods of texture and rheology has been provided. For a more extensive reviews on this topic the reader is directed to Derkach (2009), Tabilo-Munizaga and Barbosa-Cánovas (2005), and Tadros (2004).

## 5.3 Additional Physiological and Biological Functions

### *5.3.1 Health Effects of Natural Polymers*

In addition to their classical food formulation applications discussed above, some natural polymers, mostly the soluble non-starch polysaccharides, such as pectin, guar gum, ispaghul, beta-glucan, inulin, and gellan have additional health benefits that arise from the specific structural properties they exert in the food matrix. The effect of these polysaccharides are dependent on both the dose ingested and whether they are bound or free to form viscous solutions (Brennan et al. 1996). Generally, the health beneficial effects are achieved with higher levels than is typically used in food products. For example, the typical usage level of guar gum is <1 % in food products but to achieve health effects, the levels must be up to 3–5 % which unfortunately can be associated with a negatively slimy mouth feel (Edwards and Garcia 2009). However, despite the additional challenges of creating pleasing and functional products, natural polymers are still providing sound alternatives to traditional pharmacological approaches for treating and preventing

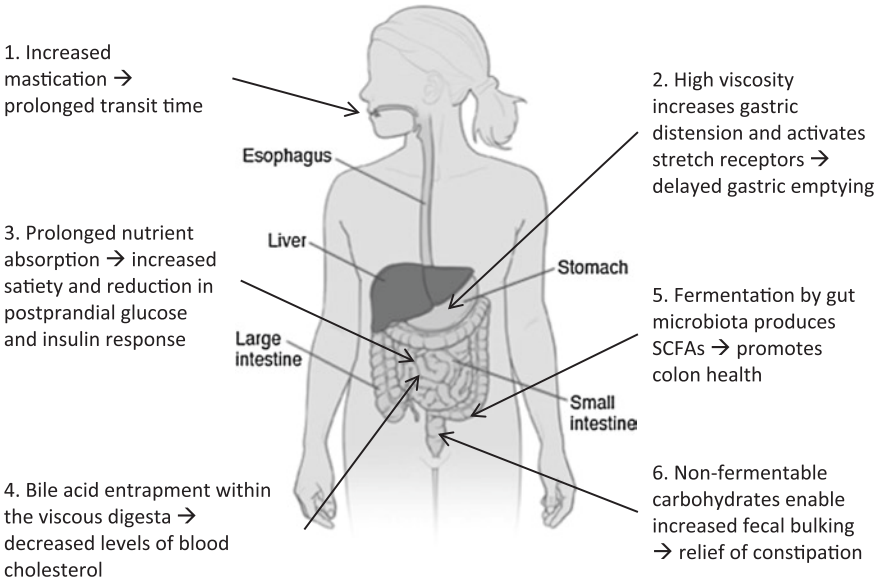



**Fig. 5.8** Health effects of natural polymers in the GI tract

a number of diet related conditions, such as obesity, blood cholesterol levels, and gut health (Fig. 5.8).

### *5.3.2 Effect of Natural Polymers in the Upper Intestine—Prolonging Satiety and Inducing Weight Loss*

Many drugs designed to facilitate weight loss usually fail due to limited efficacy, high drop-out rate in long-term treatment, concerns of side effects and safety (Lai et al. 2015; Misra 2013). From the pharmacological area, novel appetite suppressing agents, such as Rimonabant (a cannabinoid receptor blocker, initially intended as an anti-obesity and smoking-cessation dual-purpose drug) and Orlistat (a pancreatic lipase inhibitor reducing fat absorption) have been developed during recent decades. Unfortunately, Rimonabant were accompanied with psychiatric side effects and were withdrawn from the market. Orlistat is the only clinically approved drug on the market today and is also accompanied with side effects as steatorrhea, bloating, and fecal incontinence (Lagerros and Rossner 2013). However, further investigation is required due to the severe side effects and long-term safety of the pharmacological agents (Lai et al. 2015; Misra 2013). Therefore, a considerable amount of edible extracts with botanical origin are screened for their appetite suppressing properties including thylakoid membranes (Ostbring et al. 2014) and galactolipids (Chu et al. 2009) from

spinach, polyphenols from tea plant extract (Kobayashi et al. 2009), saponins from Japanese horse chestnut (Kimura et al. 2006), and terpene extract from bark of birch (Jager et al. 2009). Since the origin is food and has been consumed in many cultures for a very long time, the extracts are considered to be safe also in the long term.

Appetite is regulated by complex mechanisms and is controlled by the central nervous system. Mechanical actions involved in food intake and digestion, such as chewing, stomach distension, and peristaltic movements of the intestines play a role in the regulation of appetite signals. Also, the food composition influences appetite where fat, protein, and carbohydrate have different satiation actions. Certain hydrocolloids, such as guar gum, alginates, inulin, pectin, beta-glucan, psyllium, and ispaghula have gel forming properties that increase viscosity of the digesta which elicit effects that modulate appetite (Blundell and Stubbs 1999).

Solid or highly viscous foods are expected to elicit stronger satiation (the immediate response that initiates meal termination) and satiety (the long-term absence of hunger between meals) compared to liquids. Solid and viscous food requires increased mastication compared to liquids. Thus, the food spends longer time in the oral cavities, which prolong metabolic feedback for satiety signals to the appetite center in the central nervous system (Fujise et al. 1998).

Gel forming polysaccharides with high viscosity can change the characteristics of the liquid phase of ingested food in the stomach. Gel forming polysaccharides thereby increase gastric volume compared to high- or low viscosity meals that do not gel (Dikeman et al. 2006). The higher gastric volume increases distension in the stomach wall and activates gastric mechanoreceptors which (i) sends neural signals mediating satiety to the appetite center in the brain and (ii) sends signals that delays gastric emptying (Sturm et al. 2004). Delayed gastric emptying is a key process in the regulation of appetite as gastric distension is also an important signal to influence satiety, prevent overeating, and hence, weight control (Edwards and Garcia 2009). High viscosity, gel forming polysaccharides ingested in high concentrations increase gastric volume and enhance fullness compared to high- or low viscosity meals that do not gel and are more homogeneously diluted in the stomach (Dikeman et al. 2006; Hoad et al. 2004).

When the transit of nutrient from the stomach to the intestines is slowed down, the absorption will be prolonged. Slowed absorption results in a reduction in postprandial glucose and insulin response, which also modulates appetite responses (Jenkins et al. 1978). The ingestion of different types of insoluble and soluble viscous hydrocolloids including pectin, inulin, beta-glucan, psyllium, ispaghula husk, guar gum and modified cellulose, blunted postprandial glucose, and insulin responses (Dikeman et al. 2006; Hoad et al. 2004; Maki et al. 2008). Furthermore, ingestion of high viscous non-starch polysaccharides caused reduction in glucose and insulin concentrations after ingestion. The result was explained by retarded gastric emptying and reduced rate of absorption (Leclere et al. 1994). The slowed down transit of viscous digesta also allow nutrients to pass further down the intestine to the lower part, called the ileum. When nutrients are accumulated in the ileum, a feedback mechanism called the ileal brake is activated

which in turn promotes secretion of satiety promoting hormones and peptides, such as peptide YY (PYY), cholecystokinin (CCK), and glucagon-like peptide 1 (GLP-1) (Maljaars et al. 2007). In response to the hormones, the gastric emptying rate of the next meal is reduced and hence reduced postprandial levels (levels after a meal) of nutrients in the second meal, and even a shorter time to reach satiety from that second meal (Nilsson et al. 2008). This phenomenon is called the second meal effect: if the digestion of the first meal is prolonged, the systemic appetite regulation will be affected in various ways, and a lower amount of energy will be ingested in the second meal.

Natural polymers in the GI tract also affect the absorption of nutrients by mechanically hindering digestion. Guar gum in the intestine appears to form a gel, hindering digestion, and absorption of available carbohydrates, and thereby, decreases the rate of glucose absorption into the hepatic portal vein that normally follows a starchy meal. Starch fragments are thought to be caught in the highly viscous network, making them less available for digestive enzymes (like alpha-amylase). Thylakoid membranes from spinach has been demonstrated both to retard uptake and passage of glucose, larger carbohydrates, and proteins (Montelius et al. 2011). Thylakoids are thought to attach to the mucosal surface, hindering absorption of nutrients by steric hindrance. Thylakoids have also been demonstrated to prolong absorption of lipids by specifically inhibiting pancreatic lipase and colipase (Ostbring et al. 2014). Alginate incorporated in bread has been demonstrated to inhibit lipase/colipase and prolong lipid digestion and absorption. In agreement with guar gum above, the mechanism is suggested to be enzyme entrapment within the viscous gel, decreasing the interaction between enzymes and substrate (Houghton et al. 2015). Since digestion is a complex process, there is likely more than one mechanism to describe the influence of hydrocolloids in the human gut. It has also been suggested that an increase in the viscosity of the intestinal content reduces the mixing movements caused by intestinal contractions (Edwards et al. 1988). The reduced intestinal movements will produce laminar flow, rather than turbulent flow. Laminar flow will increase the unstirred water layer at the intestinal wall and would affect the rate at which starch fragment and other nutrients are exposed to the epithelial surface and further absorption into the hepatic portal vein (Li and Nie 2015).

Supplementation of guar gum and other hydrocolloids together with energy-controlled diets has shown promising effects on weight loss and maintenance. Obese subjects following a fixed energy diet supplemented with 40 g guar gum/day over a week significantly decreased the energy intake compared to control (Pasman et al. 1997). Modified guar gum (highly purified galactomannan) added to a low-energy diet (7.5 g/day over 2 weeks) was significantly reducing weight and prevented increases in appetite, hunger, and desire to eat compared to control (Kovacs et al. 2001). Alginate supplemented to a beverage three times/day (totally 15 g fibers/day) together with a restricted diet significantly resulted in a greater weight loss compared to control. The effect was attributed to lower percentage of body fat. However, alginate supplementation showed no effect on appetite sensation such as the hunger hormone ghrelin (Jensen et al. 2012).

### 5.3.3 *Effect of Natural Polymers on Blood Cholesterol Levels*

There is substantial evidence that hydrocolloids, which have the potential to increase viscosity, also reduce the absorption of bile. This is probably due to entrapment of molecules inside the polysaccharide network. Charged polysaccharides as pectin, may bind bile acids thus reduce reabsorption, but most binding sites are already occupied by other substances in the food and may therefore not be available for binding new molecules (Edwards and Garcia 2009).

Bile salts are synthesized from cholesterol in the liver, stored in the gall bladder and secreted into the intestine after meals to promote digestion and absorption of fat. Synthesis of bile is an energy consuming process. To minimize the production, and still allow the large physiological need, an efficient circulation of bile is performed. After taking part in the lipid digestion, bile is reabsorbed by active transport in the ileum and transported back to the liver in a circulation called the enterohepatic circulation. When bile is trapped in a polysaccharide gel in the intestine, they pass through the GI tract without being reabsorbed, and the systemic bile pool is decreased. To maintain the physiological needs of bile, new molecules are being synthesized from circulating blood cholesterol, thus reducing the overall cholesterol levels in the body. Supplementation of pectin, psyllium, beta-glucans, and guar gum has been demonstrated to reduce total cholesterol and LDL cholesterol in several human studies (Brown et al. 1999; Cicero et al. 2015; Salas-Salvado et al. 2008).

### 5.3.4 *Effect of Natural Polymers in the Lower Intestine*

Dietary fibers are defined as polysaccharides and lignin which are resistant to the endogenous enzymes in the human digestive tract. Thus, dietary fibers are not digested during transit through the small intestine. When dietary fibers reach the colon, they are fermented by the colonic microflora. Examples of hydrocolloids being substrate for colonic fermentation are pectin, beta-glucan, and non-digestible oligosaccharides such as fructooligosaccharides and inulin. The fermentation produces short chained fatty acids (SCFAs), mainly acetate, propionate, and butyrate, but also carbon dioxide, hydrogen, and methane gases. These fermentation products have several benefits for the human health. The absorption of the SCFAs promotes water absorption and helps prevent diarrhea (Crump et al. 1980). SCFAs stimulate electrolyte absorption by the mucosa and enhance transport through improving colonic blood flow. Production of SCFAs increases gut acidity, which reduces putrefaction and activity of pathogenic bacteria, which lowers toxins and thus reduces bad odors and bad smelling feces.

Butyrate production has received the most research attention due to its potential anti-inflammatory effects. Butyrate is the preferred energy source for the colonic

microflora and is thought to be essential for colonic health (Roediger 1982). It also stimulates the proliferation of intestinal cells (Sakata 1987) and promotes colonic healing from surgery and after inflammation (Scheppach et al. 1992; Topcu et al. 2002). Inflammation is a major factor in many diseases such as cardiovascular diseases and cancer and epidemiological studies have shown that populations with high intake of fibers in their diet have reduced risk of colon cancer. Protection may be through the colonic production of butyrate which inhibits the growth of tumor cells in vitro by stimulating programmed cell death (Hague and Paraskeva 1995).

Propionate, another SCFA is used mainly in the liver where it is thought to reduce the synthesis of lipids from acetate (Wolever et al. 1995) and possibly cholesterol synthesis (Chen et al. 1984). Another SCFA, acetate, is thought to increase plasma lipids, which increases the risk of thrombosis and atherosclerosis. Different food compositions give rise to different amounts of acetate, propionate, and butyrate and a lower proportion of acetate to propionate may be important in promoting a healthier plasma lipid profile (Wolever et al. 1991).

Fermentation can be associated with increased gas production and may cause discomfort if the gas is retained in the colon. Gas production will however stimulate stretch receptors in the colonic muscle and this will increase the transit rate through the colon and may feed back to the stomach and cause delayed gastric emptying which is associated to satiety (Edwards and Garcia 2009).

Some hydrocolloids such as ispaghula, gellan, and psyllium are resistant to gut fermentation and cannot be utilized by the microbiota, but they do have other health benefits. These carbohydrates have a much greater effect on stool output compared to fermentable carbohydrates. Guar gum, pectin, inulin, and beta-glucan are likely to be completely fermented in the colon but non-fermentable carbohydrates retain their water holding capacity through GI transit (Edwards and Eastwood 1995). This enables increased fecal bulking which ease laxation very efficiently, leading to relief of constipation, one of fiber's best-documented effects.

### *5.3.5 Natural Polymers Can Improve Bioavailability of Vitamins and Other Sensitive Components*

Several natural and essential nutrients, such as vitamins, carotenoids and ω-3 polyunsaturated fatty acids are prone to degrade when subjected to heat, light, or oxygen (Mao and Miao 2015). Furthermore, they are often poorly soluble in water and these characteristics together limit their wider application in the food industry. To overcome these challenges, a wide variety of colloidal delivery systems such as structured emulsions have been designed so that the sensitive nutrients can be dispersed into aqueous-based food and beverage products with improved physicochemical stability, process ability, and bioavailability (Garti and Yuli-Amar 2008; Ozturk et al. 2015; Saberi et al. 2013; Velikov and Pelan 2008).

During transit through the GI tract, the structure of food emulsions is largely modified before entering the intestine where most nutrient absorption is taking place. Food emulsions are prone to microstructural changes, such as flocculation, coalescence, and creaming during digestion and the intensity of these processes greatly affect the delivery efficacy such as bioavailability of the nutrients (Mao et al. 2009). Accumulated evidence has shown that conventional oil-in-water emulsions can only provide limited protection for nutrients during digestion, and it is difficult to control the delivery (McClements 2010). Many efforts have therefore been spent on creating desired structures in the water and oil phases and the interface between them. Three examples of successful approaches are multilayer emulsions, multiple emulsions, and gelled emulsions. The delivery systems improve emulsion stability and facilitate targeting of nutrient delivery during digestion.

Multilayer emulsions are emulsions where the droplets are surrounded by two or more layers. The layers are attached by the layer-by-layer technique (Hou et al. 2010). The first layer to be deposited onto the droplet surface is often a charged emulsifier (e.g. protein or lecithin). The second layer is an oppositely charged emulsifier (e.g. protein or SDS) or a polymer (e.g., polysaccharide). The second layer is thereby electrostatically attracted to the previously adsorbed layer, which increase the stability. Multilayer emulsions have been reported to have better stability against heating, freeze thawing, high ionic strength and pH change compared to conventional emulsions (Guzey and McClements 2006). They can therefore be used to protect and control release of sensitive nutrients in a controlled manner. Hou et al. (2010) used multilayer emulsions to protect beta-carotene from degradation during storage. The layers surrounding the emulsion droplets were soybean polysaccharide and chitosan. By adding chitosan as a second layer, the loss of beta-carotene were significantly reduced during storage in different temperatures, compared to emulsions with only soybean polysaccharide as surrounding monolayer. Guzey et al. reported that the lipid oxidation of fish oil could be reduced by more than 50 % using a double layer (SDS-chitosan) or triple layer (SDS-chitosan-pectin) emulsion compared to a single layer emulsion (SDS) (Guzey and McClements 2006).

Multiple emulsions are emulsions dispersed in the same phase as the emulsion droplets and are sometimes referred to as double emulsions. They contain two water and one oil domain (w/o/w emulsions) or two oil and one water domain (o/w/o emulsions). This structure allows prolonged delivery and higher encapsulation efficacy. Another feature with this delivery system is that it makes it possible to control the release of both lipophilic and hydrophilic substances in the same system (Mao and Miao 2015). O'Reagan et al. found that encapsulation of Vitamin B12 in double emulsions improved the chemical stability during storage (O'Regan and Mulvihill 2010). Multiple emulsions have been successfully used for encapsulation of probiotics. The viability of lactic acid bacteria decreased rapidly when directly dispersed in gastric juice, and less than 1 % was viable after 0.67 h of incubation. When lactic acid bacteria were encapsulated in the inner phase of a w/o/w emulsions, 49 % of the bacteria were alive after 2 h incubation. The viability was dependent by the inner phase ratio and the diameter of the oil droplets

where larger droplets resulted in higher viability (Shima et al. 2006). W/o/w emulsions can be used not only to improve bioavailability of sensitive ingredients, but also to substitute milk fat in low-fat dairy products. When the oil content in the oil phase are partly displaced by water in the inner phase, the caloric content can be reduced while at the same time keeping the desired viscoelastic properties such as creaminess (Lobato-Calleros et al. 2006).

In gelled emulsions, oil droplets are trapped within gel particles. The particles decrease the mass transfer and diffusion rate of the nutrients incorporated in the oil droplets. The gel particle can be broken down under certain environment conditions, such as salt concentration and temperature, which allows controlled release of the incorporated nutrients (Mao et al. 2009). Gelled emulsions are used for controlled release of lipid soluble nutrients, such as incorporation of ω-3 fatty acids, fish oil, flavor oil, etc. (Kim et al. 2006; Lamprecht et al. 2001; Weinbreck et al. 2004). Hydrocolloids, such as alginate, pectin, gelatine, and starch (Malone and Appelqvist 2003; Marefati 2015; Marefati et al. 2015) are used to create the gel surrounding the oil droplets in gelled emulsions. The nutrients incorporated in the gel are by this arrangement protected from exposure to oxygen, light, and enzymes, and they usually have improved chemical stability (Kim et al. 2006).

Structuring emulsions in different ways is a promising approach to control nutrient delivery through digestion and at the same time increase the chemical stability and bioavailability. The research field is still young and most studies are performed in vitro. Digestion in vivo is a complex process with large individual differences, such as health state, volume of digestive juice, varying enzyme release, and different microflora composition in the GI tract. Digestive models must be developed to closer mimic the in vivo digestion so that the performance of structured emulsions can be better characterized and the valuable nutrients be protected and released at the optimal location.

### *5.3.6 Antioxidative and Antimicrobial Properties of Natural Polymers*

In addition to biological functionality within the human GI tract, some natural polymers also have additional biological function that can be adapted into useful properties in food formulations, such as antioxidative and antimicrobial functions.

One such example of a biological function being transferred into food formulations is the antioxidative action of oleosins and soy fibers. Lipid oxidation is a major problem for food manufactures as oxidation products are associated with decreased food quality in terms of taste, texture, appearance, and shelf life (Berton-Carabin et al. 2014). Lipid oxidation is a major impediment in enriching food with polyunsaturated fats, such as fish oil (Kargar et al. 2011; Wijesundera and Shen 2014). Oleosin, a protein stabilizing oil bodies inside the seeds of oil plants such as canola, has been shown to not only stabilize emulsions but also to

decrease the rate of lipid oxidation (Wiejesundra 2013). Fish oil-in-water emulsions stabilized by oleosin had remarkably lower levels of the oxidation marker heptadienal, compared to emulsions stabilized by Tween 40 or sodium caseinate. Furthermore, the depletion of the sensitive fatty acids EPA (eicosapentaenoic acid) and DHA (docosahexaenoic acid) in the fish oil were lower for the oleosin-stabilized emulsions (20 % of initial value) compared to emulsions stabilized by Tween 40 (70 % of initial value) (Wijesundera et al. 2013). The antioxidative effect is thought to be due to oleosins' structure with an amphipathic domain with both hydrophilic and hydrophobic residues, a fully hydrophobic domain penetrating into the oil, and a second amphipathic domain situated near the C-terminus. This arrangement of oleosin at the oil–water interface may act as a barrier to oxygen and reactive hydroperoxides, preventing the oleosin-stabilized oil droplet from oxidative deterioration processes (Gray et al. 2010). It has also been demonstrated that fibers from soy (SSPS) prevents oxidation of oil and flavor oils. The mechanism is suggested to be stabilization of free radicals by the pectic polysaccharides included in the SSPS structure (Maeda and Nakamura 2009).

In the fruit and vegetable sector, it is desirable to control growth of a wide variety of microorganisms to prolong the storability of fresh products. Chitosan has been demonstrated to have potential as an antibacterial and antifungal preservative, aiding in increasing fruits, and vegetables storability (Shiekh et al. 2013). Coating the entire fruit with chitosan reduced the respiration rate of cucumber, strawberries, and tomatoes. The chitosan film also reduced the ripening and desiccation rate of strawberries and tomatoes. The antimicrobial effect of chitosan is suggested to be due to penetration of chitosan into the microbial cells. Inside the cells, chitosan form a complex with phosphate negative charges of the DNA helix, hindering further growth (Kubota and Kikuchi 1998). Chitosan is also used in wound dressings, due to the antimicrobial function. Wound dressing impregnated with a combination of chitosan and alginate are proven to be effective in controlling bacterial invasion in wounds (Muzzarelli and Muzzarelli 2009). OSA-modified inulin (In-OSA) has been reported to have antibacterial activity against *S. aureus* and *E. coli* (Zhang et al. 2015). The effect was concentration dependent and 1 % and 0.5 % In-OSA completely inactivated growth of *E. coli* and *S. aureus,* respectively. OSA-modified inulin interacted with the cell walls and cell membranes of the microorganisms and destroyed them severely, in some cells the walls was reported to disappear completely (Zhang et al. 2015).

## 5.4 Regulatory Aspects

Natural polymers added to foods are regulated either as additives or ingredients where most are classified as additives. Gelatin is an exception and is classified as ingredient. Ingredients are listed in the products' list of content with their name, whereas additives must be listed by a specific number (E-number in the European Union and INS number international) and it is voluntary if the manufacture wants

**Table 5.7** Approved EFSA health claims for products containing natural polymers

| Claim | Hydrocolloid |
|---|---|
| Maintenance of normal blood cholesterol concentrations | Beta-glucan, konjacmannan glucomannan, pectins, guar gum |
| Maintenance or achievement of a normal body weight | Konjacmannan glucomannan |
| Reduction of postprandial glycaemic responses | Beta-glucan, pectins |

to list additives also with their names. Additives are regulated by JECFA (Joint/WHO Expert Committee on Food Additives) in the US and by the European Commission within the EU. The regulation is used to protect the consumers' health and to ensure fair practice in the food trade. The objective of the regulation of additives is to establish safe levels of intake and to develop specifications for purity of the different compounds. Once accepted, an international number (INS, International Number System) or an E-number is allocated to the additive together with a specification of the acceptable daily intake (ADI) which cannot be exceeded. The INS/E-number is an acknowledgment of its acceptability.

When it comes to health claims of natural polymers as additives, it is regulated by EFSA (European Food and Safety Agency) within the EU. EFSA is evaluating available scientific evidence of the health claim and take a decision whether the evidence is sufficient enough or not. Only health claims approved by EFSA is legal to market on food packages within the EU. Most applications fail due to too low quality of the provided studies (Randomized Controlled Trials (RCT) are preferred), too few studies conducted, or due to too few test subjects in the studies. However, some natural polymers have passed EFSAs review and have approved health claims (Viebke et al. 2014) summarized briefly in Table 5.7.

## 5.5 Market Information

This section aims to provide some market information on the main categories of natural polymers discussed in this chapter including revenues, volumes, and averages prices, as well as main application areas, and leading manufactures of the various types of additives/ingredients. This data is not exhaustive but more to give an idea of the commercial importance of natural polymers in the food industry. The world natural polymer market (for all applications including foods) is valued at ~$4.4 billion US. By total sales, this market consists of ~70 % starches, ~12 % gelatin, ~5 % carrageenan, ~5 % pectin, and ~4 % xanthan gum, followed by LBG, alginates, carboxymethylcellulose (CMC), and many others. The total volume production volume is estimated to be 260,000–300,000 metric tons. It should be noted that nearly all-natural polymers are also used in nonfood industrial applications. The main customers being the textile and paper industries which use them as sizing and coating agents. Nevertheless, there are a few types (e.g., starch,

gelatin, pectin, carrageenan, and some other natural gums), which find their major applications in foods (Nussinovitch and Hirashima 2013). Despite the fact foods are often produced in large volumes, the natural polymer ingredients used in formulating them only represent small quantities, since these additives and ingredients are only required in minor amounts (maximum a few %) to impart the desired functional properties to these products.

Natural polymers in foods as food additives and ingredients make up a significant portion of the *Sensory and Textural Food Additives Market*. Where sensory additives are colors and flavors, and textural additives have the function of thickening and gelling agents, as well as emulsifiers and stabilizers. According to Frost and Sullivan (2013a, b), the total market revenue for the Sensory and Textural Food Additives Market was over $16 billion USD (US dollars) in 2012, of which Europe and North America account for 72 % of all sales revenue (see Table 5.8). Within this market there are several subsegments that are relevant in the context of natural polymers, specifically, the natural emulsifiers segment, the modified starch segment (which is considered to be a synthetic additive in market reports) and the gelling agents segment (Tables 5.9, 5.10, 5.11, 5.12, 5.13).

**Table 5.8** Total sensory and textural food additives market: revenue and compound annual rate of growth (CAGR) by segment and additive type for Europe and North America 2012–2017 (Frost and Sullivan 2013a, b)

| Segments | Europe | | North America | |
|---|---|---|---|---|
| | Revenue 2012 ($ Millions) | CAGR (2012–2017) | Revenue 2012 ($ Millions) | CAGR (2012–2017) |
| *Sensory food additives* (*i.e., colors and flavors*) | | | | |
| Natural | 991.0 | 6.3 % | 995.1 | 6.9 % |
| Synthetic | 2062.1 | 4.0 % | 3 665.0 | 2.4 % |
| *Textural food additives* (*i.e., emulsifiers, thickeners, gelling agents*) | | | | |
| Natural | 610.1 | 7.6 % | 470.4 | 3.5 % |
| Synthetic | 1749.4 | 3.2 % | 1 554.7 | 4.4 % |
| Total | 5412.6 (32 % of global) | | 6685.3 (40 % of global) | |

All values are in US dollars, base year 2012

**Table 5.9** Modified starches market sub-segment revenue and pricing trends for Europe and North America 2012–2017 (Frost and Sullivan 2013a, b)

| Additive | Europe | | | North America | | |
|---|---|---|---|---|---|---|
| | Revenue 2012 ($ Millions) | CAGR (2012–2017) (%) | Price per kg (2012, $) | Revenue 2012 ($ Millions) | CAGR (2012–2017) (%) | Price per kg (2012, $) |
| Modified Starches | 1100.0 | 3.8 | | 1050.0 | 5.2 | |
| Potato | | | 1.7–2.0 | | | – |
| Maize | | | 1.4–1.7 | | | 1.4–1.7 |
| Wheat | | | 1.2–1.4 | | | 1.2–1.4 |
| Rice | | | – | | | 1.6–2.0 |

All values are in US dollars, base year 2012

**Table 5.10** Key suppliers of modified starches, company market share ranking 2012 (Frost and Sullivan 2013a, b)

| Europe | North America |
|---|---|
| 1. Cargill Inc.<br>2. Roquette<br>3. Tate & Tyle PLC<br>4. Avebe<br>5. National Starch and Chemical Co. | 1. Cargill Inc.<br>2. Archer Daniels Midland Company<br>3. Tate & Tyle PLC<br>4. National Starch |

**Table 5.11** Gelling agents market sub-segment revenue and pricing trends for Europe and North America 2012–2017 (Frost and Sullivan 2013a, b)

| Additive | Europe | | North America | | Pricing Trends |
|---|---|---|---|---|---|
| | Revenue 2012 ($ Millions) | CAGR (2012–2017) (%) | Revenue 2012 ($ Millions) | CAGR (2012–2017) (%) | $ per kg (2012) |
| Carrageenan | 127.9 | 2.5 | 98.0 | 3.5 | 10–12 |
| Pectin | 114.8 | 2.5 | 88.2 | 3.1 | 12–15 |
| Xanthan Gum | 127.7 | 2.5 | 98.0 | 3.0 | 5–8 |
| Agar-agar | 29.6 | 2.5 | 22.9 | 3.4 | 20–23 |
| Total | 400.0 | | 307.1 | | |

**Table 5.12** Key suppliers of gelling agents

| Company Name | Carrageenan | Pectin | Xanthan gum | Agar-agar |
|---|---|---|---|---|
| FMC Biopolymer | ● | | | |
| CP Kelco | ● | ● | ● | |
| Danisco Dupont | ● | ● | ● | |
| Shemberg Corporation | ● | | | |
| Cargill | ● | ● | ● | |
| Jungbunzlauer | | | ● | |
| Hispanagar | | | | ● |
| Industrias ROKO | | | | ● |
| Iber Agar | | | | ● |

Leading global suppliers of **gelatin** include: Gelita USA Inc., Rousselot Inc., PB Leiner USA, Nitta Corporation, Kraft Foods Inc., Lapi SpA, Italgelatine SpA, Sterling Biotech, Ewald Gelatine, Weishardt (Frost and Sullivan 2012)

**Table 5.13** Emulsifier market sub-segment revenue and pricing trends for Europe and North America 2012–2017 (Frost and Sullivan 2013a, b)

| Additive | Europe | | North America | | Pricing trends |
|---|---|---|---|---|---|
| | Revenue 2012 ($ Millions) | CAGR (2012–2017) (%) | Revenue 2012 ($ Millions) | CAGR (2012–2017) (%) | $ per kg (2012) |
| Natural emulsifiers | 210.1 | 7.3 | 163.3 | 4.1 | 5–12 |
| Synthetic emulsifiers | 649.4 | 5.6 | 504.7 | 2.8 | 2–7 |
| Total | 859.5 | | 668.0 | | |

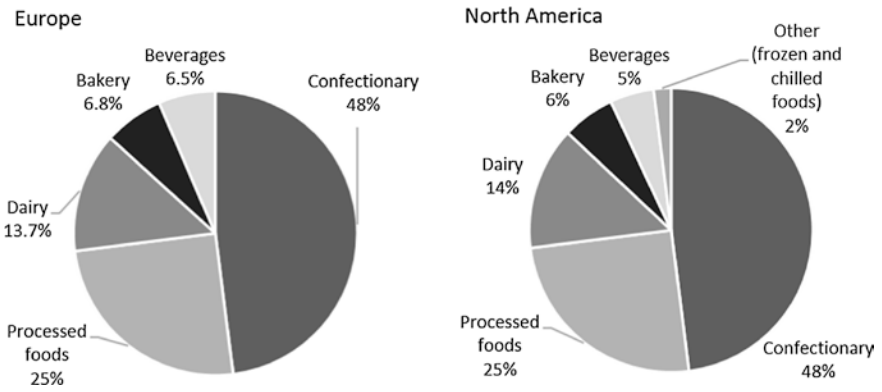



**Fig. 5.9** Modified starch subsegment market size by end application 2012 (Frost and Sullivan 2013a, b)

### *5.5.1 Modified Starch Market*

Modified starches are primarily used to provide better mouth feel and enhance the texture of foods, as well as in the stabilization of emulsions and foams. The average price of modified starch varies between $1.20 and $2.00 USD/kg however, the price of both modified starches and native starches depends heavily on the prevailing raw material supply and demand in the agricultural commodity markets (Fig. 5.9).

### *5.5.2 Gelling Agents Market*

Gelatin is not classified as an additive but rather an ingredient as part of the global animal protein ingredients market. Globally, the volume of animal protein ingredients was 2.3 million metric tons in 2012 with a compound annual growth rate of 4.8 %. Of this approximately 11.3 % was gelatin selling (0.26 million metric tons) at an average market price of $7–$8 per kg (Frost and Sullivan 2012). Thus, the approximate gelatin sale globally is estimated to be in the order of $2 billion USD per year in 2012.

Multifunctional ability of many hydrocolloids helps them find use in a wide array of applications. Processed food (including savory), dairy, and bakery are the most prevalent application areas for gelling agents (Fig. 5.10). All of the hydrocolloid based gelling agents are intrinsically "natural." Carrageenan is mainly used in processed food and savory products, while pectin is used extensively in bakery applications, and xanthan gum is used predominantly in dairy and beverage application areas (Frost and Sullivan 2013a, b). Historically, animal-based gelatin is the most commonly used gelling agent, but due to outbreaks of bovine spongiform

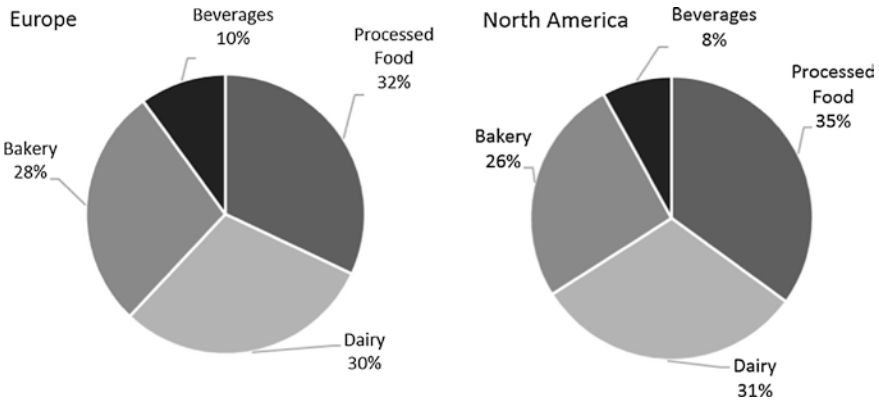



**Fig. 5.10** Gelling agents subsegment market size by end application 2012 (Frost and Sullivan 2013a, b)

encephalopathy (mad cow disease) as well as religious dietary customs, there has been substantial interest in substitute sources of gelatin, such as fish skin. The carrageenan market has also seen introduction of cheaper grades, which can be used as an alternative in cases where gel clarity is not important (Nussinovitch and Hirashima 2013).

### *5.5.3 Natural Emulsifiers Market*

The natural emulsifiers market is dominated by lecithin (which is not a polymer), however, dairy proteins and modified starches are also widely used for emulsion stabilization but are seen and regulated as protein ingredients or included within the modified starch segment. Although, the natural emulsifier segment is smaller, the growth rate is generally higher indicating a shift toward more natural ingredients and additives in general. Furthermore, there are new multifunctional emulsions stabilizers being developed from natural sources and this segment will likely see growth both at the expense of synthetic emulsifiers as well as total volume as new applications areas open up.

## 5.6 Future Outlook

The introduction of totally new natural polymers for food use is unlikely as it is restricted by the large investment cost associated with obtaining the necessary legislative and regulatory approval. Therefore, it is likely that advancements will be made with respect to new combinations, applications areas, or technological

advances with respect to processing and manufacture of existing approved natural polymer-based additives or ingredients.

The use and development of natural polymers in foods is likely to continue and increase in coming years, however, there may be shifts from one source to another due to factors like sourcing issues, varying prices, and consumer preference changes. Frost and Sullivan (2013a, b) have identified several market drivers that are increasing the use of textural food additives and ingredients in general and natural polymers in particular, including:

**Adoption of new technologies**: The advent of novel technologies such as micro/nano-encapsulation in the food sector has allowed for the application of many ingredients, such as modified starches, hydrocolloids, and macromolecular emulsifiers to create core shell materials, or even serve both as shell material and as binding agents that improve process stability and textural properties of the final product. Micro/nano-encapsulation is used to improve chemical stability or bioavailability of other sensitive ingredients such as vitamins, functional food ingredients, and volatile aromas.

**A significant shift from synthetic to natural ingredients**: Health, wellness, and well-being are a mega trend where "natural" tags on products has a significant impact on consumer choice. This has led producers to develop all-natural products or to partially replace synthetic ingredients with natural ingredients/additives in their product offerings.

**Increasing consumption of convenience and performance foods**: High growth in the convenience food and prepackaged food sector has created more opportunities for natural polymer based textural food ingredients, especially in combination with the "natural" trend. In addition to convince food, textural ingredients play a key role in performance foods that tend to rely on specialized and sophisticated formulations that require functionally advanced ingredients. Although natural polymers have historically been used in the food industry to control the stability and improve the texture of food products, many consumers are becoming increasingly aware of their nutritional and health benefits. Examples include maintaining appealing texture in low-fat food products, prebiotics, and the use of structural approaches to enhance satiety.

In addition, the classical use of natural polymer in formulations, the manufacture of natural polymer-based microgels is likely to see an increase as well. This is due to the fact that microgels have potential in fat replacement as well as rheology and texture control, and they can be tuned for encapsulation, targeted delivery, controlled release, and satiety control applications (Shewan and Stokes 2013). Although it is believed that industrial scale manufacture is achievable for microgels in the food industry (as many processes are based on standard dairy unit-operations such as heating, shearing, membrane filtration, and spray drying), there is still considerable capacity for major advancements with respect to their manufacture and novel application areas.

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# Chapter 6
# Current Application and Challenges on Packaging Industry Based on Natural Polymer Blending

**S.T. Sam, M.A. Nuradibah, K.M. Chin and Nurul Hani**

## 6.1 Introduction

Currently, the packaging sector is a major consumer in the most industries. Plastic packaging is being increasingly used in medical products and healthcare as well as in the beverages and packaged foods. In year 2002, large amounts of different synthetic plastics, totaling about 200 million tons per year, are produced throughout the world (Zhang et al. 2002). Among them, packaging is the largest single market for plastics, about 12 million tons per year. Another statistic released by Pardos Marketing, an industrial market research company which specializes in plastics and their applications, shows that the global consumption of plastics in 2005 comprises mainly of packaging plastic, up to 33 million tons, polyethylene, whereas 4.8 million tons composed of polypropylene (Anonymous 2005).

The demand of synthetic petrochemical-based polymers as packaging materials has been rising because of their desirable mechanical properties, and thermal stability as well as their performance as good barriers to carbon dioxide, oxygen, and aromatic compounds. The main reasons why synthetic petrochemical-based polymers are being chosen as packaging materials are because of their relatively low cost and large availability. Although the synthetic petrochemical-based polymers have been widely used in a variety of packaging materials, the disadvantage is that they become a major source of waste after use due to their poor biodegradability. Hence, due to the increasing demand in the packaging industries with a concern of the environmental issue, the usage of natural polymers to produce biodegradable packaging materials is the correct action in terms to reduce waste disposal problems and to guarantee the quality of the product (Sam et al. 2014).

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O. Olatunji (ed.), *Natural Polymers*, DOI 10.1007/978-3-319-26414-1_6

**Table 6.1** Benefits of natural polymer-based packaging materials

| |
|---|
| – Biodegradable |
| – Supplement the nutritional value for foods |
| – Reduced packaging volume, weight, and waste |
| – Incorporated antimicrobial and antioxidants |
| – Low cost and abundant |
| – Annually renewable resources |

These degradable packaging options can be produced from two major types of natural sources:—(1) polysaccharides—such as starch, cellulose, chitin, and chitosan; and (2) proteins—such as soya, wheat gluten, and collagen/gelatine; derived from plant and animal resources as the substitution for their non-biodegradable petrochemical-based counterparts. Table 6.1 shows the advantages of natural polymer-based packaging materials.

Normally, industries' techniques to produce packaging-based natural polymers are injection moulding and blown film extrusion. Injection molding is a method to obtain molded products by injecting plastic materials molten by heat into a mold, and then cooling and solidifying them. The method is suitable for the mass production of products with complicated shapes, and takes a large part in the area of plastic processing. This type of technique is applied in food packaging industries.

Blow molding is a molding process in which air pressure is used to inflate soft plastic into a mold cavity. It is an important industrial process for making one-piece hollow plastic parts with thin walls, such as bottles and similar containers. Since many of these items are used for consumer beverages for mass markets, production is typically organized for very high quantities. The technology is borrowed from the glass industry with which plastics compete in the disposable or recyclable bottle market. The application for natural polymers blending is widely used in food packaging, bottles packaging as well as in medical/pharmaceutical industries.

## 6.2 Sources of Natural Polymers to Produce Packaging

### *6.2.1 Polysaccharides*

Starch, cellulose, chitin or chitosan, and pectin contribute to the formation of polysaccharide films. The impart hardness, crispness, viscosity, and gel forming ability to produce a variety of films. The nontoxic properties allow the biodegradation by enzymes and do not produce environmentally harmful byproducts. It also exhibits excellent gas permeability properties that improve the shelf life of the product without creating anaerobic conditions. Basically, the hydrophilic and composition of the polymeric chains that exhibit low moisture barrier properties is known as polysaccharide-based products (Coma 2013).

### 6.2.1.1 Starch

Starch is a natural polysaccharide that accumulates in plant seeds, leaves, tubers, and stalks. The main sources for the commercial production of starch are potatoes, corn, wheat, and rice. Starch has two main polymeric constituents which are amylose in which the glucose units are 1,4-α-D-linked together in straight chains and amylopectin in which the glucose chains are highly branched of 1,4-α-D-linked and 1,-α-D-linked glucose residues as shown in Figs. 6.1 and 6.2 (Bertuzzi et al. 2007).

Table 6.2 shows the amylase and amylopectin content in natural starches.

Starch is one of the less expensive biodegradable materials used for many non-food items such as textile sizing, cardboard, and paper making. In recent times, starch has been employed as the major polymer in thermoplastic compositions and has been processed into various materials such as utensils and it also has been used as raw material for film production (Canigueral et al. 2009).

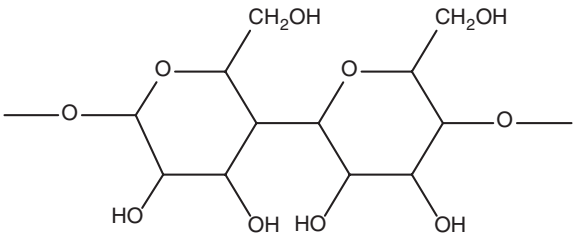


**Fig. 6.1** Amylose 1,4-α-D-linked glucose unit

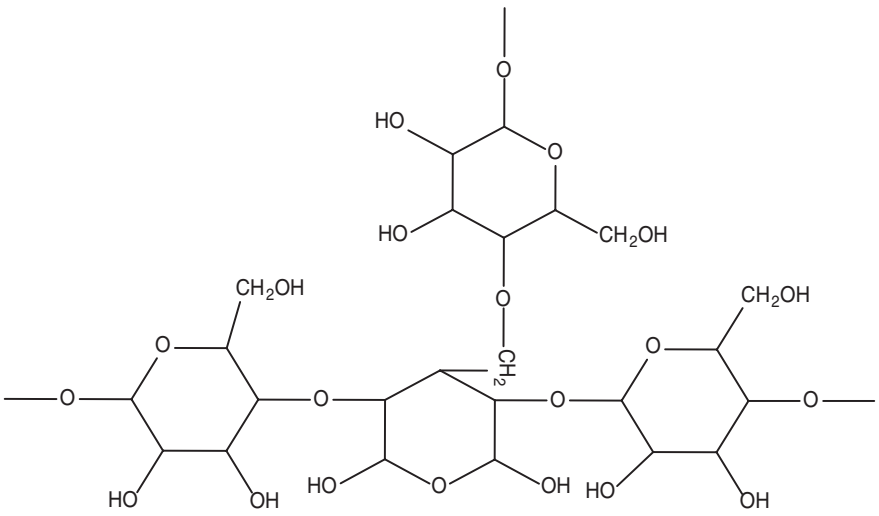


**Fig. 6.2** Highly branched amylopectin

**Table 6.2** Amylose and amylopectin content in starches (Veronica 2013)

| | Amylose (%) | Amylopectin (%) |
|---|---|---|
| Potatoes | 23 | 77 |
| Wheat | 20 | 80 |
| Rice | 15–35 | 65–85 |
| Corn | 25 | 75 |
| Banana | 17 | 83 |

The proportions of amylose and amylopectin in starch depend on the source, amylose content ranges from 10 to 20 %, and that of amylopectin is 80–90 %. Amylose is soluble in water and appears as a helical structure, whereas amylopectin chains are crystallized helical structure and cause the starch to occur physically as discrete granules. The starch granules show hydrophilic properties and strong intermolecular group through hydrogen bonding formed by the hydroxyl groups on the granule surface (Pillai et al. 2005).

Pure starch is a white, tasteless, and odorless powder and it is insoluble in cold water and alcohol. Starch can be used as a gluing or as thickening agent because it can dissolve in warm water. For starch-based materials, it is extremely brittle and has poor mechanical properties for packaging material. Starch alone cannot form films with suitable mechanical properties (high percentage elongation, tensile, and flexural strength) unless it is plasticized, blended with other materials, chemically modified, or modified with a combination of these treatments. Frequent plasticizers used include glycerol and other low-molecular-weight polyhydroxy compounds, polyethers, and urea (Peelman et al. 2013).

Starch is a fully biodegradable polymer where it can hydrolyze into glucose via microorganisms or enzyme and after that it will be metabolized into carbon dioxide, $CO_2$, and water, $H_2O$ (Lu et al. 2009). The starch itself has poor mechanical properties; this limitation is overcome by blending with other polymers. To prepare completely biodegradable starch-based biocomposites, starch is usually blended with aliphatic polyesters (PLA and PHA), polyvinyl alcohol (PVA), and other types of biopolymers. The most common polyesters to be used with starch is poly(β-hydroxyalkanoates) (PHA), which is obtained by microbial synthesis, and polylactide (PLA) or poly(ε-caprolactone) (PCL), which is derived through fermentation and chemical polymerization, respectively (Wang et al. 2008).

For starch-based materials, the hygroscopic properties depend on the temperature, relative humidity, RH, and nature of the substituent. The availability of hydroxyl groups on the starch chains has potential to display reactivity specific to where they can oxidize and reduce and might take part in the formation of ethers, esters, and hydrogen bonds (Tomasik and Schilling 2004).

#### 6.2.1.2 Cellulose

Application of cellulose nanofibers in polymer reinforcement is a relatively new research field. Cellulose is the most abundant organic molecule on earth, since it

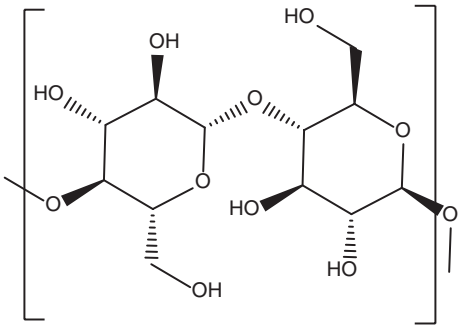


**Fig. 6.3** Chemical structure of cellulose

is the main component of plant cell walls like cotton, hemp, and other plant-based material. Uniquely, cellulose also can be synthesized by algae, tunicates, and some bacteria (Iwamoto et al. 2007). The glucose units in cellulose are linked by glycosidic bonds, but there are different α glycosidic bonds found in glycogen and starch. Cellulose has more hydrogen bonds which make it tougher fiber compared to glycogen or starch.

Regardless of its virtual chemical simplicity, the physical and morphological structure of native cellulose in higher plants is complex and heterogeneous. Besides, the molecules of the cellulose are thoroughly connected with other lignin and polysaccharides which cause more complex morphologies. It is a linear polymer of β-1,4-linked D-glucose between the anhydroglucose repeating units that contain highly ordered crystalline regions with more disoriented amorphous parts. Due to their high stiffness, strength, biodegradability, renewability, and light weight, the application and production of nanoscale cellulose fibers in composite materials have gained much attention (Kamide 2005).

The limited application of cellulose nanofibers to date may be due to the separation of plant fibers into smaller basic element which is a challenging process. Besides the nature of starch is hydrophilic, the packaging materials from this material have low water vapor barrier that causes poor mechanical properties and limited long-term stability. Addition of cellulose fibers to starch-based films will reduce 35 % of the water vapor permeability after plasticized with glycerol and decreased about 14 % after the addition of cellulose fiber. The tensile strength and Young's modulus will increase without changing the value of elongation at break (Dias et al. 2011). Figure 6.3 shows chemical structure of cellulose.

#### 6.2.1.3 Chitin and Chitosan

The most abundant polysaccharide on earth after cellulose is chitosan. Chitosan is produced from chitin by deacetylation to remove the acetyl group. Chitin is a main constituent of the shells of crustaceans like crab, shrimp, and crawfish. It is inexpensive, biodegradable, biocompatible, and nontoxic. Compared to chitin, chitosan

is more versatile due to its structural features and potential to develop films, having different properties and barriers (Fernandez-Saiz et al. 2010).

Chitosan is the second most abundant polysaccharide on earth after cellulose. This biopolymer is mostly available from waste products in the shellfish industry, and therefore commercial supplies are currently in abundance. It can also be acquired from fungal cell walls of the chitin component. There are three reactive functional groups chitosan which are amino/acetamido group, primary hydroxyl group, and secondary hydroxyl group at positions of C-2, C-3, and C-6, respectively. The main reasons for the differences between their physiochemical and structural properties are the amino contents (Chen et al. 2008a, b).

The properties of chitosan are biocompatible, biodegradable, and nontoxic which make it a suitable material for packaging films. Besides the positive charge of chitosan, it readily binds to negative-charged surfaces thus making chitosan a bioadhesive material. The presence of $NH_2$ causes the reaction of chitosan much more versatile compared to cellulose (Rinki and Dutta 2008). Chitosan is readily soluble in dilute acidic solutions less than pH 6.0. Chitosan possesses primary amino group with a pH value of 6.3 and that can be considered as a strong base. The pH significantly changes the charged state and properties of chitosan due the presence of amino groups. Starch and chitosan blends exhibit good film property which featured to intramolecular and intermolecular hydrogen bondings that appeared between amino and hydroxyl groups on the backbone of two components (Lu et al. 2009).

## *6.2.2 Proteins*

### 6.2.2.1 Soya

Soya products including soya powder and soya concentrate are commercially available. The cost of soya powder is cheaper than other soya products such as soya protein concentrate and soya protein isolate. In fact, the soya powder is similar to polysaccharide-based natural polymer as it is hydrophilic in nature. According to Swain et al. (2004), the soya beans contain 18–20 % of oil, 40–55 % of protein, 25–30 % of carbohydrate, and 3 % others. Figure 6.4 shows the major constituents of soya bean uses.

The soya bean began to gain popularity in Asia starting in the mid 1960s. The awareness of the soya beans as a low-cost and high-quality fortifier for traditional grains, primarily the weaning foods, increases the demand of soybeans. The production of the soya beans to become flour or powder has undergone several processes (David et al. 2006).

The soya powder which is a byproduct in the commercial extraction process of soya protein isolate (SPI) seems to have high protein compared to other flour as it is produced from carbohydrate-rich grains. The whole soya bean was heated and grinded with hammer mill, and 97 % will pass through a mesh screen. The flour

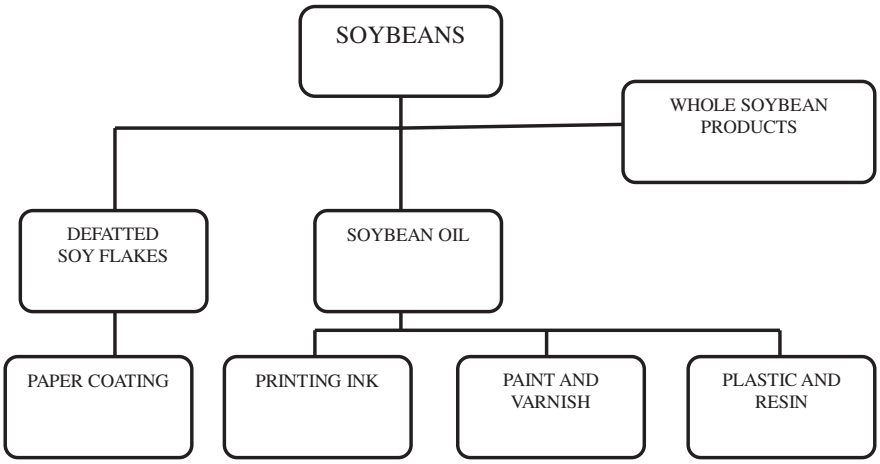


**Fig. 6.4** Major constituents of soya bean uses (Swain et al. 2004)

that passing through the finest mesh screen has the highest protein content and the moister heat treatment produces more quality and nutritional value (David et al. 2006).

Soy-based plastics can be divided into two main segments which are polyurethane using soy polyols and thermo sets. Each segment has great growth potential, from the farmers who grow the soybeans to the manufacturers who utilize them to the end user who benefits from a high-quality product (Stepto 2006).

The first documented work in producing plastic from renewable resources came from Henry Ford around 1910. He was interested in making plastic from plastic waste and he succeeded in 1940 by producing a 'plastic car' from soya bean waste mixed with other components to increase strength. Then, a new awareness in relation to the human impact on earth gave way to do research in the area of plastic. The alternative way that has been taken is by producing biodegradable plastics (Narayan 2009).

As more manufacturers look for options to high petroleum prices, soy-based plastics offer a possible choice. The multipurpose and lower production costs make soy plastics the main area for rapid growth.

#### 6.2.2.2 Wheat Gluten

Plant protein from wheat such as wheat glutenins is the abundant co-product with low price that derive from readily available resources and it is biodegradable. Wheat is one of the three most important crops in the world which include maize and rice. India becomes the second largest producer of wheat in the world. The main components of groups in wheat are starch and protein. Wheat gluten is a large extended polypeptide polymer without globular structure (Shewry and Halford 2002).

**Table 6.3** Wheat protein classification based on solubility (Wieser 2007)

| Groups | Proteins | Function | Molecular weight | Solubility | Distribution | Average protein content (%) |
|---|---|---|---|---|---|---|
| Non-gluten proteins | Albumins | Metabolic and cyto-plasmic proteins | 20,000 | Water | Embryo | 15 |
| | Globulins | Storage and cyto-plasmic proteins | 20,000–200,000 | Dilute salt solutions | Embryo and aleuronic layer | |
| Gluten Proteins | Gliadins | Storage proteins | 30,000–60,000 | Ethanol (70–80 %) | Endosperm | 45 |
| | Glutenins | Storage proteins | 8000 several millions | Dilute acid/alkali solutions | | 40 |

The term "gluten" mainly refers to the proteins due to the role in determining the unique baking quality of wheat by conferring water absorption capacity, cohesiveness, viscosity, and elasticity on dough. Basically, wheat gluten is attained when the wheat dough is washed to remove starch granules and water-soluble constituents. It contains hundreds of protein components that are present either as monomers or linked by interchain disulfide bonds as oligo- and polymers (Lagrain et al. 2010).

Table 6.3 shows the classification of wheat gluten based on the solubility. Basically, they are classified into two main groups which are non-gluten proteins and gluten proteins. Gluten proteins show low solubility in water or dilute salt solutions due to the presence of nonpolar amino acid. Besides, it is also due to the presence of high amount of glutamine and proline residues as it has nonpolar side chains (Wieser 2007).

There are about 75 % proteins with 35–45 % glutenins and 40–50 % gliadins content in industry. The difference between gliadins and glutens is that gliadins have a single-chain polypeptides whereas glutenins have multiple-chain polymeric proteins that interlinked by intermolecular disulfide and hydrogen. Wheat gluten can fully degrade without releasing toxic products, so it is the best candidate to develop biodegradable materials (Yuan et al. 2010).

#### 6.2.2.3 Collagen/Gelatine

Gelatine is generally produced by partial hydrolysis of collagen that was extracted from the bones, connective tissues, organs, and some intestines of animals. Gelatine is a translucent, colorless, odorless, brittle, and nearly tasteless solid substance, derived from the collagen inside animals' skin and bones. It is a high

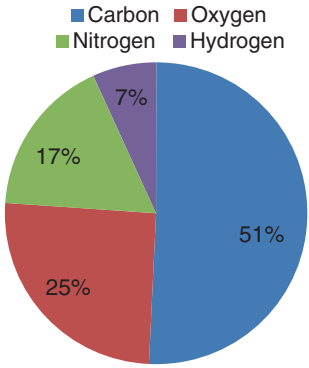


**Fig. 6.5** Composition of gelatine

molecular weight polypeptide composing of amino acids mainly glycine (27 %), hydroxyproline, and proline (25 %) (Iwai et al. 2005).

Pie chart in Fig. 6.5 shows the composition of gelatin. It is composed of 50.5 % carbon, 25.2 % oxygen, 17 % nitrogen, and 6.8 % hydrogen. Gelatine consists of rigid bar resembling molecules that are arranged in fiber and interconnected by covalent bonds. These molecules have three polypeptide chains arranged in a triple helix that is stabilized by hydrogen and hydrophobic bonds (Wang et al. 2012).

Gelatine has unique functional properties which make it widely used in cosmetic, pharmaceutical, cosmetic, food, and packaging industries. However, the pure gelatine is brittle and has high moisture absorption. Therefore, gelatine is usually blended with other polymers to prevail over the weakness. For example, blend of gelatine with hydrophilic molecules like chitosan could significantly improve the properties (Lin et al. 2012).

## 6.3 Industries' Techniques to Produce Packaging-Based Natural Polymers

### *6.3.1 Injection Molding*

Injection molding is a process where polymers are heated to an elevated plastic state and pushed at a high pressure into a mold cavity, which subsequently causes the polymer to solidify into a desired shape. The molded part, or better known as the molding, will then be removed from the cavity. Figure 6.6 depicts the process of injection molding which starts from clamping, injection, cooling, and finally ejection of the product. The cycle of production commonly varies in between 10 and 30 s, but cases of cycle that exceed one minute are not uncommon. Multiple moldings can be produced per cycle as the mold can have more than one cavity. Figure 6.7 shows a typical 2D drawing of an injection molding machine which consists of two major segments, injection segment and clamping


**Fig. 6.6** Process cycle of injection molding

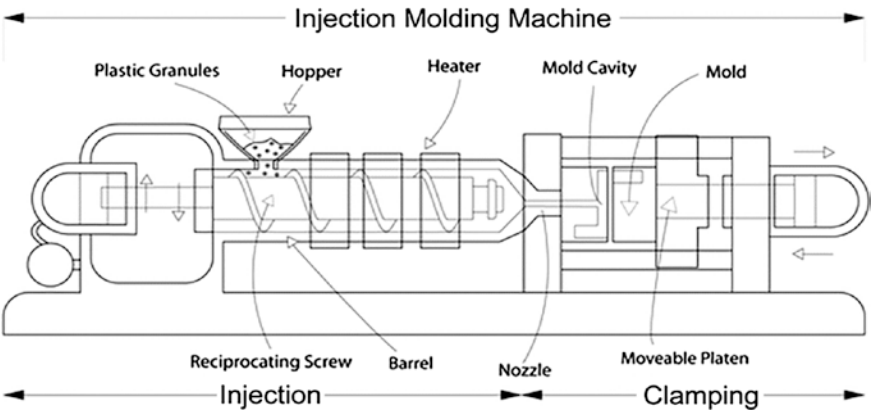


**Fig. 6.7** Injection molding machine

segment. In manufacturing process, this method is the most popular method in fabricating plastic parts which varies greatly in their complexity, size, and application. For example, injection molding is used to fabricate thin-walled plastic parts such as plastic housings, which are then used in a variety of materials including consumer electronics, household appliances, power tools, automotive dashboards, and medical devices such as syringes and valves. Open containers such as buckets and items such as toothbrushes and plastic toys are also products made from injection molding. It can be said that injection molding is generally the most common molding process in thermoplastic manufacturing. One of the main advantages of injection molding is the possibility of producing intricate and complex-shaped products and it is also very precise. However, this method is only feasible when there is a requirement for mass production of products with complicated shapes as this process is costly. In addition, thermoplastic moldings may contain defects such as weld lines, shrinkage, splash marks, and distortion but corrective measures and control of the process itself usually play a vital part in achieving an excellent quality product.

Recently, many researchers have utilized lignocellulosic filler to replace conventional fiberglass fillers in thermoplastic composites in manufacturing plastic parts (Nourbakhsh et al. 2011; Rahman et al. 2011; Azaman et al. 2013). Processing temperature of lignocellulosic thermoplastic composites is usually below 230 °C in order to prevent/reduce fiber degradation (Sanadi et al. 1998). A study had been conducted by Azaman et al. (2014) on the suitability of

lignocellulosic polymer composites in forming a shallow, thin-walled part mold with minimal residual stress distribution with injection molding method. There are three important parameters involved which are the mold temperature, cooling time, and packing pressure, and the optimal conditions for each of the parameters had been investigated. From the report, it had stated that if the mold temperature is too low, crystallization problems start to occur but if the mold temperature is too high, the properties of lignocellulosic polymer composites will degrade. An increase in cooling time will cause a drop in the tensile residual stresses near the wall of the mold while an increase in packing pressure will create higher inner stresses within the parts. Therefore, through numerical distribution analysis done by the authors, they had found out that the optimum parameter range for the mold temperature would be around 40–45 °C. As for the cooling time, the optimal range is between 20 and 30 s while the optimal packing pressure is $0.85P_{inject}$.

Yuqiu et al. (2012) studied on pultrusion technique to produce long fiber biocomposite pellets which comprises jute fiber and poly(lactic acid), a biodegradable thermoplastic matrix, for the purpose of injection molding. Jute/PLA composites were successfully fabricated by injection molding process and its mechanical properties were then investigated. It was reported that 250 °C molding temperature is the most suitable temperature for pultrusion process of jute/PLA long fiber pellets because of several factors which include less degradation of jute due to heat, improved impregnation and production efficiency as well as satisfactory mechanical properties. In addition to this, with the incorporation of jute fibers, the tensile modulus and the izod strength had improved but the tensile strength suffered a slight drop. This suggests that injection molding method has the capability to produce high-quality products that are environmental friendly as it can fabricate products made from natural polymers.

A 100 % natural-based biocomposite formed by blending egg albumen (EA), a natural source of protein with chitosan (CH), a source of glycerol was successfully made through injection molding method (Martín-Alfonso et al. 2014). In particular, CH acted as a physicochemical modifier additive in different concentrations of blends. The general idea of fabricating this biocomposite is to improve the suitability of these composites for specific applications and its properties. From the results shown in the report, the DMTA spectra were found out to be comparable to low-density polyethylene (LDPE), a commercial polymer. EA/CH composites had showed intensified behavior at high temperature when compared to LDPE. Tensile strength and elongation at break were reported to decrease with increasing CH content. The glass transition temperature, $T_g$, of the composites as well as the water absorption capacity was reduced. Biocidal activity against gram-negative bacteria (*E.* coli) was not significant. From the results, it can be deduced that there is an apparent limitation of these biocomposites in areas such as food packaging but the low diffusion efficiency of chitosan had opened up the possibilities in areas such as surgical dressings, water filtration, fruit coating, tissue engineering, and drug encapsulation.

Another innovative process that is widely used in plastic manufacturing industry to enhance molding quality using a lower amount of polymer is the

gas-assisted injection molding process. The principle of operation is basically to void out the thick internal sectional area with high-pressure gas injection to further lower down the use of polymers as compared to the conventional method. The gas acts on the molten resin by pushing it forward and then keeps it at high pressure during cooling. Over the past years, researches on this particular method had been focused only on conventional petroleum-based polymers in areas such as filling simulations (Chen et al. 2008a, b), gas channel design (Marcilla et al. 2006), and molding quality (Castany et al. 2003). However, Yam and Mak (2014) had successfully extended this gas-assisted injection molding process by utilizing eco-composites polymers made from rice husk-filled polypropylene in dissimilar compositions. The weight ratio of the product made from this technique had reduced a total of nearly one-third of the weight ratio of the product made through conventional injection method, which indirectly lower the amount of petroleum-based polymer required. It was also reported that this method also reduced the mold clamping force and injection pressure used, which in turn saved up a total 20 % energy cost. This approach had not only utilized an agricultural waste to minimize the dependency of petroleum-based polymer, but also help to reduce environmental problems and increase the manufacturers' economic benefits.

### *6.3.2 Blown Film Extrusion*

Blown film extrusion process is one of the most common polymer packaging processes in the world. Figure 6.8 shows a general blown film extrusion process, where thin-walled tube was formed from the vertical extrusion of plastic melt through an annular slit die. At the center of the die, air is introduced to blow up the tube like a balloon. A high-speed air ring, which is mounted on top of the die, cools the hot film by blowing air onto it. The tube of film is continuously cooled down as it moves upward until it is flattened by nip rolls to create 'lay-flat' tube of film. This lay-flat tube is then moved down the extrusion tower via rollers. Polymers such as low-density polyethylene and high-density polyethylene are the common plastic materials used in blown film production. Typical applications of the blown film product include industry packagings such as shrink film, stretch film, and bag film, and also consumer packagings such as food wrap film, fill & seal packaging film, and packaging bags. Blown films are also being utilized in other areas such as medical and agricultural industries.

The possibility of thermoplastic starch films made from blown film extrusion technique had gained interest of researchers over the past decade. Mats et al. (2008) had successfully investigated the suitability of TPS made from the mixing of potato starch, glycerol, and water on blown film extrusion method. The results on melt tenacity showed that plasticizer such as glycerol is important in order for the extrudate to expand satisfactorily. The tendency for bubbles to form in the extrudate and rupturing of the stretched melt portrayed the weakness of this material for this particular method. However, Olivia et al. (2013) successfully showed

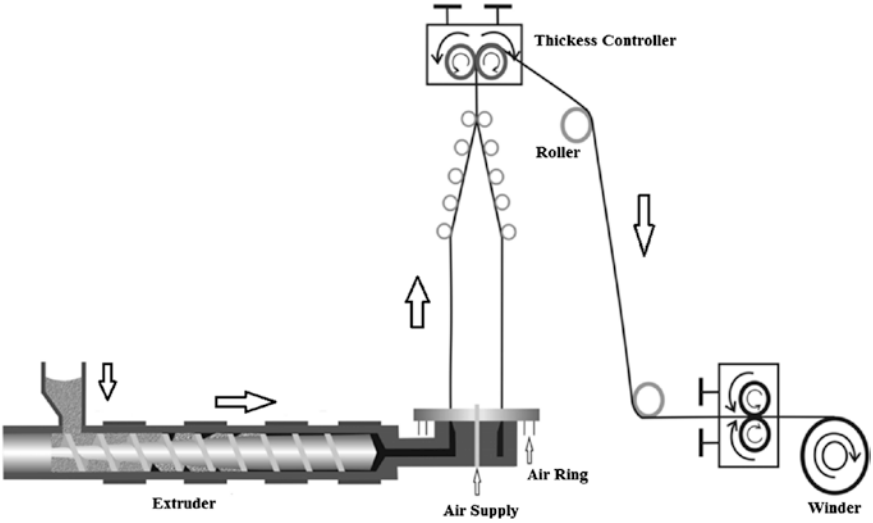


**Fig. 6.8** Process flow diagram of an extrusion blown film (Li et al. 2014)

that natural polymeric films that are suitable for food packaging applications can be developed by this blown film extrusion technique through the development of films made from native and acetylated corn thermoplastic starches (TPS). The processability of the films had been proven by the ability to withstand the airflow pressure and the tension exerted by rolling, without signs of tearing of the films. The blowing process used had developed homogeneous films without defect/bubbles on all TPS formulations, supported by visual observation and SEM imaging. However, the films appeared to be sticky due to the exposure to a humid environment and the nature of glycerol being hydrophilic. Acetylated corn TPS had lower water vapor permeability than native corn TPS. As for gas permeability, all films presented selective gaseous permeability which can be proven useful in developing food packaging materials. An increase in tensile strength and a decrease in flexibility and water vapor permeability were shown by the films that were stored in a controlled environment of 20 °C and 65 % RH.

Although there is a bright future for packaging materials to be made solely from plasticized starch (TPS) through blown film technique, the limitations in their mechanical and water barrier properties had restricted their areas of utilization. Patrícia et al. (2014) developed a novel approach to use natural biodegradable polymer, poly(butylene adipate-co-terephthalate) (PBAT) with citric acid (CA) as a compatibilizer with TPS made form cassava starch in an effort to improve these properties. PBAT was known to be flexible and able to fully degrade in a span of few weeks through enzymatic actions (Ren et al. 2009). The authors also studied the effect of uncatalyzed and catalyzed CA on the properties of the blown films. The catalyst used in their experiment, sodium hypophosphite (SHP), had enhanced the action of citric acid in the microstructure of the blown films and their

tensile strength and modulus. TPS/PBAT films with catalyst show higher thermal stability than uncatalyzed films. Most importantly, the reactive extrusion process was smooth and efficient when it comes to films with CA which acted as a compatibilizer.

Thermally imposed shrinkage is a common issue when it involves shrink films produced through blown film technique. Supak and Sirilux (2011) had attempted to reduce shrinkage of blown films by incorporating natural runner (NR) latex in low-density polyethylene (LDPE) to form LDPE/NR composite films. It was found that with increasing NR content, the degree of crystallinity also showed similar trend as well. This result was due to the semicrystalline LDPE acting as a nucleating agent, which then induced crystallization of the NR phase during the blown film process. The impact resistance and tear strength improved with increasing NR latex content but the mechanical properties such as tensile strength and hardness of LDPE/NR composite films declined. Heat shrink ability test was employed to determine the shrink ability of the LDPE/NR composite films and the results showed increased shrink ability with higher NR content. Since NR possesses a higher entropy level, heat was applied to the films. The films were able to recover to its original form.

### *6.3.3 Drawbacks in Industrial Techniques to Produce Packaging-Based Natural Polymers*

There are several drawbacks that the polymer processing industry will face when packaging-based natural polymers were to be produced in an industrial scale. Generally, natural-based polymers such as starch, cellulose, chitin, and protein might face microbial and dust contamination due to their prolonged exposure to the external environment during the period from collection, transport, and storage up until the point of processing (Kulkarni et al. 2012). The difference in each batch of raw materials used is also one of the disadvantages as natural polymers may come in different physical and chemical compositions due to the difference in climate, geography, collection, and storage time (Oliviero et al. 2010; Kulkarni et al. 2012). Hence, the production output from the process will be greatly affected due to the inconsistency in terms of physical, mechanical, and chemical properties of the raw material. Natural polymers are also sensitive to high temperature, causing degradation to occur during the processing. For example, a film of oat starch was produced using two methods which are solution casting and blown film extrusion (Galdeano et al. 2009). In comparison, both the films showed drastic difference in terms of tensile strength as the films produced through casting method were approximately eight times higher than films that were produced through extrusion method. As compared to solution casting, it was reported that the higher temperature employed during the extrusion processing, coupled with shear stress, had caused degradation of the starch chains to occur, and thus affecting the mechanical properties of the film. Similar results were also obtained when

equal parts of soy protein blended with acetylated high-amylose corn starch were injection molded, where sample degradation starts to occur at temperature above 150 °C (Huang et al. 1999). In another case, the feasibility of producing thermoplasticized blown film of zein which is typically found in corn and classified in the class of prolamine protein was investigated (Oliviero et al. 2010). From the tensile results in the report, only one batch of the thermoplasticized zein-based material was able to form film with excellent tensile properties. Protein agglomeration and the lack of α-helical structures in the films were reported to be the contributing factors in the decrease in film quality in terms of mechanical strength. In addition, the inconsistency in the properties of the films obtained for each batch of processing had further proved the downside in utilizing blown film extrusion technique for natural polymers. Next, complications during injection molding in terms of mechanical constraint were clearly shown due to the lackluster characteristic of sunflower oil cake in terms of plasticity behavior, which is a natural polymer made up of mixture of lignocellulosic fibers and proteins (Rouilly et al. 2006).

## 6.4 Application of Natural Polymers Blending in Packaging Industries

### *6.4.1 Food Packaging*

Biodegradable films have the ability to reduce, or completely replace some traditional polymeric packaging materials for specific applications. Naturally, biodegradable packaging materials were produced from natural polymers that are capable of being degraded by microorganisms (bacteria, fungi, and algae) through composting processes to produce breakdown compounds such as carbon dioxide, water, methane, and biomass. To compete with the existing food packaging, hence, bio-based packaging must perform such as conventional packaging and present all the requirement functions of containment, protection, preservation, information, and convenience in a legally and environmentally compliant manner, and cost-effectively.

Biodegradable polymers from natural source were divided into two groups: those which are non-edible and edible. Biodegradable materials derived from food resources such as polysaccharides, proteins, and lipids are edible; various researches have been reported due to their potential abilities to replace traditional plastics and act as food contact edible films and/or coatings. Table 6.4 illustrates the potential source to produce food packaging.

An edible/biodegradable film is produced from food-derived ingredients in a thin layer using wet or dry manufacturing processes. The resulting film should be a free-standing sheet used over the food as wrapping or could be used between food components for separation. In contrast, edible coatings are materials which can be applied directly to the surfaces of food products by dipping, spraying, or panning. Edible packaging formats can be consumed with, or as part of, the food

**Table 6.4** Sources of food packaging (Hanani et al. 2014)

| Non-edible | Edible | | |
|---|---|---|---|
| Starch + PE | Polysaccharides | Protein | Lipid |
| Polysaccharides | Chitin/Chitosan | Collagen/gelatins | Bees wax |
| Polylactic acid (PLA) | Starch | Soy proteins | Carnauba wax |
| | | Wheat gluten | Free fatty acids |
| Polyvinyl alcohol | Pectines | Whey | Oils |
| | | Corn zein | |

product in question, but they may fulfill other functions like acting as carriers for target food additives (antimicrobial agents, antioxidants, flavorings). Edible films and coatings may also be used to inhibit migration of moisture, oxygen, and carbon dioxide, and/or to improve the mechanical integrity or handling characteristics of the food (O'Sullivan et al. 2006). Table 6.4 summarizes about the natural polymers and its blends that can be applied in the food packaging industries.

### *6.4.2 Pharmaceutical Industries*

Pharmaceutical packaging can be described as the technology to protect the products for distribution, storage, and until the process involved in the finishing of pharmaceutical products. Packaging of pharmaceutical products is important in the maintenance of their quality and effectiveness. Thus, all packaging materials must be carefully evaluated via testing of selected materials, sterilization, storage, and stability studies (Singh et al. 2011). Table 6.5 describes about the functions of packaging for the pharmaceutical industries.

In maintaining the quality of products, the type of materials used for packaging must not produce any adverse affect on the quality of pharmaceutical product

**Table 6.5** Functional parameters of eco-friendly pharmaceutical packaging material

| Parameters | Description |
|---|---|
| Barrier Protection | Provides protection against moisture, light, oxygen and temperature variations |
| Biology protection | Provides protection against biological contaminants |
| Physical protection | Ensures protection against any physical damage |
| Information communication | Conveys information on the correct usage of dosage forms, their contents, their provenance, side effect, and warnings |
| Identification | Easy identification of the product |
| Security | Protection from small children and against counterfeiting |
| Convenience | Increase consumer access to products and improve distributions, handling, selling, and using such products |
| Marketing | Differentiate a product and/or to convey a certain message or brand image to highlight the pharmaceutical aspects for consumers |

through absorption, chemical reactions, or leaching of packaging materials. In addition, it must also be fabricated with minimal complexity, low cost, and good consumer acceptance (World Health Organization 2003).

There is much concern for eco-friendly, natural resource-based packaging in the pharmaceutical industry. Advent of new technology has promoted the biodegradable packaging as cost-effective materials. This has indeed prompted many companies to switch over to biodegradable packaging. However, the development of eco-friendly pharmaceutical packaging materials technology is still in the phase of growth.

Various development projects and research exist at the early stage targeted at developing biodegradable and eco-friendly packaging materials. Thus, the design of the packaging needs to meet the standard requirement to compete with the existing packaging materials. There has been relatively limited focus on developing packaging for pharmaceutical industries compared to food packaging. Rubber and cellulose have received the bulk of the attention to produce pharmaceutical packaging. Rubber is obtained from latex found in the sap of some plants. It is used in pharmaceutical packaging as closures (Cooper 1974). Among the derivates of cellulose, cellulose acetate is widely used in pharmaceutical packaging and other laboratory works (Haugaard and Festersen 2000).

### *6.4.3 Plastics Packaging*

The biodegradable plastic market is gradually gaining significance in the vast global packaging industry. Rising concerns over environmental hazards, carbon emission, and waste reduction lead toward 'green packaging,' which are the factors likely to boost the market for biodegradable plastic packaging solutions. Contributing further to the growth of the biodegradable plastic packaging market includes consumers' and retailers' acceptance for eco-friendly packaging; support for biodegradable bottle and biodegradable packaging from retailers; and escalating oil prices boosting the demand for alternative packaging materials. Furthermore, manufacturers are opting for better materials made from renewable sources for packaging purposes thus keeping them out of the landfills.

Environmental friendliness and sustainability have become basic qualifying criterions for all packaging products. In this regard, the biodegradable plastic packaging market is at a distinctive advantage since biodegradable plastic naturally has properties which make it one of the easiest materials to recover and recycle, or else decompose in nature. Biodegradable plastic packaging has a competitive advantage over other packaging materials, which makes it easier to recycle, reduce, and reuse to raise its eco-friendly profile. Table 6.6 shows the various literature reports on the potential sources of natural polymers blends that can be used in the packaging application. Blends from the natural polymers are classified as the polymer that is easy to biodegrade; hence, their usage in packaging industries should be expanded.

**Table 6.6** Literature reports on the potential source of natural polymers blends that can be used in the packaging application

| Title of paper | Polyolefins | Reference |
|---|---|---|
| Electret-thermal analysis to assess biodegradation of polymer composites | LDPE/starch blends | Ratanakamnuan and Aht-Ong (2006) |
| Effect of compatibilizer on the biodegradation and mechanical properties of high starch content/low-density polyethylene blends | LDPE/starch blends | Thakore et al. (2001) |
| Photo biodegradation of low-density polyethylene/banana starch films | LDPE/starch blends | Roy et al. (2007) |
| Studies on biodegradability, morphology and thermo mechanical properties of LDPE/modified starch blends | LDPE/starch blends/starch phthalate | Garg and Jana (2007) |
| Soil burial of Polyethylene-g-(Maleic Anhydride) Compatibilized LLDPE/Soya powder blends | LDPE/soya powder blends | Sam et al. (2011) |
| Thermal degradation of biodegradable blends of polyethylene with cellulose and ethylcellulose | LDPE/cellulose/ethylcellulose | Pedroso and Rosa (2005) |
| Linear low-density polyethylene/soya powder blends containing PE-g-MA copolymer as a compatibilizer | LDPE/soya powder blends | Sam et al. (2009) |
| A new approach for morphology control of poly(butylene adipate-co-terephthalate) and soy protein blends | poly(butylene adipate-co-terephthalate) (PBAT)/soy protein concentrate (SPC) | Choi et al. (2006) |

## 6.5 Conclusion

The rising ethical awareness and 'green consumerism' among the consumers had leaded the researchers to put more efforts in the development of green products. To this effect, there has been a rapid increase in the interest in environmental and ethical issues in consumer attitudes. Consumers are playing the important roles in the environmental problems by recycling and choosing environment friendly products and ways of life. There are relatively few studies about the impact of environmental preferences in the actual product or brand choice situations, instead of intention to buy.

Many consumers fail to admit the connection between their buying decision and various environmental consequences if there is no environmental information, such as labels, to remind them of it. Other reasons include the lack of

supply of environment friendly packaging options in the marketplace and consumers' inability to distinguish between the more and less environment friendly package alternatives (Bech-Larsen 1996; Thøgersen 1994). As a final conclusion, the production of green packaging polymers made up by incorporation of natural polymer into plastic-based petroleum has opened a new chapter in the packaging industry.

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# Chapter 7
# Application of Natural Polymers in Engineering

**Amany A. Aboulrous, Tahany Mahmoud, Ahmed M. Alsabagh and Mahmoud I. Abdou**

## 7.1 Introduction

### *7.1.1 Role of Natural Polymers in Nonrenewable Energy (Drilling Muds)*

A drilling fluid or muds is used in a drilling process in which the fluid is pumped from the surface, down the drill string, through the bit, and back to the surface via the annulus (Fig. 7.1). The drilling fluid or muds is essential to maintain an effective and productive oil well drilling process. Drilling muds are mainly composed of liquid (i.e., water, brine, or oil) and solid materials (i.e., clay, barite, polymer, and chemical additives). Unfortunately, drilling fluid's composition has become more complex to satisfy the demand and challenges of drilling operations. The materials used to satisfy these demand can be corrosion inhibitors, weighting agents, lubricants, biocides, detergents, defoamer, emulsifiers, surfactants, lost

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O. Olatunji (ed.), *Natural Polymers*, DOI 10.1007/978-3-319-26414-1_7

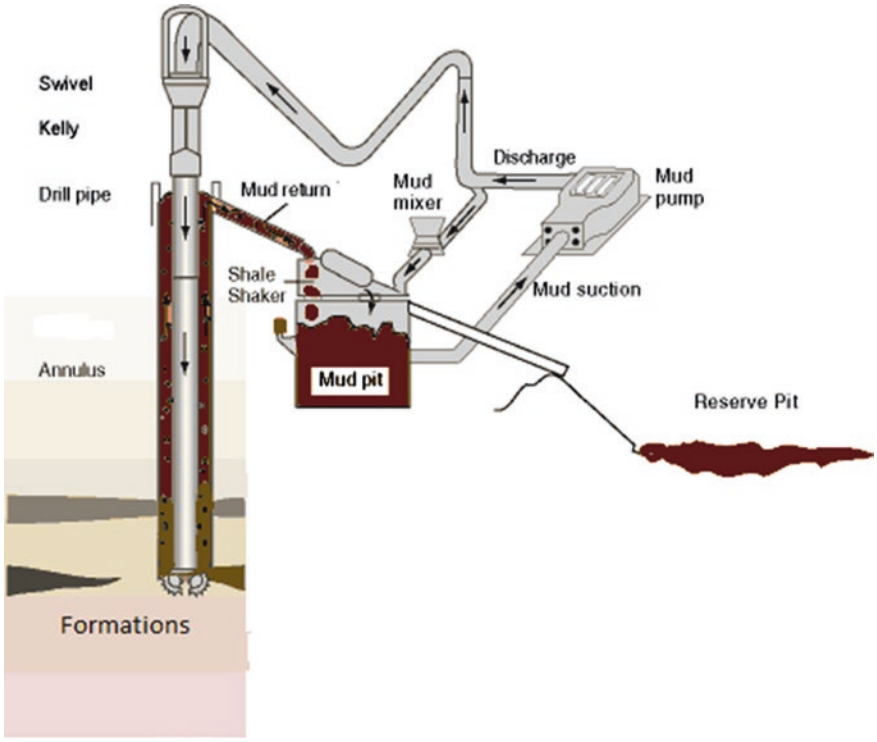


**Fig. 7.1** Drilling fluid circulating system

circulation agents, viscosifiers, shale inhibitors, and others (Darley and Gray 1988; Fink 2003; United States Government 2015).

Drilling muds perform many tasks during its circulation into the well (Growcock and Harvey 2005) as shown in Fig. 7.1 such as:

1. Generate, suspend, and remove drill solids (cuttings) from borehole in the ground.
2. Cool, clean, and lubricate the bit.
3. Maintain the stability of the borehole.
4. Sealing the permeable formations.
5. Control the corrosion.

#### 7.1.1.1 Classification of Drilling Muds

The drilling muds can be divided into five categories as follows:

***Gas-Based Drilling Muds***

This type of drilling muds is used when special conditions exist (i.e., hard rocking drilling). Compressed dry air, natural gas, mist, or foams can form gas-based

drilling muds plus chemical additives (Quintero 2002). There are two major limitations for this type of drilling muds:

A. The possibility of explosion, so it is recommended to use gas detectors while drilling with gas-based drilling muds.
B. This type was not recirculated and materials were added continuously.

***Water-Based Drilling Muds***

They were the simplest, oldest, and cheapest type of drilling fluids. They mainly consist of three components: water (fresh, brine, or saturated salt), clay (bentonite, kaolinite, or illites), and other chemicals. The type and the quantity of the other chemicals depend on the local conditions at the well and on the salt concentration. The primary functions for the clay are to provide the initial viscosity to suspend the drilling cuttings and decrease the fluid loss by forming film on the formation of the well. This type is generally nontoxic to the environment and humans (U.S. Environmental Protection Agency 1993).

***Polymer-Based Drilling Muds***

Natural polymers are added to inhibit both corrosion and degradation of polymers by $O_2$, $CO_2$, and $H_2S$ and they prevent shale sloughing so it is suitable for drilling shale well (American Petroleum Institute 2004). They have high shear-thinning ability at high shear rate

It consists of fresh or sea water, KCl, viscosity building polymer (xanthenes), CMC or stabilized starch, caustic soda, and lubricants. This type has also high shear thinning and high true yield strength.

The main advantages of this type are: It supports the bit hydraulics and the bore hole stability. This type does not cause formation damage due to its low solid contents. It is suitable for drilling at temperature up to 250 °F (121 °C) (Luheng 2014).

***Oil-Based Drilling* Muds**

They consist of oil (i.e., diesel oil, mineral oil, and so on) and minimum quantity of water if they had higher quantity of water, they would be called invert emulsion Muds. The water is added in this type of muds to react with the other additives and enhance the rheological properties. Organophilic clays or colloidal asphalts were used also to control the rheological and the filtration properties (Rodolfo and Tailleur 1955). Emulsifiers are used to stabilize the formulation of this kind of muds (Zuzich and Blytas 1994).

This type of muds has been used to gain good lubricity at high temperature (i.e., high angle drilling) where water-based muds may be thermally unstable, for shale formation drilling and to minimize the corrosion (Zuzich et al. 1995; Blytas et al. 1992).

The main disadvantages of this kind of muds are the environmental limitations and the cost of its formulation (Blytas and Frank 1995).

**Synthetic-Based Drilling Muds**

Due to the toxicity of the oils used in oil-based drilling fluids, the synthetic-based drilling muds appears as a substitute for oil-based drilling muds by replacing the oil by synthetic ones (such as ester and ether) (Munro et al. 1993).

They have the same desirable properties as these of the oil-based muds so they were often called pseudo-oil muds. They are considered more expensive than oil-based muds. This type of muds is useful for deepwater and deviated hole drilling.

### 7.1.1.2 Drilling Muds Properties

A variety of properties are monitored to satisfy the drilling process and guide formulation and treatment of muds.

**Muds Weight (Muds Density)**
It is measured by a muds balance and is normally measured in pounds per gallon (lbm/gal) or (ppg). The muds weight can be increased by the addition of barite, ilmenite, halite, or calcium carbonate (Abdou and Ahmed 2010).

**Filtration**
One of the most important functions for the muds is the ability of the muds to seal the permeable formation by forming thin, low permeable filter cake. There are two types of materials which enter the formation; the first type is fine particles which called muds spurt and the second type is liquid which is known as the filtrate (Cerasi and Soga 2001).

The model suggests that the filtration rate and the suspended fine particles are the responsible factors for the formation of the filter cake (Fink 2012; Kabir and Gamwo 2011) as shown in Fig. 7.2.

The filtration performance is determined using standard API filtration test. In this test, the cell equipped with filter paper, is full of drilling fluids and then 100 psi pressure is applied to the cell and finally the filtrate volume after 30 min is calculated (American Petroleum Institute 2009).

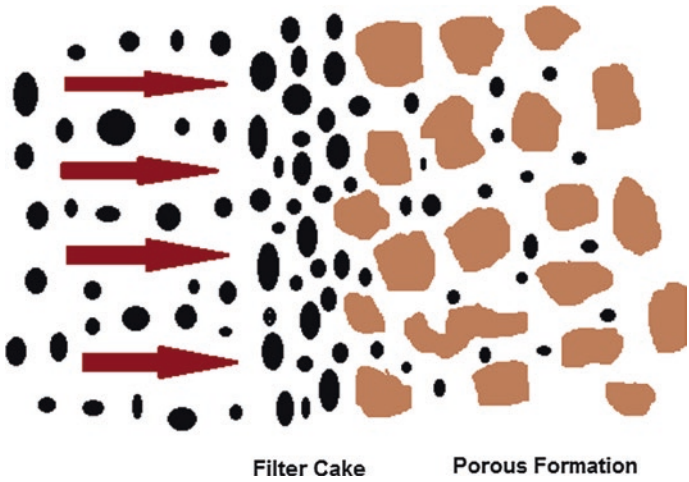


**Fig. 7.2** The formation of a filter cake in a porous formation from suspension (*filled circle*) in a drilling fluid

**Muds Rheological Properties**

The rheological properties played a very important role in determining the success of the drilling process.

It can be measured by two methods (American Petroleum Institute 2009):

A. Marsh funnel, the funnel is filled by 946 ml of muds and then notes the time required for the discharge of this amount and the time should be less than 1 min.
B. Fann V-G meter, different parameters (i.e., plastic viscosity, apparent viscosity, yield point, and gel strength) are measured by taking six reading at 600, 300, 200, 100, 6, 3 rpm.

**Plastic Viscosity (PV)**

The value of plastic viscosity is derived from two readings from Fann meter (600 and 300 rpm). The low value of plastic viscosity is desirable as the drilling process is rapid due to the low viscosity of the muds existing at the bit. The high values indicate the existence of excess solids or viscous base fluid. By dilution, we can lower the value of plastic viscosity (Negm et al. 2014).

$$\text{PV (in centipoise)} = \phi 600 - \phi 300$$

where $\phi 600$ is the reading of the viscometer at speed 600 rpm and $\phi 300$ is the reading of the viscometer at speed 300 rpm.

**Apparent Viscosity (AV)**

The viscosity of a fluid is measured at a given shear rate at a fixed temperature. In order for a viscosity measurement to be meaningful, the shear rate must be stated or defined. It is a rheological property calculated from viscometer readings performed by a Muds engineer on drilling fluid. It is normally abbreviated as AV (sometimes denoted $\eta$). It is expressed in cP (centipoise). These calculations and tests help the muds engineer develop and maintain the properties of the drilling fluid to the specifications required (Rosa et al. 1995).

**Yield Point (YP)**

The yield point is the resistance of the fluids to initial flow or the stress required to start fluid movement. The higher value of yield point is desirable as the drilling muds had the ability to carry cuttings better than fluid with the same density but with lower yield point (Aboulrous et al. 2013).

$$\text{YP}\left(\text{lb}/100\ \text{ft}^2\right) = 2(\text{AV} - \text{PV})$$

where AV is the apparent viscosity measured and PV is the plastic viscosity measured in centipoise.

The true yield point (Yt) is affected by the concentration of solids, their electrical charge, and surface properties of the muds.

$$\text{Yt}\left(\text{lb}/100\,\text{ft}^2\right) = 3/4\ \text{YP}$$

### Gel Strength

The gel strength is the measure of the minimum shear stress required to produce movement of muds. Gel strength played a very important role in suspending cuttings. Excessive gel strength can cause many problems as stuck pipes. It is measured using Fann meter at 3 rpm reading at 10 s and it can be measured also at 10 min (Van Oort et al. 2004).

### Muds Additives

*Muds Thickeners*

Thickener polymers include polyacrylamide, polyesters, polyacrylates, natural polymers, and modified natural polymers (Doolan and Cody 1995). Table 7.1 illustrates some examples for the thickener polymers that are used in drilling fluids. The main advantage of polymers is that they cause little change in solid contents of muds.

***Muds Filtrating Reducing Agents***

There are numerous cellulose-based fluid loss additives which are used to minimize the invasion of drilling fluids through the permeable formations. An apparent viscosity in water of at least 15 cP is needed to achieve an API fluid loss of less than 50 ml/30 min (Raines 1986).

A mixture containing polyanionic cellulose (PAC) and a synthetic sulfonate polymer has been tested to minimize the drilling fluid loss and thermal stability for a water-based drilling fluid at high well drilling temperatures up to 300 °F (150 °C) (Hen 1991).

Hydroxyethyl cellulose (HEC) with a degree of substitution of 1.1–1.6 has been used for fluid loss reduction in water-based drilling fluids (Raines 1986). While Chang et al. (1998) have used cross-linked HEC for high-permeability formations.

**Table 7.1** Thickener polymers

| Compound | References |
|---|---|
| Polyethylene glycol | Lundan and Lahteenmaki (1996) |
| Carboxymethyl cellulose | Lundan et al. (1993) |
| Combination of a cellulose ether with clay | Rangus et al. (1993) |
| Amide-modified carboxyl-containing polysaccharide | Batelaan and van der Horts (1994) |
| Copolymers acrylamide–acrylate and vinylsulfonate–vinylamide | Waehner (1990) |
| Cationic polygalactomannans and anionic xanthan gum | Yeh (1995) |
| Copolymer from vinyl urethanes and AA or alkyl acrylates | Wilkerson et al. (1995) |
| 2-Nitroalkyl ether–modified starch | Gotlieb et al. (1996) |
| Polymer of glucuronic acid | Courtois-Sambourg et al. (1993) |
| Ferrochrome lignosulfonate and carboxymethyl cellulose | Kotelnikov et al. (1992) |
| Cellulose nanofibrils | Langlois (1998), Langlois et al. (1999) |
| Chitosan | House and Cowan (2001) |

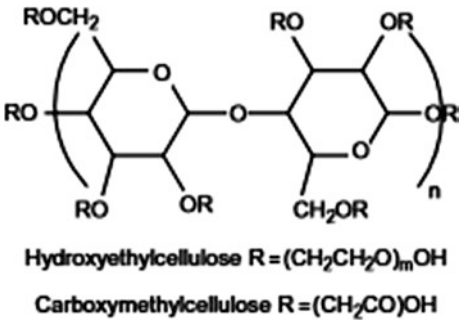


**Fig. 7.3** Starch derivates

The etherified or esterified form of HEC can be used as fluid loss control additives (Audibert et al. 1997; Chang and Parlar 1999). It was found that a derivatized HEC polymer gel has little or no damage to the formation permeability (Nguyen et al. 1996).

Succinoglycan is a natural biopolymer, which can be used as fluid loss control additive during oil field drilling (Lau 1994). Succinoglycan does not depend on viscosity to reduce fluid loss. Unfortunately, it can cause formation damage as it forms easy-to-remove filter cake.

Some cellulosic materials are shown in Fig. 7.3 Mixtures that contain metal hydroxides and a polysaccharide, partially etherified with hydroxyethyl and hydroxypropyl groups, are used to reduce fluid loss in water-based drilling fluids (Plank 1993).

Johnson (1996) has used to minimize the fluid loss a mixture of graded calcium carbonate particle sizes, a nonionic polysaccharide of the scleroglucan type, and a modified starch. Gellan has been used as a filtrate reducer in water-based drilling fluids (Dreveton et al. 1998).

#### 7.1.1.3 Drilling Problems

There are some problems in drilling process which exist due to the wrong values of muds parameters. These problems can be overcome or minimized by addition of some materials (Aboulrous et al. 2013).

Some of the problems are:

A. Muds losses during circulation
B. Stuck pipe
C. Corrosion of the drill pipe.

#### 7.1.1.4 Lost Circulation Problem

Lost circulation is leaking of drilling fluids into the well formations. The lost circulation is one of the biggest contributors to drilling nonproductive time and ruins

the specifications of the drilling process. This problem may lead to complete loss of the well due to the reduction of the pressure gradient manageable (Aboulrous et al. 2013).

### 7.1.1.5 The Classification of Drilling Muds According to Losses

**Seepage Loss Muds (SLM)**
It is called seepage losses muds when losses are 1–5 bbl/h during drilling process. Once it was determined that the fluid was being lost, the operator must make a decision of whether to tolerate or treat these losses. It might be possible to continue the drilling if the fluid was cheap and the pressures were manageable (Aboulrous et al. 2013; Nayberg and Petty 1986).

**Partial Loss Muds (PLM)**
It is the drilling fluids which lost 5–100 bbl/h (Nayberg and Petty 1986)

**Severe Loss Muds (SVLM)**
When the drilling fluid loss was more than 100 bbl/h (Nayberg and Petty 1986).

The last two types of muds require immediate treatment for these losses.

### 7.1.1.6 Types of Loss Circulation Zones

The idea that the pressure of specific zone exceeded the muds weight pressure, was the dominated reason for the lost circulation until (Gockel et al. 1987) indicated otherwise. They had found four types of formations that were responsible for the lost circulation (Howard and Scott 1951) (as in Fig. 7.4)

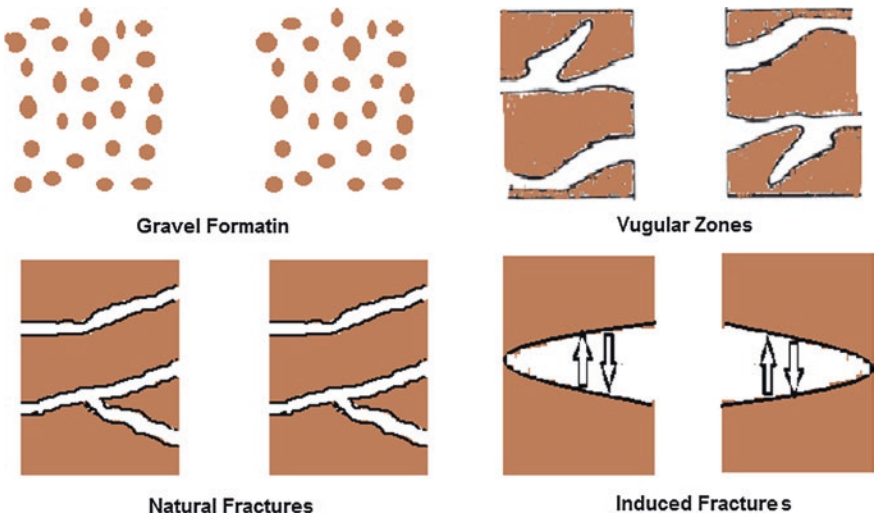


**Fig. 7.4** Illustrates four types of formations which are responsible for the lost circulation

1. High-permeability unconsolidated gravels where lost circulation caused a cavity. This type of loss can be controlled by muds weight.
2. Low-pressurized cavernous or vugular zones which are found in carbonate or volcanic formations due to two reasons:

   A. Continuous water flow through the dissolved parts of the rock in limestone.
   B. The cooling of magma.

3. Natural fractures or fissures, faults, and transition zones in carbonate.
4. Induced fractures due to the extensive hydraulic pressures.

#### 7.1.1.7 Loss Circulation Treatment

Rojas et al. (1998) demonstrated six ways for controlling the muds losses during drilling which can be done through the planning and execution of the well.

**Drill String Geometry and Casing Design**
The equivalent circulating density depends on casing design, drill string geometry, and hole size. These parameters should be taken in operator's mind during the planning stage. It is advisable to use bicentered bits to reduce the equivalent circulating density and select casing seats to minimize the exposure time of loss zones.

**Muds Rheology**
The muds rheology and flow rate should satisfy all drilling functions such as hole cleaning and cuttings removal as well as minimizing the equivalent circulating density.

**Muds Weight Selection**
In practice, we cannot reduce the equivalent circulating density by lowering the muds weight due to the increasing possibility of wellbore collapse.

**Sealing Properties of Drilling Muds**
The size of the solids, which exist in the drilling muds, control losses to high-permeability formation and small fractures as they function as bridging materials.

**Hole Cleaning Efficiency**
Failure to transport cuttings would result in cuttings accumulation in the annulus which led to higher frictional pressure drops in the well and higher equivalent circulating densities.

**Lost Circulation Control Materials (LCM)**
There are a variety of lost circulation additives shown in Table 7.2 but the polymeric materials have the largest impact in the reduction of fluid loss during drilling due to their viscosity as superabsorbent materials (Fink 2003; Alsabagh et al. 2013).

Lost circulation materials were evaluated using permeability plugging apparatus using the ceramic disks with different pore throat diameters as a filter medium at differential pressures to simulate the conditions of the well. The filtration

**Table 7.2** Lost circulation additives

| Material | References |
|---|---|
| Encapsulated lime | Walker (1986) |
| Encapsulated oil-absorbent polymers | Delhommer and Walker (1987) |
| Hydrolyzed polyacrylonitrile | Yakovlev and Konovalov (1987) |
| Poly(galactomannan) gum | Kohn (1988) |
| Partially hydrolyzed polyacrylamide 30 % hydrolyzed, cross-linked with Cr3+ | Sydansk (1990) |
| Oat hulls | House et al. (1991) |
| Rice products | Burts (1992, 1997) |
| Waste olive pulp | Duhon (1998) |
| Nut cork | Fuh et al. (1993), Rose (1996) |
| Pulp residue waste | Gullett and Head (1993) |
| Petroleum coke | Whitfill et al. (1990) |
| Shredded cellophane | Burts (2001) |

parameters can be made from the data collected at 7.5 and 30 min intervals according to the following formulas (American Petroleum Institute 2009):

$$\mathbf{PPT} = 2 \times V_{30\ \mathrm{min}}$$
$$\mathbf{SL} = 2 \times \left[V_{7.5\ \mathrm{min}} - \left(V_{30\ \mathrm{min}} - V_{7.5\ \mathrm{min}}\right)\right]$$
$$\mathbf{SFR} = 2 \times \left[V_{30\ \mathrm{min}} - V_{7.5\ \mathrm{min}}\right]/2.739$$

where **PPT** is the permeability plugging tester value(ml); $V_{30\ \mathrm{min}}$ (ml) is the total filtrate collected in 30 min; **SL** is the spurt loss (ml); $V_{7.5\ \mathrm{min}}$ (ml) is the filtrate collected in 7.5 min; and **SFR** is the static filtration rate (ml/min$^{1/2}$).

#### 7.1.1.8 Water-Soluble Natural Polymers as Lost Circulation Control Materials (LCM)

Cellulosic natural polymers (i.e., carboxymethyl cellulose, guar gum, and starch) are available in abundance so they are low cost. The carboxymethyl cellulose (CMC) is a cellulose derivative with carboxymethyl groups ($ACH_2ACOOH$) bound to some of the hydroxyl groups of the glucopyranose units that form the main backbone of cellulose. The guar gum is a polysaccharide that contained the sugars galactose and mannose. The backbone of gum is a linear chain of 1,4-linked mannose units to which galactose units are 1,6-linked at every second mannose, forming short side branches. Starch is composed of anhydroglucose units having 1, 4-linkages (Fink 2003; Alsabagh et al. 2014).

**Filtration Parameters for Natural Polymers**

From Tables 7.3, 7.4, and 7.5, by changing the ceramic disks (60 and 90 μ) at 100 and 300 differential pressures, the CMC exhibited the best performance in

**Table 7.3** Filtration parameters for carboxymethyl cellulose (CMC) using different ceramic disks at different pressures

| Conc. % | $V_{7.5\ min}$ (ml) | | $V_{30\ min}$ (ml) | | PPT value (ml) | | Spurt loss (ml) | | Static filtration rate ($ml/min^{1/2}$) | | Filter cake (mm) | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 100 psi | 300 psi | 100 psi | 300 psi | 100 psi | 300 psi | 100 psi | 300 psi | 100 psi | 300 psi | 100 psi | 300 psi |
| *At* 60 μ *ceramic disks* | | | | | | | | | | | | |
| 0.1 | 20.2 | 22 | 23.8 | 26.5 | 40.1 | 44 | 33.2 | 35 | 2.6 | 3.3 | 0.17 | 0.12 |
| 0.3 | 30.8 | 35.2 | 34.9 | 41 | 61.6 | 70.4 | 53.4 | 58.8 | 2.9 | 4.2 | 0.19 | 0.15 |
| 0.6 | 43.9 | 50.2 | 50 | 57 | 87.8 | 100.4 | 75.6 | 86.8 | 4.5 | 4.9 | 0.2 | 0.17 |
| *At* 90 μ *ceramic disks* | | | | | | | | | | | | |
| 0.1 | 23.7 | 27.2 | 28 | 32 | 47.4 | 54.4 | 38.8 | 44.8 | 3.1 | 3.5 | 0.17 | 0.12 |
| 0.3 | 42.6 | 48.4 | 48 | 54.5 | 85.2 | 96.8 | 74.4 | 84.6 | 3.9 | 4.5 | 0.19 | 0.15 |
| 0.6 | 51 | 58.3 | 58 | 65.6 | 102 | 116.6 | 88 | 102 | 5.1 | 5.3 | 0.2 | 0.17 |

**Table 7.4** Filtration parameters for guar gum (MG) using different ceramic disks at different pressures

| Conc. % | $V_{7.5\ min}$ (ml) | | $V_{30\ min}$ (ml) | | PPT value (ml) | | Spurt loss (ml) | | Static filtration rate ($ml/min^{1/2}$) | | Filter cake (mm) | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 100 psi | 300 psi | 100 psi | 300 psi | 100 psi | 300 psi | 100 psi | 300 psi | 100 psi | 300 psi | 100 psi | 300 psi |
| *At* 60 μ *ceramic disks* | | | | | | | | | | | | |
| 0.1 | 32.7 | 37.8 | 36.6 | 42.7 | 73.2 | 85.4 | 57.6 | 65.8 | 2.8 | 3.6 | 0.25 | 0.21 |
| 0.3 | 21.3 | 23.8 | 24.8 | 28.2 | 49.6 | 56.4 | 35.6 | 38.6 | 2.5 | 3.3 | 0.27 | 0.25 |
| 0.6 | 46.4 | 53.3 | 51.4 | 58.5 | 102.8 | 117 | 82.8 | 96.2 | 3.7 | 4 | 0.3 | 0.27 |
| *At* 90 μ *ceramic disks* | | | | | | | | | | | | |
| 0.1 | 43.6 | 51.2 | 47.7 | 56.3 | 95.4 | 112.6 | 79 | 92.2 | 3 | 3.5 | 0.25 | 0.21 |
| 0.3 | 25.1 | 29.3 | 28.9 | 34.1 | 57.8 | 68.2 | 42.6 | 49 | 2.7 | 3.5 | 0.27 | 0.25 |
| 0.6 | 54 | 62.3 | 59.2 | 67.8 | 118.4 | 135.6 | 97.6 | 113.6 | 3.8 | 4.1 | 0.3 | 0.27 |

**Table 7.5** Filtration parameters for potato starch (MS) using different ceramic disks at different pressures

| Conc. % | $V_{7.5\ min}$ (ml) | | $V_{30\ min}$ (ml) | | PPT value (ml) | | Spurt loss (ml) | | Static filtration rate (ml/min$^{1/2}$) | | Filter cake thickness (mm) | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 100 psi | 300 psi | 100 psi | 300 psi | 100 psi | 300 psi | 100 psi | 300 psi | 100 psi | 300 psi | 100 psi | 300 psi |
| *At* 60 μ *ceramic disks* | | | | | | | | | | | | |
| 0.1 | 33.8 | 42.5 | 37.3 | 47.7 | 74.6 | 95.4 | 59.4 | 74.6 | 3 | 3.8 | 0.18 | 0.16 |
| 0.3 | 30 | 40.2 | 34.8 | 45.5 | 69.6 | 91 | 50.4 | 69.8 | 3.5 | 3.9 | 0.26 | 0.2 |
| 0.6 | 23.5 | 32 | 27 | 36 | 54 | 72 | 40 | 56 | 2.6 | 2.9 | 0.26 | 0.23 |
| *At* 90 μ *ceramic disks* | | | | | | | | | | | | |
| 0.1 | 43.6 | 51.2 | 47.7 | 56.3 | 95.4 | 112.6 | 79 | 92.2 | 3 | 3.5 | 0.2 | 0.18 |
| 0.3 | 37.1 | 47.2 | 42 | 53 | 84 | 106 | 64.4 | 82.8 | 3.6 | 4.2 | 0.24 | 0.18 |
| 0.6 | 32.7 | 37.8 | 36.6 | 42.7 | 73.2 | 85.4 | 57.6 | 65.8 | 2.8 | 3.6 | 0.23 | 0.2 |

all the filtration parameters such as filtrate volume after 30 min, PPT value, spurt loss, and static filtration at 0.1 % concentration. While the maximum efficiency for the guar gum and potato starch is pronounced at 0.3 and 0.6 %, respectively (Alsabagh et al. 2014).

The filtrate loss after 30 min (ml) was 16.7, 18, and 24.2 against the CMC, guar gum, and potato starch, respectively. On the other hand the spurt loss decreased from 35.6, 24, and 22.6 ml against the potato starch, guar gum, and CMC, respectively. By investigating the results of permeability plugging tester value, it was found that the CMC pronounced the best results among the guar gum and potato starch. The same result was exhibited by examining the static filtration rate values with the same ranking. By analyzing the filter cake data, it was found that the filter cake for CMC is more elastic and without any bubbles (ranging from 0.12 to 0.2 mm) among the coming results by the guar gum and the potato starch (ranging from 0.17 to 0.3 mm) and their filter cakes having instability and bubbles (Alsabagh et al. 2014).

The obtained good results by the CMC in the filtration parameters may be due to the CMC having surface active properties and forming micellar solution so that the micelles may form an external filter cake which leads to complete plugging of the pores to prevent the filtration loss (Alsabagh et al. 2014) as shown in Fig. 7.5.

**Surface Tension Parameters for Natural Polymers**

From Table 7.6 the CMC forms critical micelle concentration formation (CMCF). These data mean that it has surface active properties. Meanwhile the guar gum and the potato starch have cleared undistinguished CMCF. These results illustrated the reason that the CMC exhibited good results among the guar gum and the potato starch. The $\Delta G_{ads}$ (−4.1) of the CMC in Table 7.6 means that its adsorbability on the surface of the rocks leads to maximum stability for the formed filter cake layer (Alsabagh et al. 2014).

#### 7.1.1.9 Water-Insoluble Natural Polymers as Lost Circulation Materials

Three natural water-insoluble cellulosic materials were investigated as lost circulation control material depending on their physical and chemical properties (particle size distribution and chemical composition).

**Effect of Particle Size Distribution of Natural Materials on Filtration Parameters**

All fine-sized materials have the best results in filtration volume, PPT value, and spurt loss and that is because the fine-sized material gives better filling properties. A bridge may be initiated when several particles of lost circulation material lodge against each other in the pore throat. The smaller particles may then bridge the openings between the larger, previously bridged particles. This process continues until the pore plugged. The fine-sized materials have more surface area so they possess more resistance to pressure and they can plug pore (Alsabagh et al. 2016).

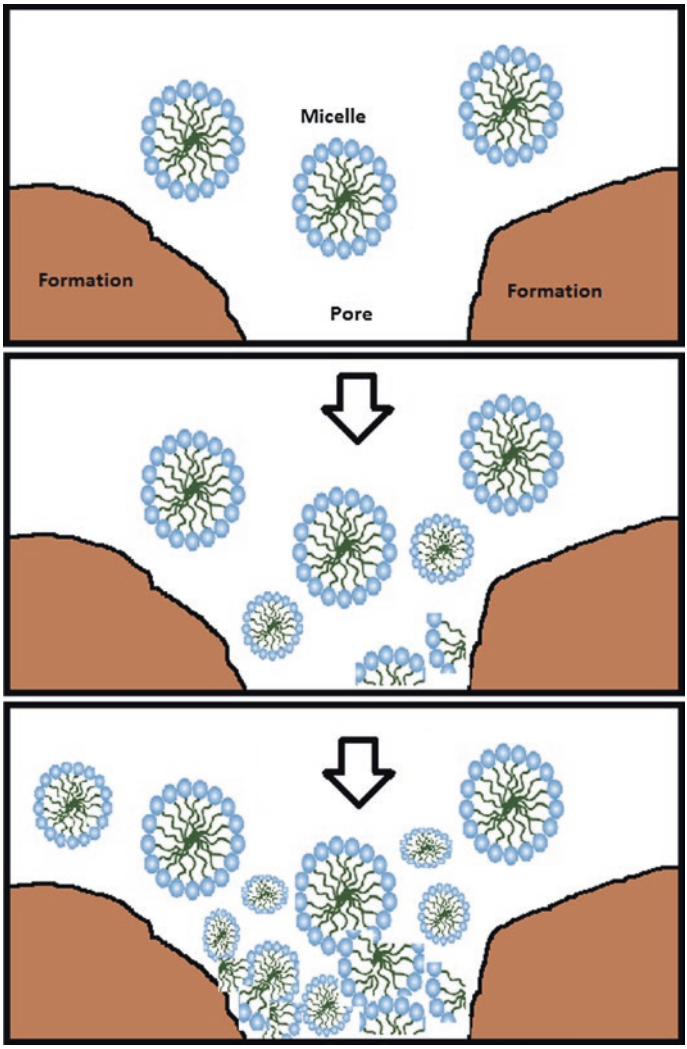


**Fig. 7.5** Shows the mechanism of CMC as lost circulation control materials through micelle formation. Adapted from Alsabagh et al. (2014)

**Table 7.6** Thermodynamic parameters for natural water-soluble polymers at 25 °C

| Material | γ CMC | $\Gamma_{max} \times 10^{-10}$ | $A_{min} \times 10^{2}$ | πCMC | $\Delta G_{mic}$ | $\Delta G_{ads}$ |
|---|---|---|---|---|---|---|
| CMC | 55 | 0.42 | 4.2 | 17.3 | +0.55 | −4.1 |
| Guar gum | NA | 0.48 | 3.4 | NA | NA | NA |
| Starch | NA | NA | NA | NA | NA | NA |

**Effect of Concentration of Natural Polymers on Filtration Parameters**

From Fig. 7.6a–c, it can be concluded that if the concentration of the three investigated cellulosic materials increases (at concentration 0.6 %), the filtration performance will be better in all filtration parameters (Alsabagh et al. 2016). These results meet with what Abram in 1977 stated; high concentration provides better sealing.

This concentration is considered to be optimum as it is the best concentration with changing the applied differential pressure and the permeability of ceramic disks.

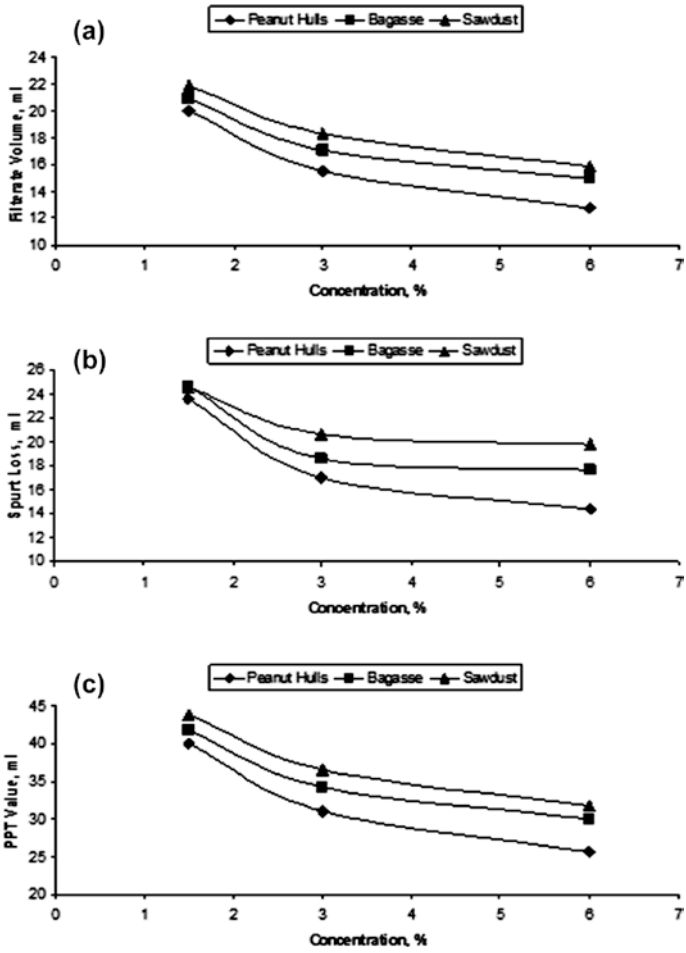


**Fig. 7.6** Illustrates the filtration parameters for peanut hulls, bagasse, and sawdust (in fine size) with 90 μ ceramic disks at 100 psi where **a** filtrate volume (vs.) concentration. **b** PPT value (vs.) concentration. **c** spurt loss (vs.) concentration. Adapted from Alsabagh et al. (2016)

**Table 7.7** The composite of the investigated water-insoluble natural polymers

| Materials | Cellulose (%) | Crude fiber (%) | Water (%) | Ash (%) | Lignin (%) | Other (%) |
|---|---|---|---|---|---|---|
| Peanut hulls | 25 | 60 | 8 | 2 | – | 5 |
| Bagasse | 55 | – | 5 | 4 | 24 | 12 |
| Sawdust | 58.2 | – | 4.8 | 0.21 | 28.4 | 5.1 |

**Effect of Cellulosic Content of Natural Material on Filtration Parameters**
All filtration parameters enhanced with all investigated materials and all investigated materials decrease the flow rate of the water-based muds drastically. The peanut hulls show the better performance in reducing the loss circulation of drilling fluids than the bagasse and sawdust as shown in Fig. 7.6a–c. These results may be because the peanut hulls contain crude fiber (60 %) and the least content of cellulose (25 %) and the sawdust is the worst one because it has the highest content of cellulose (58.2 %) (Alsabagh et al. 2016) as shown in Table 7.7 and that makes it more friable under pressure.

#### 7.1.1.10 Scanning Electron Microscope (SEM) for the Formed Internal Filter Cakes

The ceramic disks have been photographed by SEM to investigate the plugging quantity of investigated materials. Best filtration result of 60 μ ceramic disk is shown in Fig. 7.7a–c (Alsabagh et al. 2016).

### *7.1.2 Role of Natural Polymers in Renewable Energy (Biomass)*

The world currently depends heavily on coal, oil, and natural gas for its energy. Fossil fuels are nonrenewable as they draw on finite resources that will eventually dwindle. This type of energy is becoming too expensive, too environmentally damaging and the reason for global warming. In contrast, the many types of renewable energy resources such as wind, solar energy, and biomass are constantly replenished and will never run out (McKendry 2002).

According to Renewable Energy Policy Network for the 21st Century (2010, 2011, 2012) renewables contributed 19 % to our energy consumption and 22 % to our electricity generation in 2012 and 2013, respectively; while it contributes 16.7 % to our energy consumption during 2010 as shown in Fig. 7.8. For both modern renewables, such as hydro, wind, solar, and biofuels, and traditional biomass, worldwide investments in renewable technologies amounted to more than US$214 billion in 2013. Figure 7.9 shows global growth of renewables throughout 2011.

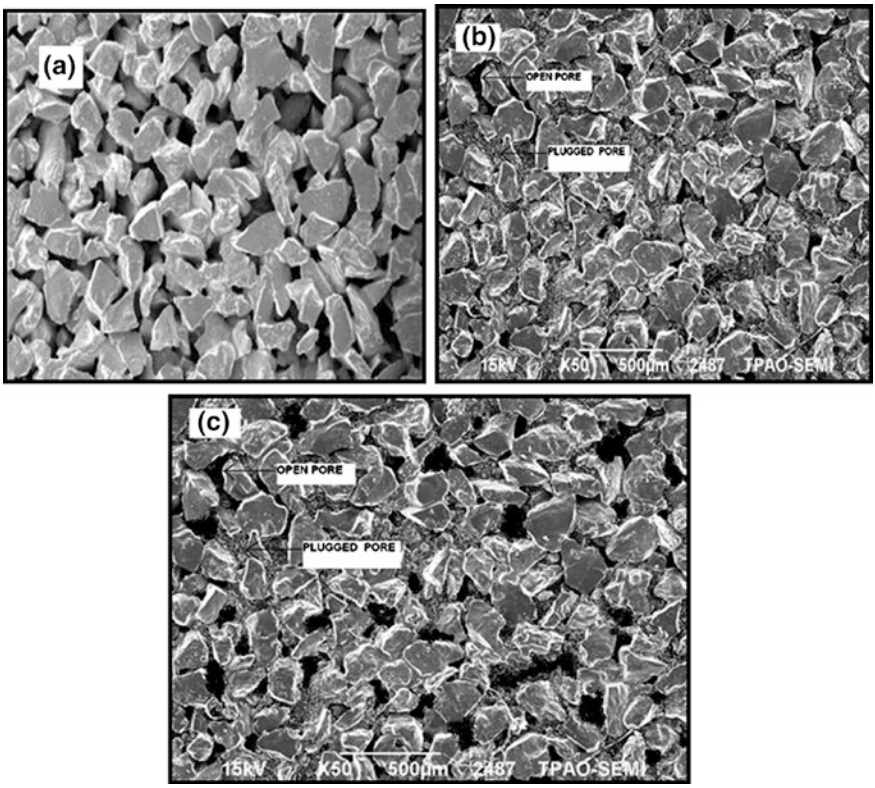


**Fig. 7.7** Represents 60 μ ceramic disk **a** before PPT, **b** after PPT (6 % of fine-sized peanut hulls), **c** after PPT (6 % of fine-sized sawdust). Adapted from Alsabagh et al. (2016)

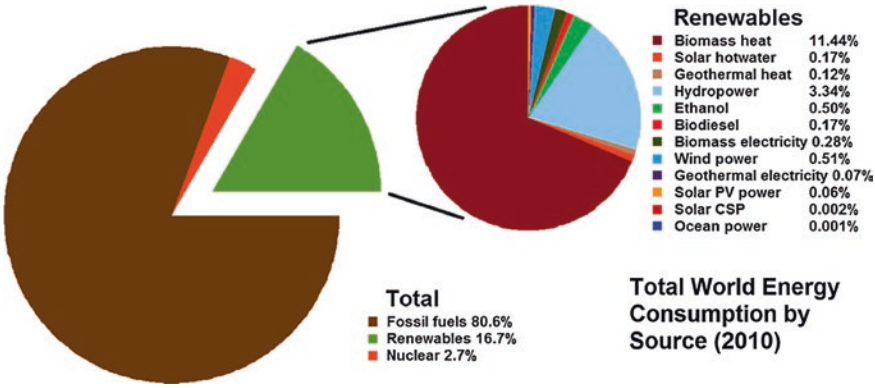


**Fig. 7.8** Total world energy consumption by 2010. Adapted from Renewable Energy Policy Network for the 21st Century (2010)

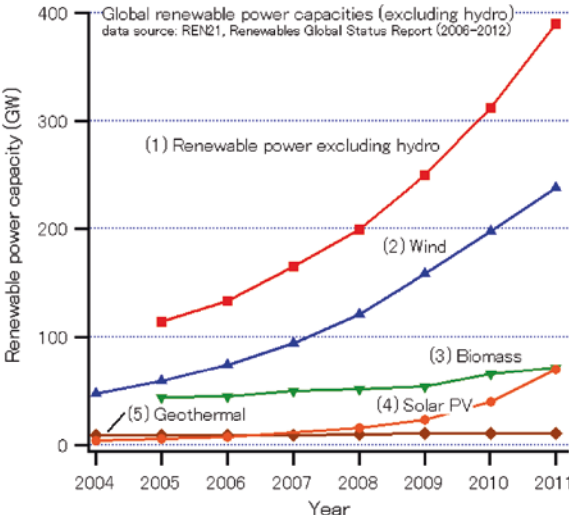


**Fig. 7.9** Global growth of renewables throughout 2011. Adapted from Renewable Energy Policy Network for the 21st Century (2011)

### *7.1.3 Types of Renewable Energy*

There are so many kinds of renewable energy (Renewable Energy Policy Network for the 21st Century 2010) such as

- Electricity generation. Renewable energy provides 21.7 % of electricity generation worldwide in 2013 (British Petroleum Company 2014). Renewable power generators are spread across many countries, and the percent for usage of wind to produce electricity in some areas is, for example, 14 % in the U.S. state of Iowa, 40 % in the northern German state of Schleswig-Holstein, and 49 % in Denmark (Renewable Energy Policy Network for the 21st Century 2010).
- Transport fuels. Biofuels have contributed to a significant decline in oil consumption in the United States since 2006 (Renewable Energy Policy Network for the 21st Century 2010). The 93 billion liters of biofuels produced worldwide in 2009 displaced 68 billion liters of gasoline, equal to about 5 % of world gasoline production (Renewable Energy Policy Network for the 21st Century 2010).
- Solar energy. Solar hot water makes an important contribution to renewable heat in many countries, most notably in China, which now has 70 % of the global total. Direct geothermal for heating is growing rapidly (Renewable Energy Policy Network for the 21st Century 2010).
- Biomass. In Sweden, national use of biomass energy has surpassed oil. The use of biomass for heating continues to grow as well.

#### 7.1.3.1 Biomass

The use of biomass as renewable energy source is becoming increasingly necessary, if we are to achieve the changes required to address the impacts of global warming. Biomass is the most common form of renewable energy, widely used in the third world until recently.

Biomass is considered natural, renewable, and high molecular weight material which can produce energy. The renewable energy is used mostly to generate electricity but it can be used also to create alternative fuel (biofuel). Biomass denotes living and recently dead biological materials which can be used as fuel (Ellabban et al. 2014).

The building blocks of the biomass are the carbohydrates which produce from the photosynthesis of the plant materials between carbon dioxide ($CO_2$) in the air, water, and sunlight. The solar energy which is stored in the chemical bonds of carbohydrate can be extracted chemically or biologically.

Oxygen is extra product of the extraction process which oxidized carbon to produce carbon dioxide ($CO_2$) and water. This process is cyclical as carbon dioxide can produce new biomass. The chemical and physical properties of the high molecular weight materials determine the value of a particular type of biomass. Biomass is more secure source for energy as biomass is available in most countries (McKendry 2002).

Many crops are being tested for commercial energy forming. Energy crops include woody crops, grasses, starch, sugar, and oil seeds. These include also poplar trees and *Miscanthus giganteus*. The premier energy crop is sugarcane, which is a source of the readily fermentable sucrose and the lignocellulosic by-product bagasse (ADAS 1992). The desired characteristics for the energy crops are:

1. Low cost
2. Low nutrient requirement
3. Low energy requirement to produce
4. High yield (maximum production of dry materials per hectare)

Biomass can be converted into three main types of products.

#### 7.1.3.2 Electrical/Heat Energy

In the UK, the government tries to generate 10 % of the national electricity supply of 60 GW/year from renewable sources especially biomass (Price 1998; U.S. Energy Information Administration 2012). It has been reported that electricity can be produced when microbial foods, such as glucose and acetate, or even organic compounds in wastewater are fed to the bacteria. Figure 7.10 shows the top five countries generating electricity from biomass.

#### 7.1.3.3 Transport Fuel (Biofuel)

Since the middle of the twentieth century, the interest of biomass as a precursor to liquid fuels has increased. The fermentation of lignocellulosic biomass to ethanol

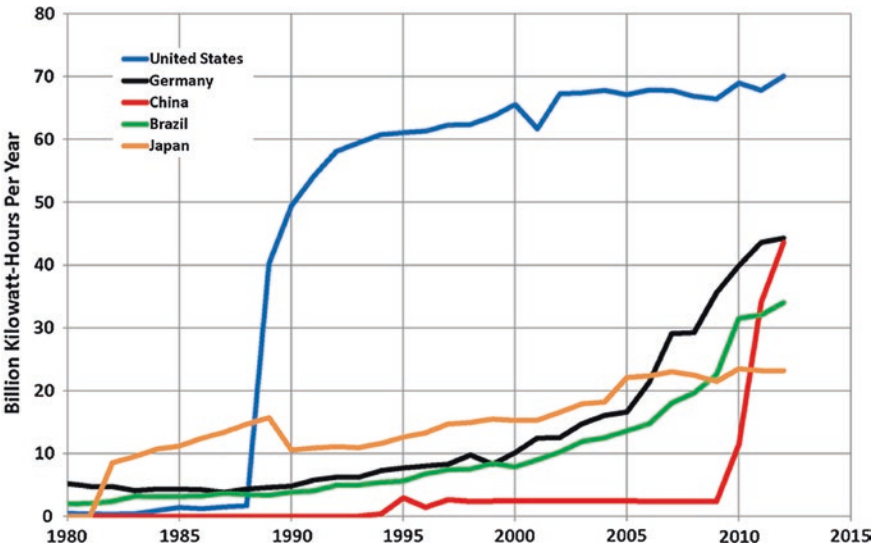


**Fig. 7.10** The top five countries generating electricity from biomass. Adapted from U.S. Energy Information Administration (2012)

(Allen and Bennetto 1993) is an essential supply to fuels instead of the fossil fuels. This process produces no net carbon dioxide in the earth's atmosphere. There are so many other lignocellulose-derived fuels such as butanol, dimethylfuran, and gamma-Valerolactone (Mecheri et al. 2011; Logan 2004).

Among biological fuel cells, enzymatic fuel cells (EFCs) have attracted interest in the last decade due to their use as power sources for portable electronics, and implantable medical devices (Minteer et al. 2007; Barton et al. 2004; Moehlenbrock and Minteer 2008). Enzymes possess merits over chemical catalysts, such as biocompatibility and biodegradability. By encapsulation technique, it is possible to entrap the biomolecule in the polymeric matrix while retaining sufficient mobility. This immobilization procedure depends on the entrapment of the enzyme in polymer networks without any covalent associations. Several polymer networks have been proposed, among which the use of natural polymers has been found to provide good environment for enzyme immobilization (Moore et al. 2004; Thomas et al. 2003; Klotzbach et al. 2006).

Glucose oxidase (GOx) is the most widely used enzyme in the field of biosensors due to its high stability and specificity (Wilson and Turner 1992; Tsai et al. 2005). Based on research advances leading to commercially available biosensors, materials and strategies to design GOx-based biofuel cell have been explored (Ivnitski et al. 2006).

The hybrid fuel cell combines some features of solar cells, fuel cells, and redox flow batteries which convert biomass to electricity with the help of a catalyst activated by solar or thermal energy at low temperature. The hybrid fuel cell can be any type of biomass sources, including starch, cellulose, lignin—and switch grass, powdered wood, algae, and waste.

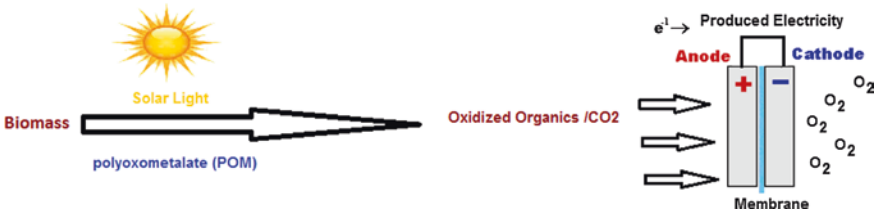


**Fig. 7.11** Shows the hybrid fuel cell

In this hybride fuel cell, the biomass is ground up and mixed with a polyoxometalate (POM) catalyst in solution and then exposed to light from the sun—or heat. The fuel cell uses polyoxometalates as the photocatalyst and charge carrier to generate electricity at low temperature. POM oxidizes the biomass under photo or thermal irradiation, and delivers the charges from the biomass to the fuel cell's anode. The electrons are then transported to the cathode, where they are finally oxidized by oxygen through an external circuit to produce electricity as shown in Fig. 7.11. This type of cell is not sensitive to impurities unlike the other cell technologies as it has reported that it is inert to organic and inorganic impurities present in the fuels (Sapra 2014).

#### 7.1.3.4 Chemical Feedstock

Lignocellulosic biomass is the feedstock for the pulp and paper industry. This industry focuses on the separation of the lignin and cellulosic fractions of the biomass. The biomass can be converted to raw materials for polymer synthesis and modification.

This can be done by liquefaction which is a widely known technology to convert gaseous and solid products to liquids. This technique can even produce novel thermoset nanocomposites.

#### 7.1.3.5 Lignocellulosic Biomass

Lignocellulosic biomass is the most abundantly available raw material on the earth for the production of biofuels.

Lignocellulose refers to plant dry matter of higher plants, softwood or hardwood. It is composed mainly of carbohydrate polymers (cellulose, hemicellulose), and an aromatic polymer (lignin). Cellulose provides mechanical strength and chemical stability to plants. Solar energy is stored in the form of cellulose during the photosynthesis process. Hemicellulose is a copolymer of different sugar monomers (six and five carbon sugars) which are tightly bound to lignin and also exist in the plant cell. Lignin is polymer of aromatic compounds that produce reinforcement to the plant walls. It has been reported that about $7.5 \times 10^{10}$ tons of cellulose are consumed every year (Kirk-Othmer 2001).

There are two main types of linkages identified in the lignocellulose complex. The main types of bonds that provide linkages within the individual components of lignocellulose (intrapolymer linkages), and connect the different components to form the complex (interpolymer linkages). The position and bonding function of the latter linkages is summarized in Table 7.8 (Faulon et al. 1994).

The content of cellulose, hemicellulose, and lignin in the lignocellulosic biomass highly depends on its source, whether it is wood, softwood, or grasses (Sun and Cheng 2002) as shown in Table 7.9.

**Table 7.8** Overview of linkages between the monomer units that form the individual polymers lignin, cellulose, and hemicellulose, and between the polymers to form lignocellulose

| | |
|---|---|
| *Bonds within different components (intrapolymer linkages)* | |
| Ether bond | Lignin, (hemi)cellulose |
| Carbon to carbon | Lignin |
| Hydrogen bond | Cellulose |
| Ester bond | Hemicellulose |
| *Bonds connecting different components (interpolymer linkages)* | |
| Ether bond | Cellulose–lignin<br>Hemicellulose–lignin |
| Ester bond | Hemicellulose–lignin |
| Hydrogen bond | Cellulose–hemicellulose<br>Hemicellulose–lignin<br>Cellulose–lignin |

Adapted from Faulon et al. (1994)

**Table 7.9** Composition of lignocellulose in several sources on dry matter

| Lignocellulosic materials | Cellulose (%) | Hemicellulose (%) | Lignin (%) |
|---|---|---|---|
| Hardwoods stems | 40–55 | 24–40 | 18–25 |
| Softwood stems | 45–50 | 25–35 | 25–35 |
| Nut shells | 25–30 | 25–30 | 30–40 |
| Corn cobs | 45 | 35 | 15 |
| Grasses | 25–40 | 35–50 | 10–30 |
| Paper | 85–99 | 0 | 0–15 |
| Wheat straw | 30 | 50 | 15 |
| Sorted refuse | 60 | 20 | 20 |
| Leaves | 15–20 | 80–85 | 0 |
| Cotton seed hairs | 80–95 | 5–20 | 0 |
| Newspaper | 40–55 | 25–40 | 18–30 |
| Waste papers from chemical pulps | 60–70 | 10–20 | 5–10 |
| Primary wastewater solids | 8–15 | NA | 24–29 |
| Swine waste | 6 | 28 | NA |
| Solid cattle manure | 1.6–4.7 | 1.4–3.3 | 2.7–5.7 |
| Coastal Bermuda grass | 25 | 35.7 | 6.4 |
| Switchgrass | 45 | 31.4 | 12 |

Lignocellulosic biomass can be classified into virgin biomass, waste biomass, and energy crops. Virgin biomass is all naturally occurring plants such as trees, bushes, and grass. Waste biomass is produced as a low-value by-product of various industries such as agriculture. Energy crops are crops with high yield of dry matters (lignocellulosic biomass) produced to be used in production of energy such as switch grass (*Panicum virgatum*) and elephant grass (Carioca et al. 1985).

### *7.1.4 Other Applications of Natural Polymers in Engineering*

Significant volumes of wastewaters, with organic and inorganic contaminants such as suspended solids, dyes, pesticides, toxicants, and heavy metals, are discharged from various industries. These wastewaters create a serious environmental problem and pose a threat to water quality when discharged into rivers and lakes (Lee et al. 2014). Thus, such contaminants must be effectively removed to meet increasingly stringent environmental quality standards. It is increasingly recognized that the nontoxic and biodegradable biopolymer chitosan can be used in wastewater treatment (Peniston and Johnson 1970).

The need for the environmentally friendly materials in treating water and wastewater continue to increase during last decade so bioflocculants have emerged to replace conventional commercial ones. Polysaccharides or natural polymers may be of great interest because they are natural polymers, environmentally friendly materials (biodegradable polymers), and easily available from agricultural resources (Bolto and Gregory 2007). They are not used only in food and fermentation processes, pharmaceutical, cosmetic, downstream processing but also in water and wastewater treatment.

#### 7.1.4.1 Mechanism for Natural Bioflocculants

For example, the chitosan behaves as cationic bioflocculant (reactive amino and hydroxyl groups) and have high molecular weight, so it can treat wastewater by both mechanisms, coagulation by charge neutralization and flocculation by bridging mechanism (Li et al. 2013) as shown in Fig. 7.12. In a study that reported coagulation and flocculation of dye-containing solutions using the chitosan, the anionic dye was electrostatically attracted by protonated amine groups from chitosan and then neutralizes the anionic charges of dyes and finally the agglomerates settle down by the flocculation which was enhanced by the bridging mechanism (Guibal and Roussy 2007). The behavior of chitosan involves two factors, hydrophobic interactions and the formation of hydrogen bonds. Anionic bioflocculants (cellulose, tannin, and sodium alginate) cannot flocculate anionic contaminants from the wastewater without the assistance to neutralize the negatively charged impurities, so we must add inorganic metal salts (e.g., aluminum and ferric salts) or cationic

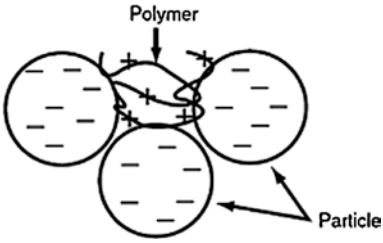


**Fig. 7.12** Schematic view of a flocculation mechanism. Adapted from Dobias and Stechemesser (2005)

polymer (e.g., chitosan) (Khiari et al. 2010; Özacar and Şengıl 2003; Roussy et al. 2005; Suopajärvi et al. 2013; Wu et al. 2012; Dobias and Stechemesser 2005). For many years, bioflocculants such as chitosan, tannins, cellulose, alginate, gums, and mucilage have been attracting wide interest for treating the wastewater.

### 7.1.4.2 Chitosan

Cationic biopolymers or polyelectrolytes are of increasing interest as flocculants in wastewater. Chitosan is a valuable polymeric waste produced from the shells of crustaceans. Crab shells consist of chitin, protein/caroteins, chitin, and calcium carbonate (Peniston and Johnson 1970). Prawn, lobster, and crab shells are a particularly rich source of this chemical, containing 15–20 % of chitin (the chitosan source). Chitin is a polymer of the polysaccharide class, a cellulose-like biopolymer containing mainly of β-(1→4)-2 acetamido-2-deoxy-D-glucose units. The structure of chitin is shown in Fig. 7.13. The main components of chitins are shown in Fig. 7.14. Chitosan is a partially deacetylated polymer obtained from the alkaline deacetylation of chitin. It is a linear hydrophilic amino-polysaccharide with a rigid structure containing both glucosamine and acetylglucosamine units. The structure of chitosan is shown in Fig. 7.15. Chitin has been found in a wide range of natural sources, such as crustaceans, fungi, insects, annelids, mollusks, etc. The world's market for seafood crustaceans, particularly prawns, shrimp, crab, crayfish, and lobster, is several million tons per year, of which 50 % is discarded as shell waste.

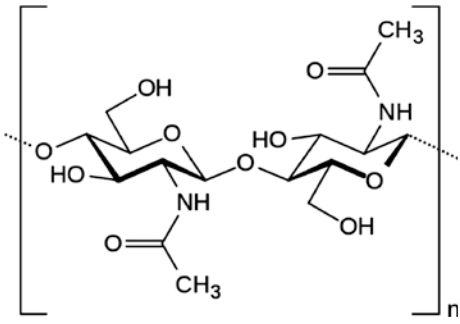


**Fig. 7.13** Structure of Chitin

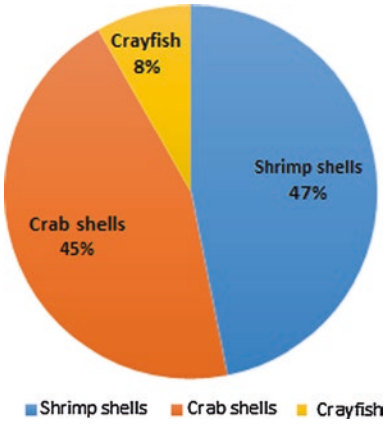


**Fig. 7.14** Percentage of chitin from different sources

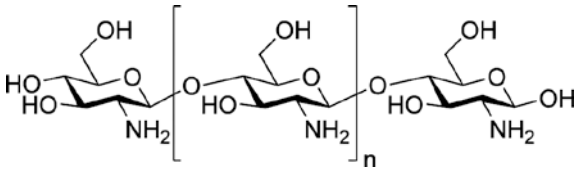


**Fig. 7.15** Structure of Chitosan

The shells contain significant amounts of calcium carbonate and the polymer chitin (15–20 % w/w), which can be *N*-deacetylated, using concentrated sodium hydroxide to produce the polysaccharide chitosan. Actually, chitin is the world's second most abundant naturally occurring polysaccharide. In fact, these biopolymers are considered to be a key material in the external protective structure of living systems, so chitin and chitosan have several outstanding properties (Gerente et al. 2007).

To facilitate electrostatic interactions between polymer chains and the negatively charged impurities in wastewater, we should dissolve chitosan in acids to produce protonated amine groups along the biopolymer chains (Renault et al. 2009; Muzzarelli 1977).

Numerous works have reported its promising coagulation and flocculation properties for dye molecules in dye-containing solutions (Guibal and Roussy 2007) or organic matter (e.g., lignin and chlorinated compounds) in pulp and paper mill wastewater (Rodrigues et al. 2008), heavy metals and phenolic compounds in cardboard-mill wastewater (Renault et al. 2009), and inorganic suspensions in kaolinite suspension (Li et al. 2013).

### 7.1.4.3 Tannin

Tannin is an anionic biopolymer (Özacar and Şengıl 2000) which extracts from vegetal secondary metabolites such as bark, fruits, leaves, and others (Beltrán

Heredia and Sánchez Martín 2009). It has been tested in removal of colloidal impurities in drinking water treatment (Özacar and Şengıl 2003), removal of suspended matters from synthetic raw water (Özacar and Şengıl 2000), and removal of dyes, pigments, and inks from ink containing wastewater (Roussy et al. 2005). Some studies showed that the coagulant such as aluminum sulfate with the negatively charged colloidal particles estabilized with anionic tannin acted as flocculant to bridge the aggregates together to settle the flocs. In order to eliminate the need for the coagulant, modified tannin (Tanfloc flocculant) has been investigated recently to remove heavy metals from polluted water (Beltrán Heredia and Sánchez Martín 2009) and in wastewater treatment (Beltrán Heredia and Sánchez Martín 2009).

#### 7.1.4.4 Gums and Mucilage

In recent years, bioflocculants based on gums and mucilage extracted (as illustrated in Fig. 7.16) from plant species that include Hibiscus/*Abelmoschus esculentus* (Okra), *Malva sylvestris* (Mallow), *Plantago psyllium* (Psyllium), *Plantago ovata* (Isabgol), *Tamarindus indica* (Tamarind), and *Trigonella foenum-graecum* (Fenugreek) have been examined.

These biopolymers have shown excellent results in treatment of landfill leachate (Al-Hamadani et al. 2011), biologically treated effluent (Anastasakis et al. 2009), textile wastewater (Mishra and Bajpai 2005), tannery effluent (Lee et al. 2014; Mishra et al. 2004), and sewage effluent (Mishra et al. 2003). At least 85 % of total suspended solids (TSS) removal, 70 % of turbidity removal, 60 % of chemical oxygen demand (COD) reduction, and 90 % of color removal have been established in these studies. Some of them were effective in low concentrations compared to chemical ones. More than 85 % removal of suspended solids from sewage wastewater and tannery effluent was achieved using 0.12 mg/L of okra gum and 0.08 mg/L Fenugreek mucilage, respectively (Mishra et al. 2004; Agarwal et al. 2001).

#### 7.1.4.5 Cellulose

Cellulose is one of the most abundant natural polysaccharide (Das et al. 2012). Anionic sodium carboxymethylcellulose (Na-CMC) was tested as environmentally friendly flocculants with addition of aluminum sulfate as coagulant for the removal of turbidity in drinking water treatment (Khiari et al. 2010). Sodium carboxymethylcellulose (Na-CMC) can be extracted from an agricultural waste date palm rachis. In another study, anionized dicarboxylic acid nanocellulose (DCC) flocculant showed promising results with addition of ferric sulfate as coagulant in treating the wastewater (Suopajärvi et al. 2013).

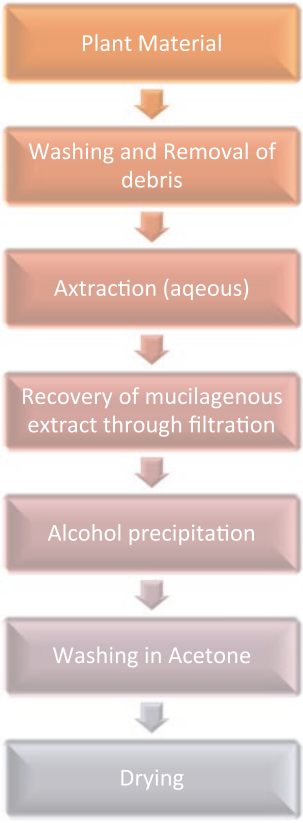


**Fig. 7.16** General processing steps in preparation of plant-based flocculants

## 7.2 Conclusion

Natural polymers play a significant and important role in production of oil and gas (drilling fluid). They are not only a type of drilling fluids which support a conducive environment for carrying out effective drilling operations but also enhance the different properties of drilling fluids by adding them as viscosifier, filtrate reducing agent, or lost circulation control agent. Besides their role in nonrenewable energy, they also produce biomass especially lignocellulosic biomass to support the renewable energy. Biomass can be converted into three main types of products; **Electrical/heat energy, Transport fuel (biofuel), and chemical feedstock**. They contribute to the new hybrid fuel cell which combines some features of solar cells, fuel cells, and redox flow batteries which convert biomass to electricity with the help of a catalyst activated by solar or thermal energy at low temperature. Their applications in other fields of engineering are infinite but in this chapter, we show their application in wastewater treatment. The need for the environmentally friendly materials in treating water and wastewater continue to increase during last decade so bioflocculants

have emerged to replace commercial ones. High molecular weight bioflocculant can treat wastewater by both mechanisms, coagulation by charge neutralization and flocculation by bridging mechanism. Chitosan, tannin, gums, mucilage, and cellulose are considered to be the most important examples for bioflocculant.

**Acknowledgments** The authors would like to acknowledge all staffs of Egyptian Petroleum Research Institute for encouragement and support.

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# Chapter 8
# Cosmetics and Personal Care Products

**Géraldine Savary, Michel Grisel and Céline Picard**

## 8.1 Introduction

For many years, manufacture, labelling and supply of cosmetic products are being submitted to Regulations, depending on the area (European Union, U.S., Canada, Brazil, Japan, China, etc.). Definition of cosmetics and personal care products therefore varies depending on the countries or world regions. Following the Regulation (EC) N°1223/2009 of the European parliament and of the council of 30th November 2009, cosmetic products in Europe means "any substance or mixture intended to be placed in contact with the external parts of the human body (epidermis, hair system, nails, lips and external genital organs) or with the teeth and the mucous membranes of the oral cavity with a view exclusively or mainly to cleaning them, perfuming them, changing their appearance, protecting them, keeping them in good condition or correcting body odours". The term 'substance' means a chemical element and its compounds in the natural state or obtained by any manufacturing process, including any additive necessary to preserve its stability and any impurity deriving from the process used but excluding any solvent which may be separated without affecting the stability of the substance or changing its composition (Cosmetic Products 2013; Official Journal of the European Union 2009).

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O. Olatunji (ed.), *Natural Polymers*, DOI 10.1007/978-3-319-26414-1_8

In the U.S., The Food and Drug Administration (FDA) Act regulates cosmetics and defines them as "articles intended to be rubbed, poured, sprinkled, or sprayed on, introduced into, or otherwise applied to the human body… for cleansing, beautifying, promoting attractiveness, or altering the appearance" [FD&C Act, sec. 201(i)].

Among the important differences between requirements for cosmetics in the United States and various other countries are the legal definitions of drugs and cosmetics, restrictions on the use of colour additives and other ingredients, and registration requirements. Some products regulated as cosmetics in Europe, for instance, are regulated as drugs in the United States. Sunscreens are a case in point. There are also differences regarding prohibited and restricted ingredients, particularly colour additives and preservatives. Some countries may require cosmetic companies to register their establishments and list products and ingredients with the government; in the United States, cosmetic registration is highly recommended but remains voluntary (Cosmetics and U.S. Law 2005).

Taking these definitions all together, cosmetic products may include creams, emulsions, lotions, gels and oils for the skin, face masks, tinted bases (liquids, pastes, powders), make-up powders, after-bath powders, hygienic powders, toilet soaps, deodorant soaps, perfumes, toilet waters and eau de Cologne, bath and shower preparations (salts, foams, oils, gels), depilatories, deodorants and antiperspirants, hair colourants, products for waving, straightening and fixing hair, hair-setting products, hair-cleansing products (lotions, powders, shampoos), hair-conditioning products (lotions, creams, oils), hairdressing products (lotions, lacquers, brilliantine's), shaving products (creams, foams, lotions), make-up and products removing make-up, products intended for application to the lips, products for care of teeth and the mouth, products for nail care and make-up, products for external intimate hygiene, sunbathing products, products for tanning without sun, skin-whitening products and anti-wrinkle products, as well as any material intended for use as a component of a cosmetic product (Official Journal of the European Union 2009; Cosmetics and U.S. Law 2005).

In order to formulate varied delivery systems, cosmetic industries, from ingredients producers to end-products distributors are responsible for checking the cosmetics' compliance with the requirements of applicable regulations and other relevant legislation including REACH, restriction of hazardous substances, good manufacturing practices, etc. Thus, ingredients used to formulate cosmetic and personal care products are usually cosmetic grade that means produced and sold by manufacturers that checked the safety according to regulations. The Cosmetic, Toiletries, Fragrance Association (CTFA), now The Personal Care Products Council, created the first edition of the Cosmetic Ingredient Dictionary in 1973. The first edition of this Dictionary contained a listing of 5000 trade and chemical names together with their CTFA adopted names, definitions, structures, Chemical Abstract Service Registry (CAS) numbers and other information. In 1994, the fifth edition contained more than 6000 chemical names and was called the International Cosmetic Ingredient Dictionary first edition of the Cosmetic Ingredient. Since then, most countries have adopted this nomenclature and today, cosmetic

ingredients are described and referred on packaging and in the ingredients list on the label with their INCI name, a systematic name coined by the International Nomenclature Committee. The 2014 International Cosmetic Ingredient Dictionary and Handbook provided the most comprehensive listing of ingredients used in cosmetic and personal care products with 21,000 monographs of INCI labelling names (Personal Care Products Council 2015).

Cosmetic products are used by consumers for specific function or a promise of efficiency but also mostly for the pleasure it brings to them. Thus, during many years, cosmetic ingredients and products have been developed and produced to fulfil these attempts, thus partly explaining the high number of ingredients available. However, consumers nowadays have become increasingly cautious on safety and environmental issues. As a consequence, in relationship with the deep evolution of the different regulations in the world since the 1970s, consumers' concerns are also to use products with a promise of safety and with a respect for living systems and environment. So today, consumers are also particularly sensitive to raw material selection and are looking for more "natural products". Consequently, different ingredient families such as animal-based ingredients, nanomaterials, preservatives (e.g. parabens) suffer from a low opinion. As for many others areas, brand image and marketing are very important in cosmetic industries and more products on sale today which claim to possess "naturality".

In such a context, more interests are given to ingredients issued from a natural source and for which the steps of transformation are reduced to a minimum, with few or even no chemical reagents. Among the different classes of ingredients, natural polymers and their derivatives are an important class of ingredients, widely used in a lot of delivery cosmetic products. The aim of this chapter is to describe the place, the role and the use of such polymers in the cosmetic field. The first part of this chapter gives general information on type and structure of the different natural polymers generally encountered and their place among the different polymers used in cosmetic. In order to improve their functional properties, natural polymers may be chemically modified and the principle of these modifications is presented through the example of cellulose derivatives. Then, in a second part, the role and properties of natural polymers in cosmetics are presented following three main impacts on stability, rheology and during application. In order to illustrate these two first parts, the third one details the examples of cosmetic formulations with specific focus on how natural polymers and derivatives may be handled to be formulated. Finally, a conclusion presents several promising innovations on those compounds and some perspectives (see also Chap. 12).

## 8.2 Generalities

Polymers are one of the most important class of ingredients in cosmetics and personal care and represent the second largest class of ingredients in this field (Lochhead 2007). They are referenced on the label of a cosmetic product, with

their INCI name in the ingredients list. It is important to note that one of the requirements for the labelling is to first list the ingredients in descending order of predominance by weight, if they are present at more than 1 % in the formula and then ingredients present at a concentration not exceeding 1 % may be listed in any order. Thus, as polymers are generally added at concentrations lower than 1 % (see Table 8.1), they can be found at the bottom of the ingredients list.

INCI assignments for polymers are based on starting monomers rather than resultant polymer as they are not always easily defined and can be a complex mixture of reactants and by-products. So, for synthetic polymers, guidelines for INCI assignments can be found in the following references. Biological materials are named specifically (e.g. hyaluronic acid) when the material has been isolated, purified and chemically characterized. When the end product is produced from fermentation or microorganism culture, it has a common or usual name, such name may be used, e.g. gellan gum, xanthan gum. Finally, botanicals are cosmetic ingredients directly derived from plants. Generally, these ingredients have not undergone chemical modification and include extracts, juices, waters, distillates, powders, oils, waxes, gels, saps, tars, gums, unsaponifiables, and resins. As an example, INCI name of carob or locust bean gum is Ceratonia Siliqua Gum as it is a gum obtained from the ground endosperms of Ceratonia siliqua (INCI Nomenclature Conventions 2015; Abrutyn 2010).

Polymer can be defined as an organic or inorganic compound, with large dimension and a high molecular weight. It is composed of large macromolecular chains made up with the covalent assembly of a great number of repetitive units or monomers. In the INCI dictionary, polymers can be categorized as: organic polymers, inorganic polymers, siloxane polymers and naturally occurring polymers, classes that can be further sub-categorized (Abrutyn 2010).

This chapter only focuses on organic polymers. There are several ways to classify organic polymers; according to their source, there are natural polymers obtained from biosynthesis, semi-synthetic polymers obtained by chemical modifications of natural polymers and synthetic polymers, obtained through polymerization reactions (step-growth or chain-growth reaction). In the case of cosmetic products, it may also be interesting to classify those polymers according to their electric charge, especially in the case of water-soluble polymers, which represent an important part of this class of ingredients in this field. Thus, among polymers, natural, modified ones (so-called artificial), and synthetic ones, nonionic as well as anionic, cationic or amphoteric substances are available.

Polymers can be characterized by the arrangement of the atoms and repetitive units in the chain: homopolymers are derived from one type of monomer; copolymers are derived from two or more species of monomers and as a consequence can be distinguished by the sequence of their monomer units (random, alternating, diblock, triblock, grafted).

Two key parameters should be known to characterize polymers: its molecular weight and its architecture. With the exception of naturally occurring proteins, all polymers are mixtures of many molecular weights and are polydisperse and the knowledge of the distribution of molecular weights is very important as it may

**Table 8.1** Main natural polymers used in cosmetics[a]

| Name | Origin/source | Function | Level (%) | Current applications in cosmetics | Examples of derivatives used in cosmetics |
|---|---|---|---|---|---|
| Xanthan | Biotechnology | Thickener; emulsion stabilizer; suspending agent | 0.1–1 | Skin care; haircare; conditioners; toothpaste; aftershave; shower gel; shower cream; body lotion; shampoo; sunscreen; cleanser… | None |
| Hyaluronic acid + hydrolysis products | | Moisturizer, softening agent | 0.1–2 | Moisturizing cream and lotion; hydrating gels, anti-ageing and anti-wrinkle products, pre/after sun lotions, protecting and nourishing products… | None |
| Sclerotium gum | | Thickener; emulsion stabilizer; suspending agent | 0.02–1 | Skin care: lotions, creams, face masks… sun care lotions; bath and shower gels and washes; hair care (shampoo)… | None |
| Cellulose + Microcrystalline cellulose | Vegetal | Thickener; film former; absorbant; opacifiant; Charge; softening agent | 0.5–2 | Skin care; lipstick; foundation; face, body and hand products; eyeliner; moisturizing products; mascara; hair dyes and colours; bath preparation; shampoos; toothpaste; antiperspirant… | See detail in Table 8.2 |

(continued)

**Table 8.1** (continued)

| Name | Origin/source | Function | Level (%) | Current applications in cosmetics | Examples of derivatives used in cosmetics |
|---|---|---|---|---|---|
| Starch (maize, potato, tapioca…) Including maltodextrin | Vegetal (plant seed) | Thickener; conditioner; powder (charge): softening agent | 3–10 | Conditioning; body and make-up powders; antiperspirant; colour cosmetics; creams; lotions; eye cosmetics; face scrub; liquid make-up; liquid talc… | Aluminium starch octenyl succinate<br>Distarch phosphate<br>Hydroxypropyl starch phosphate<br>Starch hydroxypropyltrimonium chloride |
| Galactomannan gums (guar and locust bean) | | Thickener; film former, stabilizer | 0.1–1 | Skin care; hair care | Hydroxypropylguar (hpg)<br>Guar hydroxypropyltrimonium chloride<br>Locust bean hydroxypropyltrimonium chloride |
| Hydrolyzed wheat (hydr wheat) | | Conditioner; film former; tensor; antistatic | 0.5–5 | Skin care, haircare | Hydr wheat protein dimethicone peg-7 acetate<br>Hydr wheat protein peg-20 acetate copolymer<br>Hydr wheat protein polysiloxane copolymer |
| Acacia gum | Vegetal (plant exudate) | Thickener; dispersing agent; foam and emulsion stabilizer; adhesive; film former | 1–10 | Cleanser; creams; lotions; balms; pomades; shampoos; body washes; make-up products (e.g. Mascara, brow and lash gels)… | None |
| Carrageenan gum (kappa, iota, lambda) | Vegetal (seaweed) | Thickener; gelling agent; film former | 0.2–1.2 | Toothpaste; skin care; cream | None |
| Alginate and alginic acid | | Thickener, suspending agent; film-forming | 0.2–2 | Skin care; styling products; toothpaste | Propylene glycol alginate |

(continued)

**Table 8.1** (continued)

| Name | Origin/source | Function | Level (%) | Current applications in cosmetics | Examples of derivatives used in cosmetics |
|---|---|---|---|---|---|
| Hydrolyzed keratin (hydr.keratin) | Animal or vegetal | Conditioner; moisturizer | 0.2–5 | Shampoos; hair conditioners; hair balms; hair pomades; skin care products including lotions and creams… | Cocodimoniumhydroxypropylhydr. keratin<br>Cocodimoniumhydroxypropylhydr. keratin<br>Hydr.keratinpg-propylmethylsilanediol |
| Collagen, gelatin, and hydrolyzed collagen (hydr.collagen) | Animal | Conditioner; moisturizer; hydrating; film-forming | 0.2–2 | Skin care; haircare; anti-ageing and moisturizing lotions; serums; sun care and after sun products; make-up products; hair conditioners; shampoos; hair masks… | Cocodimoniumhydroxypropylhydr. collagen<br>Lauryldimoniumhydroxypropylhydr. collagen<br>Isostearoylhydr.collagen |
| Chitosan, hydrolyzed chitosan and chitin | | Thickener; conditioner; chelating agent; hydrating, film former | 0.25–1 | Hair care, skin care | Chitosan lactate<br>Chitosanpyrrolidonium carboxylate |
| Hydrolyzed silk (hydr. silk) | | Hair conditioner; +antistatic; humectants | 0.2–2 | Haircare; shampoo; mask | Hydr.silkpg-propylmethylsilanediol<br>Sodium lauroylhydr.silk |

[a]*Sources* Le Flacon (2015), Lochhead and Gruber (1999), Making Cosmetics (2015), Official Journal of the European Union (2009)

influence properties such as the rheology of melts and solutions, adhesion and ageing behaviour. Furthermore, architecture of a polymer affects physical, functional and/or chemical properties. Chains can be structured in many different ways: linear, branched, side chains, rigid rod, macrocycle, star polymers, comb polymers, brush polymers, dendrimers, cross-linked polymers. Finally, polymers can be amorphous or semi-crystalline, depending on the chains arrangement and ordering.

Due to their marked properties, even at low content, polymers are used in small quantities to exert various functions in formulations: rheology modifiers, e.g. thickeners/surface active modifiers such as surfactants, emulsifiers and wetting agents/solubility modifiers including coupling agents and dispersants/bulking agents, preservatives, skin and hair conditioners, sunscreen agents/coating agents, encapsulants/abrasive, exfoliants (Abrutyn 2010).

Natural polymers or biopolymers include proteins, polysaccharides, natural rubber, resins and gums. Proteins and polypeptides are constituted of amino acids linked by an amide linkage or peptide bond between the amino group of one molecule and the carboxyl group of another. Most proteins derivatives for cosmetic purposes are obtained from simple proteins (fibrous and globular) while conjugated proteins (proteoglycans and nucleoprotein derivatives) are far less frequently used. Main proteins and protein derivatives used in cosmetic products are obtained from animal and vegetable sources. Collagen, elastin, keratins, milk and silk proteins are the first and most successfully used in the modern cosmetics industry and are from animal sources. They are currently used as water-soluble derivatives, suitable for cosmetic use, and are obtained from partial hydrolysis of native form. The success of such ingredients is also related to their wide availability at low cost and high-purity but also because of their high tolerance as human skin and connective tissues are constituted by the same proteins. Due to their animal sources and loss of popularity since last decades, proteins issued from vegetable and plant sources have been more developed; in particular, interest in proteins and hydrolyzed derivates from wheat gluten and soy have been growing a lot. These last ingredients are reported in Table 8.1 with their level of use and current functions in cosmetic products. The first rational use of proteins and peptides in cosmetics dates to the 1950s and since the beginning of the 1960s, their binding properties to skin and hair and substantively to hair were investigated and demonstrated. Today, numerous protein derivatives are developed to enhance their functionalities but also to find new protein sources. As they are mainly used as actives, their roles will be detailed in Sect. 8.3.3 dealing with the sensory and properties during application (Teglia and Secchi 1999).

Polysaccharides are composed of simple carbohydrates linked to each other by acetal bonds. Main polysaccharides used in the cosmetic industry are reported in Table 8.1. This list is not exhaustive and we decided to highlight the ones whose occurrence is most important in industrial products. Like alginates, pectins and carrageenans, xanthan is an anionic polysaccharide. It is obtained by bacterial fermentation and as a complex structure comprising a primary chain of glucose which has, on alternating glucose moieties, a branching trisaccharide side chain. Thus, in solution, xanthan generally forms helical coils characterized by a rigid backbone and is an excellent suspending agent. Its properties are mainly described

in Sects. 8.3.1 and 8.3.2 concerning stabilizing and rheological properties of natural polymers; in addition, sensory characteristics of this important cosmetic ingredient are also presented in Sect. 8.3.3.

Hyaluronic acid is also an anionic polysaccharide, isolated from various animal tissues and commercially manufactured by bacterial fermentation. It is made of two repeating monosaccharides: glucuronic acid and *N*-acetyl-glucosamine. It is mainly used for topical purposes and as an active, as it is described in Sect. 8.3.3. Finally, among anionic polysaccharides, acacia gum is one of the oldest and most commercially well-established. It is extracted from exudate gums of specific trees (Acacia Senegal for instance) and is comprised of a neutral backbone of galactose units that have multiple branching glycans. It is characterized by a relatively low molecular weight and thus is used in applications where high levels of polysaccharide are desired without enhancing viscosity. It is an emulsifying agent supplying stabilization properties to complex multiphase systems as noted in the Sect. 8.3.1.

Chitosan is the only naturally occurring polysaccharide to be cationic. This property is only shown at pH below seven. The advantage of being cationic is the ability to bind strongly to anionic surfaces like human and hair skin. Chitosan is a random copolymer comprised of two monosaccharides, *N*-acetyl-b-d-(1,4)-glucosamine and b-d-(1,4)-glucosamine generally in a 1:4 ratio in commercial materials. Besides the substantive application to hair and skin owing to the cationic property; chitosan is also used as a film-forming agent in fixative products and 2-in-1 shampoos. This polymer is principally described in Sect. 8.3.3. The two other cationic polysaccharides extensively used in cosmetic are cationic derivatives of cellulose and guar, cited in Sects. 8.3.1 and 8.3.3.

Cellulose, starch, galactomannan and sclerotium gums are nonionic polysaccharides. Together, cellulose and starch represent the most abundant polysaccharides available for commercial exploitation. They are composed of one repeating monosaccharide, glucose, linked to each other by β-D (1,4) or α-D (1,4) bonds, respectively. Sclerotium gum is also composed of repeating glucose moieties but linked through β-D (1,3) linkage together with a branching of glucose and is a good suspending agent like xanthan. However, unlike cellulose or starch, sclerotium gum has limited uses in personal care.

Galactomannans, guar and locust bean gum more specifically, have a backbone of β-D-(1,4)-mannose with a branching of α-D-(1,6)-galactose. Guar is more substituted than locust bean and can be characterized as a comb-like polymer. Although locust bean gum has received limited use in the personal care industry, guar is an important natural thickening agent for aqueous compositions and brings lubriciousness or silky feel to those compositions (Gruber 1999).

Due to their chemical composition and also the conformation of their macromolecular chains, those nonionic polymers often show a weak or complex solubility in water; thus, in order to improve and enhance their interactions with different solvents, many semi-natural derivatives are prepared from cellulose, guar or starch polysaccharides. Those derivatives are extensively used in personal care products when compared to the native ones. Few examples are mentioned in Table 8.1, such as hydroxypropyl guar or maltodextrin (Gruber 1999).

To better understand the principle of such modifications, a focus on cellulose modification is proposed (Table 8.2). Cellulose is a polydisperse linear homopolymer, consisting of β-1,4-glycosidic linked D-glucopyranose units [so-called anhydroglucose units (AGU)]. The polymer contains free hydroxyl groups at the C-2, C-3 and C-6 atoms.

The abundance of hydroxyl groups and concomitant tendency to form intra- and intermolecular hydrogen bonds results in the formation of linear aggregates of helical structures. In the solid state, highly ordered crystalline areas are interspersed between less ordered amorphous zones. Consequently, as cellulose is insoluble in water, conversion to water-soluble derivate forms is usually required for cosmetic uses. This can be done either physically or chemically (Gruber 1999; Zecher and Gerrish 1999).

Disruption of the hydrogen bonds can be accomplished by cellulose derivatization. To that purpose, the native polymer is first submitted to aqueous alkali conditions to induce swelling of the cellulose fibres prior to further treatment. Then, alkali-cellulose may be treated by sodium chloroacetate to produce carboxymethylcellulose, an anionic derivative, or with various alkylating agents, to produce nonionic cellulose ethers: hydroxyethyl cellulose (HEC), hydroxypropyl cellulose (HPC), methyl cellulose (MC) and hydroxypropylmethyl cellulose (HPMC) are among the most popular and useful rheology modifiers employed in the personal care industry (Gruber 1999; Zecher and Gerrish 1999).

The corresponding polymer properties are governed by the extent of the substitution. This last parameter is expressed as the degree of substitution (DS) or the molar substitution (MS). As each anhydroglucose unit (AGU) contains three free hydroxyl groups available for reaction, the polymer may have a maximum degree of substitution (DS) of three where DS is defined as the average number of substituent groups per anhydroglucose unit.

When alkylene oxides (HEC, HPC, HPMC, etc.) are used, new hydroxyl substituent groups are formed that can further react. Thus, the extent of substitution is better characterized as the molar substitution (MS), where MS is defined as the average number of moles of substituent groups per AGU. For instance, hydroxyethyl cellulose is commonly manufactured with a MS of 1.8–2.5 but various grades range from an MS of 1.5–3.0. Cellulose gum or carboxymethylcellulose is currently manufactured with DS ranging from 0.65 to 1.45. For both, solution viscosities greatly vary, depending also on the molecular weight of the product (Review Expert Panel 2009).

Hydroxyethyl cellulose (HEC) can be further derived with various cationic reagents to randomly add quaternary cationic charges along the HEC backbone. Known by their INCI name as polyquaternium-10 or polyquaternium-4, those cationic derivatives are extensively employed as conditioner or conditioning and fixative adjuvant, respectively, in hair and skin care formulations (Gruber 1999).

At last, cellulose can be physically treated to produce microcrystalline cellulose (MCC) which is prepared by treating wood pulp and linters with dilute mineral acid and is described as purified, partially depolymerised cellulose with a degree of polymerisation (DP) below 350. MCC is basically made of crystallites of

**Table 8.2** Main modified celluloses[a]

| INCI Name | Description | Function | Examples |
|---|---|---|---|
| Cellulose | Natural polysaccharide derived from plants fibres<br>Linear polymer of β-1,4-d-glucose | Absorbent, bulking, opacifying, viscosity controlling | Foundation, facial scrub, face mask, eyeliner |
| Microcrystalline Cellulose | Purified, partially depolymerised fraction of α-cellulose. Isolated, colloidal crystalline portions of cellulose fibres | Absorbent, anticaking, bulking, emulsion stabilizing, opacifying, viscosity controlling | Moisturizing cream, shower gel, anti-ageing fluid, hand cream |
| *Anionic cellulose derivatives* | | | |
| Cellulose gum (sodium carboxymethylcellulose) | Sodium salt of the polycarboxymethyl ether of cellulose. Reaction of sodium chloroacetate with alkali-treated cellulose | Binding, emulsion stabilizing, film forming, masking, viscosity controlling | Toothpaste, moisturizing cream, anti-wrinkle fluids and creams, skin care |
| *Nonionic cellulose derivatives* | | | |
| Cellulose Acetate Butyrate | Butyric acid ester of a partially acetylated cellulose | Film forming | Serum, moisturizers, skin care, nail care |
| Cetyl Hydroxyethylcellulose | Ether of cetyl alcohol and hydroxy-ethylcellulose. Reaction of alkali-cellulose with ethylene oxide followed by a cetyl substitution | Emulsion stabilizing, film forming, viscosity controlling | Hair care, shaving foam, hair lotion, body gel |
| Ethylcellulose | Ethyl ether of cellulose | Binding, film forming, viscosity controlling | Skin care, skin cleansers, lip balm |
| Hydroxyethylcellulose | Ethylene glycol ether of cellulose<br>Reacting alkali-cellulose with ethylene oxide in the presence of alcohol or acetone | Binding, emulsion stabilizing, film forming, stabilizing, viscosity controlling | Skin care, deodorant, serum, hair care, shaving gel, mascara |
| Hydroxypropylcellulose | Propylene glycol ether of cellulose (reacting propylene oxide with alkali-treated cellulose) | Binding, emulsifying, emulsion stabilizing, film forming, viscosity controlling | Colognes and toilet waters, hair conditioners, aftershave lotions, moisturizers |

(continued)

**Table 8.2** (continued)

| INCI Name | Description | Function | Examples |
|---|---|---|---|
| Hydroxypropyl Methylcellulose | Propylene glycol ether of methyl cellulose. Methyl chloride treatment of hydroxypropyl cellulose | Binding, emulsion stabilizing, film forming, surfactant, viscosity controlling | Facial scrub, paste and treatment mask, masks, bubble baths, shaving cream |
| Methylcellulose | Methyl ether of cellulose. Reaction of methyl chloride with alkali-treated cellulose | Binding, emulsion stabilizing, viscosity controlling | Body lotion, shampoos, cleansers |
| Nitrocellulose | Nitrate esters of cellulose. Treatment of cellulose by nitric and sulfuric acids | Film forming | Nail polishes and enamels |
| *Cationic cellulose derivatives* | | | |
| Polyquaternium-10 | Cationic hydroxyethyl cellulose Reaction of alkali-treated hydroxyethyl cellulose with a cationic epoxy (2,3-epoxypropyltrimethylammonium chloride) | Antistatic, film forming | Shampoos, body cleansers, hair conditioners |

[a]*Sources* Le Flacon (2015), Lochhead and Gruber (1999), Official Journal of the European Union (2009), Review Expert Panel (2009)

colloidal size. The crystallite aggregates, forming particles, which in turn agglomerate during drying of the cellulose slurry to reach a final mean particle size between 20 and 200 μm. Microcrystalline cellulose is a diluent with very good binding properties for direct compression (compaction of tablets for instance) and due to its insolubility, it provides a "gel" network with pseudoplastic, highly shear thinning and thixotropic properties (Thoorens et al. 2014).

To conclude, polysaccharides in the solution can exist as loose random coils or rigid helices. They can be anionic, cationic, nonionic or even amphoteric depending on their chemical composition. They can be single coils, double coils and even aggregates of coils; the nature of which can be influenced by, among other things, temperature, concentrations and other species such as salts.

For all these reasons, natural polymers, gums and resins have been used in the industry since the early 1940s as water-soluble binders, thickeners and film-forming agents. Those properties are highlighted in Sects. 8.3.1 and 8.3.2 dealing with the stabilizing and rheological properties of natural and nature modified polymers as illustrated through examples in the cosmetic field.

Unfortunately, use of polymers obtained from natural sources has some disadvantages: they vary in purity and physical appearance which imply variations in viscosity and microbial contamination, and are relatively expensive when compared to the ones obtained by synthetic routes. These variations are due to the difficulty to obtain stable supplies. As a consequence, those features historically led to a change to synthetic or semi-synthetic substitutes (Winnick 1999). At the beginning, in the 1950s, synthetic or semi-synthetic polymers have been developed to match the properties of gums and resins. Since 1970s, carbomers, polymers obtained from acrylic acid, have dominated the market of thickening and stabilizing agents used in emulsions and lotions. In the 1990s, hydrophobically-modified versions of carbomers (Acrylates/C10-30 alkyl Acrylate Crosspolymer) were introduced, combining emulsifying and rheology-modifying properties. Other synthetic polymers used for cosmetic purposes are acrylamides copolymer, simple vinyl polymers, crosspolymers like acrylates/VA (Vinyl Acetate) crosspolymer, alkoxylatedhomopolymeric ethers based on ethylene oxide or propylene oxide. So, until recently, chemical synthesis of synthetic polymers made it possible to tune several required properties (thickening, associative properties, emulsifying) with one ingredient or a mixture of synthetic ingredients leading to improved formulations.

However, today there is a growing consumer demand for natural products, safety profile of ingredients and use of renewable resources which give a renewed interest in natural polymers. Section 8.3.3 of this chapter presents new research on the sensory properties brought by natural and natural modified polymers. Finally, it is also important to keep in mind that most part of cosmetic products and personal care must comply with quite a long period after opening (PAO), at least 6 or 12 months. Thus, stabilizing and maintaining physicochemical as well as sensory properties and, of course, the consumer security for these products over a wide period of time is a challenge. To do so, as can be noticed in Sect. 8.4 of this chapter, dealing with examples of cosmetic formulations including polymers, synthetic

and natural polymers coexist with relatively high amounts of synthetic emulsifiers that are conjugated with fatty alcohol, in order to create organized structures in the emulsions (liquid crystalline phase) and to obtain products with consistency that can support long-time ageing. Further details on synthetic polymers used and role of polymers in cosmetic product can be obtained in Goddard and Gruber (1999), Lochhead (2007, 2010).

## 8.3 Functions of Natural Polymers in Cosmetic Products

### *8.3.1 Impact on the Stability*

#### 8.3.1.1 Cosmetic Products: Complex Systems Subjected to Destabilization

When cosmetic and toiletry products are developed, they have to fulfil a number of requirements: they have to provide a function (cleaning hair and skin, protecting against sunburst, etc.), to enhance the psychological well-being of consumers by increasing their aesthetic appeal (for example impart a pleasant odour and making the skin feel smooth) while insuring medical safety as they come in close contact with various organs and tissues like hair and skin, and sometimes the mucous membrane. The different ingredients constituting the formulations must be chosen with respect to the biological and physicochemical properties of those substrates; in a formulation, they are numerous and could be oil, water, surfactants, pigments, UV filters, colouring agents, fragrant, preservatives, conditioning agents, vitamins amongst others. Different delivery systems—emulsions, suspensions, foams, solutions—are prepared to optimize the effects and benefits of the different components (Tadros 2008). These complex systems are generally included as colloidal systems.

Emulsions are one of the most common delivery system used in cosmetics. They consist of mixtures of at least one liquid dispersed in another in the form of droplets, both liquids being immiscible or poorly miscible. They are classified as follows:

- Macroemulsions: simple emulsions that can be Oil-in-Water (O/W) or Water-in-Oil (W/O) like lotions and creams. Droplet sizes generally range between 0.1 and 100 μm.
- Nanoemulsions: simple emulsions (O/W or W/O) for which droplet sizes range between 20 and 200 nm.
- Multiple emulsions: More complex systems like oil-in-water-in-oil or water-in-oil-in-water with droplet sizes similar to the ones in macroemulsions.
- Microemulsions: system of water, oil and both surfactant and co-surfactant which is a single optically isotropic and thermodynamically stable liquid solution. Droplet sizes range from 10 to 100 nm.

Solid/liquid dispersions or suspensions are dispersed systems currently used in cosmetics. These can be classified as follows:

- Suspensions: dispersions of solid particles in a liquid continuous media (pigments, solid actives, clay, mechanical facial scrubs particles, polyamide particles,etc.) like lipsticks or nail polishes and also shampoos or shower gels containing particles. Particle sizes generally range from 0.1 to 100 μm;
- Nanosuspensions: particle sizes range from 20 to 200 nm.

Both emulsions and suspensions are combined to form emulsions–suspensions mixture or suspoemulsions like in the case of foundations where pigment particles are usually dispersed in the continuous phase of an O/W or W/O emulsion.

Except for microemulsions, all previous systems are thermodynamically instable and submitted to different destabilization mechanisms described below.

Similar for emulsions and suspensions, creaming and sedimentation depend on the size of the particles/droplets and the density difference between the particle and the medium. Those phenomena are more intense for sizes larger than 1 μm and density difference larger than 0.1 which occurs very frequently in cosmetic products. Creaming and sedimentation can be avoided or strongly reduced by enhancing viscosity of the continuous phase which can be done by using "thickeners" like polymers. If the droplet size or the particle size is reduced to 20–200 nm like in nanoemulsions or suspensions, respectively; then, Brownian diffusion overcome gravity and the systems are physically stable, without apparition of other destabilization mechanisms.

Flocculation is the result of an attractive interaction between particles or droplets. It can be weak or strong depending on the magnitude of the attractive energy. Weak flocculation is in some cases reversible by re-stirring and may also occur by two other mechanisms: bridging and depletion. Bridging flocculation may arise when a single polymer macromolecule weakly adsorb at the surface on more than one suspension particle or emulsion droplet. Depletion flocculation is produced by the addition of a non-adsorbing polymer. Increase of osmotic pressure around droplets results in exclusion of polymer species from the surface of particles and the formation of depleted zones and weak attraction between particles. For further information, see Tadros (2008) and Bouyer et al. (2012).

Strong flocculation leads to formation of aggregates that can further sediment or cream; in the case of highly concentrated suspension or emulsion, the particles or droplets create a three-dimensional "gel" structure. When flocculated structures are not re-dispersible or in the case of strong flocculation, this is the starting point of further sedimentation or creaming phenomena and especially coalescence in the case of emulsions or coagulation in the case of suspensions are nonreversible mechanisms. Coalescence is first the thinning and then the disruption of the liquid interfacial film between droplets until macroscopic oil–water phase separation. Coagulation is the formation of strong aggregates sediment or clusters forming compact structures. Both structures must be avoided.

Finally, emulsions may undergo Ostwald ripening that is a diffusion mechanism of smaller droplets, due to their solubility in the external phase, into larger ones. This phenomenon may lead to the separation of the phases and is also nonreversible.

#### 8.3.1.2 Stabilizing Properties of Natural Polymers in Cosmetic Emulsions and Suspensions

Natural and semi-synthetic polymers are used in personal care as rheology modifiers to achieve stability against settling during storage. Natural polymers concerned here include casein, alginates, guar gum, xanthan gum, tragacanth gum and semi-synthetic include modified cellulose such as carboxymethyl cellulose, methylcellulose, hydroxyethyl cellulose, hydroxypropyl cellulose (Lochhead 2007, 2010). Unlike the food area, in the cosmetic field, proteins and their derivatives are mostly used as active ingredients and polysaccharides are often used to stabilized emulsions and suspensions, all together combined with synthetic polymers like carbomers (see Sect. 8.4—Examples of formulas) and, in addition, small molecular weight emulsifiers, in order to confer the desired delivery characteristics such as smoothness. Those properties are focused in Sects. 8.3.2 and 8.3.3 of this chapter. As they are, for the most part of them, hydrophilic, it generally concerns formulations in which the continuous liquid phase is aqueous and they are mainly used to prevent creaming and sedimentation.

The mechanism of stabilization depends on adsorption ability of the macromolecules. Some adsorb at the oil–water interface while others only modify the aqueous phase viscosity due to their non-adsorbant nature. Rozanska et al. (2013) have compared the stabilizing effects of guar gum (GG), hydroxypropylmethyl cellulose (HPMC), carboxymethyl cellulose (Na-CMC) and xanthan gum (XG). O/W emulsions containing 20 and 40 vol% of dispersed phase were produced with 0.4 wt% GG and HPMC, 0.5 % Na-CMC and 0.1 and 0.2 wt% for XG. As non-adsorbing polysaccharides, XG, GG and Na-CMC exhibit emulsions with aggregated droplets due to depletion flocculation (Fig. 8.1a, e and f). The depletion forces are higher with increasing molar mass of the polymer and with polyelectrolytes (Na-CMC emulsion more flocculated that one with GG) and are stronger at low polymer concentration (0.1 wt% XG emulsion show bigger agglomerates than 0.2 wt% XG emulsion). HPMC adsorbs at the droplets surface and bridging flocculation is evidenced thus producing agglomerates similar to GG and 0.2 wt% XG emulsions. Authors show that those different flocculated states have an impact on rheological properties, as at low shear rate the rheological properties of emulsions depend on the size of aggregates made up of single oil droplets, which in turn may have an impact on stability of the emulsion.

Xanthan gum is one of the most widely occurring polysaccharide in cosmetic emulsions, as can be seen in the different formula given to illustrate utilization of natural polymers in the Sect. 8.4. Thus, a great number of research papers, dealing with cosmetic emulsions (Mostefa et al. 2006) or “simplified” or model emulsions

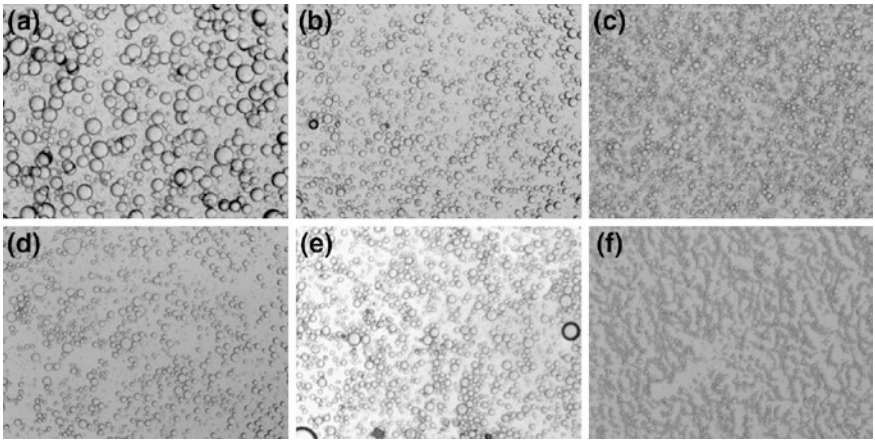


**Fig. 8.1** Microscopic pictures of emulsions with addition of GG 0.4 wt%, $\phi = 20$ vol% (**a**); HPMC 0.4 wt%, $\phi = 20$ vol% (**b**); XG 0.1 wt%, $\phi = 20$ vol% (**c**); XG 0.2 wt%, $\phi = 20$ vol% (**d**); XG 0.1 wt%, $\phi = 40$ vol% (**e**); Na-CMC 0.5 wt%, $\phi = 20$ vol% (**f**) (from Rozanska et al. 2013) with permission from Elsevier, Licence number 3634200640618

(Krstonosic et al. 2009, 2015; Vianna-Filho et al. 2013; Ye et al. 2004) have studied the effect of this polymer on the emulsions stability. The major results of those studies is that stability of emulsions mainly depends on xanthan gum concentration: in the study of Krstonosic et al. (2015), whatever the xanthan gum concentration (between 0.01 and 0.2 wt%) in the continuous phase, droplets flocculation occurs. Under a certain value (0.08 wt%), creaming is enhanced, and produces a phase separation in the emulsion, while above this value, emulsions containing higher xanthan concentration exhibit a delayed time in creaming. It has been reported that above a critical concentration, xanthan gum induces the establishment of a three-dimensional gel-like droplets network (Ye et al. 2004; Krstonosic et al. 2009; Aben et al. 2012). When xanthan concentration is still increased, less flocculation appears (>0.6 % in the study of Ye et al. 2004) and emulsions are then mostly stabilized by the continuous phase viscosity increase. Thus, Mostefa et al. (2006) show with experimental design that the most important parameter is the xanthan concentration. It has a positive influence in the range of [1 and 2 %] on the stability of a depilatory cream, in relationship with high viscosity of the aqueous phase of the oil-in-water emulsions. Hydroxyethyl cellulose is also widely used as thickener and rheology modifier to stabilize emulsions and suspensions. As Starch, alginates, carrageenans, hyaluronan, chitosan, it is considered as non-adsorbing polysaccharides.

Some other polysaccharides such as acacia gum, naturally occurring galactomannans (guar and carob), pectin and chemically modified starch or cellulose derivatives exhibit interfacial activity (Bouyer et al. 2012). Due to their amphiphilic character, they adsorb at the interface of the oil droplet, stabilizing the emulsion and through electrostatic and/or steric repulsive forces hinder flocculation and

coalescence. In the case of acacia gum and pectin, this surface activity is related to the presence of a protein fraction in the structures such as for, but less obviously, galactomannans (Bouyer et al. 2012; Vianna-Filho et al. 2013).

In order to improve interfacial properties, starch and cellulose have been chemically modified to introduce hydrophobic/hydrophilic groups along the macromolecules backbone. Hydroxypropylmethyl cellulose, hydroxypropyl cellulose and new derivatives from hydroxyethyl cellulose such as ethyl hydroxyethyl cellulose, methyl hydroxyethyl cellulose and hydrophobically-modified ethyl hydroxyethyl cellulose are known to exhibit high surface activity when compared to HEC (Asad 2011). Sun et al. (2007) studied the adsorption and thickening effect of hexadecyl modified hydroxyethyl cellulose compared to the hydroxyethyl cellulose. More than a polymeric surfactant, such a hydrophobically-modified polymer behaves as an associative polymer: it adsorbs at the oil/water interface due to penetration of the alkyl chains into the oil phase and shows much better thickening ability which is caused by the intermolecular association of the hydrophobic alkyl chains. Therefore, emulsions stability is the result of an associative thickening mechanism caused by alkyl chains, combined with the adsorption of hydrophobically-modified hydroxyethyl cellulose at the oil–water interface, which can form a solid film preventing droplets coalescence.

Starch may be hydrophobically-modified via octenyl succinic anhydride to produce OSA starch that can be used as emulsifier in oil-in-water emulsions (Krstonosic 2015). OSA starch may play the role of both an emulsifier and an emulsion stabilizer: the short octenyl succinate side chains adsorb at the oil–water interface while the large amylopectin backbone provides steric stabilization against flocculation. Recent studies focused on formation of Pickering emulsions, that are particle stabilized emulsions and so surfactants free emulsions, with hydrophobically-modified starch particles (Marku et al. 2012) or hydrophobized cellulose nanocrystals (Capron and Cathala 2013).

#### 8.3.1.3 Role of Natural and Semi-synthetic Polymers in Cleansing Products

Shampoos and conditioners are the highest volume of products sold in personal care. The principal function of a shampoo is to cleanse the hair. However, modern shampoos should at least cleanse, make the hair easier to style, and fragrance the hair with a pleasant, lingering smell (Lochhead 2012). Shampoos consist essentially of water, primary surfactant, one or more co-surfactants and soluble salt. Other ingredients are added for fragrance, preservation, conditioning and styling attributes. Primary surfactant is generally an anionic surfactant and the co-surfactant often called the foam booster is generally a betaine.

One essential attribute of a shampoo is its ability to produce rich foam. As complex systems previously described, foams may also be included in colloidal

complex systems as they are heterogeneous multiphasic systems composed of high volume fraction of gas and liquid. During cleaning process, foams are created by incorporating air during friction of shampoo on the wet hair. Foams are made of gas bubbles separated from each other by lamellae that are thin liquid films between two bubbles and plateau border, the region were three lamellae are joining together. During shelf life of foams, bubbles turn from spherical shape to polyhedral shape due to continuous drainage of the liquid and consequently thinning of the film between bubbles. Dramatic situation arises when lamellae are disrupt and bubbles burst. These are the two main mechanisms of foams destabilization.

It has been demonstrated that utilization of cationic polymers hinders drainage of the lamellar liquid; for this reason cellulose and guar cationic derivatives are extensively used in this field of cleansing personal care.

Thus, polyquaternium 24, a hydroxyethyl cellulose reacted with a lauryl dimethyl ammonium epoxide, provides conditioning attributes but also increases stability of oil-in-water emulsions and increases foam stability of aerosol mousses. Guar hydroxypropyltrimonium chloride is an excellent thickener, with suspending and stabilizing properties, combined with conditioning properties (Hoshowski 1997).

Polyquaternium-10 (see cellulosic derivatives Sect. 8.2, Table 8.2) is a hydroxypropyltrimethyl ammonium chloride ether of hydroxyethyl cellulose. With cationic guar, it is one of the most occurring cationic conditioning polymers in hair and skin care products, and more specifically in shampoos. Those polymers impart great deposition on hair for the corresponding shampoos.

In order to improve properties of conditioning and cleansing products, a lot of works have been realized to understand the interactions between surfactants and polymers in solution and to further use those interactions in formulations. For further details, see Lochhead (2007, 2010, 2012), Goddard (1999), Llamas et al. (2014) and Bureiko et al. (2014).

At last, as they are compatible with most shampoo ingredients, cellulosic derivatives such as methyl cellulose, hydroxypropyl cellulose and hydroxyethyl cellulose may also be added to the formulation; they are widely used in shampoo as thickening agents, to achieve desired viscosity; such cellulose derivatives also provide stabilizing effects in the case of conditioning shampoos or more complex shampoo formulations incorporating emollients like silicones or oils, and also solid particles.

Finally, it is noteworthy that cosmetic products are complex mixtures of many ingredients in interaction. Natural polymers are stabilizing agents but their ability may be reduced or improved according to the presence of the other ingredients. For this reason, it is not always possible to predict the impact of the polymer on the stability of a blend.

In this section, we mention that polymers may stabilize colloidal systems owing to an enhancement of the viscosity. In the following section, it is explained how the impact of polymers on the rheological properties exceeds largely a simply stabilizing function.

## *8.3.2 Impact on the Rheological Properties*

### 8.3.2.1 Rheology of Cosmetics: A Key from Manufacturing to End-User

Developing cosmetics requires controlling the rheological properties at the different steps of product life, from the initial raw material processing until the final utilization of product by consumers. Like in many other domains dealing with complex mixtures elaboration, rheology allows understanding and optimizing product development; rheology dimension has therefore to be considered for the entire manufacturing process: raw material and mixture quality control, production steps, stability considerations, final product characteristics and usage performance. The ease of picking of a cream from its container, the lotion pumping ability, the nail varnish spreading and film-forming capacity when drying, the hair-conditioning ability, the hair shaping/fixing of a hair fixer, the toothpaste squeezing out of a tube and shape integrity once on the brush, the soap flow capacity, etc., are few examples where product rheology has to be considered. In addition, more than in many other fields, the rheological properties are of primary importance for the consumer sensory perception and acceptance, as criteria for choosing a cosmetic product are unambiguously associated to texture, performance (e.g. cream hydration, lipstick film thickness and homogeneity) and pleasure sensation all over the product usage, ranging from the product shape before application to the final perception once the product applied (e.g. residual film softness). As cosmetic manufacturers permanently need to adapt the product to the consumer expectations, aim to fit to the market changes and also to develop innovating products, controlling the products rheology is a key aspect to be considered. For all these reasons, since many years the cosmetic industry considers rheology as one of the most promising tools allowing predicting the product sensory attributes and so the consumer's final choice (Tranchant et al. 2001).

Like in several other domains, rheology is currently used in the cosmetic industry to investigate the role of functional ingredients (such as polymers used as thickeners), the resulting microstructure and the stability of complex mixtures, the scale up of new developments and the process reproducibility. In addition, recently, few studies using rheology have been published with the aim to correlate sensory data to the rheological properties of cosmetic products (Dimuzio et al. 2005; Lukic et al. 2012a; Gilbert et al. 2013b).

### 8.3.2.2 Natural Polymers and Derivatives as Rheological Agents in Cosmetics

Cosmetic products cover a wide diversity of forms, ranging from monophasic systems including fluids, viscous solutions or gels, highly elastic emulsions, semi-solid or solid dispersions and powders. Among the various ingredients governing

the mixtures physical characteristics, like in many other domains polymeric species are widely used for controlling the general product flow and viscoelastic properties. Furthermore, biopolymer dispersions show a variety of rheological behaviours in relation with their molecular structure and conformation. Among the numerous cosmetic applications, polysaccharides and derivatives are more currently incorporated in the continuous phase of oil-in-water (O/W) emulsions to control the consistency (Bais et al. 2005; Tadros 2004).

#### 8.3.2.3 Natural Polymers to Control Formulations Stability and Texture

As previously mentioned in Sect. 8.3.1, cosmetic products have first of all to be stable over a fairly long period of time (often over 30 months) and the polymers stabilizing efficacy is currently employed for reaching sufficient lifetime. Basically, natural polymers are efficient to stabilize complex mixtures as a consequence of their high molecular weight, thus inducing large hydrodynamic volumes for the chains when hydrated in appropriate solvent. Biopolymers (polysaccharides and proteins) do efficiently act as stabilizers due to their ability to induce steric and electrostatic interactions, change the interface viscosity and viscoelasticity and to increase the continuous phase viscosity thus improving the whole mixture's stability. In addition, the interfacial tension may be significantly lowered by pure proteins and also due to the presence of proteins covalently linked to the polysaccharide backbone. A recent review focused on pharmaceutical potentiality of biopolymers brings further details on these crucial properties related to natural polymers (Bouyer et al. 2012).

In cosmetics, viscosity enhancement and/or weak gel establishment may be induced by weak interactions and/or chains overlap (e.g. xanthan, starch and hydroxyethylcellulose), while strong gels may be obtained by intermolecular complex occurrence (e.g. gelatin, carrageenan and alginate). Depending on the expected texture level at rest, formulator therefore has a variety of natural polymers and derivatives available when developing a new product. If considering the whole cosmetic market, the most common natural polymer used is xanthan as it provides high viscosity enhancement at rest, even at very low concentration, and remarkable flow properties under shear. Such remarkable viscosity enhancement and suspending ability is related to the xanthan well-known secondary, semi-rigid, helix strand conformation. As an example, toothpastes are concentrated dispersions, currently owing from 30 to 50 % of abrasive and/or polishing silica particles and are classically stabilized using xanthan due to its high suspending efficacy.

An interesting illustration is given by examining the rheological data related to an emulsion formula only differing by the polymer used as stabilizer and texturing agent (natural or artificial). Gilbert et al. (2012) investigated the effect of polymers of the whole rheological properties of a given O/W non-commercial emulsion, specifically developed at lab scale thus only differing by the polymer, most being natural or artificial, used at a unique level (1 % w/w).

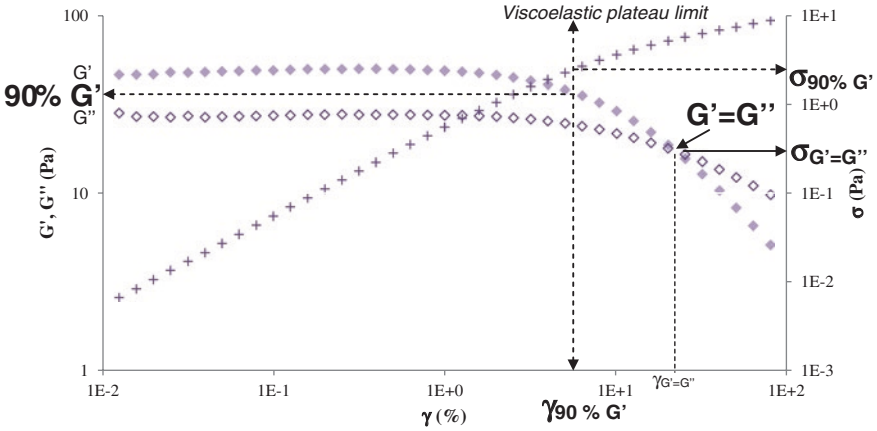


**Fig. 8.2** An example of viscoelastic data collected within and over the linear viscoelastic plateau. G′, G″ and τ are measured as a function of the strain at 1 rad $s^{-1}$ (*close symbol* G′; *open symbol* G″; *cross* oscillatory stress) (Gilbert 2012)

Data are obtained by viscoelastic measurements within and upon the linear viscoelastic plateau. As represented on Fig. 8.2, it is possible to get different data referring to the product properties: the elastic and viscous moduli (G′ and G″, respectively), tan δ or the critical strain and stress, corresponding to the cross-over point of G′ and G″ ($\sigma_{G'=G''}$ and $\gamma_{G'=G''}$, respectively).

Tested biopolymers, either natural or artificial, cover a wide range of properties as reported in Table 8.3; data are compared to a "control" emulsion with no added polymer. The emulsions viscoelastic parameters indicate distinct behaviours, ranging from viscoelastic liquids with tan δ close to 1 (e.g. carob, HE cellulose) to weak gel tendency for xanthan containing system (lower tan δ close to 0.1), this latter system being therefore efficient for reaching long-term stability. In addition, both the viscoelastic plateau limit and the recovery after shear appear highly dependent from the polymer type thus indicating distinct behaviours when

**Table 8.3** Rheological data (means ± SD) obtained from the strain and time sweep tests for O/W emulsions without polysaccharide (control) and with added polysaccharide

| Products | G′ (Pa) | G″ (Pa) | tan δ | $\gamma_{G'=G''}$ (%) | $\tau_{95\%\ G'}$ (s) |
|---|---|---|---|---|---|
| Carob | 58.9 ± 0.0 | 51.3 ± 0.1 | 0.870 ± 0.002 | 7.2 ± 0.2 | 297 ± 4 |
| Control | 84.3 ± 1.6 | 31.0 ± 0.5 | 0.368 ± 0.001 | 38.4 ± 11.2 | 141 ± 12 |
| HE cellulose | 46.6 ± 0.3 | 36.2 ± 0.4 | 0.776 ± 0.005 | 15.2 ± 0.0 | 264 ± 11 |
| HP guar | 56.5 ± 0.9 | 35.0 ± 0.4 | 0.619 ± 0.002 | 40.2 ± 0.1 | 227 ± 5 |
| HPM Cellulosecellulose | 48.6 ± 0.3 | 27.2 ± 0.4 | 0.559 ± 0.005 | 22.5 ± 0.1 | 257 ± 4 |
| Xanthan | 62.6 ± 0.3 | 17.6 ± 0.1 | 0.282 ± 0.001 | 123.8 ± 6.1 | 182 ± 2 |

The values of G′, G″ and tan δ correspond to the linear viscoelastic region; $\tau^{95\%\ G'}$ corresponds to the time necessary for G′ to recover 95 % of its initial value after being submitted to shear (Gilbert et al. 2013)

submitted to shear strain. The different emulsions were also characterized using sensory analysis. Data computation clearly illustrates the key role of polymers on the whole rheological on a cosmetic emulsion as, more than its lonely stability, it also directly affects its perception by the consumer.

Moreover, in complex mixture, polysaccharide-surfactant mixtures may lead to complex formation between both species thus allowing adjusting the rheological behaviour of the final product (emulsion or non-emulsion systems) to get suitable texture properties (Lindman et al. 1993). Such association phenomenon is depending on both the surfactant type (ionic, zwitterionic or nonionic) and the polymer structure: main backbone, functional groups, pendant species, stiffness, electrostatic properties, hydrophilic/hydrophobic moieties amongst others. Obtaining stability and expected mechanical properties makes it necessary to consider all these aspects carefully (Bais et al. 2005). A recent paper interestingly illustrates the different possible effects of protein—polysaccharide association for stabilizing O/W emulsions; as an example, sodium caseinate-maltodextrin and caseinate-xanthan combinations are described, showing that polysaccharide cannot simply be considered as continuous phase viscosity enhancer as it affects droplet network formation and dynamic, and so the whole mechanical properties (Liang et al. 2014).

#### 8.3.2.4 Controlling End-User Expectations

The key properties of natural and semi-synthetic polymers are unambiguously their ability, even at low level, to efficiently thicken or gel aqueous media thus allowing the control of products viscosity at rest, but also when submitted to mechanical stress during usage. Such mechanical stress may include the pressure induced by finger during pick-up and spreading over the skin surface, the shear when spreading varnish over a nail surface using a brush, the pumping of a cream out of its container and the spraying of a hair fixer. Each of these situations corresponds to a specific range of shear intensity; few examples are listed in Fig. 8.3 (Barnes 1994; Brummer and Godersky 1999; Tranchant et al. 2001).

From a general point of view, cosmetic products containing polymer mostly show non-Newtonian behaviour under shear; this is due to polymer chains coil deformation and, in the case of emulsions, to the droplet network disruption combined with the ellipsoidal shape adopted by droplets when submitted to shear. In addition, yield stress parameter is often observed in the presence of polymer. Once

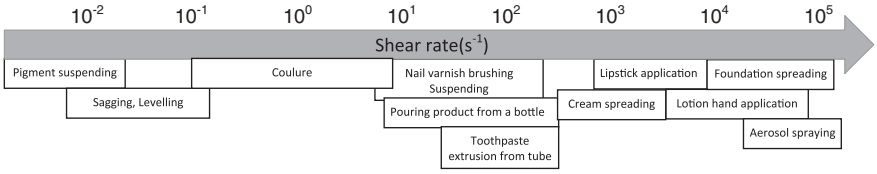


**Fig. 8.3** Values of shear rate corresponding to different situations when using cosmetics

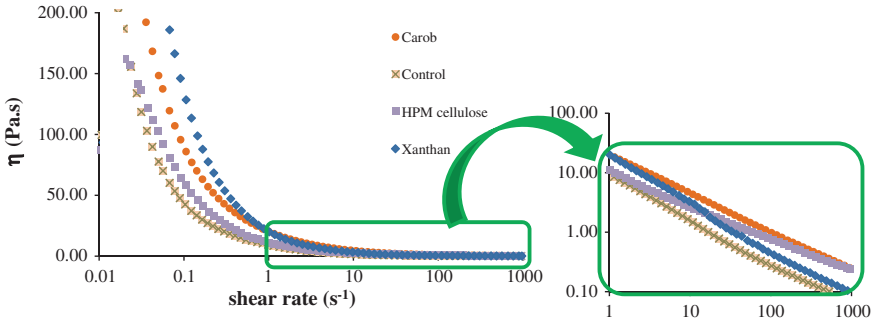


**Fig. 8.4** Flow behaviour of O/W emulsions containing without (control) and with various polysaccharides: carob, HPM cellulose and xanthan, respectively (from Gilbert et al. 2013a)

the product flowing, the viscosity loss is often over several decades depending on the conformation and sensitivity to shear of the polymeric specie.

Figure 8.4 gives an interesting illustration of this phenomenon for a series of emulsions only differing by the thickening agent used, being natural (xanthan, carob) or artificial (HPM cellulose), compared with the same emulsion with no added (Control).

As expected, the presence of polymer induces a higher viscosity when compared to the control emulsion with no added polymer. In addition, it is obvious that viscosity at low shear is higher for the xanthan containing emulsion, while on the contrary, when submitted to high shear, the emulsions containing carob or HPMC keep a higher viscosity. Such a dramatic difference makes the products very different for the user as its feeling during emulsion spreading onto the skin appears "richer" for the latter's when compared to the control, while spreading the emulsion containing xanthan may allow a "lighter" sensation combined with a quicker product penetration during application. Such a remarkable behaviour is directly related to the polymer structure, molecular weight and chain conformation. It allows the formulator optimizing the product performance by judiciously choosing the polymer, the natural and artificial ones offering the widest versatility.

Texture analysis is a complementary technique which has been intensively used for many years in the food industry to characterize the mechanical properties of complex systems; it is a useful tool for analysing the product texture, and is therefore, more recently, becoming more considerable for cosmetics. Publications related to texture analysis of cosmetic emulsions were published recently (Roso and Brinet 2004; Smewing and Jachowicz 2007; Jachowicz and Smewing 2008) compared to food. Lukic et al. (2012a, b) combined together texture analysis and rheology to predict W/O emulsions sensory properties.

Gilbert et al. (2013a) described the rheological and texture characterization of cosmetic emulsions having exactly the same microstructure (identical oil content and droplet size) but differing for the polymer (either natural, artificial or synthetic) used to modify the aqueous phase rheology; one of the main objectives of

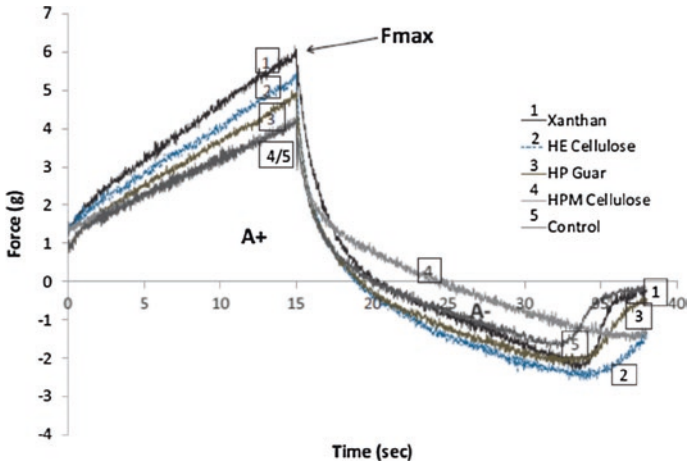


**Fig. 8.5** Penetration curves with the different collected parameters for an emulsion without (control) or with natural/artificial polymer (from Gilbert et al. 2013a)

this work was to establish relationships between both series of data. Viscometric and viscoelastic data were obtained through flow, oscillatory and creep methods, while texture analysis were mainly issued from penetration to compression tests, with considering various experimental conditions such a probe diameter, speed and depth or container dimensions. All data were computed to attempt linking together both categories of physical properties. The results obtained for natural and artificial polymers interestingly indicate that the different texture parameters (e.g.: $F_{max}$, see Fig. 8.5) strongly correlate with emulsions viscosity measured with shear rate varying from 0.1 $s^{-1}$ to 10 $s^{-1}$. In addition, harsher operative conditions in compression tests make it possible to correlate texture data to viscosity measured at much higher shear rate, currently around 1000 $s^{-1}$. Other interesting correlations were established with further experimental data: (1) negative area as recorded with penetration test versus final deformation as obtained through creep-recovery experiments; (2) compression parameters versus relaxation time after shear exposure.

Among the various texturing properties characterizing cosmetic products, a particular sensory attribute related to stretching phenomena is currently considered. This attribute, expressed as Cohesiveness or Stringiness (Civille and Dus 1991 and 2005; Lee et al. 2005), is evaluated during the pick-up, and corresponds to the properties perceived in the hand when the product is taken from its container. Civille and Dus (1991) defined the stringiness as "amount sample deforms or strings rather than breaks when fingers are separated". This definition, a bit confused, means that the stringier a product, the more it makes long filaments.

As a mechanical parameter, the sensory evaluation of this attribute is strongly associated with samples' extensional properties. Such a filament forming ability resulting from sudden material's stretching is depending on many parameters

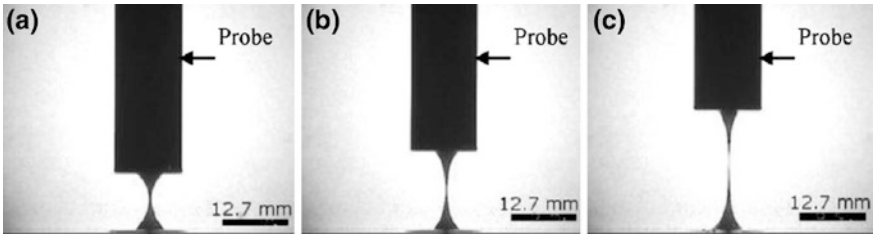


**Fig. 8.6** Images of the stretching properties ($L_{max}$) of different emulsions containing different polymers: control (**a**), HPM cellulose (**b**) and HP guar (**c**) emulsions. Experiments were performed at 40 mm/s, with the P/0.5R probe and a gap of 0.8 mm over 1 cycle (Gilbert et al. 2013c)

related to the product's composition and structure. Among the other ingredients of the formulae, polymers of course play a major role due to their well-known elongational properties.

Gilbert et al. (2013c) tested the role of polymers neither natural, artificial or synthetic, on the stretching properties of a series of emulsions, each different from another by the polymer used; both sensory assessment and instrumental stretch experiments were performed and compared together as visible on Fig. 8.6.

The xanthan-based emulsion showed the highest extensional properties, followed by the HP guar and HE cellulose emulsions; the carob and the HPM cellulose emulsions presented stretching properties to a lesser extent. Nevertheless, the aqueous solutions of polymers obtained lower maximum breaking lengths, especially the xanthan, which suggests that the different ingredients present in the emulsions could interact together to enhance or attenuate the polysaccharide's intrinsic extensional properties.

For ingredients as well as the raw material formulation, the general structural properties gradually under the action of viscoelastic and capillary forces, contracts, and finally breaks.

The whole data clearly indicate that using natural and artificial polymers when formulating allows getting emulsion with markedly different shear thinning and weak gels properties; such versatility is of great interest for formulator when developing products owning innovative texture.

In addition, it is of primary importance to keep in mind that beside their rheological modifier function, polymers bring additional benefits for the cosmetic formulations performance; examples are film former, skin hydration, conditioner, softener, occlusive amongst the other, thus making it real multifunctional ingredients. Numerous examples concern algae for example the microalgal capacity for producing a variety of metabolites such as proteins and carbohydrates offers a wide variety natural extracts owing thickening properties with additional interest as active ingredient such as anti-ageing, emollient, anti-irritant, etc. (Priyadardshani and Rath 2012). Alginic acids, which are polysaccharides isolated from algae, bring gel properties and also allow water absorption thus preventing cell collapsing; Agar polysaccharide is efficient as gelling agent, but is also of interest for cosmetic use due to emollient properties (Wang et al. 2014).

The growing utilization of polysaccharides and derivatives for cosmetic applications is clearly linked to such a multiple benefit, as it can be illustrated for polymers issued from biotechnology.

## *8.3.3 Impact on the Properties During Application*

A cosmetic product is attractive for consumer use as a result of its function, its promise of efficiency but also the pleasure it brings to them. The cosmetic products are intended for contacting the superficial parts of the body, or with the teeth and mucous membranes. During application, consumers have a primary expectation which could be for example moisturizing the skin with a cream, washing the hair with a shampoo, protection against UV with a sunscreen, colouring and protection of nails with a varnish and secondary expectations such as a non-sticky face cream, a shampoo easy to spread on the hair or a varnish simple to apply on the nails.

As showed in the previous paragraph, polymers made possible to monitor the rheological behaviours of cosmetics. This will largely affect the properties during the handling of the product, during its use and after application. Among polymers, some are used only to modify the intrinsic properties of the cosmetic product (such as its appearance, consistency, firmness and spreading on the skin or the hair). Others are used for their ability to form a film at the surface of the skin, the nails or the hair. These film-forming polymers are added in hair fixatives or in varnish and give a protection against dehydration and against chemicals and pollutants from environment.

Furthermore, polymers may be used as active, moisturizer, hydrating agent or conditioners. In this case, the polymer (mostly hydrolyzed) is able to penetrate tissues and to bring a beneficial action at the cellular level, such as water-retention into the skin, reconstruction of the damaged tissues and stimulation of the production of key elements amongst other properties.

### 8.3.3.1 Impact of Polymers on the Sensory Properties

The evaluation of these properties before, during and after application uses directly human persons either through sensory evaluations or through clinical trials.

The sensory evaluation is a measuring instrument of the sensations perceived by a consumer when applying a cosmetic product. For that, a “panel”—a group of assessors—is used with specificities according to the objective of the study and to the test to be carried out. The sensory evaluation gathers together different tests that use the five human senses to evaluate the properties of a product: sight, hearing, touch, taste and smell.

The sensory evaluation was developed at first in the food field and that made possible to establish standardized test conditions that are nowadays available for the cosmetic field. It is necessary to make a distinction between, on the one hand, the hedonic tests that are performed to evaluate the personal appreciation of a product by consumers. These tests are carried out by questioning a large panel of "naïve" assessors that are among the potential targets for the cosmetic product. Tests may also be made directly at home. On the other hand, discriminative and descriptive tests are performed to analyse and characterize the cosmetic products with more experienced assessors or even with experts. Such tests are realized in a sensory laboratory and often require several evaluation weeks. Products are evaluated directly in the container, during application onto the skin, the nails, or the hair; in addition, hair care products are often tested using hair tresses.

In the cosmetic field, the five human senses are involved in the perception of the product. The sense of smell is of course essential to evaluate the perfume of a cream or soap and is a key element for the emotional point of view. The sight makes possible to evaluate the colour of a make-up, a hair colouring, the gloss attribute of a cream, etc. The sense of hearing is secondary in cosmetic, whereas the sense of taste concerns only the products which are in contact with the oral mucosa (toothpaste, mouthwash, lipstick, gloss, etc.). The sense of touch is particularly important in cosmetic; it is involved in the perception of the somatic sensations including several modalities such as pressure, skin stretch, vibration, pain and temperature perceived by many receptors and mechanoreceptors localized at various depth in the skin and the mucous membranes.

Polymers are commonly named texturing agents because they fully contribute to the texture of the products; this parameter is a complex and multidimensional parameter. The procedure for the sensory evaluation of the texture is generally split in four categories, namely "appearance", "pick-up", "rub-out" and "residual appearance and after feel". However, the influence of natural polymers on sensory skin feel properties for cosmetic products has been very little investigated. Gilbert et al. (2012) were interested in the impact of polymers on the texture properties of cosmetic creams. The study focused on eight hydrophilic polymers, either natural (xanthan and caroub), derivate (hydroxy ethyl cellulose, hydroxyl propyl guar and hydroxyl propyl methyl cellulose) or synthetic (carbomer, polyacrylamide, and ammonium acryloyldimethyltaurate/VP copolymer). Polymers were incorporated at a concentration of 1 % w/w in an O/W emulsion and a formulation without any polymer was also prepared. The contribution of each polymer to the sensory properties was investigated using the Spectrum Descriptive Analysis (SDA) method. In order to properly discriminate the texture properties of the nine emulsions, eight attributes were selected: *Gloss* and *Integrity of shape* evaluated during the first phase, named "appearance"; *Penetration Force*, *Compression Force* and *Stringiness* evaluated during the "pick-up"; *Difficulty of spreading* and *Absorbency* evaluated during the "rub-out" and *Stickiness* evaluated in the last phase, named "residual appearance". Results highlighted significant differences between the texture of creams according to the polymer used and its origin (see Fig. 8.7).

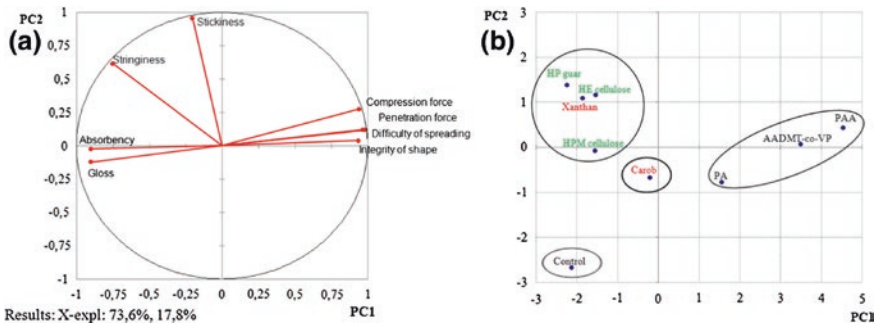


**Fig. 8.7** Results of the sensory characterization of cosmetic O/W emulsions containing different polymers at 1 % w/w: xanthan, caroub, hydroxy ethyl cellulose (HE cellulose), hydroxyl propyl guar (HP guar), hydroxyl propyl methyl cellulose (HPM cellulose), laureth-7, C13-14 isoparaffin, polyacrylamide (PA), carbomer (PAA) and ammonium acryloyldimethyltaurate/VP copolymer (AADMT-co-VP). The "Control" emulsion was prepared without polymer. The results of PCA: loading plot of the attributes (**a**) and of emulsions (**b**) (Gilbert et al. 2012)

The emulsions with synthetic polymers exhibited a higher firmness and consistency than those with natural or modified polymers. Otherwise, emulsions containing natural polymers showed better spreading properties on the skin, which is an important criterion during application. It is noteworthy that natural and modified polymers confer also stringiness during pick-up and stickiness feeling after application of the cream to the skin.

As a consequence, natural polymers are not the more appropriate ingredient to modify the lonely consistency and the firmness of cosmetic creams when compare to the synthetic polymers. For this reason, natural polymers are often associated with synthetic ones in order to control properties during application as for instance the spreading performance of the product during use (see example of formulation in Sect. 8.4: body lotion with 0.2 % of carbomer and 0.1 % of xanthan).

The sensory evaluation also concerns the hair care product. Derivates from natural polysaccharides are for example widely included into hair conditioners to achieve sensory improvement. Hair conditioners are generally used after shampooing the hair by taking a small portion on the palm, applying on the wet hair, spreading, rinsing, wiping with a towel and drying with a blower. It is commonly admitted that the feel during application can be improved with polymers such as polyquaternium-10 or hydroxyl ethyl cellulose (Lochhead 2007). Nevertheless, such results remain largely unpublished.

Natural polymers are used in cosmetic products as texturing agent but some of them are also able to protect or penetrate tissues and are used as active ingredients, film formers, moisturizers, hydrating agents or conditioners. This is discussed in the following sections.

#### 8.3.3.2 Polysaccharides Used as Conditioning Agents and Active Ingredients

Compounds that can improve the skin or hair surface are so-called conditioning agents. The mechanisms by which conditioning compounds do this vary depending on the type of compound and surface to which they are applied to. One of the primary methods by which conditioning ingredients act consists on regulating the amount of moisture of skin or hair (Gesslein 1999).

The skin consists of epidermis, the most exposed part, directly in contact with the external environment. It is assembled by multiple superposed cell layers that form an effective protection barrier. Over the years, however, epidermal primary functions may gradually falter. Molecular, cell-related, and morphological changes in aged epidermis not only compromise its protective role, but also contribute to the appearance of skin symptoms as for example excessive dryness, formation of wrinkles and skin irritation. The possible therapeutic strategies include the use of moisturizing compounds and the application of active ingredients able to stimulate biological responses or to reactivate biological pathways. Among the active ingredients, some polymers are used in cosmetic formulations.

Different polysaccharides are notably added to skin care products because of their water-retention properties that contribute to the epidermis hydration. As an example, that is the case of chitosan that is a natural polymer abundantly found in crustaceans obtained by deacethylation of chitin. Chitosan is used as thickening and gelling agent and as active since its water-retention properties are also efficient to maintain skin moisture. Chitosan has also attracted the attention owing antimicrobial activity in oral care (toothpaste), peculiar biological properties in wound healing and specific characteristics for applications in hair care. As the only cationic polysaccharide in nature, chitosan in aqueous solutions interacts with negatively charged damaged hair via electrostatic interactions. It forms a film that improves suppleness of hair and reduces static electricity. However, chitosan is normally insoluble in aqueous solution above pH 7 because of the stable, crystalline structure. To improve the solubility of chitosan and exploit its application, different methods of chemical modification (PEG-grafting, hydroxylation, sulfonation, quaternization and carboxymethylation) are commonly applied (Rinaudo 2006).

Polysaccharides used as active also include hyaluronic acid (HA). HA is a glycosaminoglycan (GAG) widely distributed throughout the dermis and the epidermis. HA is synthesized by skin fibroblasts and is involved in the tissue repair and in skin's moisture balance due to its high performance in water-retention. HA can absorb water about 1000 times its own volume. Nowadays it is mainly obtained by biotechnology and is used as active ingredient in topical applications for skin care including anti-ageing products. It is often used as a sodium salt (sodium hyaluronate) or hydrolyzed forms owing various molecular weights. As HA is naturally found in the dermis, its biocompatibility with skin is a key point. According to its molecular weight, HA forms an elastic and permeable film on the surface of the

skin or penetrates the stratum corneum and may act in skin renewal (Bourguignon et al. 2013; Lorencini et al. 2014).

Other natural polysaccharides are used as active ingredients in cosmetics. Wang et al. (2014) indicate for example that polysaccharides from marine algae may act as hair conditioners and wound-healing agents, and can also moisturize, hydrate and emolliate. Several yeasts and yeast-like fungi are also known to produce extracellular polysaccharides. Most of these contain D-mannose, either alone or in combination with other sugars and phosphate. Almost all of the yeast exopolysaccharides are known to display some sort of biological activity and some of them already find applications in cosmetics as moisturizer (Van Bogaert et al. 2009). Exopolysaccharides may also be obtained by bacterial fermentation and display protective effects against pollution, heavy metals and ultra violet light. The case of exopolysaccharides produced by marine microorganisms is also detailed in the literature Finore et al. (2014), as well as the possible applications of such polymers as GAG-like molecules to replace hyaluronic acid or heparin (Delbarre-Lachat et al. 2014).

#### 8.3.3.3 Proteins Used as Conditioning Agents and Active Ingredients

Proteins are widely used in skin care and hair care products as moisturizing agents, film formers and also used for their ability to repair skin tissues. Widely used proteins include collagen, keratin, silk protein and soybean protein. There are hydrolyzed products of these proteins of various molecular weights. Molecular weight primarily determines a number of properties of hydrolyzates. The molecular weights cited for hydrolyzates represent average values for relatively broad distribution. Thus, a range of 1000–5000 Da for hydrolyzate may be considered "narrow". Humectancy (hygroscopicity) is greatest for individual amino acids, which can absorb several times their weight in water. Therefore, humectancy performance diminishes exponentially as the size of the polypeptide increases, while non occlusive protective colloidal film-forming properties concurrently increase. Concerning hair conditioning, substantial quantities of at least some hydrolyzates penetrated through the cuticle into the cortex. The amount of hydrolyzate bound increased markedly with increasing damage (virgin < bleached ≪ bleached and waved). Evaluation of hydrolyzates applied to human skin revealed that penetration was limited to the outer layers of the stratum corneum; consequently, hydrolyzates mainly function as film formers and moisturizers (Neudahl 1999).

As an example, collagen is naturally present in connective skin tissues; therefore, collagen hydrolyzates are currently used in cosmetic formulations for properties such as skin structure and function protecting, thus enhancing its appearance. Collagen is unique in its ability to form insoluble fibres that have a high tensile strength and right-handed triple super helical rod consisting of three polypeptide chains. Collagen has been, traditionally, isolated from the skins of land-based animals, such as cow and pig. Collagen is usually incorporated into hydrating cream at 1 %. However, in recent years, the uses of collagen and collagen-derived

products of land animal origin have become of more concern. As a consequence, alternative sources of collagen especially from aquatic animals including freshwater and marine fish and molluscs have received increasing attention (Veeruraj et al. 2013).

Another interesting example is keratin, a highly specialized intracellular epidermal protein. It comprises the main bulk of the horny layer of the skin, and with modification forms specialized structures such as hair or nails. Keratin is a fibrous film-forming protein used in hair and skin care products. It is thought to bring different benefits to hair and skin, such as linking to structural proteins, restoring the surface damages, enhancing the surface moisture content, and surface coating. Water-soluble hydrolyzed keratin, often derived from sheep's wool, is a cosmetic active and consists in peptides of about 10–20 amino acids. Cocodimoniumhydroxypropyl hydrolyzed keratin is a hydrolysed keratin which has been modified with a quaternary ammonium group. This truly cationic polymer is found in various hair care products in which it prevents damages and repairs the hair. Hair mainly consists in keratin and can be more generally repaired from damage by supplying proteins. Proteins are included in hair conditioners to that purpose. Since many years, protein derivatives have been developed to improve molecular binding with hair; examples are cationated, acylated, and silylated proteins (Bolduc and Shapiro 2001).

Small peptide fragments are also common components of anti-ageing topical formulations. They penetrate through the skin epidermal layer and may be able to induce synthesis of dermal extracellular matrix, thus restoring damaged tissues. Many are thought to act as 'matrikines', a concept that peptide fragments produced naturally during extracellular matrix protein processing—most commonly collagen or elastin processing—can act as signalling intermediates, thus simulating cells to increase extracellular matrix production. Bradley et al. (2015) present a review of the various peptide fragments, mainly consisting on tetra-, penta- and hexapeptide used to repair photo-aged skins.

Finally, it should be noted that protein products are generally used as active and they have almost no influence on the sensory characteristics of cosmetic products because the current amount used in the cosmetic formulae remains fairly small.

## 8.4 Examples of Cosmetic Formulations Including Polymers

Natural and artificial polymers are commonly used in a large range of cosmetic products. They appear among the minority ingredients with amount below 1 % wt but are indispensable to satisfy requirements in term of stability, rheological behaviours, sensory and active properties. Generally, only one polymer is not enough and a mix of different polymers is required. Most of the time, natural polymers are found as powder but are sometime commercialised as a liquid

form (aqueous solutions at 1 or 2 % including preservatives). Natural polymers are mainly hydrocolloids and their dissolution in the solvent medium is one of the critical steps in the preparation procedure. That is the reason why the polymer is usually added alone as a separated phase by following specific conditions in term of stirring, time or temperature. In the cosmetic field, the cold water-soluble polymers are preferred in order to avoid heat treatment during processing. However, heating speeds up the dissolution and is sometime obliged to hydrate certain natural polymers, highly ordered or with an important crystalline phase, as for instance locust bean gum (temperature required around 80 °C). Always in order to facilitate dissolution, it is possible to prepare a premix of the polymer powder with the other dry ingredients or to pre-disperse it in a non-solvent medium (oil, alcohol, polyols, etc.). Dissolution depends on the product in which the material is being used and/or the type of equipment available.

Below are given several examples of cosmetic products quantitative formula including natural and artificial polymers. General information and preparation procedure are given for each example. The role of natural polymers and derivatives is explained. See the book Personal Care Formulas (2006) for more formula.

### *8.4.1 Skin Cleansers*

Body cleanser and shower gel, also known as bodywash, is liquid soap used for cleaning the body. It is a water-based product with high detergent concentration (e.g. sodium lauryl sulfate, ammonium laurethsulfate, Triethanolaminecocoyl glutamate) used as a skin cleansing agent in the shower or bath. If compared to classical soap, it is less irritating to the skin, lathers better even in case of hard water and does not leave a mineral residue on the skin after usage. Thickening water solution polymer (e.g. Hydroxyethyl cellulose) is added to reach suitable viscosity. It may contain ingredients with a long-lasting cooling and stimulating sensation on the skin (e.g. menthol, menthyl lactate), and it is often designed for hair and body combined utilization. Shower gels contain milder surfactant bases than shampoos and in addition to being pH-friendly to the skin, most are also prepared with gentle conditioning agents. Conditioning polymers are polycations (e.g. Guar hydroxypropyltrimonium chloride) as keratin substrates (especially hair) carry a net negative charge, thus involving strong surface-product interactions. This formulation has strong foaming power and very low skin irritation. It also leads to moisturization and silky after-feel (Table 8.4).

### *8.4.2 Hair Cleanser and Hair Conditioner*

A shampoo is a cosmetic care product that is used for cleaning hair. The goal of using shampoo is to remove the unwanted build-up without stripping out so much

**Table 8.4** Composition of a cooling shower gel (Sino Lion) from Personal Care Formulas (2006)

| Phase | INCI name | wt% |
|---|---|---|
| A | Water (Aqua) | Qsp 100.00 |
| | **Hydroxyethyl cellulose** | 0.80 |
| B | Disodium EDTA | 1.00 |
| | Ammonium laurethsulphate, 25 % | 28.00 |
| | Triethanolaminecocoyl glutamate | 20.00 |
| C | **Guar hydroxypropyltrimonium chloride** | 0.30 |
| | Lauramide MEA | 2.00 |
| | Menthyl lactate | 0.30 |
| | Saffloweramide DEA (and) isostearamide DEA | 0.50 |
| | Sodium isostearyllactylate | 0.50 |
| | DMDM hydantoin (and) IPBC | 0.30 |
| D | Citricacid, 20 %, to pH 6.50 | Qs |
| | Fragrance (parfum) | Qs |
| | Sodium Chloride, 20 % | Qs |
| E | Styrene/acrylates copolymers | 0.80 |

*Procedure* Heat part of water* to 50 °C and add hydroxy ethyl cellulose; mix until dissolved. Add disodium EDTA and agitate for 5 min. Add the remaining B ingredients with agitation. Heat up to 70 °C. Add C and mix until uniform. Premix E with 4 times amount of water and add into the vessel, mix for 15 min

*Reserve amount necessary for addition of E

Bold corresponds to the polymers used in the list of ingredients.

sebum thus leaving hairs unmanageable. Shampoo is generally made by combining surfactant(s) (e.g. ammonium lauryl sulfate, ammonium laurethsulfate, cocoamidopropylbetain) in water to form a thick, viscous liquid. Other essential ingredients include salt (sodium chloride) used to adjust the viscosity by micellar mechanism and polymers as thickening agents (e.g. xanthan gum). Substantive conditioning properties may be controlled by using appropriate polymeric ingredients (e.g. polyquaternium-10, Hydrolysed wheat protein PG-propyl silanetriol). Preservatives and fragrance are also added. Many parameters such as foam formation and stability, skin and eye irritation, hair protection or damage repair, biodegradability, etc., have to be considered when developing the product (Table 8.5).

The basic formula of hair conditioners is fairly similar to shampoo. The conditioning mechanisms can be various, but require ingredients to bind with hair keratin thus inducing resistance to rinse and mechanical strain. Different kinds of interactions may be involved, but electrostatic are the main ones. Examples are cationic polymers (such as quaternized cellulose or guar gums), protein and protein hydrolysates (issued from, e.g. corn, milk, silk, soy, wheat and yeast) all being commonly used as cosmetic ingredients with conditioning properties (Table 8.6).

**Table 8.5** Composition of a Moisturizing Shampoo (Stepan) from Personal Care Formulas (2006)

| Phase | INCI name | wt% |
|---|---|---|
| A | Water (Aqua), deionized | Qsp 100.00 |
| B | **Polyquaternium-10** | 0.30 |
| C | **Xanthan gum** | 0.50 |
| D | Disodium EDTA | |
| | Ammonium lauryl sulphate | 25.00 |
| | Ammonium laurethsulphate | 18.00 |
| | Cocamidopropylbetain | 3.60 |
| | PEG5-cocamide | 0.50 |
| | Sodium laurethsulfate (and) ethylene glycol distearate (and) cocamide MEA | 3.00 |
| | Glycol stearate | 0.75 |
| | Dimethiconecopolyol | 1.00 |
| E | Polyquaternium-7 | 3.00 |
| | Panthenol | 0.15 |
| | Fragrance (parfum) | Qs |
| | Dye | Qs |
| | Preservative | Qs |
| F | Citric acid | Qs |
| G | Sodium Chloride | Qs |

*Procedure* In a suitable vessel equipped with heating and agitation capabilities, Charge A. Sprinkle B into A. Mix until well dispersed. Sprinkle C into AB. Mix until well dispersed and heat at 72–75 °C. Add D under moderate agitation. Keep heating at 72–75 °C, and mix for at least 30 min until completely dissolved. Cool to 40 °C with adjusting mixing speed to avoid minimize aeration. At 40 °C, add E and continue mixing. Cool to 25 °C. Adjust pH with F, if necessary. Adjust viscosity with G, if necessary

Bold corresponds to the polymers used in the list of ingredients.

### *8.4.3 Skin Care*

Skin care products are used to improve the skin appearance and health, formulated for different types of skin: normal, dry or oily. Skin care products include cleansers, facial masks, moisturizers, sunscreen, tanning oils and lotions, skin lighteners, serums, etc. Most skin care products are O/W emulsions. Normal skin is neither greasy nor dry, and usually appears clear with no spots or blemishes, and therefore requires gentle treatment. Such a skin requires common maintenance. Dry skin tends to flake easily due to its no efficacy to retain moisture and insufficient production of sebum by sebaceous glands. In that case, using a moisturizer for both day and night creams may be essential. Finally, oily skin is more or less greasy, which is caused by the over secretion of sebum. The excess oil on the surface of

**Table 8.6** Composition of a thermal protection hair conditioner from Personal Care Formulas (2006)

| Phase | INCI Name | wt% |
|---|---|---|
| A | Water (Aqua) | Qs 100.00 |
| B | **Hydroxyethyl cellulose** | **0.30** |
| C | Quaternium-82 | 1.00 |
| | Cetrimoniumchloride | 3.33 |
| D | Cetyl alcohol | 1.50 |
| | Stearyl alcohol | 2.00 |
| | Pentaerythrityltetracaprylate/tetracaprate | 2.50 |
| | Phenyl trimethicone | 0.50 |
| E | **Wheat amino acids** | **1.00** |
| | **Hydrolized wheat protein PG-propyl silanetriol** | **1.00** |
| F | Sodium hydroxide | Qs |
| G | Citric acid | Qs |
| H | Preservative, colour, fragrance (Parfum) | Qs |

*Procedure* Disperse B into A. Add F to raise pH to 7.0–8.0. When solution is clear, adjust pH with G to a pH of 4.0–5.0. Add C and mix well. Start heating to 76–82 °C. Add D at 77 °C. Mix well for 20 min. Start cooling to room temperature. Add E at 38 °C. Mix well. Add F or G, if necessary, to adjust pH. Add H. Mix well
Bold corresponds to the polymers used in the list of ingredients.

the skin causes dirt and adhesion of dust from the environment. Consequently, it needs to be cleansed thoroughly every day; moisturizing with an oil-free, water-based and non-comedogenic moisturizer is required, and efficient exfoliation may be necessary so to improve the skin's appearance. In all cases, the texture of skin care products is of primary importance, thus requiring viscosity adjustment by hydrocolloids for reaching suitable viscosity and improving the systems stability (e.g.: xanthan gum, cellulose ether). Further functional properties such as skin adhesion of mask may be obtained by adding colloids (e.g. Acacia gum). Below are examples of two O/W emulsions, obtained by hot and cold process, respectively (Tables 8.7 and 8.8).

### *8.4.4 Toothpaste*

Toothpaste is a semi-solid product (often paste) designed to clean teeth and leave breath smelling and feeling fresh. The primary function of toothpaste is to remove debris from the teeth surface. It has to be easily extruded from its tube, to keep stiff enough to remain on the toothbrush and have a consumer acceptable taste. Toothpastes are a blend of surfactants, abrasives (e.g. hydrated silica), water, humectants, anti-caries actives, thickening agents (e.g. xanthan gum, cellulose gums and carrageenan), flavouring, and other aesthetic ingredients. Mechanical

**Table 8.7** Composition of a Moisturizing Facial cream with sunscreen from Personal Care Formulas (2006)

| Phase | INCI Name | wt% |
|---|---|---|
| A | Water (aqua), dionized | Qs 100.00 |
| B | **Xanthan gum** | **0.17** |
| C | Propylene glycol | 0.75 |
| | Glycerin | 1.25 |
| | Aloe barbadensis gel | 0.50 |
| | Sodium PCA | 0.25 |
| | Preservative | 0.10 |
| D | Petrolatum | 3.50 |
| | Octylmethoxycinnamate | 5.25 |
| | Meadowfoam seed (Limnathes alba) oil | 1.75 |
| | Oxybenzone | 2.35 |
| | Octyl salicylate | 1.50 |
| | Neopentylglycoldicaprylate/dicaprate | 2.30 |
| | Glyceryl stearate | 1.50 |
| | PEG-150 distearate | 1.75 |
| | Stearic acid, triple press | 1.25 |
| | Emulsifying wax, NF | 0.50 |
| | Cetyl alcohol | 0.50 |
| E | **Cellulose ethers, 2 % soln** | **16.50** |
| F | Water (aqua), deionized | 1.00 |
| | Imidazolidinyl urea | 0.25 |
| G | Citric acid, 50 % soln | Qs |

*Procedure* Heat A to 60 °C under propeller mixing at medium speed. Add B slowly, continue mixing until completely in solution and hydrated, approximately 10 min. Premix C and add to batch. Pre-blend D and heat to 65–70 °C under propeller mixing until completely clear. Then add D to batch on a Homomixer at medium speed for 2 min. Premix/prepare E. Heat to 55 °C with mixing. Add to batch on Homomixer at medium speed for 2 min. Reduce speed on Homomixer to low setting and cool to 40–45 °C. Place on mixer using sweep blade at low speed, cooling to 35 °C. Premix F and add to batch at 35 °C. Then cool to 25 °C, adjust pH, if necessary, with G
Bold corresponds to the polymers used in the list of ingredients.

action of abrasive agents allows stain removal; the large proportion of particles makes it necessary to use efficient suspending agent to stabilize the mixture (Table 8.9).

**Table 8.8** Composition of a 0/W PEG-free body lotion, cold processing from Personal Care Formulas (2006)

| Phase | INCI Name | wt% |
|---|---|---|
| A | Sorbitanoleate (and) polyglyceryl-10 laurate | 2.00 |
| | Isononyl stearate | 2.50 |
| | Isopropyl palmitate | 6.00 |
| | Avocado (*perseagratissima*) oil | 5.00 |
| | Jojoba (Simmondsiachinensis) oil | 2.50 |
| B | Water (*Aqua*) | 40.00 |
| | Carbomer | 0.20 |
| | **Xanthan gum** | **0.10** |
| C | Water (*Aqua*) | Qs 100.00 |
| | Glycerin | 3.00 |
| | **Water (and) propylene glycol (and) *Acacia senegal*** | **8.00** |
| D | Triethanolamine, 99 % | pH 6.00–6.50 |
| E | Tocopherol | 0.05 |
| | Tocopheryl acetate | 0.20 |
| | Fragrance (Parfum) | Qs |
| | Preservative | Qs |

*Procedure* Premix A, B and C separately to obtain homogeneous phases. Add C to B while stirring. Add A to BC. Homogenize for 2 min. Add D and E while stirring
Bold corresponds to the polymers used in the list of ingredients.

**Table 8.9** Composition of a toothpaste product

| Phase | INCI Name | wt% |
|---|---|---|
| A | Water | Qs 100.00 |
| | Sodium benzoate | 0.60 |
| | ChlorhexidineDigluconate | 0.05 |
| | Sodium Saccharin | 0.08 |
| | Sodium Monofluorophosphate | 0.76 |
| | Glycerin | 10.00 |
| | Sorbitol | 10.00 |
| B | **Xanthan gum** | **0.80** |
| | **Cellulose gum** | **0.30** |
| C | Tetrasodium Pyrophosphate | 1.00 |
| D | TitaniumDioxide | 0.30 |
| | HydratedSilica | 30.00 |
| E | Sodium Lauryl Sulphate 29 % | 1.50 |
| F | Fragrance (Parfum) | 0.50 |

*Procedure* Mix Phase A ingredients together. Gently add Phase B under vigorous stirring, keep stirring until complete powders dispersion. Gently add Phase C until complete dissolution. Phase D: Slowly add Titanium dioxide/half of hydrated silica quantity premix to previous mix. Append the rest of Phase D to the mixture once the mixture homogeneous. Mix under vacuum using high speed rotor–stator for 15 min. If necessary, keep stirring to reach complete homogenization. Poor Phase E under vacuum using gentle stirring and then add phase F

Bold corresponds to the polymers used in the list of ingredients.

## 8.5 Conclusions

As illustrated in this chapter, natural polymers are commonly used in any kind of cosmetic products; the utilization of proteins, polysaccharides and corresponding derivatives in the cosmetic industry is due to their wide range of properties such as stabilizer, texturing agent, hydrating, film former and sensory ingredient. A variety of natural and artificial polymeric raw material is nowadays available, and the interest for such ingredients is growing year after year due to several reasons:

- The good image of natural ingredients by consumers makes it of great interest from a marketing point of view;
- The ability for natural polymers to significantly increase the dispersions stability;
- The wide variety of textures available, ranging from low viscous to highly gelled systems;
- The development of "eco-labels" and "natural cosmetics" requires relevant substitution of synthetic raw materials;
- The Life Cycle Assessment (LCA) requires considerations such as biodegradability and/or low Carbon Footprint;
- The general biocompatibility requirements with skin and mucus is much better with natural ingredients;
- Natural "active" ingredients allow improving product efficacy;
- The reaching of higher aesthetic and sensory performance;

Consumer may decide to buy a product on the basis of a complex compromise between sensory expectations and allegations (e.g. ease of pick-up, pleasure during application, skin softness and multifunctional), efficacy (e.g. anti-ageing, hair conditioning, make-up resistance to water and sunscreen protection), specific requirements (e.g. natural or "bio" products and anti-allergenic) and, of course economic considerations.

Natural cosmetic ingredients market in Western Europe is estimated to cross $800 million in 2017, while it was $6592 million in 2012 (Source: Frost and Sullivan, January 2014). For all these reasons, like in other domains, the cosmetic industry requires constant innovation, and is permanently searching for new ingredients or technologies; among the other natural ingredients categories, research for new developments of natural polymers is very active, with a market growing rapidly over the world. Few examples are given in the following perspectives.

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# Chapter 9
# Pharmaceutical Applications of Natural Polymers

**Atul Nayak, Ololade Olatunji, Diganta Bhusan Das and Goran Vladisavljević**

## List of Abbreviations

| | |
|---|---|
| API | Active pharmaceutical ingredients |
| BTCA | Butanetetracarboxylic dianhydride |
| CMC | Carboxymethyl cellulose |
| CNS | Central nervous system |
| DB | DamarBatu |
| DMAP | 4-dimethylaminopyridine |
| HGH | Human growth hormone |
| HPMC | Hydroxypropylmethyl cellulose |
| Lo | Lecithin organogel |
| NaCMC | Sodium carboxy methyl cellulose |
| N-IPAAm | *N*-isopropylacrylamide (NIPAAm) |
| pAA | Polyacrylic acid |
| PEG | Polyethylene glycol |
| PELA, PLA | Polylactic acid |
| PLGA | Poly(DL-lactic-*co*-glycolic acid) |
| PLLA | Poly(L-lactic acid) |

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O. Olatunji (ed.), *Natural Polymers*, DOI 10.1007/978-3-319-26414-1_9

| | |
|---|---|
| PSA | Pressure sensitive adhesives |
| PVA | Polyvinyl alcohol |
| SPG | Shirasu porous glass |
| TDD | Transdermal drug delivery |

## 9.1 Introduction

Natural polymers have a very broad range of applications in both the polymer and pharmaceutical industries. The pharmaceutical industry is a very broad field where there is a continued need to consider various applications. It is logical, therefore, to state that understanding the roles of natural polymers in the pharmaceutical industry helps in turn the polymer industry to determine the broader applications of these polymers and incorporate the desired requirements to meet the end applications (e.g. provide various functionalities). Drug delivery methods form a key part of the pharmaceutical applications of polymers. In the next section of this chapter, we discuss portals of drug administration into the human body which gives an overview of the possibilities of applications of natural polymers. The chapter then discusses some specific applications in detail. Transdermal drug delivery, nasal drug delivery, vaginal, ocular, oral drug delivery methods using natural polymers are discussed with some example case studies. As hydrogels play important roles in drug delivery, a separate section is dedicated in discussing the applications of natural polymer-based hydrogels in drug delivery.

## 9.2 Portals of Drug Administration in the Human Body

The controlled delivery of drug molecules requires either a device or a vehicle for administration into specific localised tissues or systemic distribution via plasma fluid in blood. The human body has several portal entries for drug administration as outlined in Fig. 9.1. These portals are intramuscular (Suh et al. 2014), percutaneous (Ge et al. 2014), intrathecal (Freeman et al. 2013), subcutaneous (Kinnunen and Mrsny 2014), gastrointestinal (Varum et al. 2013), ocular (Mignani et al. 2013), intravenous (Mignani et al. 2013), nasal (Tian et al. 2014), pulmonary (Beck-Broichsitter et al. 2012), sublingual (Patel et al. 2014), baccal (Patel et al. 2014), rectal (Lautenschläger et al. 2014) and vaginal (Valenta 2005). Intravenous, intramuscular, percutaneous, intrathecal, subcutaneous and transdermal are collective terminologies associated with parenteral administration. Pulmonary drug administration through the lungs is the least common portal delivery because of a limited number of excipients, especially natural polymeric excipients with reduced polydispersity of size and ideal particle densities concerning the drug particle formulation (Sanders 1990; Pilcer and Amighi 2010).

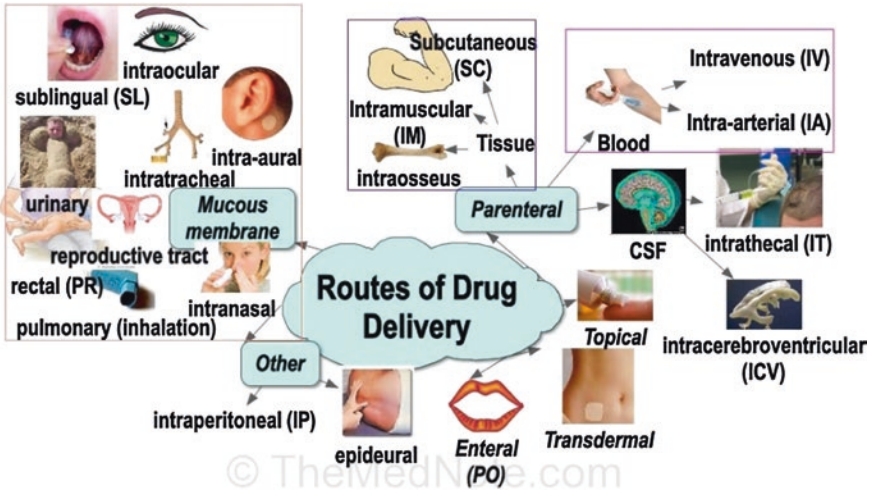


**Fig. 9.1** An outline of main portals for drug administration (Adopted from www.themednote.com with permission)

## 9.3 Transdermal Drug Delivery Devices

Polymers are used extensively in transdermal drug delivery systems. They control the rate of drug release from the device, act as primary packaging parts, coatings, penetration enhancers and provide ease in drug device handling and structural support to the device in the form of a backing layer. Their unique properties make them ubiquitous component of transdermal patches. As petrochemical-based resources for the production of synthetic polymers become more expensive and in short supply, the production of transdermal drug delivery device components from more readily available natural polymers becomes eminent. This section of the review looks at the application of natural polymers in transdermal drug delivery. The different parts of the transdermal drug delivery system are discussed such that the use of natural polymers in each individual part, namely, the matrix, adhesive layer, rate controlling membrane, backing layer, release liner and penetration enhancer are then discussed. Further areas to be explored are also suggested.

Polymers are used more extensively in transdermal drug delivery (TDD) than any other material as they possess unique properties which are significant to the drug delivery process (Kim 1996). They are effective in aiding the control of drug release from carrier formulations (Cleary 1993). Polymers commonly used in TDD include cellulose derivatives, polyvinylalcohol, chitosan, polyacrylates, polyesters such as PLGA, PELA, and PLA and silicones. Natural polymers are a preferable option in TDD as they are readily available, inexpensive, potentially biodegradable and biocompatible and can undergo various chemical and surface modifications to fit the requirement of the TDD system. A TDD system comprises

of a combination of one or more polymers and an embedded drug to be delivered into or through the skin in a controlled and sustained manner (Tojo 2005).

Polymers used for TDD systems are required to be chemically inert and pure according to high analytical product yields. It should also possess adequate physical properties which correspond with the intended application. The material must not age easily and be suitable for processing. Furthermore, biodegradability and safety are paramount properties in the design of a TDD patch system due to the long-term exposure of the skin in contact with the patch (Pietrzak et al. 1997).

This section focuses on the application of natural polymers in transdermal drug delivery. The next subsections discuss the different types of transdermal drug delivery systems explaining each one is separate subsection. Section 9.3.2 discusses the use of polymers in transdermal drug delivery with specific focus on natural polymers. Within the section the different parts of a transdermal drug delivery system are discussed. The properties and function of each is first described and some recent studies of developing natural polymers in the specific area are then outlined.

## *9.3.1 Types of Transdermal Drug Delivery Systems*

TDD systems are classified into three types, namely, reservoir, matrix and microreservior system (Kandavilli et al. 2002; Chein 1987). Each of these is described below.

### 9.3.1.1 Reservoir System

The reservoir system comprises of a reservoir of drug in the form of a suspension, solution or liquid gel embedded between an impervious backing layer and a rate controlling membrane. Suspensions and solutions are two distinct types of liquid mixtures. The definition of a suspension and a solution is well understood. The definition of a liquid gel can sometimes be difficult to formally express. A gel is a semi-solid, colloidal solution consisting of one or more crosslinked polymers dispersed in a liquid medium. A liquid gel is softer, less resilient and easily spreadable colloid gel. The reservoir could also be the drug dispersed within a solid polymer matrix. An adhesive polymer is often placed between the rate controlling membrane and the skin.

### 9.3.1.2 Matrix System

The matrix system comprises of drug molecules dispersed within a polymer matrix. The matrix system is of two types, the drug in adhesive system and the matrix-dispersed system. In the drug in adhesive system, the drug is dispersed in a polymer

adhesive. The drug loaded adhesive polymer is then spread by solvent casting or in the case of hot-melt adhesives, where, it is melted onto an impervious backing layer. Additional layers of adhesive polymer are then applied on top of the reservoir. *In the matrix-dispersed system,* the drug is dispersed homogeneously in a polymer matrix which is either lipophilic or hydrophilic. The polymer is then placed on a backing layer and above this matrix, an adhesive layer surrounds the matrix perimeter.

#### 9.3.1.3 Microreservoir System

This system combines the reservoir and matrix-dispersed systems. The drug is first suspended in aqueous solution in a water soluble polymer. This is then dispersed homogeneously in a lipophilic polymer, which results in the formation of microscopic spheres of drug reservoirs dispersed within a polymer matrix.

### *9.3.2 Natural Polymers in Transdermal Drug Delivery*

Polymers have been used in transdermal drug delivery as far back as the 1980s. Most transdermal patches contain a matrix of cross-linkage of linear polymer chains from which the drug is to be absorbed into the skin (Tojo 2005). Polymers used in transdermal drug delivery include cellulose derivatives, polyvinyl alcohol, polyvinylparrolidone, polyacrylates, silicones and chitosan. Both natural and synthetic polymers have been used either as matrices, gelling agents, emulsifiers, penetration enhancers or as adhesives in transdermal delivery systems. For example Sun (1986) reported the successful delivery of testosterone into lab rats using a transdermal delivery system with a silicone elastomer as synthetic polymer matrix. Another group explored the use of pectin hydrogels for the transdermal delivery of insulin. Pectin hydrogels loaded with insulin were administered to diabetic rats with type 2 diabetes mellitus. The results obtained showed that the transdermal patch delivered insulin across the skin in a dose dependent manner with pharmacological effect (Tufts and Musabayane 2010). More recent studies explored the use of natural polymers such as rubber latex as backing layer adhesive in nicotine patches (Suksaeree et al. 2011). There is, therefore, scope for research into the use of natural polymers in transdermal drug delivery.

Although synthetic polymers seem to be more commonly employed in the development of TDD systems, natural polymers from plant and animal sources are emerging as a preferred alternative as they pose the advantage of being biocompatible, biodegradable, degrading into non-toxic monomers and are more readily available (Sharma et al. 2011; Chang et al. 2010). Synthetic polymers derived from petroleum sources and synthetically modified polypeptides are known to have limited pharmaceutical implementations due to toxicity and slow biodegradation rates (Shi et al. 2014; Deming 2007; Kim et al. 2014). The following section discusses the use of natural polymers in the different parts of a transdermal patch system.

#### 9.3.2.1 Controlled Release Systems

Natural polymers in combination with other natural and/or synthetic polymers have been used in hydrogels for pharmaceutical application. A recent study looked at the development of controlled release system based on thermosensitive chitosan-gelatin–glycerol phosphate hydrogels for ocular delivery of latanoprost, a drug used in the treatment of glaucoma (Cheng et al. 2014). The formulation can be delivered via subconjunctival injection reducing the need for repeated dose administration and possible side effect from conventional treatments of the condition (Gaudana et al. 2010; Cheng et al. 2014)

#### 9.3.2.2 Matrix

Polymers are attractive for use as matrices in transdermal patches due to certain useful properties which they possess. In addition to being biodegradable and biocompatible, they contain various functional groups that can be modified as required and combined with other materials and tailored for specific applications.

When exposed to biological fluids, biodegradable polymers will degrade releasing the drug that is dissolved or dispersed within them (Gilding and Reed 1979). There are on-going research studies into the application of natural polymers in TDD as polymer matrices. In this area biocompatibility and biosafety are a paramount requirement (Pietrzak et al. 1997). Release of APIs (active pharmaceutical ingredients) from a polymer matrix occurs via various mechanisms including polymer erosion, diffusion, swelling followed by diffusion and degradation. The mechanism initiated depends on the type of system (Sharma et al. 2011).

The use of various natural polymers as matrices has been explored by different research groups. These include natural polymers of chitosan, a polycationic (pH 6.5 or less in solvent) natural polysaccharide which is obtained from one of the most abundant polysaccharides in nature, chitin (Pillai et al. 2009). Chitin is a natural polymer which forms the shells of crustaceans, some insects, fungi, yeasts and plants. Chitosan is deacetylated chitin with a degree of deacetylation ranging from 60 to 95 % (Zheng et al. 2001; Knaul et al. 1999).

The rate of drug delivery from a chitosan matrix can be controlled by varying the manner in which the chains are crosslinked (Säkkinen et al. 2004). The most common crosslinkers used for fabrication of chitosan gels are glutaraldehyde, formaldehyde, glyoxal, dialdehyde starch, epoxy compound, diethyl squarate, pyromellitic dianhydride, genipin, quinone and diisocyanate (Berger et al. 2004; Mohamed and Fahmy 2012). Preparations of chitosan in the form of beads, microspheres and gels have been shown to deliver drugs such as local anaesthetic drugs, lidocaine hydrochloride and anti-inflammatory drugs, prednisolone (Sawayanagi et al. 1982; Nishioka et al. 1990; Hou et al. 1985). Chitosan has also been used as a matrix for transdermal delivery of large protein molecules such as insulin. It

is robustly physicochemically stable and possesses mucoadhesive property which makes a good candidate for TDD (Dodane and Vilivalam 1998; Krauland et al. 2004; Pan et al. 2002; Ma and Lim 2003; Mao et al. 2005).

Pectin is also another natural polymer used in TDD matrices. Pectin is a water soluble polysaccharide composed of different monomers, mainly D-galacturonic acid, sourced from the cell walls of plants which grow on land. Pectin is commercially extracted from fruits and its appearance ranges from a white to light brown powder. Recent studies on application of pectin in TDD have looked at modifying pectin to act as matrix for TDD (Graeme et al. 1999). In a study by Musabayane et al. (2003), pectin was used as a matrix for delivery of chloroquine through the skin; The results showed that pectin was effective as a matrix for TDD delivery of chloroquine resulting in more effective and convenient treatment of malaria (Musabayane et al. 2003). Soybean lecithin has also been used as gel matrices to deliver scopolamine and dcoxatenol transdermally (Willimann et al. 1992). Lecithin is a component of cells that is isolated from soya beans or eggs. It is processed into Lecithin organogel (LO) to act as a matrix for topical delivery of many bioactive agents into and through the skin. When purified and combined with water it shows excellent gelating properties in non-polar solvents. LO provides a temperature independent resistant to microbial growth as well as being a viscoelastic, optically transparent and non-birefringent micellar system. LO is a dynamic drug delivery vehicle as it dissolves both lipophilic and hydrophilic drugs. It effectively partitions into the skin thereby acting as an organic medium to enhance permeation of otherwise poorly permeable drugs into the skin (Raut et al. 2012).

A combination of more than one polymer can also be used in a TDD matrix and this also applies to natural polymers. For example Siddaramaiah (2009) developed a matrix comprising of xanthan gum and sodium alginate. In vitro evaluation of the TDD system showed good compatibility and controlled release of the model drug Domperidone following in vitro release in a glass diffusion cell.

Other natural polymers that are being explored for use as matrices in TDD include collagen, gelatin, agarose from seaweed, natural rubber, polyethylene obtained from bioethanol, and polylactide (PLA), a polyester of lactic acid which is produced from starch or cane sugar fermentation by bacteria (Sharma et al. 2011).

#### 9.3.2.3 Rate Controlling Membrane

Rate controlling membranes are used when the TDD patch is a reservoir type such that the rate at which the drug leaves the device is regulated by the membrane which is either a porous or non-porous membrane. Various natural polymers are being explored for use as rate controlling membranes. These polymers usually have attributes such as good film forming properties and variable film thickness. Mundada and Avari (2009) developed an optimised formulation of DamarBatu (DB), a natural gum from the hardwood tree of the Shorea species such as *S. virescens* Parijs, *S. robusta* and *S. guiso*. The optimised formulation was shown

to successfully deliver Eudragit RL00, the model drug. Following in vitro drug release, skin permeation studies and other analysis concluded that Eudragit RL100 is a suitable film for TDD (Mundada and Avari 2009). In other studies DB has also been evaluated as a rate controlling membrane for TDD of a model drug diltiazem hydrochloride (Mundada and Avari 2009).

Gum copal, a biological polymer gum has also been tested as a film for TDD (Mundada and Avari 2009). The effect of different plasticisers was tested on the effectiveness of gum copal as a rate controlling membrane. The effectiveness of the film produced was estimated from tensile strength of the film, uniformity of the thickness, moisture absorption, water vapour transmission, elongation, foldability and drug permeability. PEG400 was found to be the plasticizer which gave the best permeability amongst those tested. However, a more sustained delivery was achieved in vitro with a formulation containing 30 % w/w DPB (dibutylphalate).

Another natural polymer with good film forming properties is zein. It is a protein obtained as a by-product from the processing of corn. Zein shows potential as a low cost and effective alternative to synthetic films for TDD (Elisangela et al. 2007).

#### 9.3.2.4 Adhesives

Adhesives are required in TDD systems to ensure the device remains in contact with the skin. For TDD the selected adhesive must meet certain criteria such as skin compatibility, biodegradability and good adhesion over long period due to the long-term contact with the skin and drug formulation (Kandavilli et al. 2002).

Pressure sensitive adhesives (PSA) are materials which adhere or stick to the surface following application of normal finger pressure and remains attached exerting a strong holding force. When removed from the attached surfaces, PSAs should ideally leave no residues (Pocius 1991). Adhesion refers to a liquid-like flow which causes wetting of the skin surface as pressure is applied with the adhesive remaining in place after the removal of the applied pressure. The adhesion is achieved as a result of the elastic energy that has been stored during the breaking of bonds caused by applied pressure. The effectiveness of the PSA is, therefore,an attributable to the relation between viscous flow and stored elastic energy (Franz et al. 1991). Synthetic polymers seem to have dominated the adhesives used in TDD. Commonly, used ones include acrylic, polyisobutylene and silicones (Dimas et al. 2000; Barnhart and Carrig 1998; Tan and Pfister 1999).

Use of adhesives on skin is an idea that has been around for many decades, one of the earliest applications being in bandages for wound healing by Johnson and Johnson company in 1899 (Subbu and Robert 1998). When deciding on what kind of polymer to incorporate as an adhesive, an understanding of the properties of the skin is essential. The surface energy of the skin, which acts as the adherent in the case of TDD, must be greater than or equal to the surface energy of the adhesive (Subbu and Robert 1998). Furthermore the skin properties vary with the factors

such as age, gender, race and environmental conditions. Therefore, the effect of properties such as moisture content of skin and the viscometric property of the adhesive should be established (Subbu and Robert 1998).

Adhesives in transdermal patches may exist as a single adhesive layer or a drug in adhesive type, the latter is preferred as the simplest to apply however, it is rather complicated to produce. For drug-in-adhesive type patches, issues which must be addressed include the tendency of the drug or adhesive to crystalize. This will have an effect on the drug delivery rate as it permeates through the adhesive layer (Variankaval et al. 1999).

Pressure sensitive adhesives generally comprise an elastomeric polymer, a resin for tack, a filler, antioxidants, stabilisers and crosslinking agents. Although synthetic polymers seem to be more commonly used as adhesive in TDD systems, the development of adhesives from natural polymers is becoming a rather attractive area of interest (Doherty et al. 2011). Various sources in nature have been explored for obtain adhesives.

Carbohydrates are readily available polymers of plants. Cellulose, starch and gums are the most common forms that are used in production of adhesives (Baumann and Conner 1994). There are studies which have been focused on the production of adhesives obtained from cellulose recovered from domestic and agricultural waste. These include soy protein, raft lignin and coffee bean shells (Weimer et al. 2003; Chung and Washburn 2012; Khan and Ashraf 2005). Adhesives formed from carbohydrates include carboxymethyl cellulose (CMC), hydroxyethyl cellulose, ethyl cellulose, methyl cellulose, cellulose acetate and cellulose nitrate. Those formed from starch such as tapioca, sago and potatoes can be more readily converted to adhesives following modification through heating, alkali, acidic or oxidative treatment (Baumann and Conner 1994). The adhesives often require further additives during processing. Recent studies focused on extracting natural polymeric adhesives include that by Hoong et al. (2011) which studies acacia mangium bark extracts as a source of natural polymer adhesives. The dicotyledonous tree bark which is commonly grown in Malaysia as a source of raw material for veneer, pulp and paper showed a promising prospect as an alternative to adhesives produced from petrochemicals.

In other works adhesive production from waste materials such as de-inked waste paper has been studied (Mishra and Sinha 2010). In a particular study de-inked waste paper from magazines were washed using detergent under stirring. This was then followed by further processing under heat at 150 °C and treatment with acid and ethylene glycol. The glycosides which resulted from the breaking down of the cellulose were then transesterified using rice-bran castor and soy oils to convert it to polyols. Polyurethenes are then produced from the polyols. The adhesives produced using the methods described when tested showed strong adhesive properties than the commercial adhesives and also showed significant water resistance. Marine organisms (Waite 1990) and bacteria have also been shown to be the sources of natural adhesives. The main limitation with these sources is the expensive production process.

#### 9.3.2.5 Penetration Enhancers

Polymers are also used as penetration enhancers to aid the permeation of drugs across skin. Polyethylene glycol solution is an example of such penetration enhancers of prodrugs across skin models (Hikima and Tojo 1993). However use of polymers as additives in formulations also carries some limitations such as inhibiting the bioconversion of the drug (Tojo 2005). Transdermal films incorporating 0.5 % tenoxicam have been developed from varying ratios of glycerol, PEG 200 and PEG 400. Using Fourier transform infrared spectroscopy, it was found that increasing the concentration of PEG enhanced the penetration of tenoxicam into the skin (Nesseem et al. 2011). Polymers are also employed as other formulation additives in the form of viscosity enhancers and as emulsifiers. Chitosan, a natural polymer has been used as a penetration enhancer, which acts by opening up the tight junctions which exists between epithelial cells (Cano-Cebrián et al. 2005; Mao et al. 2005; Gao et al. 2008; Avadi et al. 2005; Kotzé et al. 1997).

Recently, research studies aimed at fabricating micron-sized penetration enhancers which partially disrupt the stratum corneum layer creating a more permeable pathway for drugs to enter into the skin via natural polymers is emerging. For example a study by You et al. (2011) where dissolving polymer microneedles were fabricated from silk Fibroins obtained from bombyx mori silk worm. The resulting structures were rapidly dissolving microneedles with adjustable mechanical parameters and were biocompatible with skin. Maltose has also been used to fabricate dissolving polymer microneedle using traditional casting methods as well as using the extrusion drawing method (Lee et al. 2011). More recent studies have looked at the application of hydrolyzed collagen extracted from fish scales for production of microneedles as mechanical penetration enhancers (Olatunji et al. 2014).

#### 9.3.2.6 Backing Layer

The backing layer comes in contact with the drug matrix or reservoir therefore the chemical inertness of the material used for the backing layer is required. The backing layer must also be compatible with the excipient formulation. Back-diffusion of the drugs, penetration enhancer or excipient must not occur even over a long period of contact. While maintaining chemical inertness it must also be ensured that the backing layer is flexible enough to allow movement, transmission of moisture vapour and air in order to prevent skin irritation during long-term contact with skin. Adequate transmission of moisture vapour and air also prevents the weakening of the adhesive hold on the skin surfaces (Kandavilli et al. 2002; Rolf and Urmann 2000a). In more modern designs of TDD patches, the backing layer could be solidified with the reservoir to form a single structure such that it serves as a storage space for the reservoir (Rolf and Urmann 2000b; Kandavilli et al. 2011). More recent studies have explored the use of natural polymers as backing layer of nicotine transdermal patches from natural rubber latex (Suksaeree et al. 2011).

#### 9.3.2.7 Release Liner

The adhesive side of the transdermal patch is usually covered with a liner which protects the adhesive and the rest of the patch during storage. Although mostly for packaging purpose, the liner is in direct contact with the adhesive layer throughout the storage period. The material used as a release liner should be chemically inert (Wokovich et al. 2006) and resistant to the permeation of the drug, penetration enhancer and moisture. The liner should also not cross link with the adhesive such that it becomes difficult to remove (Pfister and Hsieh 1990). Example of a release liner used in commercial TDD is the ScotchPak$^{TM}$ 1022 and Scotchpak$^{TM}$ 9742 liner which are produced from fluoropolymers by 3M Drug Delivery Systems (available in 3M product catalogue Product ID 70000065659).

Although currently the use of synthetic polymers seem to dominate that of natural polymers in TDD, there is increasing research interest in incorporating natural polymers in new ways in TDD systems (Valenta and Auner 2004). This is attributable to the desire to produce pharmaceutical products with more desirable environmental impacts, reduce dependency on fast diminishing petrochemical resources and developing more sophisticated TDD systems with better effectiveness and biosafety (Klingenberg 2013). However, there is yet to be a transdermal drug delivery system which is developed fully from natural polymers. The dependency on synthetic polymers therefore still persists. Future research efforts directed towards developing novel natural polymers from new biological sources. Consequently as new polymers emerge, extensive studies will be required to identify the physical and chemical properties of the new biomaterials. Furthermore developing newer processing methods and new combinations of polymers could be optimised leading to improved effectiveness in transdermal drug delivery.

Natural polymers have proven valuable in transdermal drug delivery systems. They have a wide range of applicability and pose several advantages over synthetic polymers in this application. Nature offers an abundant supply of polymers with numerous properties. Understanding these sources and properties allow us to further modify these polymers to suit specific requirements. The area of transdermal drug delivery still faces certain limitations such as skin irritation and limited range of drugs which can be delivered through this means. Exploring new polymers from natural sources could provide new solutions and offer clinical and commercial development in the area of transdermal drug delivery.

## 9.4 Topical Drug Delivery

Delivery of drugs into the body topically can be employed to treat conditions which exist on or close to the surface of the skin. This could vary from aches and bruises to severe burns and mild and chronic conditions such as eczema and psoriasis. This form of delivery refers to when a drug formulation is applied directly to the external skin surface or surface of the mucous membrane of the vaginal, anal,

oral, ocular or nasal area for local activity (Joraholmen et al. 2014; Mekkawy et al. 2013; Gratieri et al. 2011; Singla et al. 2012). Topical delivery through the other entry routes (i.e. oral, vaginal, ocular, etc.) is not to be confused with the other forms of delivery which are discussed in other sections of this chapter.

### *9.4.1 Advantages and Disadvantages*

Topical delivery is relatively convenient and has relatively better patience compliance than, e.g. oral or intravenous injection which could impose adverse impacts such as nausea, low bioavailability due to metabolism of drug in the gastrointestinal tract, needle phobia and general preferences. The specificity of topical delivery is also advantageous as it can be directly applied to the affected area to act locally, similarly the medication can be easily terminated by simply cleaning off the medication. Topical delivery particularly becomes a favourable option where other routes of entry into the body are deemed unnecessary or unsuitable depending on the individual or nature of drug. In cases where for instance oral delivery of the drug could induce adverse effect which could even is more severe than the actual condition being treated. For instance many of the adverse effect associated with antifungal drug fluconazole are gastrointestinal related and could be avoided by applying a topical formulation for effective delivery of the drug (Mekkawy et al. 2013).

Main challenges in the area of topical drug delivery alongside skin irritation and allergic reaction include skin penetration into target region especially for drugs with large particle size. In particular, situations such as in fungal infection where the penetration into the stratum corneum is further inhibited as an attack mechanism of the pathogen to prevent shedding of the stratum corneum, penetration enhancement of the topical agent becomes of relative importance in the effectiveness of the drug formulation (Del Palacio et al. 2000; Mekkawy et al. 2013).

### *9.4.2 Composition of a Topical Formulation*

The main components of a topical formulation includes a vehicle which could be in the aqueous form, mainly water or alcohol, or it could be an oil such as mineral oils, paraffin, castor oil, fish liver oils, cotton seed oil, etc. A vehicle should maintain effective deposition and even distribution of the drug on the skin; it should allow delivery and release to the target site and maintain a pharmacologically effective therapeutic concentration of the drug in the target site. In addition to these properties a suitable vehicle should be well formulated to meet patient's cosmetic acceptability and be well suited for the anatomic site.

Emulsifiers are important to maintain stability and the distribution of the water and oil emulsion throughout the shelf and usage lifespan of the formulation.

Typical synthetic emulsifiers include polyethylene glycol 40 stearate, sorbitan monooleate (commercial name: Span 80), polyoxyethylene sorbitan monooleate (commercial name Tween 80), stearic acid and sodium stearate. Natural polymers used as emulsifiers include starch, gum acacia, alginates, xanthan gum, irvingia gabonensis mucilage, and tragacanth gum (Ogaji et al. 2011). Gelling agents are also important in increasing the bulk of the drug and thicken the topical formulation according to stable viscoelasticity. Examples include sodium alginate, cellulose in modified forms as sodium carboxymethyl cellulose (NaCMC), hydroxypropylmethyl cellulose (HPMC) and hydroxypropyl cellulose (HPC) (Mekkawy et al. 2013).

### *9.4.3 Types of Topical Formulations*

Topical drug delivery systems could be in the form of gels, emulgels, emulsions, liposomes, liquids, powders and aerosols. Gels and emulgels are relatively new forms of topical delivery formulations. Gels are formed when a large amount of aqueous or hydro-alcoholic solutions are entrapped within a network of colloidal solid particles or macromolecules, while emulgels are a combination of a gel and emulsion. Emulgels are targeted at addressing the limitation of gels to delivery of hydrophilic compounds by enabling the delivery of hydrophobic compounds better than using gels or emulsions. To create emulgels for hydrophobic drugs, oil-in-water (o/w) emulsions are needed to entrap the hydrophobic drugs followed by addition of a gelling agent to the emulsions, while for hydrophilic drugs; a water-in-oil (w/o) emulsion is used. The desirable features of an emulgel include more effective cutaneous penetration, greaseless, spreadability, extended shelf life compared to gels or emulsions, biofriendly, non-staining, water soluble, moisturising and a generally transparent and pleasing appearance.

### *9.4.4 Natural Polymers in Topical Delivery Systems*

Natural polymers are used in topical drug delivery as gelling agents, emulsifiers, stabilizers, thickeners, etc. Cellulose, alginates, chitosan, albumin, starches and xanthan gum are examples of natural polymers which have been applied in the production of topical formulations (Timgren et al. 2013; Gratieri et al. 2011; Laxmi et al. 2013). The derivatives of cellulose such as HPMC or CMC are particularly common candidates in topical formulations and they pose a good alternative to the commonly used carbopol, a synthetic polymer (Singla et al. 2012).

Gels are of interest for topical delivery of pharmaceutical agents as they are easy to apply, spread and remove, thus encouraging patience compliance. Excipients used in topical delivery of psoralen using natural polymers; pectin, xanthan gum, egg albumin, bovine albumin, sodium alginate and guar gum are compared in

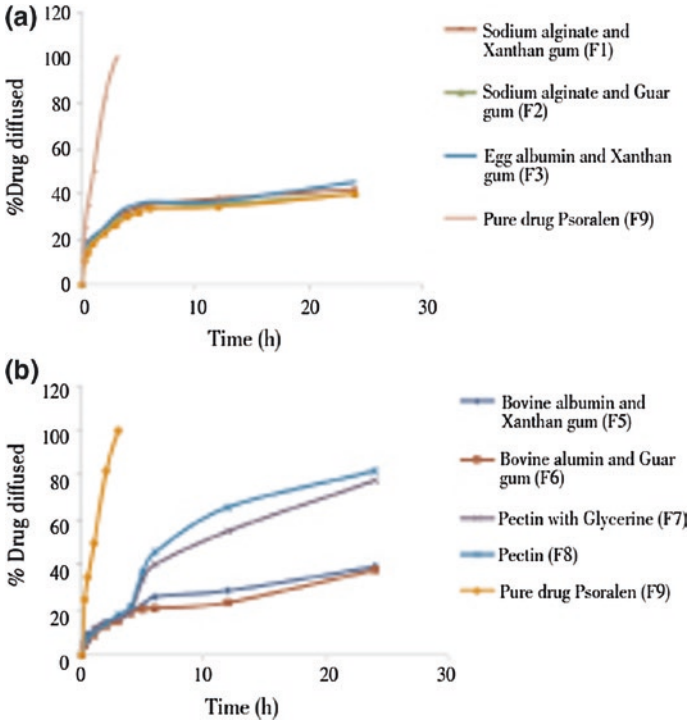


**Fig. 9.2** Comparing diffusion profiles of topical drug, psoralen using various natural polymer-based excipients (**a**) and (**b**). Sourced from Laxmi et al. (2013) under creative commons attributed licence

Fig. 9.2. Table 9.1 shows the reagent component concentrations of the respective polymer, humectant, drug, solvent, antioxidant and preservatives in a developmental formulation of Psoralen, labelled F1–F8 (Laxmi et al. 2013). Psoralen is a drug used in the treatment of skin conditions such as psoriasis, vitiligo, mycosis fungoides and eczema, but also possesses antitumor, antibacterial and antifungal properties. It belongs to a class of furanocoumarins compounds found in the *psoralea corylifolia* L. plant (Ahmed and Baig 2014).

The psoralen gel formulations were prepared by first mixing the polymer in water and stirring continuously at 37 °C. This was followed by addition of gelling agent and continued mixing until a homogenous dispersion was attained. The required drug dissolved in methanol was then added followed by addition of antioxidant, preservatives and humectants. The mixture was then stirred until a homogenous mixture was obtained.

All polymers used showed good compatibility with the drug. This is important as an interaction between the excipient and the drug formulation will likely affect the drug activity and could also pose some adverse health effects. This is not to say that all natural polymer excipient do not interact with the drug compound or

**Table 9.1** Various formulations of Psoralen using natural polymer excipients adopted from Laxmi et al. (2013) under creative commons Licence

| Materials | Formulation code | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | F1 | F2 | F3 | F4 | F5 | F6 | F7 | F8 |
| Psolaren (g) | 0.05 | 0.05 | 0.05 | 0.05 | 0.05 | 0.05 | 0.05 | 0.05 |
| Sodium alginate (g) | 0.75 | 0.75 | – | – | – | – | – | – |
| Egg albumin (g) | – | – | 0.75 | 0.75 | – | – | – | – |
| Bovine albumin (g) | – | – | – | – | 0.75 | 0.75 | – | – |
| Pectin (g) | – | – | – | – | – | – | 4 | 5 |
| Xanthan gum (g) | 0.50 | – | 0.75 | – | 0.75 | – | – | – |
| Guar gum (g) | – | 0.50 | – | 0.75 | – | 1.75 | – | – |
| Menthol (g) | 0.25 | 0.25 | 0.25 | 0.25 | 0.25 | 0.25 | 0.25 | 0.25 |
| σ-Tocopherol (g) | 0.50 | 0.50 | 0.50 | 0.50 | 0.50 | 0.50 | 0.50 | 0.50 |
| Barbaloin (g) | 0.005 | 0.005 | 0.005 | 0.005 | 0.005 | 0.005 | 0.005 | 0.005 |
| Glycerin (mL) | – | – | – | – | – | – | 5 | – |
| Eugenol (mL) | 0.01 | 0.01 | 0.01 | 0.01 | 0.01 | 0.01 | 0.01 | 0.01 |
| Methanol (mL) | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 10 |
| Distilled water to make (mL) | 50 | 50 | 50 | 50 | 50 | 50 | 50 | 50 |

psoralen in particular. The tendency of interaction between excipient and drug compound depends in the specific drug and specific polymer. While a polymer might show the desired biomechanical properties, release kinetics, bioactivity, etc. the applicability may be limited if there is interaction between the polymer being used as excipient and the active drug compound. For instance, nanofibrillar cellulose gels show good potential for drug delivery (Laurén et al. 2014); however, nanofibrillar cellulose possesses various carboxyl and hydroxyl groups which may interact with drug compounds in different ways. This, therefore, must be investigated for every new formulation.

Interaction between excipient and drug compound is commonly evaluated using FTIR. Compatibility is indicated when the characteristic peaks of the pure drug are retained in the FTIR spectra of the drug formulation with the excipients present. Figure 9.3 shows the FTIR spectra of pure psoralen next to that of formulation of psoralen in albumin and xanthan gum as polymer excipients.

Of the polymers investigated, the formulation containing xanthan gum and egg albumin showed the best drug incorporation, release kinetics and in vitro antipsoriatic activity (Laxmi et al. 2013).

Topical delivery system should possess sufficient pseudoplasticity and controllable release kinetics. Sodium alginate and derivatives of cellulose, sodium carboxymethyl cellulose, hydroxypropylmethyl cellulose and hydroxypropyl cellulose when applied as excipients for topical delivery of fluconazole showed desirable pseudoplastic behaviour. This pseudoplastic behaviour is a shear thinning property that allows the topical formulation to be effectively spread with ease on the affected area while remaining in the required region for localised and sustained

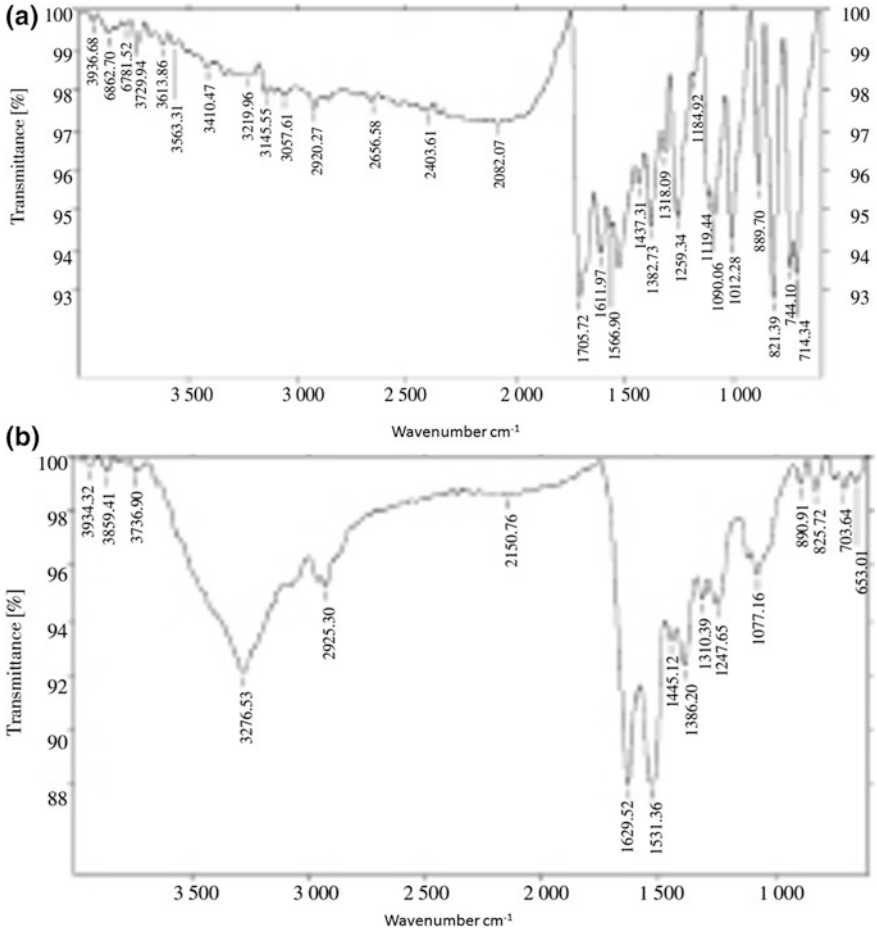


**Fig. 9.3** FTIR spectra of psolaren (**a**) and psolaren in a formulation of egg albumin and Xanthan gum (**b**). Sourced from Laxmi et al. (2013) under creative commons attributed licence

delivery. The release kinetics and viscosity also vary with the concentration of the polymer such that the release rate and viscosity can be varied as required by varying the concentration of the polymer as desired. Although a synthetic gelling agent, carbopol showed the best drug release profile and anti-fungi activity; the other polymers also had sufficient antifungal activity and drug release rate (Fig. 9.4).

Over the 3 h observed, the release rate of the fluconazole increased as the concentration of the polymer id reduced (Mekkawy et al. 2013). This can be attributed to increased porosity as polymer concentration reduces, allowing easier permeation of the drug compound through the polymer matrix of the gel.

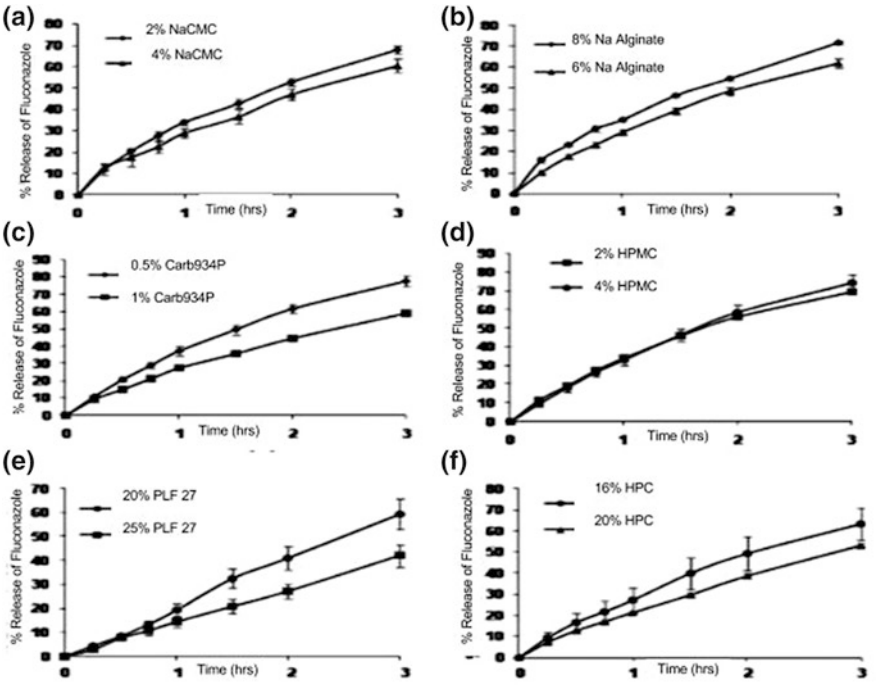


**Fig. 9.4** Effect of various polymer excipients on the release profile of fluconazole from prepared gel

The ability to control and predict release kinetics of drug formulation is important in the effective drug delivery. Here, we see gels from natural polymers showing controllable parameters comparable to that of synthetic polymers.

In the treatment of fungal keratitis, delivery and bioavailability of the antifungal agent can be enhanced by using chitosan-based formulations either in gel or solution. Topical formulations of fluconazole using chitosan solution and a gel system of chitosan with a thermoresponsive polymer poloxamer as vehicles showed improved bioavailability of fluconazole in the eye compared to aqueous solutions. The aqueous solutions used as eye drops have limited effectiveness due to the eye's inherent defence mechanism which prevents penetration of foreign substances (Fig. 9.5). The chitosan-based formulation in solution and gel when tested on rabbit models in vivo and across porcine cornea ex vivo at a time of nearly 2 h retained the drug in the desired area allowing more of the drug to penetrate leading to increased bioavailability (Fig. 9.5) (Gratieri et al. 2011).

The mucoadhesive property of chitosan also makes it applicable for application in topical gels for localised and effective delivery topically. In the case of pregnant women where care must be taken to avoid systemic absorption of certain drugs such that the drug being administered to treat the mother does not get to the child as the drug, although beneficial to the mother might pose harm to the child. It is therefore desired that the drug be localised to the affected tissue as

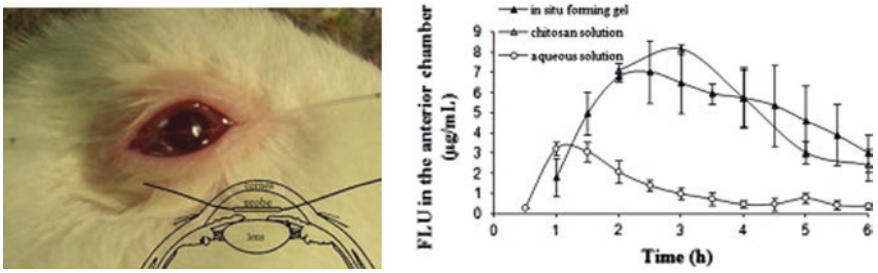


**Fig. 9.5** Enhanced topical ocular delivery of fluconazole using chitosan-based solution and gel (Gratieri et al. 2011). Reproduced with permission from Elselvier (Licence number 3631870446393)

best as possible. An example is the delivery of clotrimazole using chitosan-coated liposomes for the treatment of vaginal infection which occurs during pregnancy (Joraholmen et al. 2014). Vaginal infection although might heal without treatment in non-pregnant women, in pregnancy must be treated to prevent complications at child birth or affect development of the child. Drug treatment provides adverse effects involving current drug regimens because of very high therapeutic levels in the bloodstream despite favourable long durations of action. For example, trichomoniasis is a vaginal infection when treated with metronidazole before 37 weeks pregnancy substantially increases the adverse effects of preterm labour and low birth rate babies (Hainer and Gibson 2011). The drug metronidazole is commonly prescribed to pregnant women in oral dosage form (500 mg or 250 mg) (Hainer and Gibson 2011). Further research in decreasing the adverse effects, maintaining an ideal therapeutic level and long sustainable duration of action for metronidazole is much sought after. Chitosan-coated liposomes containing 0.1, 0.3 and 0.6 % w/v concentration of chitosan and a drug concentration of 22 g/mg lipid of Clotrimazole, show good localised delivery of the drug (Joraholmen et al. 2014). The retention of the drug in the vaginal tissue was also significantly increased by use of chitosan, (Fig. 9.6). Interestingly, it was also shown that the

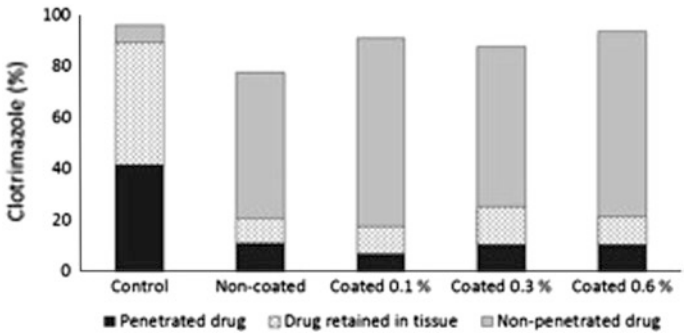


**Fig. 9.6** Comparing retention of the drug clomirazole at vaginal site using varying concentration of chitosan. Reproduced with permission from Elselvier Licence number 3631861429984

clotrimazole-containing liposome system with lower concentration of chitosan showed better mucoadhesive property than the higher concentration of chitosan. The topical formulation effectively adheres to the tissue preventing penetration into the systemic flow such that the drug does not cross the placenta to the child but remains in the tissue where it is needed to act.

## 9.5 Oral Drug Delivery Systems

Drug delivery through the oral route is one of the most common forms of drug delivery into the body (Elsayed et al. 2009; Muheem et al. 2014). Oral drug delivery refers to the intake of medicaments into the body through the mouth by swallowing, chewing or drinking. These 87 dosage forms could be in form of solid or liquids as tablets, capsules, powders, liquids. Oral dosage forms could be targeted at any tissue in the body and for a variety of purposes from general pain relief to regulation of insulin in diabetes patients.

### *9.5.1 Advantages and Disadvantages of the Oral Route*

In certain cases, the oral route becomes more than just an alternative to other routes of drug delivery. For example, insulin delivery, where oral route provides an administration which is closer to the natural physiology of the body by delivering the drug into the liver which is the target tissue. The drug passes into the liver via the pancreatic β cells through the hepatic portal vein. This is unlike in the case of other delivery routes such as parenteral or nasal which aim to deliver the drug directly into the systemic circulation. While this route is favourable in avoiding the first pass metabolism, it is not in line with insulin's natural physiological pathway (Rekha and Sharma 2013; Muheem et al. 2014).

Protein drugs such as insulin pose a particular challenge in oral delivery as they are more likely to follow the paracellular route rather than the lipophilic membrane route which most other drugs follow. This makes them more susceptible to enzymatic degradation.

The main limitations in oral delivery route are the first pass metabolism and biodegradation in the gastrointestinal tract which adversely impacts on the bioavailability of the drug in vivo. Scientific focus in the area of oral drug delivery looks at developing oral formulations which can successfully pass through the gastrointestinal tract while still remaining potent, resist enzymatic degradation at the mucous membrane, can be effectively transported through the complex structure of the mucous membrane, get absorbed into the targeted tissue and have the desired pharmacological activity after passing through the mucous layer (Muheem et al. 2014).

### 9.5.2 Current Challenges and Natural Polymer-Based Innovations in Oral Drug Delivery

Mucoadhesive polymers are applied with the aim of developing a delivery system which enables the drug to attach to the mucous membrane for enhanced permeation and sustained delivery. However, limitation of this procedure lies in the constant renewal of the mucous layer which inhibits mucoadhesive drug delivery systems (Muheem et al. 2014; Ponchel and Irache 1998).

Although rate of drug absorption using any kind of route (e.g. oral, nasal, topical) depends on factors such as age, diet and state of health of the patient (Morishita and Peppas 2006), the drug properties also has a significant effect on the rate of absorption and effectiveness. The drug properties which affect oral delivery include molecular weight, particularly drugs with molecular mass greater than 500–700 Da like protein drugs such as insulin. Lower molecular weight drugs are generally easier to absorb.

While their oral delivery would be of much significance pharmaceutically, delivery of proteins and peptides-based drugs orally have particularly proven challenging. This is mainly due to their generally large molecular weight and the tendency to be digested in the body without serving their purpose. There are about two known oral protein and peptide drugs in clinical development and these are Interferon-alpha and human growth hormone (HGH) while more are being studied for potential pharmaceutical application. Of much interest is the oral delivery of insulin.

Research approaches in enhancing the oral delivery of proteins include reducing the particle size and using biodegradable nanoparticles (Bakhru et al. 2013).

## 9.6 Parenteral Drug Delivery Systems

Parenteral delivery concerns the delivery of drugs invasively through the skin, eye, vein, artery and spinal cavity. Substantial efforts in formulating a documented plan in the development of hypodermic needles was first initiated by Lafargue in 1836 (Howard-Jones 1947). Lafargue immersed the lancet in morphine and diluted the morphine by a once repeated immersion into water before self-injection (Howard-Jones 1947). The hypodermic needle is a cylindrical tube with an elliptical shaped bevel end forming a sharp tip for the purpose of cutting into skin (Hamilton 1961). Hypodermic needles are conventionally fabricated from medical grade stainless steel. The luer lock is the plastic connector between the hypodermic needle and syringe body. Polyethylene and polypropylene are medical grade thermoplastics moulded into the luer lock (Gilson and Windischman 1983). The syringe body is composed of medical grade plastic. Medical grade thermoplastics can be moulded into complex geometries in a process known as injection moulding. Medical grade plastics are regulated by USP with the aim of analysing if a grade of plastic reacts

with mammalian cells cultures. There is no published material about syringes constructed from natural polymer materials. This is because most natural polymers may not be easily mouldable by injection moulding and end product assurance towards medical grade is less likely due to the risk of by-product toxicity if a reagent in a natural polymer blend is unstable despite high desirable yields. Hypodermic needles and syringes are usually disposable and single use only. Complex blended natural polymers such as sorn starch blended with clay, mineral montmorillonite and modified natural rubber latex were injection moulded thus resulting in good tensile strength and elastic modulus properties (Mondragón et al. 2009). The constraints for complex blended polymers are greater costs than conventional process, longer duration in process manufacturing and end product can be unaesthetically pleasing. In the past, syringes were constructed from borosilicate glass and autoclavable for reuse thus producing less of an ecological impact.

### *9.6.1 Advantages and Disadvantages of Parenteral Drug Delivery*

Parenteral drug delivery is still a common and widely accepted route to drug administration. The main advantages are bypassing gastrointestinal tract metabolism, rapid drug delivery with target-based response and is an alternative route for patients with difficulty ingesting their medication or are completely sedated (Breymann et al. 2010; Jain 2008). The disadvantages are depth-related localised pain, likelihood of peripheral nerve injury and accidental piercing of a blood vessel at hypodermis level (Jain 2008).

### *9.6.2 Properties of Parenteral Drug Molecules*

Injection-based parenteral drug molecules are usually high molecular weight, more ring-based structural configuration, high counts for proton acceptors and lowest $\text{Log}_{10}$ o/w (Vieth et al. 2004). Fluid-based drug formulations are ideal for flow-based transfer along hollow hypodermic needles. Surface tension forces are the usual forces that allow fluid to travel along capillary tube. The volumetric flow rate of a fluid inside a microcapillary is defined by the Hagen–Poiseuille (Eq. 9.1) (Holzman 1998; Allahham et al. 2004).

$$Q = \Delta P\left(\frac{\pi r^4}{8\,\mu L}\right) \tag{9.1}$$

where $Q$ is the volumetric flow rate inside the hypodermic needle, $\Delta P$ is the pressure difference from Eq. 9.2, $F$ is the injection force, $f$ is the frictional force from the tube and syringe walls, $A$ is the interior cross-sectional area of the tube

and $r$ is the internal tube radius, $\mu$ is the fluid viscosity and $L$ is the hypodermic needle length.

$$Q = \Delta P\left(\frac{\pi r^4}{8\,\mu L}\right) \tag{9.2}$$

The characteristic of fluid flow is expressed by the Reynolds number, *Re* (Eq. 9.3) (Ashraf et al. 2010)

$$Re = \frac{\rho \mathrm{d} V}{\mu} \tag{9.3}$$

where $\rho$ is fluid density, $d$ is the internal tube diameter, $V$ is the fluid volume. A Reynolds number of 2100 or less indicates laminar flow and turbulent flow is above this value (Ashraf et al. 2010).

### *9.6.3 Current Proprietary Parenteral Devices*

Parenteral devices are commonly injectables and examples of current devices available on the market are mentioned. Injectable devices for the delivery of soft implants subcutaneously are patented and commercially available from Rexam (www.rexam.com). Also pre-filled drug syringes is registered Safe 'n' Sound, patented and commercially available from Rexam (www.rexam.com). A self-injector trademarked SelfDose for the safe delivery of drugs is in the format of an adaptor for fitting syringe formats is commercially available from West Pharma (www.westpharma.com). Another self-injector device has a window indicator regarding usage and is trademarked Project, patented and commercially available from Aptar (www.aptar.com).

### *9.6.4 Future Challenges of Parenteral Devices*

In this chapter, we have discussed microneedles as minimal invasive parenteral devices because the needles are fabricated to penetrate a known depth in skin layers than a hypodermic needle. Natural polymers have the potential to support the sustained release of drugs in the skin and can prove advantageous for the biodegradable class of microneedles. However, the challenge arises to strengthen the microneedles with the result of all microneedles piercing the skin at a reproducible depth. Synthetic biodegradable polymer such as poly(DL-lactic-*co*-glycolic acid) PLGA and poly(L-lactic acid) (PLLA) possess high mechanical strength (Ishaug et al. 1994; Leung et al. 2008). The possibility of enhancing the natural polymeric formulation with blended synthetic, polymeric fibres in providing improved mechanical strength properties is one direct solution.

## 9.7 Nasal Drug Delivery Systems

Nasal delivery is one of the oldest drug delivery systems originating from Ancient Indian Ayurveda called Nasya Karma. The mucosal epithelium inside the nasal cavity is an area for non-invasive drug delivery. This epithelial layer located in the inferior turbinate of the nasal cavity is highly vascularised with a significant absorption area (150 $cm^2$) and projections of microvilli in epithelial cells (Grassin-Delyle et al. 2012; Lan Kang et al. 2009). The nasal cavity is covered with mucous membrane comprising of goblet cells, columnar cells and basal cells (Fig. 9.7). Most cells of the nasal cavity have cilia apart from columnar cells in the anterior cavity (Fig. 9.7). A collective group of microvilli are known as cilia. Cilia move rhythmically in waves with a function to clear mucus from the nasal cavity into the nasopharynx followed by the oesophagus before finally moving towards the gastrointestinal tract. The microvilli contribute to the large surface area thus highly desirable for effective drug absorption into the nasal mucosa. The nasal mucosa is neutral pH and permeable to numerous drug molecules. Mucosa is usually comprised of lipids, inorganic salts, mucin glycoproteins and water. The main functions of mucus are lubrication of surfaces and protection. The function of protection are goblet cells and mucus glands of nasal epithelium that prevent the absorption of foreign chemicals and decrease residence time for any applied drugs that are in surface contact with the epithelial lining. The purpose for nasal drug delivery is to target the drug systemically such as peptides or proteins in the bloodstream locally (Illum 2012) such as a nasal allergy, nasal congestion, sinus, and to target the central nervous system (CNS) such as bypassing the blood-brain

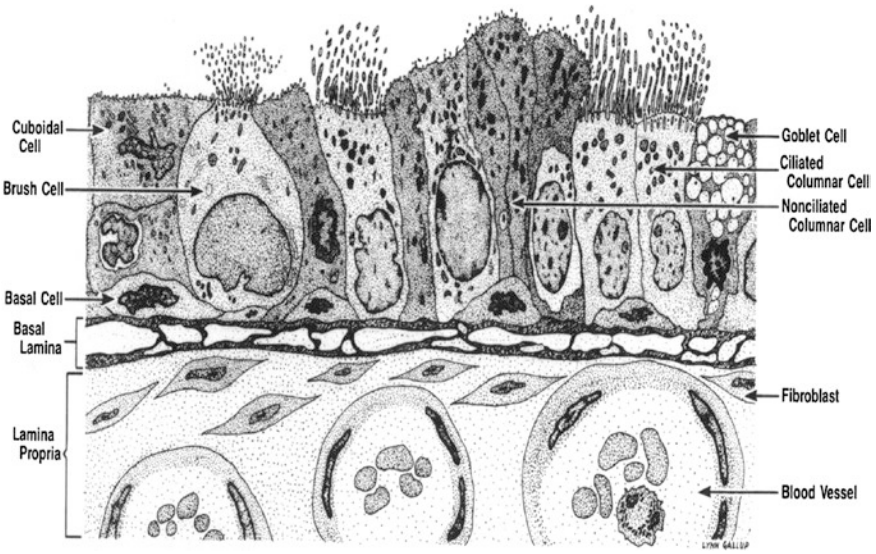


**Fig. 9.7** Histology of the nasal cavity morphology (Uraih and Maronpot 1990)

barrier (Illum 2012). The purpose of targeting the CNS is to develop drugs for rapid treatment of migraine, headaches, advanced neurodegenerative illnesses such as Alzheimer's and Parkinson's disease.

### *9.7.1 Advantages and Disadvantages of Nasal Drug Delivery*

The advantages of nasal drug delivery are avoidance of potential gastrointestinal and hepatic first pass metabolism (Grinberg and Gedanken 2010; Lan Kang et al. 2009), low molecular weight drugs have a good bioavailability via the nasal route, straight forward self-administration and protein-based drugs are able to absorb through the nasal mucosa as an alternative to parenteral drug delivery (Grassin-Delyle et al. 2012). The disadvantages of nasal drug delivery are possibility of irreversible cilia damage on the nasal mucosa caused by the drug formulation (Grassin-Delyle et al. 2012), high molecular weight molecules and polar molecules may not permeate or result in low permeation thorough nasal membranes (molecular weight threshold: 1 kDa) (Illum 2012; Grassin-Delyle et al. 2012), clearance of mucosa frequently by cilia has the potential to decrease or prevent full drug absorption (Patil and Sawant 2009), nasal mucosa could denature and change the structure of some drugs through enzymes and possible incompatibility observed between drug and nasal mucosa interaction (Grassin-Delyle et al. 2012).

### *9.7.2 Natural Polymers in Nasal Drug Delivery*

Mucoadhesive microspheres, liposomes, solutions, gels and Mucoadhesive hydrogels are vehicles commonly adopted in the nasal delivery of drugs. Starch, Chitosan, alginate, dextran, hyaluronic acid and gelatin are natural polymers adopted for nasal drug delivery. Mucoadhesion is defined as the contact between the drug formulation and the mucin surface. The concept of mucoadhesion is to allow sustained drug delivery in nasal membranes by prolonging the contact time between the drug formulation and nasal mucosa layers in the cavity (Duan and Mao 2010). Mucoadhesion promotes drug absorption and lowers the chances of complete mucociliary clearance (Patil and Sawant 2009).

Starch is a biodegradable polysaccharide which can be readily processed into microspheres (Grinberg and Gedanken 2010). Starch microspheres commercially available under the name Spherex are used in nasal drug delivery (Pereswetoff-Morath 1998; Grinberg and Gedanken 2010). Drugs such as Insulin (Duan and Mao 2010), morphine (Illum et al. 2002), inactivated influenza (Coucke et al. 2009) and Salbutamol (Xu et al. 2014) are examples of starch loaded intranasal drugs at developmental stage.

Chitosan is a natural polysaccharide with mucoadhesive properties thus it has very good binding properties to nasal epithelial cells and the covering mucus layer

(Illum 2003). The cationic nature of chitosan readily permits the electrostatic attraction with the negatively charged mucosal surface (Martinac et al. 2005). There has been a wealth of research published on chitosan for intranasal delivery according to variable salt forms, degrees of acetylation, variation in derivatives, variation in molecular weights and variation in physical form such as gel, microspheres (Casettari and Illum 2014). Drugs such as Loratadine (Martinac et al. 2005), Zolmitriptan (Alhalaweh et al. 2009) and Insulin (Chung et al. 2010) are examples of loaded chitosan-based intranasal drugs at developmental stage. However, there is yet to be a marketed nasal drug product containing chitosan as the drug absorption enhancer. A morphine intranasal formulation containing chitosan (Rylomine) has already published phase 2 clinical trials and has already pursued phase 3 clinical trails (Javelin Pharmaceuticals; Casettari and Illum 2014; the Pharma Letter).

Alginate is a divalent cation-induced rapid gelation, natural polysaccharide with greater mucoadhesion strength as compared with chitosan, PLA and carboxymethyl cellulose (Patil and Sawant 2009). Usually alginate gel is blended with one or more mucoadhesive polymers in order to improve the strength and drug loading efficiency of the vehicle (Pal and Nayak 2012). Drugs and macromolecules such as bovine serum albumin in representing a water soluble antigen (Lemoine et al. 1998) Carvedilol (Patil and Sawant 2009) and Terbutaline Sulphate (Moebus et al. 2009) are examples of alginate loaded intranasal drugs at developmental stage. There appears to be no significant proprietary drugs containing alginate as the vehicle for intranasal drug delivery.

## 9.8 Hydrogel-Based Drug Delivery Systems

The need in optimised semi-solid, biocompatible, polymeric formulations in drug loading and routes of entry in the human body is still a growing area in pharmaceutics. Gel-and ointment-based drug formulations are normally oily and thick in appearance (Mueller et al. 2012). A common purpose of such semi-solid, polymeric gel/ointment formulations are to enhance the viscoelasticity (Teeranachaideekul et al. 2008; Silva et al. 2007) and improve target-based pharmacokinetics such as enhanced permeability of luteinizing-hormone, releasing hormone (LH–RH) from polycarbophil hydrogels inside the vagina compared with solution (Valenta 2005). In terms of viscoelasticity, an example in enhancing pseudoplastic properties for oral Ibuprofen is Carbopol-based hydrogels (Silva et al. 2007). Limitations for semi-solid formulations such as topical applications concerning transdermal drug routes of delivery are one common area (Dubey et al. 2007). Hydrogels can be considered as a semi-solid matrix for the purpose of controlled drug release (Jacobs 2014; York 1996). Hydrogels can change structural configuration during certain temperature or pH-induced environments in bodily systems (Cai et al. 2013; Nguyen and Lee 2010). Usually, hydrogels are known to release trapped drug molecules by swelling in watery plasma solvent (Li et al.

2014b). Distinct variability from conventional swelling mechanism of active molecule release are thermoresponsive hydrolysis of block copolymers hydrogels and full dissociation of polycationic poly(allylamine) hydrochloride and polyanionic polystyrene sulfonate complex microgel during increase pH (Buwalda et al. 2014; Rondon et al. 2014). A growing demand for hydrogel-based drug delivery since 1980 onwards shows increasing treads (Fig. 9.8).

This section focuses on hydrogels obtained from natural polymers. It outlines the structure and function of natural polymeric hydrogels in the area of Pharmaceutics-based drug delivery. The distinct sub-classification of a less common form of hydrogels, known as microgels, explains this difference. Also, another area of this review focuses on the physico-chemical properties of hydrogels as a drug delivery system with ideal pharmacokinetic targeting areas.

A hydrogel is a solid or semi-solid hydrophilic matrix comprising of polymeric macromolecules crosslinked by varying combinations of hydrogen bonding, Van der Waals, ionic electrostatic-based and covalent-based intermolecular interactions (Laftah et al. 2011; Huang et al. 2007). Hydrogels possess matrix swelling or shrinkage properties in physico-chemical solvent media such as pH, temperature and ionic strength of electrolytes in solution (Chang et al. 2010; Li et al. 2014b). Usually, solvent ion concentrations at medium ionic strengths allow for ion exchange between polyelectrolyte gel and solvent ions resulting in osmotic pressure increases inside hydrogel and thus causing swelling (Richter et al. 2008). Polymeric hydrogels such as *N*-isopropylacrylamide (*N*IPAAm) are influenced by higher ionic strength of electrolytes and temperature in solution and they can swell above their critical solution thresholds (Díez-Peña et al. 2002; Sharpe et al. 2014). *N*IPAAm has swelling properties as the nitrogen groups' hydrogen bond with water at *N*IPAAm lower critical solution temperature of 34 °C (Lee and Fu

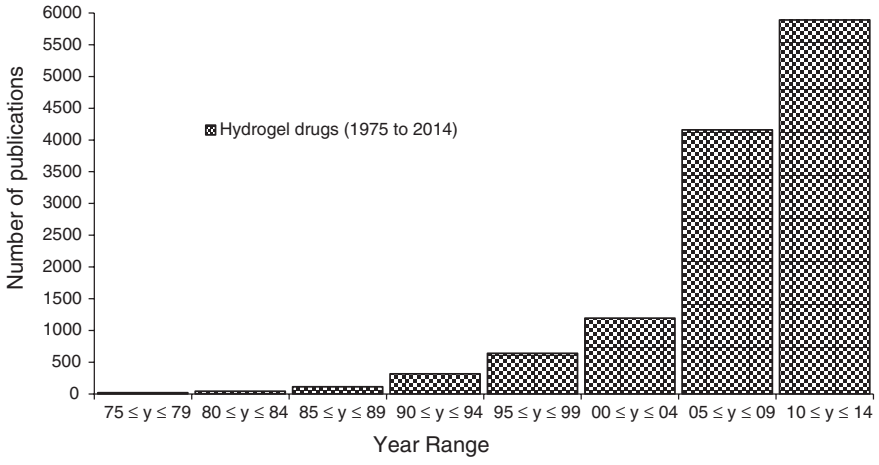


**Fig. 9.8** The number of hydrogel drug publications according to year range (Web of Science)

2003). Also the deprotonation of carboxylic acid groups in hydrogels such as polyacrylic acid (polyAA) and interpenetrating network of chitosan combined poly(sodiumacrylate-*co*-hydroxyethyl methacrylate) (SCPSC) in high pH results in ionic repulsion and induces swelling (Fig. 9.9) (Yang et al. 2011; Mandal and Ray 2014).

The equilibrium swelling ratio of SCPSC was significantly 1.6 folds greater in pH 7 buffer medium when compared with pH 3.9 (Mandal and Ray 2014). The polymeric macromolecules in hydrogels can be cationic, anionic or entirely neutral with regard to interacting with another macromolecule or drug molecules (Van Vlierberghe et al. 2011; Singh and Lee 2014). The crosslinking of hydrogels combines highly desirable characteristics such as mechanical strength, pseudoplasticity, drug and macromolecular intermolecular interactions and plasma swelling (Zhao et al. 2014; Kurland et al. 2014). The porosity of the crosslinked hydrogel

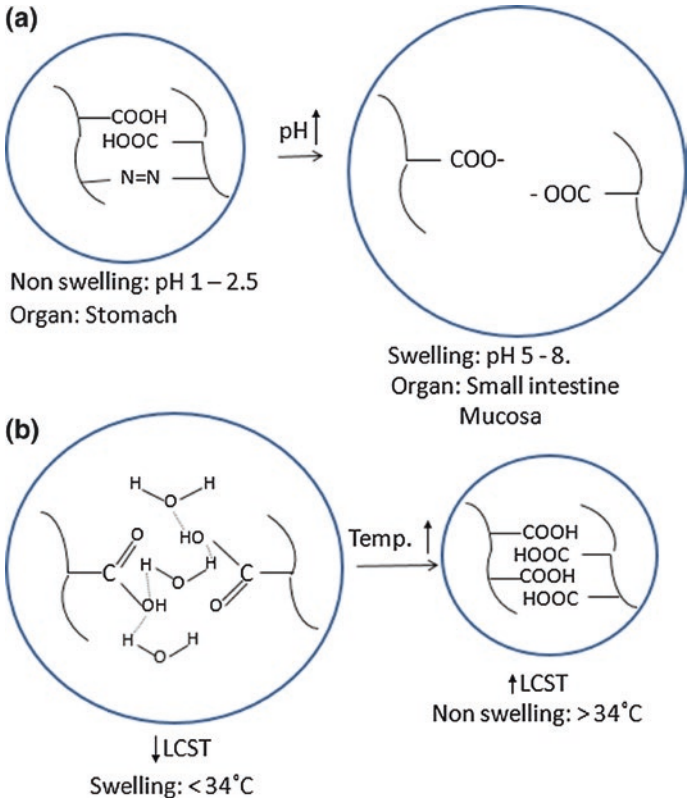


**Fig. 9.9** A schematic representation of swelling according to **a** pH with a hydrogels such as crosslinked azo polyacrylic acid (pAA) (Adopted from Yang et al. 2011). **b** Temperature with hydrogels such as PNIPAM with PNIPAM/IA (Adopted from Yang et al. 2011) with permission from Royal Society of Chemistry Licence number 3631871241621

matrix determines aqueous solvent adsorption and rate of drug release (Hoare and Kohane 2008). However, the insolubility of hydrogels to water is attributed to the networking arrangement of crosslinks between polymer chains thus maintaining physical structure (Gupta et al. 2002). Nevertheless control in the polymeric swelling release rates of drugs with possible subsequent degradation of hydrogels is very much a sought after challenge in matching the duration of drug release across a therapeutic range and target specificity in the body. There are constraints and possible major limitations in stabilising porous combination of polymers in defined mass ratios in attaining desirable controlled release of drug molecules. However, the complex chemical structures of hydrogels can pose challenging in synthesis coupled with mass reproducibility and end product purification (Martín del Valle et al. 2009). Although synthetic polymers seem to have largely dominated over natural polymers in the past decade due to their relatively long service life, high water absorption capacity and gel strength and the possibility of tailored degradation and functionality, natural polymers are highly sort after for their biocompatibility, availability and low cost. (Ahmed 2015). Hydrogels from natural source usually require inclusion of synthetic components as, for example crosslinkers or the hydrogel could be a blend of both natural and synthetic polymers for improved functionality, degradation or biocompatibility (Kamoun et al. 2015). In the following sections we look at some common natural polymers and their recent applications as hydrogels.

### *9.8.1 Hydrogels in Transdermal Patches*

The architecture of a transdermal patch comprises a drug reservoir or a polymer-drug matrix trapped between two polymeric layers as a laminated layer-by-layer arrangement (Sarkar et al. 2014). A study of the effect of mucilage derived from indigenous taro corns combined with hydroxypropylmethylcellullose (HPMC) was a patch vehicle in the slow IV drug release of an antihypertensive drug, Diltiazem (Sarkar et al. 2014). Patches have been developed for targeting the drug molecules through full skin thickness passive diffusion in the systemic circulation so that receptors or pathogens in the body are affected by the drug (Suksaeree et al. 2014; Arkvanshi et al. 2014). A cellulose polymer derived from bacteria, plasticised with glycerol using solvent evaporation techniques as a potential patch demonstrated a reduced lidocaine permeation flux in skin epidermis when compared with a hydroxypropylmethylcellulose gel (Trovatti et al. 2012). The observation of a low permeation flux is an example of implementing further optimisation-based studies by using chemical penetration enhancers effecting SC barrier properties at possible higher concentrations. Proprietary patches available as pharmaceuticals are Nicorette® (Nicorette.co.uk) in nicotine delivery to wean addiction, Ortho Evra® (Orthoevra.com) in norelgestromin/ethinyl estradiol delivery to decrease blood levels of gonadotrophins and inhibiting ovulation and chances of pregnancy and

Exelon®Patch (Novartis.com) in rivastigmine delivery to inhibit cholinesterase by reversible inhibition in delaying the progression of Alzheimers disease. Those proprietary patches mentioned are examples outlining three completely different therapeutic before current growing trends emerged since the 1980s (Wiedersberg and Guy 2014). The major benefits of patch-based delivery are reduction in adverse effects such as gastrointestinal disturbances caused by high dose oral rivastigmine as compared with a rivastigmine patch (Reñéa et al. 2014), reduction in peak plasma concentrations and interventions of prior dose adjustments periodically from oral and fast intraveneous delivery (Reñéa et al. 2014; Arkvanshi et al. 2014). The sensitivity of patient's skin to transdermal patches is a major concern because of the likelihood of allergic reactions if the patched skin area is left covered for a long duration (Reñéa et al. 2014).

### *9.8.2 Nanoparticles for Controlled Delivery*

The controlled release of active drug molecules sustained at therapeutic thresholds in specific targets of the body according to the length of treatment is a major focus in pharmaceutics research (Soppimatha et al. 2001; Ashley et al. 2014). A significant gap for nanoparticle mediated drugs to enter the pharmaceutical drugs market exists because of the sophisticated pathological targeting mechanisms and therefore traditional pharmacology cannot distinctly characterise nanoparticle drugs (Brambilla et al. 2014). Themoresponsive Poly(NIPAAm-*co*-AAm) hydrogels were shown to have a *z*-diameter of 156.0 nm after encapsulating gold-silica nanoparticles and forming nanoshells by collapsing to absorb the gold-silica at 40–45 °C at 780 nm (Strong et al. 2014). A chemotherapeutic agent, doxorubicin was loaded into the Poly(*N*-isopropylacrylamide-*co*-Acrylamide) Poly(NIPAAm-*co*-AAm) nanoshells by 1.12 folds greater than without nanoshells arrangement (Strong et al. 2014). The crosslinkers in NIPAAm-*co*-AAm hydrogels can reversibly collapse into a dehydrated globular conformation above their lower critical solution temperature, normally above physiological body temperatures, to release the drug (Sershen et al. 2000; Fundueanu et al. 2013). Poly(NIPAAm-*co*-AAm) is a synthetic polymer. Nevertheless Poly(NIPAAm) has been commonly crosslinked with natural chitosan because of pH sensitive properties of the amino groups (Li et al. 2009). The cytotoxicity of Poly(NiPAAm-*co*-chitosan) containing 5 mg/ml NIPAAm nanoparticles encapsulated with paclitaxel resulted in 60 % viability of human lung cancer cells thus proving favourable toxicity (Li et al. 2009). Complementing the 60 % cell viability, the cumulative release of Paclitaxel was increased by 1.86 fold in extracellular tumour conditions of pH 6.8 compared with pH 7.4 at the same physiological temperatures (Li et al. 2009). Nanoparticle drugs are usually between 10 and 200 nm in size with generally high efficacies (Noble et al. 2014). Liposomes are mainly natural phospholipids nanoparticles as highly advantageous drug delivery vehicles because of the potential to deliver

hydrophobic drugs and biocompatible properties (Noble et al. 2014). Liposomal synthesised PEG nanoparticles loaded anti-cancer carfilzomib allowed the inhibition in tumour growth and subsequently proved to be up to fourfolds more cytotoxic to tumours compared with unloaded carfilzomib (Ashley et al. 2014). Liposomes synthesised with PEG prevents any aggregation of nanoparticles and adsorption of plasma-based serum proteins that promote immediate clearance (Noble et al. 2014). The advantage of drug nanoparticles in drug therapy is the reduction in systemic toxicity and greater drug loading in nanospheres (Ashley et al. 2014). A huge vacuole still remains for research into drug hydrogel nanoparticles containing higher concentrations of ideal naturally sourced polymers.

### *9.8.3 Hydrogels for Wound Dressing*

Wound dressing is an immediate first aid response in superficial and chronic skin wounding injuries. The general treatment of skin wounds is to minimise scarring, microbial infection, pain, protection from further trauma and absorption of excess exudates from open lacerations (Mayet et al. 2014). Conventional gauzes and pads based on cotton and synthetic rayon polyester bandages need regular changing and tend to be more expensive than modern dressings (Boateng et al. 2008). Also conventional bandages are known to keep the wound bed dry and slow down the natural skin healing process due to restricted new cell migration and healthy tissue removal when bandage requires changing (Boateng et al. 2008; Rolstad et al. 2012). Hydrogels are an ideal dressing material for absorbing excess exudates, allowing enough moisture of the wound bed and filling irregular-shaped wound cavities (Lee et al. 2014; Tran et al. 2011). A synthesised gelatine-hydroxyphenylpropionic acid hydrogel was studied because of well-known biocompatible and tissue adhesive properties (Lee et al. 2014). A gelatine-hydroxyphenylpropionic acid hydrogel loaded with human dermal fibroblast resulted in a 1.9 fold wound closure in mice compared with phosphate buffer solution control after four days (Lee et al. 2014). The focus on hydrogels for wound dressing may seem irrelevant in the area of traditional pharmaceutics as defined in the section Portals of drug administration in the human body. The importance of a new area of study relating to emergency trauma shows the need for the application hydrogels compounds.

### *9.8.4 Polymeric Crosslinking in Hydrogels*

An important characteristic of a hydrogel is the polymeric strand crosslinking. Crosslinking of hydrogels with morphologically cross-hatched or entangled macromolecular architecture allows a 3D structure and avoids immediate dissolution of separate macromolecular strands in hydrophilic solvent (Hennick and van Nostrum 2012).

Physical crosslinking of polypeptides are attributed to ionic bonding, hydrogen bonding and hydrophobic interactions in aid of bipolymeric crosslinking (Nonoyama et al. 2012; Hu et al. 2010). Physically crosslinked hydrogels are inhomogeneous due to more than one type of intermolecular-based interaction (Hoffman 2002).

Chemically crosslinked hydrogels involve covalent linkages in bridging two different polymeric strands and the use of crosslinking agents that can react with specific functional groups in polymeric macromolecules (Hennick and van Nostrum 2012). Chemically crosslinked hydrogels permit bigger volume increases during sol-gel transition than physically crosslinked hydrogels (Jonker et al. 2012). The use of chemical crosslinking agents to bind-specific functional groups for crosslinking polymers is shown in Table 9.2. The process and target application of hydrogel and microgel polymers is outlined in Table 9.3.

### *9.8.5 Natural Polymers in Hydrogels*

Polysaccharides such as hyaluronic acid, chondroitin sulphate, chitosan, carboxymethylcellulose, hydroxypropylmethylcellulose, methylcellulose, bacterial cellulose and sodium alginate are common examples of carbohydrate derived polymers in hydrogels (Van Vlierberghe et al. 2011). Examples of proteins used in hydrogels include gelatine, collagen, elastin, ovalbumin, β-lactoglobulin and silk fibroin from both plant and animal sources (Jonker et al. 2012). Polymer strands from natural, synthetic and partially synthetic sources are acquired as drug delivery vehicles (Gupta et al. 2002). Polypeptides have straight chained or helical assemblies in their gross macromolecular arrangement such as β-pleated sheets and α-helix respectively (Woolfson 2010). Amino acids in polypeptides, containing Ala, Glu, Lys and Gln occur more in α-helices compared with Thr and Val in β-pleated sheets, in-conjunction to Gly and Pro usually located in the turn area of molecule (Woolfson 2010). Two hydrophobic regions in the macromolecular structure of anti-parallel conformation assemble to form the β-pleated sheet (Fig. 9.10) (Nonoyama et al. 2012; Woolfson 2010). Polypeptide structure hydrogels overall are the most suitable in mimicking natural extracellular crosslinking matrix (Yao et al. 2014).

Hyaluronic acid (HA)-based hydrogel particles have been investigated for drug delivery using trimethoprim (TMP) and naproxen as model drugs. Hyaluronic acid was modified with an aqueous solution of sodium bis (2-ethythexyl) sulfosuccinate (AOT)-Isoctane microemulsion system. This formed hyaluronic acid particle which were further modified by oxidizing to aldehyde (HA-O) using treatment with $NaIO_4$ followed by reacting with cysteamine thus forming thiol ligands onto the surface of the HA particles. The final HA-based hydrogel particles were formed by radical polymerization of the HA particles with anionic and cationic monomers 2-acrylamido-2-acrylamido-2-methyl-propanosulfonic acid and 3-acrylamidopropyl-trimethyl-ammonium chloride, respectively. The HA-based hydrogel particles derived demonstrated good pH dependent size variation and

**Table 9.2** Chemical agents for the chemical crosslinking of functional groups in hydrogels

| Crosslinker | Functional gps | Reaction or functional gp interactions | Chemical reaction conditions |
|---|---|---|---|
| Glutaraldehyde (Berger et al. 2004; Costa-Júnior et al.2009) | Di-aldehydes (Berger et al. 2004) | Imine group formed by Schiff base formation (Berger et al. 2004; Costa-Júnior et al. 2009). Acetal group formation from hydroxyl groups (Costa-Júnior et al. 2009) | No heat required and slow addition is usual (Costa-Júnior et al. 2009) |
| Poly(ethylene glycol)–propion dialdehyde (PEG–diald) (Luo et al. 2000) | Amine (Luo et al. 2000) | Azide addition (Luo et al. 2000) | Unimolecular addition of PEG-diald and polymer in ambient temperature conditions (Luo et al. 2000) |
| Methylene bis-acrylamide (Berger et al. 2004) | Acrylamide, ethylene (Berger et al. 2004; Bhattacharyya and Ray 2014) | Variable (Berger et al. 2004) | |
| Genipin (Song et al. 2009; Muzzarelli 2009) | Amino acid groups and secondary amino group in acidic and neutral pH (Muzzarelli 2009) | Amino acid groups (Song et al. 2009). Condensation reactions in acidic or neutral conditions and aldol condensation in basic conditions (Muzzarelli 2009) | Set pH conditions (Muzzarelli 2009) |

**Table 9.3** Recent examples of hydrogels developed in drug delivery

| Polymer | Composition | Process[a] | Target/delivery[a] | Reference(s) |
|---|---|---|---|---|
| Casein | 100 % | Temperature-based gelation | BSA molecule into buffered solution | Song et al. (2009) |
| Poly(*N*-isopropylacrylamide-*co*-Acrylamide) poly(NIPAAm-*co*-AAm) | NIPAAm and AAm, 83.3:16.7 (% mol ratio) | Poly(NIPAAm-co-AAm) synthesis: free radical copolymerisation with AIBN initiator. Microsphere process: W/O emulsification and copolymer solubilised by acidic DI water and crosslinking using glutaraldehyde | Propranolol and lidocaine | Fundueanu et al. (2009) |
| Alginate (Monomer unit: 1,4-linked b-D-mannuronic acid and a-L-guluronic acid) | Methacrylated alginate (5.7–45.3 %) | Photocrosslinking of methacrylated alginate at 365 nm and 0.05 % w/v Irgacure D-2959 photo initiator | Bovine chondrocytes for cytocompatibility for cell culture | Jeon et al. (2009) |
| Sodium carboxymethylcellulose (NaCMC): cellulose | NaCMC: cell (5:5–9:1 by wt). A hydrogel film | Solubilisation of cell and NaCMC and crosslinking with epichlorohydrin (ECH) | In vitro release of Bovine Serum Albumin (BSA) | Chang et al. (2010) |
| Poly(ethylene oxide)-poly(propylene oxide)-poly(ethylene oxide) (PF127) and Poly(methyl vinyl ether-*co*-maleic anhydride) (GZ) | GZm/PF127 molar ratio from 1 to 20 (GZm is the monomer, methyl vinyl ether-co-maleic anhydride) | Esterification between carboxyl groups of maleic anhydride and hydroxyl groups of PF127. Subsequent solvent evaporation of tetrahydrofuran followed by precipitate copolymer filtration and collection | BSA, glucoprotein rKPM-11 and dextran in PBS (pH 7.4) | Moreno et al. (2014) |

[a]The process are the main experimental conditions, reagents or crosslinking reagents in preparing hydrogels. The target/delivery is the active molecule or drug studied for encapsulation or controlled release from hydrogel

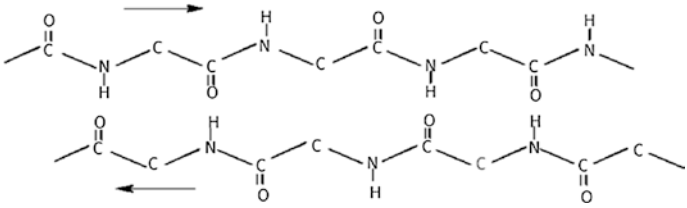

**Fig. 9.10** An anti-parallel orientation for a β-pleated sheet (Adopted from Woolfson 2010)

swelling properties. This is important for applications such as controlling and tuning the rate of drug delivery in different parts of the body. This takes advantage of the remarkable ability of HA to demonstrate variety of swelling kinetics in different pH environment (Burke and Barrett 2005; Ekici et al. 2014). Other natural polymers which tend to form hydrogels with pH dependent swelling kinetics include alginate. Arginine grafted alginate hydrogels are also potential carriers for protein drugs enabling oral delivery. This can be used to orally deliver proteins while limiting the effect of metabolism in the gastrointestinal tract prior to reaching the target area (Eldin et al. 2014).

Nanocellulose has had increasing application in the pharmaceutical area in recent times. Current interests in exploring the industrial application of nanocellulose extend to their use as hydrogels for drug delivery. Nanofibrillar cellulose derived from wood pulp was developed into injectable hydrogel for localised and controlled release of large and small compounds in vivo. Although further studies are required to establish the nature and possibility of interaction between the hydrogel material and the active drug, studies carried out so far show that nanofibrillar cellulose has good potential as an injectable hydrogel drug delivery system. This application exploits the shear thinning property of nanofibrillar cellulose hydrogel which makes it possible to inject with ease using a syringe while still maintaining its viscosity (Bhattacharya 2012). This allows for localised and targeted delivery to easily assessable regions using injections. Nanofibrillar cellulose hydrogel also has the advantage of ease of preparation without need for an external source of gel activation unlike most other hydrogels being explored for the same application. The external activators could be chemicals or irradiation methods which could invoke toxicity or complication of the delivery process. Nanofibrillar cellulose-based hydrogels, however possess intrinsic pseudoplasticity which makes them suitable an injectable hydrogels (Laurén et al. 2014).

Chitosan and its various derivatives have also been expired as hydrogels for drug delivery. Due to the robust chemical property, chitosan can be crosslinked using a crosslinker such as genipin and glutaraldehyde with a variety of other natural polymers to obtain desired functionality. For example, chitosan is crosslinked with gelatin for improved rigidity and with starch for improved flexibility and cohesion (Giri et al. 2012).

Cellulose is a highly abundant natural polymer in plants, bacteria, algae and fungi phylum. The unbranched chains consist of 1,4 glycosidic linkage of monomer units, D-glucopyranose (DGP) and presence of three hydroxyl groups per

DGP monomer (Kamel et al. 2008; Carter Fox et al. 2011). Cellulose polymers consist of amorphous and crystalline arrangements in which the hydrolysis properties of cellulose are found to be more unfavourable in higher crystalline arrangements (Walker and Wilson 1991).

Sodium Carboxymethylcellulose (NaCMC) is a cellulose derived water soluble polymer (Sannino et al. 2009). NaCMC is grossly anionic because of the negative electron density with respect to the carboxymethyl substitution region. Hence, polyanionic NaCMC has the potential to electrostatically interact with gelatine below its isoelectric point (Devi and Kumar 2009). NaCMC and gelatine are biocompatible as NaCMC is biologically excreted and gelatine is degraded by natural enzymes (Rathna and Chatterji 2003). NaCMC is able to hydrogen bond with water molecules hence hydrogel NaCMC crosslinked gelatine possesses swelling properties which is reported by Tataru et al. (2011). Individual polymers of NaCMC and gelatine have the tendency to swell in ambient temperature water. As far as we know there is no published literature comparing swelling rates of individual NaCMC and gelatine with post bipolymeric NaCMC: gelatine microgel. Ionic interactions are dominant intermolecular forces in crosslinking polyanionic NaCMC with polycationic polymers such as polyvinylamine (PVAm) (Chang and Zhang 2011). The degree of substitution (DS) defines this structure when hydroxyl groups in the glucopyranose monomer are replaced with carboxymethyl groups in which the number of substituted hydroxyls accounts to the degree of substitution (Rokhade et al. 2006). The higher the DS and quite significantly the lower the MW of NaCMC allows for increased in ionic conductivity (Lee and Oh 2013). The discharge capacity of NaCMC (0.9 DS and 250 kDa) up to 0.5 current density (C-rate) was 165 mAh $g^{-1}$ compared with NaCMC (0.9 DS and 700 kDa) at 155 mAh $g^{-1}$ (Lee and Oh 2013). Potentiometric titration with hydrochloric acid as a carboxylate proton donor coupled with Infrared spectroscopy in knowing the relative amount of carboxyl groups is implemented in calculating DS (Pushpamalar et al. 2006).

Gelatin is another natural polymer which finds wide application as hydrogels for drug delivery. Hydrogel made from gelatin and polyvinyl alcohol (PVA) has been developed for application in delivery of anti-cancer drug Cisplatin. The anti-cancer drug encapsulated within the macrocycle cucurbit(7)uril was incorporated in hydrogel formulations containing between 0 and 4 % PVA. The hydrogel formed demonstrated a controllable swelling and degradation rate which was PVA concentration dependent. As the concentration of PVA in the hydrogel formulation increases, the release rate of encapsulated drug decreases such that the release rate of the drug can be controlled by varying the concentration of the PVA in the hydrogel formulation. Hydrogel containing gelatin only inhibited cancer cell growth by 80 % while hydrogel containing 2 % PVA inhibited cell growth by 4 %. At 4 % cell growth inhibition was 20 %. When compared to intraperitoneal injection of free cisplatin at high dose of 150 μg, subcutaneous implantation of the gelatin PVA hydrogels at just 30 μg of cisplatin achieved the same effectiveness such that the use of the gelatin/PVA hydrogel improved the effectiveness of the anti-cancer drug (Oun et al. 2014).

A globular whey protein of high abundance from cow's milk is β-lactoglobulin which has the potential in binding hydrophobic molecules via hydrogen bonding and van der Waals interactions (Livney 2010; Lee and Hong 2009). Chitosan forms a complex coacervates with β-lactoglobulin at pH 6.5 (Lee and Hong 2009). Pectin which is an anionic polysaccharide coacervates with β-lactoglobulin and has an apparent mean particle diameter below 1000 nm and zeta potential reaching −40 mV above pH 6 for formulations containing pectin 0.5 % w/w (Jones et al. 2009). Here, very low zeta potential values outline particle repulsion and minimal particle aggregation (Jones et al. 2009). As far as we know there is currently studies performed in the encapsulation and release of drugs using β-lactoglobulin as a co-polymer in a hydrogel.

### *9.8.6 The Preparation Techniques of Hydrogels*

There are numerous valid engineering techniques in the preparation of natural hydrogels. Natural polymers such as gelatin, κ-carrageenan, agarose and gellan gum in hot solutions undergo random coil to helix transitions with the support of ionic salts such as $Na^{+}$ which lowers the repulsive forces between same electrostatic charges, allowing ionic interaction and the polymeric crosslinking to occur (Fig. 9.10) (Coutinho et al. 2010; Gulrez et al. 2011). The polymer κ-carrageenan can further form a superhelical network when a number of helices aggregate in the presence of ions and a gel is formed (Viebke et al. 1994).

Polymers possessing charged functional groups such as chitosan, carboxymethylcellulose, gellan, gelatin, alginates and pectin can be crosslinked with multivalent ions of opposite charges, which is known as ionotropic gelation (Patil et al. 2012). Polyanionic molecules such as alginic acid and l-carrageenan can be reversibly crosslinked by cations such as $Ca^{2+}$, $Zn^{2+}$ and $Fe^{3+}$ (Bracher et al. 2010; Agulhon et al. 2012). An ionotropic crosslinking interaction between a divalent cation and polyanionic groups between two chains of sodium alginate is by chelate complex with glucuronic acid groups (Fig. 9.11) (Ahirrao et al. 2014).

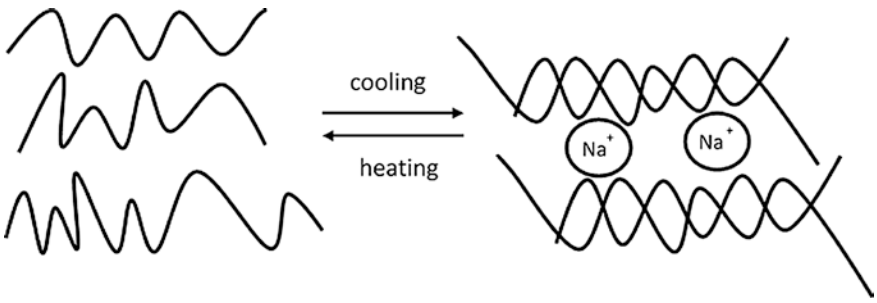


**Fig. 9.11** Illustration of random coil to helical transition of anionic, natural polymers, e.g. gellan gum during the cooling of a hot polymeric solution

A recent study by Boppana et al. (2010) combined polyanionic sodium carboxymethylcellulose with polycationic albumin via $Al^{3+}$ ions to induce electrostatic interactions by ionotropic gelation prior to chemical crosslinking using glutaraldehyde. The entrapment efficiency of a drug, simvastatin, was between 74 and 82 % in a bipolymeric sodium carboxymethylcellulose and albumin hydrogel network (Boppana et al. 2010). Slightly different to ionotropic gelation, a process known as complex coacervation involves the electrostatic attraction of oppositely charged polyelectrolytes such as precipitate or gel in solution because of change of factors such as pH, ionic strength and polymeric mass ratios (Jin and Kim 2008; Hoffman 2002). An alginate/β-lactoglobulin lipid droplets contained in hydrogel matrices were complex coacervated with alginate ($–NH_3^+$) and cationic chitosan (–COO–) at acidic pH ranges of 3.5–6.5 in the formation of beads for gastrointestinal active molecule delivery (Li and McClements 2011). An example of a complex coacervate bipolymer is sodium carboxymethylcellulose and gelatin in the formation of a complex coacervate.

Chemical crosslinking of two non-ionic polymers can be enzyme catalysed in the addition of a crosslinking agent forming covalent bonds on specific functional groups in forming a hydrogel (Hoare and Kohane 2008; Hennick and van Nostrum 2012). An example is a crosslinker, 1, 2, 3, 4-butanetetracarboxylic dianhydride (BTCA) forming ester linkages with the hydroxyl groups on β-mannose or α-galactose monomers present in guar gum with enzyme, 4-dimethylaminopyridine (DMAP) (Fig. 9.12) (Kono et al. 2014).

Monomers of low molecular weight can undergo radical polymerisation using photoinitiators forming photopolymerised hydrogels such as dextran and glycidyl acrylate (Hennick and van Nostrum 2012; Nguyen and West 2002). The

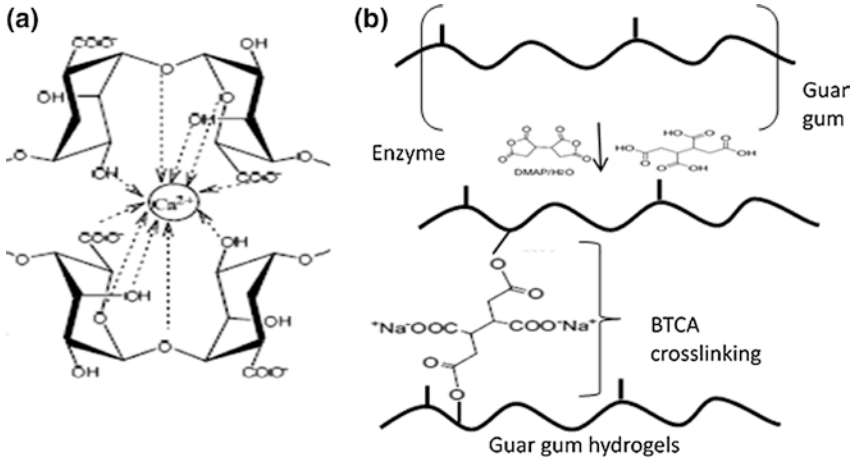


**Fig. 9.12** Schematic outlines in the preparation of hydrogels. **a** An ionotropic interaction formed by chelation between $Ca^{2+}$ and alginic acid (Adopted from Ahirrao et al. 2014). **b** Chemical crosslinking of guar gum with BTCA crosslinking agent and enzyme. Reused under creative commons attribution licence

advantages of photopolymerisation are rapid curing rates during processing, lower production of heat and spatial and temporal control of process polymerisation reactions (Nguyen and West 2002; Burdick and Prestwich 2011). Hyaluronic acid is radically polymerised with methacrylic anhydride under basic conditions in producing methacrylated hyaluronic acid (Burdick and Prestwich 2011).

The manufacturing considerations in bulk production of hydrogels of bead morphology use microengineering processes in attempting to optimise control and batch wise consistency requirements. Micromoulding is an engineering process recently employed in the production of hydrogel microneedles composed of NIPAAm particles suspended in 50/50 polylactic-*co*-glycolic acid (PLGA) (Kim et al. 2012). The micromould implemented in the fabrication of NIPAAm hydrogel microneedles were poly-di-methyl siloxane and molten PLGA was added to pre-filled NIPAAm particles in the mould followed by curing at 150 °C and −100 kPa pressure in a vacuum oven (Kim et al. 2012). Microfluidics is a specialist area concerned with the fluid dynamics and engineering of micron scale confinement of flowing fluids (Domachuk et al. 2010). A phospholipid polymer, poly(2-methacryloyloxyethyl phosphorylcholine (MPC)-*co*-*n*-butyl methacrylate (BMA)-*co*-4-vinylphenyl boronic acid (PMBV) and poly (vinyl alcohol) (PVA) were crosslinked with the aid of a microfluidic device (Fig. 9.13) (Aikawa et al. 2012). The PMBV and PVA were separately injected and droplets were pinched off after gelation induced by contact, the flow rate ratio between paraffin oil and polymer was high in order to decrease the diameter of hydrogel droplets (Aikawa et al. 2012).

The main disadvantage of microfluidics is the possibility of channel clogging due to gelation of gel beads when external gelation by ionotropic crosslinking is adopted (Mark et al. 2009). Photolithography implements a source of radiation, usually UV, directed onto the fluid material containing a photoinitiator in propagating crosslinking reactions according to polymerisation kinetics via transparent areas of the photomask that outline the pattern (Fig. 9.14) (Helgeson et al. 2011).

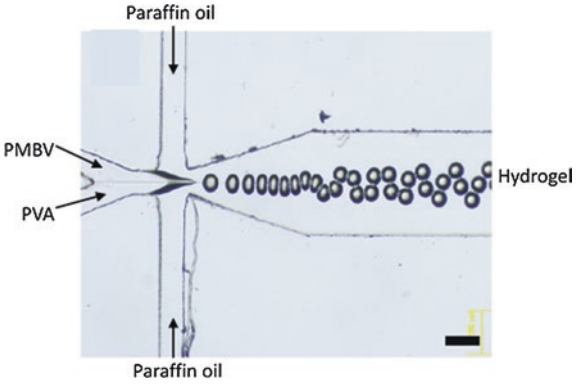


**Fig. 9.13** Microfluidic device in the generation of hydrogel microparticles of PMBV/PVA (Adopted from Aikawa et al. 2012) reused with permission from American Chemical Society Licence number 3631861429984

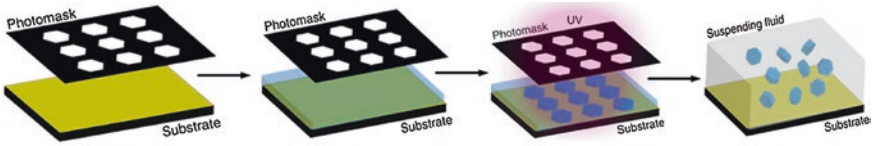


**Fig. 9.14** Outline of photolithography for a polymeric hydrogel (reproduced from Helgeson et al. (2011) with permission from Elsevier, licence number 3631910827880

Hydrogels made photoresponsive can evoke changes in degree of swelling, shape, viscosity or elasticity properties (Tomatsu et al. 2011). They are functionalised as photoresponsive when a polymer is modified with supramolecular interacting groups, formation of photoresponsive low molecular weight gelators into a supramolecular hydrogel and addition of photoresponsive groups in hydrogel modification (Tomatsu et al. 2011). A recent study by Xiao et al. (2011) fabricated methacrylated gelatine and silk fibroin interpenetrating polymer network hydrogels using 2-hydroxy-1-[4-(hydroxyethoxy)-phenyl]-2-methyl-l-propanone (Irgacure 2959) as the photoinitiator under UV radiation. The mass ratios of crystallised silk fibroin crosslinked with methacrylated gelatine defined the mechanical stiffness and the rate of degradation (Xiao et al. 2011). Photolithography and micromoulding require a lot of capital investment relating to the precision fabrication of photomasks, photocrosslinking reagents and moulds (Mark et al. 2009).

Membrane emulsification involves injection of the dispersed phase through a microporous membrane into the continuous phase of an immiscible liquid under pressure. The purpose of membrane emulsification is to obtain monodisperse particles from controlled membrane pore size and pore size distributions for average emulsion diameters (Akamatsu et al. 2010). Chitosan-coated calcium alginate particles with a diameter of 4.4 μm were produced from a w/o emulsion using Shirasu porous glass (SPG) membranes (Akamatsu et al. 2010).

### *9.8.7 Microgels*

Microgels are hydrogel microparticles that are colloidally stable in aqueous solutions (Gao et al. 2014; Vinogradov 2006). Temperature-responsive microgels undergo a rapid change in hydrodynamic particle diameters in temperature-based hydrating or dehydrating polymers in aqueous solution at the lower critical solution temperature (Yang et al. 2013). Techniques for the preparation of hydrogels can be copied or adopted for microgels as long as there is no non-particulate morphology such as film or deviation towards a pure polymeric formulation. There are three important factors in using microgels in drug delivery. The first factor concerns the stability of microgels as a stable dispersion in physiological conditions mimicking blood plasma because the microgel drug has to circulate systemically

before significant controlled release of the drug (Oh et al. 2008; Pich and Adler 2007). The second factor is the degradation kinetics in allowing sustainable release leading to clearance after complete degradation of the microgel (Oh et al. 2008). The third factor is controlling the microgel particle diameter to less than 200 nm in diameter to pass blood vessels or enter cells membranes (Oh et al. 2008).

### *9.8.8 Microgels from Natural Polymers in Drug Delivery*

Current research in formulating and pharmacokinetic-based testing of microgel drugs is still being pursued. Most recently, plasmid DNA macromolecules were loaded in microgels by an inversion microemulsion polymerisation technique with ethylene glycol diglycidyl ether (EGDE) crosslinking reagent for cancer research therapy (Costa et al. 2014). A novel pH sensitive microgel was prepared using a salt bridge interaction between polyanionic carboxymethylcellulose (CMC) and tertiary amide of cationic (2-hydroxyethyl) trimethylammonium chloride benzoate (TMACB) linked with β-Cyclodextrin (β-CD) at pH 8.0 (Yang and Kim 2010). β-CD was crosslinked with CMC using TMACB and a model drug, calcein was loaded successfully (Yang and Kim 2010).

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# Chapter 10
# Environmental Impact of Natural Polymers

**Witold Brostow and Tea Datashvili**

## 10.1 Introduction

In 1920, the Nobel laureate Hermann Staudinger recognized that natural and man-made polymers are produced according to the same blueprint: a very large number of small monomer molecules are linked together to produce high-molecular-weight macromolecules (Staudinger 1920). In both natural and man-made technologies, polymers play a prominent role as extraordinarily versatile and diversified structural and multifunctional macromolecular materials (Brostow 2000, 2009). Properties are readily tuned by varying monomer type, sequence of monomer incorporation, polymerization processes, polymer superstructures, and processing technologies (Abdel-Azim et al. 2009; Estevez et al. 2007; Brostow et al. 2007; Hagg Lobland et al. 2008; Orozco et al. 2014). Without polymers, modern life would be impossible because polymers secure the high quality of life and serve as pace-makers for modern technologies (Brostow et al. 2007, 2010a; Brostow and Pietkiewicz 2007).

During the early days of polymer sciences and engineering (PSE), almost all materials were based exclusively upon chemically modified biopolymers. Examples are sugar-based cellulose which is the major component of biomass,

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O. Olatunji (ed.), *Natural Polymers*, DOI 10.1007/978-3-319-26414-1_10

also wood, while cotton represents the most abundant organic compound produced by living organisms. In biological cells and biotechnology labs, the incorporation of 20 amino acids is precisely controlled, producing polypeptides such as spider silk, wool, enzymes, insulin, and a great variety of other synthetic proteins for industrial and biomedical applications.

We need to clarify that "green" and "natural" are not equivalent terms. As their name implies, natural polymers (or biopolymers) are polymers that occur naturally or are produced by living organisms (such as cellulose, silk, chitin, protein, DNA). By a wider definition, natural polymers can be man-made out of raw materials that are found in nature. Although natural polymers still amount to less than 1 % of the 300 million tons of plastics produced per year, their production is steadily rising. In the USA, demand for natural polymers has been predicted to expand 6.9 % annually and rise from $3.3 billion in 2012 to $4.6 billion in 2016 (Freedonia Group 2012; Transparency market research 2013). The natural polymers market is driven by a growing demand for natural polymers with pharmaceutical and medical applications. Natural polymers also are used in construction and adhesives, food, the food packaging and beverage industries, and cosmetics and toiletries, as well as the paint and inks industries. The market is led by cellulose ethers and also includes starch and fermentation polymers, exudates and vegetable gums, protein-based polymers, and marine polymers.

So, what's Green? Green polymers, on the other hand, are those produced using green (or sustainable) chemistry, a term that appeared in the 1990s. According to the International Union of Pure and Applied Chemistry (IUPAC) definition, green chemistry relates to the "design of chemical products and processes that reduce or eliminate the use or generation of substances hazardous to humans, animals, plants, and the environment" (Green Polymer Chemistry 2014). Thus, green chemistry seeks to reduce and prevent pollution at its source. In fact, many existing polymers and polymerization processes meet the demands of green chemistry. Prominent examples of successful sustainable materials are polyolefins such as polyethylene and polypropylene, which amount to around half of the global polymer production. Modern olefin polymerization has set new standards for environmentally friendly polymer production. Polymer properties can be readily tuned as a function of catalyst type and process conditions to meet the demands of specific applications. Moreover, polyolefins are very effectively recycled either by remolding or by facile thermal cleavage of the polymer backbone. Polyolefins meet the demands of sustainable development, preserving resources for future generations. In terms of their favorable ecobalance, recycling, energy-, and resource effectiveness as well as their attractive cost/performance ratio, polyolefins outperform all biopolymers and bio-based plastics. In principle, it is feasible to switch from fossil resources to bio-based feedstocks in polyolefin manufacturing to meet the demands of green chemistry. Today, polyolefin technology stands for the most effective and sustainable use of oil and gas, especially when compared with burning oil and gas in energy production. In contrast, most biotechnology processes consume significant amounts of water, produce byproduct wastes, and require energy-intensive biopolymer purification.

Further, an integral part of the green economy concept is fostering the use of renewable resources and bio-based products. Environmentalists "dream" of using solar power in biological photosynthesis to convert greenhouse gas carbon dioxide and water into biomass, which then serves as a feedstock for biofuels, biopower, and bioplastics (Fig. 11.1).

From this extremely idealistic point of view, biodegradation appears to solve the littering problem encountered when highly durable synthetic polymers are not recycled. However, we have to keep in mind that that "bio" does *not* imply quantitative and rapid degradation to produce exclusively carbon dioxide and water. Biodegradation can also produce water-soluble and even toxic metabolites that are

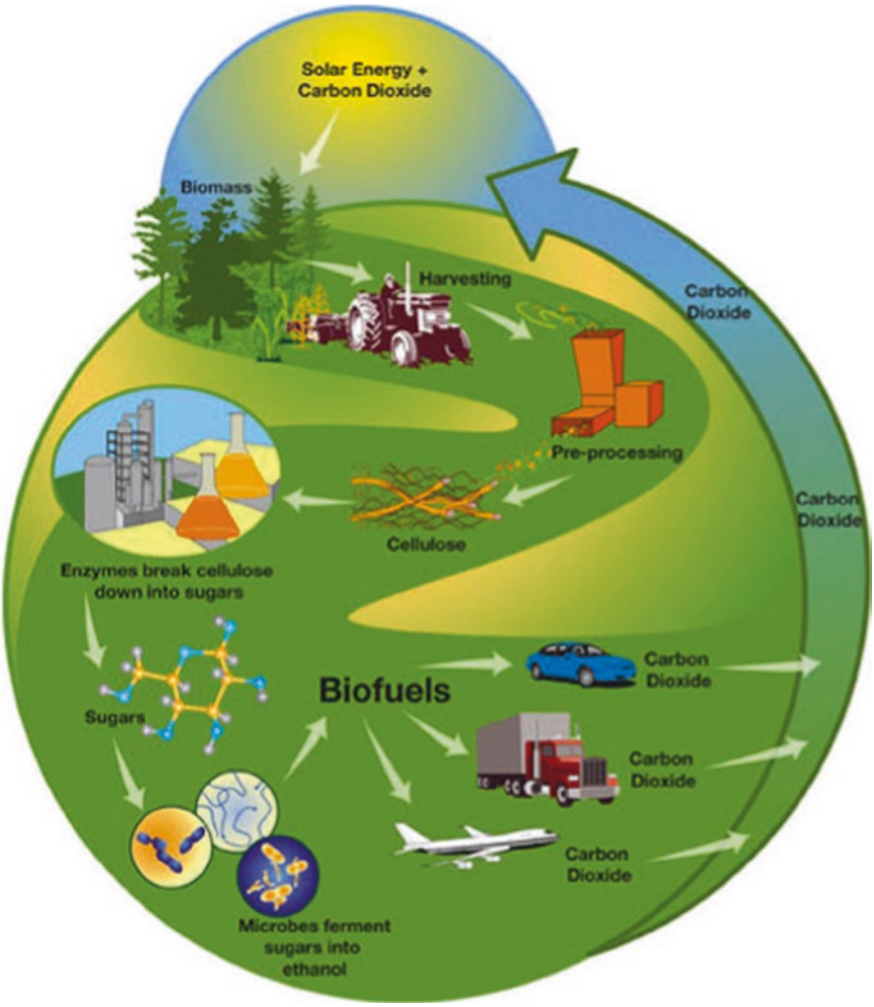


**Fig. 11.1** Biomass usage and production of the biofuels (Adapted from http://www.our-energy.com/news/biomass_production_needs_to_become_sustainable.html)

washed away by rain and thus pollute groundwater. In landfills, paper made from cellulose and other *in principle biodegradable materials* do not degrade and survive for many decades when oxygen and water are absent. Moreover, biodegradation and bioerosion render polymers brittle so that they readily disintegrate when exposed to mechanical stresses. Often, they form very small dust-like micron- and nanometer-sized particles, which are carried away by wind or rain. Although the biodegrading plastics are no longer visible to the human eye, the resulting fine and invisible particles can accumulate in the air and cause inhalation hazards. Most biodegradable polymers are coveted source of food for bacteria, other microorganisms, for example fungal spores, and even small animals, such as insects, bugs, mice, and rats.

Let us take a closer look at what drives the green and renewable polymer industries. According to Rolf Mülhaupt from the University of Freiburg, Germany (Mülhaupt 2013), the development of the green polymer industry is inevitable: at the beginning of the twenty-first century, we are experiencing a renaissance of renewable polymers and a major thrust towards the development of bio-based macromolecular materials. There are several reasons for this paradigm shift—and for the envisioned transition from petrochemistry to bioeconomy.

From the economic point of view, the dwindling oil supply is likely to further boost the oil price, especially in view of the expected surge in worldwide energy demand. Energy demands are increasing worldwide for the simple reason that *the population of the Earth is increasing* at a high rate. This could drastically impact the cost-effectiveness and competiveness of plastics. Shifting chemical raw material production to renewable resources or coal could safeguard plastics production against this expected new future oil crisis. Hence, another even more important reason is the growing concerns of consumers regarding global warming, resulting in a surging demand for sustainable and ‘green’ products. In addition, a tsunami of environmental legislation and regulations is propelling the development of environmentally friendly products with a low carbon footprint.

In the production of polymers, green principles include:

- A high content of raw material in the product
- A clean (no-waste) and lean production processes and reducing greenhouse gas emissions
- Elimination of use of additional substances such as organic solvents
- High energy efficiency in manufacturing
- Use of renewable resources and renewable energy
- Absence of health and environmental hazards
- High safety standards
- Low carbon footprint
- Controlled product lifecycles with effective waste recycling.

In addition, the use of renewable resources for green polymer production should not compete with food production, should not promote intensified farming or deforestation, and should not use transgenic plants or genetically modified bacteria; biodegradable polymers should not produce inhalable spores or nanoparticles.

There are three basic strategies to produce renewable plastics:

1. Using biomass and/or carbon dioxide to produce 'renewable oil' and green monomers for highly resource- and energy-effective polymer manufacturing processes
2. Through living cells, which are converted into solar-powered chemical reactors, using genetic engineering and biotechnology routes to produce biopolymers and bio-based polymers
3. By activation and polymerization of carbon dioxide.

Whereas Nature needs more than 300 million years to convert biomass into oil, there are several options for producing synthetic bio-based renewable oil and even "green coal" on a large scale that require only a few minutes; biofuel technologies are developed to refine biomass to produce renewable oil and green monomers. Inspired by coal liquefaction and gasification, biomass-to-liquid (BtL) conversion is based on the Fischer–Tropsch process to convert biomass into a mixture of carbon monoxide and hydrogen (called syngas), which is an important feedstock for chemicals. Although the entire plant can be gasified, this process is energy-intensive, especially when producing nonpolar olefin monomers. Less favorable energy and problematic eco-balances are typical for biodiesel, prepared by transesterification of vegetable oils with methanol, accompanied by glycerol byproduct formation. Among emerging biofuels, bioethanol is produced by fermentation of sugar obtained from sugarcane or cellulose. Bioethanol represents a very versatile raw biomaterial for producing olefin and diolefin monomers such as ethylene, propylene, and butadiene. Both BtL and bioethanol processes involve rather poor atom economy—because only part of the raw material is incorporated into the polymer product. There is another option: biomass is directly converted into renewable coal and oil in a single process step. In the catalytic pressureless liquefaction of wood and plastics wastes, developed by AlphaKat in Germany, high-quality diesel fuel is produced without requiring the high temperatures and pressures typical for coal gasification and the Fischer–Tropsch processes. Several processes have been developed to convert carbon dioxide into carbon monoxide, methanol, formic acid, and formaldehyde. In a recent advance, photocatalysis was employed to convert aqueous carbon dioxide into carbon monoxide using in situ water splitting as a hydrogen source. Going well beyond the scope of biomass utilization, the direct chemical fixation of carbon dioxide is commonly recognized as an attractive green feedstock and green solvent for the chemical industry.

## 10.2 Market Trends for the Renewable Plastics

Today the world is facing mounting global crises, ranging from global financial market distress to extreme climate-induced weather events and skyrocketing costs for energy. At present, the world population exceeds 7 billion people and is projected to reach 9 billion people by 2050; this prediction might be an

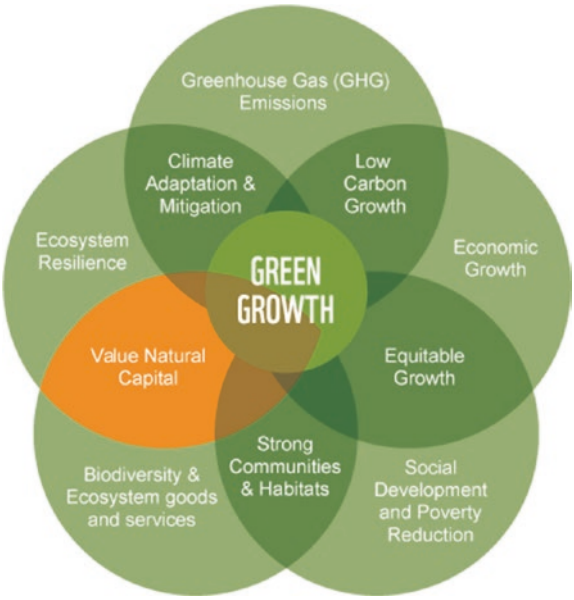


**Fig. 11.2** Integral parts of sustainable economy (Adapted from http://www.education4sustainability.org/2013/01/)

underestimate. People living in developing countries aspire to the living standards of the Western world and claim their rightful part of the world's resources and plastics production. The resulting drastically increasing hunger for energy, which is currently satisfied by consuming fossil fuels, will undoubtedly further increase emissions of the greenhouse gases, water vapor, methane, and carbon dioxide.

In green economy, it is imperative to reduce the demand for resources and energy, minimize wastes, prevent environmental pollution and hazards, reduce greenhouse gas emissions, optimize manufacturing processes, and establish effective recycling of wastes. These elements are an integral part of sustainable chemistry, which is also referred to as green chemistry, a term coined in the 1990s (Fig. 11.2).

Green polymers, renewable polymers, and bioplastics already are more common than one might think.

Bio-based polymers are closer to the reality of replacing conventional polymers than ever before. Nowadays, bio-based polymers are commonly found in many applications from commodity to hi-tech applications due to advancement in biotechnologies and public awareness. However, despite these advancements, there are still some drawbacks—which prevent the wider commercialization of bio-based polymers in many applications. This is mainly due to comparisons of performance and price with their conventional counterparts; thus, a significant challenge for bio-based polymers remains.

We all know about bioethanol as an emerging biofuel, produced by fermentation of sugar obtained from sugar cane or cellulose (Fig. 11.3).

Bioethanol also is a versatile raw biomaterial for producing olefin and diolefin monomers, including ethylene, propylene, and butadiene. In 2010, Braskem company

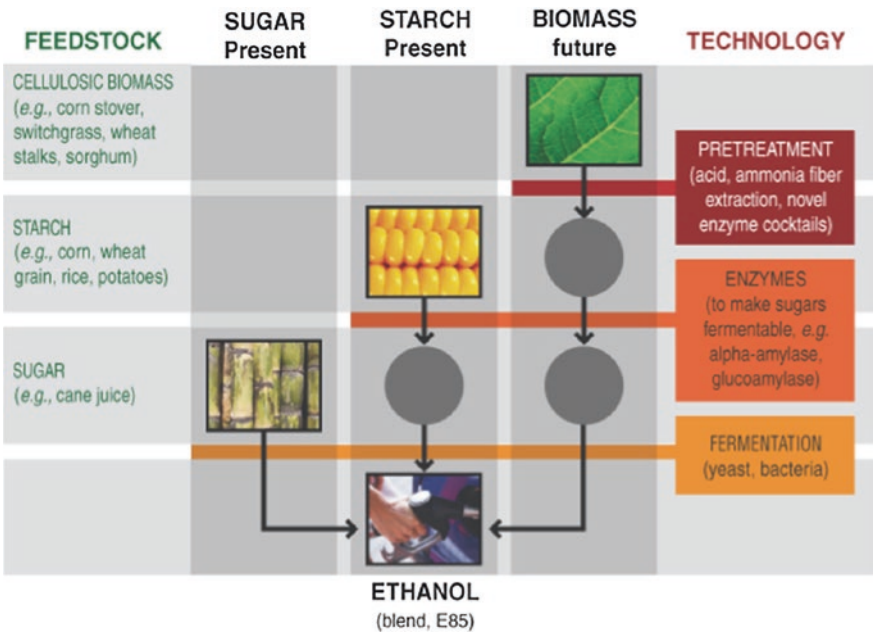


**Fig. 11.3** General schematic for producing ethanol (Adapted from http://sec.edgar-online.com/verenium-corp/10-k-annual-report/2008/03/17/Sect.3.aspx)

in Brazil inaugurated a 200 kt/year plant producing green ethylene from sugar cane bioethanol for the production of green polyethylene, which is 100 % recyclable.

Using processes that are even more energy-efficient, biomass can be directly converted into renewable coal and oil. Agricultural and forestry wastes already are used to produce renewable monomers. Processes have been developed to convert carbon dioxide into carbon monoxide, methanol, formic acid, and formaldehyde. Vegetable oils can be used to produce biodiesel and glycerol as a byproduct, which in turn can be used to make a variety of monomers such as propane diol, acrylic acid, and even epichlorohydrin for the production of epoxy resins.

Carbohydrates, terpenes, proteins, and polyesters are chemically modified and used in polymer processing and applications. Natural fibers provide excellent fiber reinforcement for thermosets and thermoplastics. Microfibrillated cellulose is used in polymer nanocomposites, including applications in medical implants. Lignin serves as renewable energy source in paper manufacturing, as a filler for cement, and in various polymers and rubbers. Thermoplastic lignin mixed with natural fibers (Arboform) combines the advantages of wood and synthetic thermoplastics. Biohybrids has been using starch as a blend component with polyolefins and compostable polyesters (Ecoflex). Chitosan and polylactic acid have numerous medical applications. Casein is used as a binder and as an adhesive.

Renewable monomers are already substituting for “oil-made” monomers. The ever-present plastic bottles are just one example. In 2011, Coca-Cola Co.

announced a goal to make plastic bottles from 100 % bio-based materials. Recyclable PET "PlantBottles," which use up to 30 % bio-based monomers, were introduced in 2009, and can still be recycled.

In spite of this progress, bio-based polymers still hold a tiny fraction of the total global plastic market. To be specific, biopolymers in 2015 take approximately 1 % of the total market (Doug 2010). Bio-based polymers offer important contributions by reducing the dependence on fossil fuels and through the related positive environmental impacts such as reduced carbon dioxide emissions. The legislative landscape is also changing where bio-based products are being favored through initiatives such as the Lead Market Initiative (European Union) and BioPreferred (USA). As a result, there is a worldwide demand for replacing petroleum-derived raw materials with renewable resource-based raw materials for the production of polymers.

The first generation of bio-based polymers focused on deriving polymers from agricultural feedstocks such as corn, potatoes, and other carbohydrate feedstocks. However, the focus has shifted in recent years due to a desire to move away from food-based resources and significant breakthroughs in biotechnology.

Carbohydrates, terpenes, proteins, and polyesters are prominent representatives of biomaterials that are chemically modified in a variety of ways to meet the demands of polymer processing and applications.

## 10.3 Renewable Polymers

Renewable polymers are obtained either from natural biopolymers or by polymerization of bio-based monomers. Carbohydrates, terpenes, proteins, and polyesters are prominent representatives of biomaterials that are chemically modified in various ways to meet the demands of polymer processing and applications; see Fig. 11.4.

**Polylactic Acid**

Polylactic acid (PLA) has been known since 1845 but it was not commercialized until early 1990 (Erwin et al. 2007). PLA belongs to the family of aliphatic polyesters with the basic constitutional unit lactic acid. The monomer lactic acid is the hydroxyl carboxylic acid which can be obtained via bacterial fermentation from corn (starch) or sugars obtained from renewable resources. Although other renewable resources can be used, corn has the advantage of providing a high-quality feedstock for fermentation which results in a high-purity lactic acid, which is required for an efficient synthetic process. L-lactic acid or D-lactic acid is obtained depending on the microbial strain used during the fermentation process.

PLA can be synthesized from lactic acid by direct polycondensation reaction or ring-opening polymerization of lactide monomer. However, it is difficult to obtain high-molecular-weight PLA via polycondensation reaction because of water formation during the reaction. Nature Works LLC (previously Cargill Dow LLC) has developed a low-cost continuous process for the production of PLA

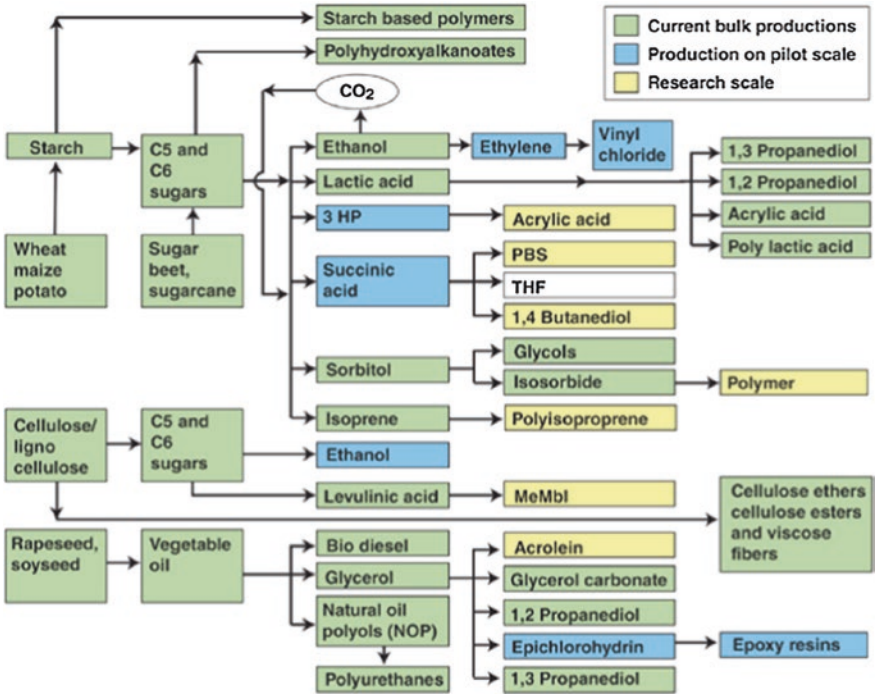


**Fig. 11.4** Renewable materials platform (Adapted from http://www.chemengonline.com/renewable-feedstocks-trading-barrels-for-bushels/?printmode=1)

(Mülhaupt 2013). In this process, low molecular weight pre-polymer lactide dimers are formed during a condensation process. In the second step, the pre-polymers are converted into high-molecular-weight PLA via ring-opening polymerization with selected catalysts. Depending on the ratio and stereochemical nature of the monomer (l or d), various types of PLA and PLA copolymers can be obtained. The final properties of PLA produced are highly dependent on the ratio of the D and L forms of the lactic acid.

PLA is a commercially interesting polymer as it shares some similarities with hydrocarbon polymers such as polyethylene terephthalate (PET). It has many unique characteristics, including good transparency, glossy appearance, high rigidity, and ability to tolerate various types of processing conditions.

PLA is a thermoplastic polymer which has the potential to replace traditional polymers such as PET, PS, and PC for packaging to electronic and automotive applications (Majid et al. 2010). While PLA has similar mechanical properties to traditional polymers, the thermal properties are not attractive due to its relatively low glass transition temperature $T_g \approx 60$ °C. This problem can be overcome by changing the stereochemistry of the polymer and blending with other polymers and processing aids to improve the mechanical properties; varying the ratio

of L and D isomer ratio strongly influences the crystallinity of the final polymer. However, much more work is required to improve the properties of PLA to suit various applications.

Currently, Nature Works LLC, USA, is the major supplier of PLA sold under the brand name Ingeo, with a production capacity of 100,000 ton/year. There are other manufactures of PLA based in the USA, Europe, China, and Japan developing various grades of PLA suitable for different industrial sectors such as automobile, electronics, medical devices, and commodity applications.

PLA is widely used in many day-to-day applications. It is mainly used in food packing (including food trays, tableware such as plates and cutlery, water bottles, candy wraps, cups, etc.). Although PLA has one of the highest heat resistances and mechanical strengths of all bio-based polymers, it is still not suitable for use in electronic devices and other engineering applications. NEC Corporation (Japan) recently produced a PLA with carbon and kenaf fibers with improved thermal and flame retardancy properties. Fujitsu (Japan) developed a polycarbonate blend with PLA to make computer housings. In recent years, PLA has been employed as a membrane material for use in automotive and chemical industry.

The ease of melt processing has led to the production of PLA fibers, which are increasingly accepted in a wide variety of textiles from dresses to sportswear, furnishing to drapes, and soft nonwoven baby wipes to tough landscape textiles. These textiles can outperform traditional textiles made from synthetic counterparts. Bioresorbable scaffolds produced with PLA and various PLA blends are used in implants for growing living cells. The US Food and Drug Administration (FDA) has approved the use of PLA for certain human clinical applications (Dorozhkin 2009). In addition, PLA-based materials have been used for bone support splints.

**Polyhydroxyalkanoates**

Polyhydroxyalkanoates (PHAs) are a family of polyesters produced by bacterial fermentation with the potential to replace conventional hydrocarbon-based polymers. PHAs occur naturally in a variety of organisms, but microorganisms can be employed to tailor their production in cells. Polyhydroxybutyrate (PHB), the simplest PHA, was discovered in 1926 by Maurice Lemoigne as a constituent of the bacterium *Bacillus megaterium* (Lemoigne 1923).

PHAs can be produced by varieties of bacteria using several renewable waste feedstocks. A generic process to produce PHA by bacterial fermentation involves fermentation, isolation, and purification from fermentation broth. A large fermentation vessel is filled with mineral medium and inoculated with a seed culture that contains bacteria. The feedstocks include cellulosics, vegetable oils, organic waste, municipal solid waste, and fatty acids depending on the specific PHA required. The carbon source is fed into the vessel until it is consumed and cell growth and PHA accumulation is complete. In general, a minimum of 48 h is required for fermentation time. To isolate and purify PHA, cells are concentrated, dried, and extracted with solvents such as acetone or chloroform. The residual cell debris is removed from the solvent containing dissolved PHA by solid–liquid separation

process. The PHA is then precipitated by the addition of an alcohol (e.g., methanol) and recovered by a precipitation process (Kathiraser et al. 2007).

More than 150 PHA monomers have been identified as the constituents of PHAs (Steinbüchel and Valentin 1995). Such diversity allows the production of bio-based polymers with a wide range of properties, tailored for specific applications. Poly-3-hydroxybutyrate was the first bacterial PHA identified. It has received the greatest attention in terms of pathway characterization and industrial-scale production. It possesses similar thermal and mechanical properties to those of polypropylene (Savenkova et al. 2000). However, due to its slow crystallization, narrow processing temperature range, and tendency to "creep," it is not attractive for many applications, requiring further development in order to overcome these shortcomings (Reis et al. 2008). Several companies have developed PHA copolymers with typically 80–95 % (R)-3-hydroxybutyric acid monomer and 5–20 % of a second monomer in order to improve the properties of PHAs. Some specific examples of PHAs include the following:

- Poly(3HB): Poly(3-hydroxybutyrate)
- Poly(3HB-co-3HV): Poly(3-hydroxybutyrate-co-3-hydroxyvalerate), PHBV
- Poly(3-HB-co-4HB): Poly(3-hydroxybutyrate-co-4-hydroxybutyrate)
- Poly(3HB-co-3HH): Poly(3-hydroxyoctanoate-co-hydroxyhexanoate)
- Poly(3HO-co-3HH): Poly(3-hydroxyoctanoate-co-hydroxyhexanoate)
- Poly (4-HB): Poly(4-hydroxybutyrate).

The copolymer poly(3HB-co-3HV) has a much lower crystallinity, decreased stiffness and brittleness, and increased tensile strength and toughness compared to poly(3HB) while remaining biodegradable. It also has a higher melt viscosity, which is a desirable property for extrusion and blow molding (Hanggi 1995).

The first commercial plant for PHBV was built in the USA in a joint venture between Metabolix and Archer Daniels Midland. However, the joint venture between these two companies ended in 2012. Currently, Tianan Biologic Material Co. in China is the largest producer of PHB and PHB copolymers. Tianan's PHBV contains about 5 % valerate which improves the flexibility of the polymer. Tainjin Green Biosciences, China, invested along with DSM to build a production plant with 10 kt/year capacity to produce PHAs for packing and biomedical applications (DSM Press Release 2008).

PHA polymers are thermoplastic, and their thermal and mechanical properties depend on their composition. The $T_g$ values of the polymers vary from −40 to +5 °C while the melting temperatures range from 50 to 180 °C, depending on their chemical composition (McChalicher and Srienc 2007). PHB is similar in its material properties to polypropylene, with a good resistance to moisture and aroma barrier properties. Polyhydroxybutyric acid synthesized from pure PHB is relatively brittle and stiff. PHB copolymers, which may include other fatty acids such as beta-hydroxyvaleric acid, may be elastic (McChalicher and Srienc 2007).

PHAs can be processed in existing polymer-processing equipment and can be converted into injection-molded components: films and sheets, fibers, laminates,

and coated articles; nonwoven fabrics, synthetic paper products, disposable items, feminine hygiene products, adhesives, waxes, paints, binders, and foams. Metabolix has received US Food and Drug Administration (FDA) clearance for use of PHAs in food contact applications. These materials are suitable for a wide range of food packaging applications including caps and closures, disposable items such as forks, spoons, knives, tubs, trays, and hot cup lids, and products such as housewares, cosmetics, and medical packaging (Philip et al. 2007).

PHAs and their copolymers are widely used as biomedical implant materials. These include sutures, suture fasteners, meniscus repair devices, rivets, bone plates, surgical mesh, repair patches, cardiovascular patches, tissue repair patches, and stem cell growth. Changing the PHA composition allows the manufacturer to tune the properties such as biocompatibility and polymer degradation time within desirable time frames under specific conditions. PHAs can also be used in drug delivery due to their biocompatibility and controlled degradability. Only a few examples of PHAs have been evaluated for this type of applications, and this remains an important area for exploitation (Tang et al. 2008).

**Polybutylene Succinate**

Polybutylene succinate (PBS) is an aliphatic polyester with similar properties to those of PET. PBS is produced by condensation of succinic acid and 1,4-butanediol. PBS can be produced by either monomers derived from petroleum-based systems or along the bacterial fermentation route. There are several processes for producing succinic acid from fossil fuels. Among them, electrochemical synthesis is a common process with high yield and low cost. However, the fermentation production of succinic acid has numerous advantages compared to the chemical process. Fermentation process uses renewable resources and consumes less energy compared to chemical process. Several companies (solely or in partnership) are now scaling bio-succinate production processes—which earlier have suffered from poor productivity and high downstream processing costs. Mitsubishi Chemical (Japan) has developed biomass-derived succinic acid in collaboration with Ajinomoto to commercialize bio-based PBS. DSM in the Netherlands and Roquette in France (but with plants also in the US) are developing a commercially feasible fermentation process for the production of succinic acid 1,4-butanediol and subsequent production of PBS. Myriant and Bioamber have developed a fermentation technology to produce monomers.

Conventional processes for the production of 1,4-butanediol use fossil fuel feedstocks such as acetylene and formaldehyde. The bio-based process involves the use of glucose from renewable resources—to produce succinic acid followed by a chemical reduction to produce butanediol. PBS is produced by transesterification, direct polymerization, and condensation polymerization reactions. PBS copolymers can be produced by adding a third monomer such as sebacic acid, adipic acid, and succinic acid which is also produced by renewable resources (Bechthold et al. 2008).

PBS is a semicrystalline polyester with a melting point higher than that of PLA. As usual, its mechanical and thermal properties depend on the crystal structure and the degree of crystallinity (Nicolas et al. 2011). PBS displays similar

crystallization behavior and mechanical properties to those of polyolefin such as polyethylene. It has a good tensile and impact strength with moderate rigidity and hardness. The $T_g$ is ≈−32 °C, and the melting temperature $T_m$ ≈ +115 °C. In comparison with PLA, PBS is tougher in nature but with a lower rigidity and Young's modulus. By changing the monomer composition, mechanical properties can be tuned to suit the required application.

PBS and their blends have found commercial applications in agriculture, fishery, forestry, construction, and other industrial fields. For example, PBS has been employed as mulch film, in packaging, and flushable hygiene products and also used as a non-migrant plasticizer for polyvinyl chloride (PVC). In addition, PBS is used in foaming. Relatively poor mechanical flexibility of PBS limits the applications of 100 % PBS-based products. However, this can be overcome by blending PBS with PLA or starch to improve the mechanical properties significantly, providing properties similar to that of polyolefins (Eslmai and Kamal 2013).

**Bio-polyethylene**

Polyethylene (PE) is an important engineering polymer traditionally produced from fossil resources. PE is produced by polymerization of ethylene under pressure, temperature, in the presence of a catalyst. Traditionally, ethylene is produced through steam cracking of naphtha or heavy oils or ethanol dehydration. *Microbial* PE or green PE is now being manufactured from dehydration of ethanol produced by microbial fermentation. The concept of producing PE from bioethanol is not a particularly new one. In the 1980s, Braskem made bio-PE and bio-PVC from bioethanol. However, low oil prices and the limitations of the biotechnology processes made the technology unattractive at that time (de Guzman 2010).

Currently, bio-PE produced on an industrial scale from bioethanol is derived from sugarcane. Bioethanol is also derived from biorenewable feedstocks, including sugar beet, starch crops such as maize, wood, wheat, corn, and other plant wastes through microbial strain and biological fermentation process. In a typical process, extracted sugarcane juice with high sucrose content is anaerobically fermented to produce ethanol. At the end of the fermentation process, ethanol is distilled in order to remove water, yielding an azeotropic mixture of ethanol + water with a high content of the former. Ethanol is then fully dehydrated at high temperatures over a solid catalyst to produce ethylene and, subsequently, polyethylene (Guangwen et al. 2007) (Fig. 11.5).

Bio-based polyethylene has exactly the same chemical, physical, and mechanical properties as petrochemical polyethylene. Braskem in Brazil is the largest producer of bio-PE with 52 % market share, and this is the first certified bio-PE in the world. Similarly, Braskem is developing other bio-based polymers such as bio-polyvinyl chloride, bio-polypropylene, and their copolymers with similar industrial technologies. The current Braskem bio-based PE grades are mainly targeted towards food packing, cosmetics, personal care, automotive parts, and toys. Dow Chemicals in the US in cooperation with Crystalsev is the second largest producer of bio-PE with 12 % market share. Solvay in Belgium is another producer of bio-PE; it has 10 % share in the current market. Solvay is also a leader in the

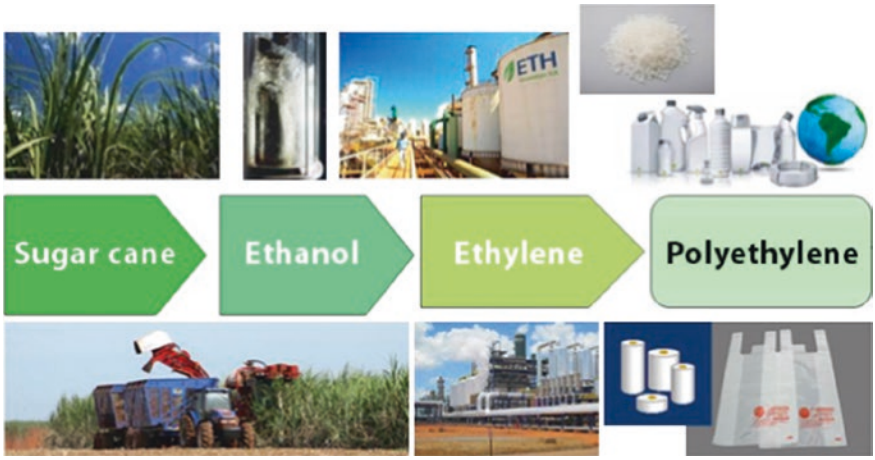


**Fig. 11.5** Process for green-PE production (http://www.sojitz.com/en/news/2012/07/20120705.php)

production of bio-PVC with similar industrial technologies. China Petrochemical Corporation also plans to setup production facilities in China to produce bio-PE from bioethanol (Haung et al. 2008).

Bio-PE can replace all the applications of current fossil-based PE. It is widely used in engineering, agriculture, packaging, and many day-to-day commodity applications because of its low price and good performance.

**Starch**

Starch is a unique bio-based polymer because it occurs in nature as discrete granules. Starch is the end product of photosynthesis in plants—a natural carbohydrate-based polymer that is abundantly available in Nature from various sources including wheat, rice, corn, and potato. Essentially, starch consists of the linear polysaccharide amylose and the highly branched polysaccharide amylopectin. In particular, thermoplastic starch is of growing interest for the industry. The thermal and mechanical properties of starch can vary greatly and depend upon such factors as the amount of plasticizer present. The $T_g$ varies between −50 and 110 °C, while the elastic modulus is similar to polyolefins (Jane 1995). Several challenges exist in producing commercially viable starch plastics. Starch's molecular structure is complex and partly nonlinear, leading to issues with ductility. Starch and starch thermoplastics suffer from the phenomenon of retrogradation—a natural increase in crystallinity over time, leading to increased brittleness. Plasticizers need to be found to create starch plastics with mechanical properties comparable to polyolefin-derived packaging. Plasticized starch blends and composites and/or chemical modifications may overcome these issues, creating biodegradable polymers with sufficient mechanical strength, flexibility, and water barrier properties for commercial packaging and consumer products (Maurizio et al. 2005; Orozco et al. 2009; Espindola-Gonzalez et al. 2011).

Novamont (an Italian company but with plants also in the US) is one of the leading companies in processing starch-based products. The company produces various types of starch-based products using proprietary blend formulations. There are other companies around the world producing starch-based products in a similar scale for various applications (Doug 2010).

Applications of thermoplastic starch polymers include films, such as for shopping bags, fishing bait bags, overwraps, flushable sanitary products, packaging materials, and special mulch films. Potential future applications could include foam loose-fill packaging and injection-molded products such as 'take-away' food containers. Starch and modified starches have a broad range of applications both in the food and non-food sectors. In Europe in 2002, the total consumption of starch and starch derivatives was approximately 7.9 million tons, of which 54 % was used for food applications and 46 % in non-food applications (Frost and Sullivan report 2009).

The largest users of starch in the European Union (30 %) are the paper, cardboard, and corrugating industries (Frost and Sullivan report 2009). Other important fields of starch application are textiles, cosmetics, pharmaceuticals, construction industry, and paints. In the medium and long term, starch will play an increasing role in the field of "renewable raw materials" for the production of biodegradable plastics, packaging material, and molded products.

**Cellulose**

Cellulose is the predominant constituent in cell walls of all plants. Cellulose is a complex polysaccharide with crystalline morphology. Cellulose differs from starch where glucose units are linked by ß-1,4-glycosidic bonds, whereas the bonds in starch are predominantly α-1,4 linkages. The most important raw material sources for the production of cellulosic plastics are cotton fibers and wood (Brostow et al. 2009, 2010b). Plant fibers are dissolved in alkali and carbon disulfide to create viscose, which is then reconverted to cellulose in cellophane form following a sulfuric acid and sodium sulfate bath. There are currently two processes which are used to separate cellulose from the other wood constituents (Fig. 11.6). These methods, sulfite and pre-hydrolysis Kraft pulping, use high pressure and chemicals to separate cellulose from lignin and hemicellulose, attaining greater than 97 % cellulose purity. The main derivatives of cellulose for industrial purposes are cellulose acetate, cellulose esters (molding, extrusion, and films), and regenerated cellulose for fibers.

Cellulose is a hard polymer and has a high tensile strength of 62–500 MPa and elongation of 4 % (Bisanda and Ansell 1992). In order to overcome the inherent processing problems of cellulose, it is necessary to modify it, plasticize, and blend with other polymers. The mechanical and thermal properties vary from blend to blend depending on the composition. The $T_g$ of cellulosic derivatives ranged between 53 and 180 °C (Picker and Hoag 2002).

Eastman Chemical is a major producer of cellulosic polymers. FKuR launched a biopolymer business in the year 2000 and has a capacity of 2800 metric ton/year of various cellulosic compounds for different applications (Doug 2010).

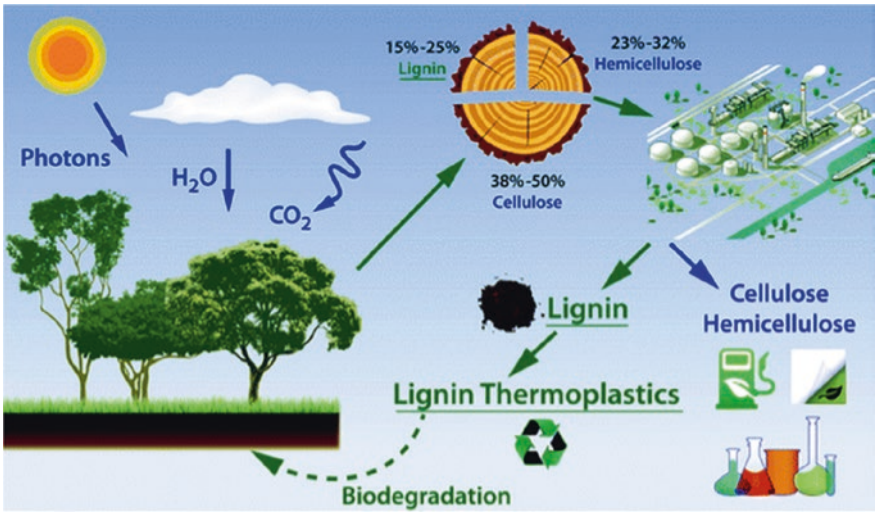


**Fig. 11.6** Wood composition reproduced with permission from Royal Society of Chemistry Licence number 3650080883796

There are three main groups of cellulosic polymers that are produced by chemical modifications of cellulose for various applications. Cellulose esters, namely cellulose nitrate and cellulose acetate, are mainly developed for film and fiber applications. Cellulose ethers, such as carboxymethyl cellulose and hydroxyethyl cellulose, are widely used in construction, food, personal care, pharmaceuticals, paint, and other pharmaceutical applications (Kamel et al. 2008). Finally, regenerated cellulose is the largest bio-based polymer produced globally for fiber and film applications. Regenerated cellulose fibers are used in textiles, hygienic disposables, and home furnishing fabrics because of its thermal stability and high modulus (Kevin et al. 2001).

Chemically pure cellulose can be produced using a certain type of bacteria. Bacterial cellulose is characterized by high purity and high strength. Currently, applications for bacterial cellulose outside food and biomedical fields are rather limited because of its high price. The other applications include acoustic diaphragms, mining, paints, oil gas recovery, and adhesives. However, the low yields and high costs of bacterial cellulose represent barriers to large-scale industrial applications (Prashant et al. 2009).

**Chitin and Chitosan**

Chitin and chitosan are the most abundant natural amino polysaccharide and valuable bio-based natural polymers derived from *shells of prawns and crabs*. Currently, chitin and chitosan are produced commercially by chemical extraction process from crab, shrimp, and prawn wastes (Roberts 1997). The chemical extraction of chitin is quite an aggressive process based on demineralization by acid and deproteination by the action of alkali followed by deacetylated into chitosan (Roberts 1997). Chitin can also be produced by using enzyme hydrolysis or fermentation

process, but these processes are not economically feasible on an industrial scale (Win and Stevens 2001). Currently, there are few industrial-scale plants of chitin and chitosan worldwide located in the USA, Canada, Scandinavia, and Asia.

Chitosan displays interesting characteristics including biodegradability, biocompatibility, chemical inertness, high mechanical strength, good film-forming properties, and low cost (Espindola-Gonzalez et al. 2011; Marguerite 2006; Virginia et al. 2011; Liu et al. 2012). Chitosan is being used in a vast array of widely varying products and applications—ranging from pharmaceutical and cosmetic products to water treatment and plant protection. For each application, different properties of chitosan are required—dependent on the degree of acetylation and molecular weight. Chitosan is compatible with many biologically active components incorporated in cosmetic product composition. Due to its low toxicity, biocompatibility, and bioactivity, chitosan has become a very attractive material in such diverse applications as biomaterials in medical devices and as a pharmaceutical ingredient (Bae and Moo-Moo 2010). Chitosan has applications in shampoos, rinses, and permanent hair-coloring agents. Chitosan and its derivatives also have applications in the skin care industry. Chitosan can function as a moisturizer for the skin, and because of its lower costs, it might compete with hyaluronic acid in this application (Bansal et al. 2011).

**Pullulan**

Pullulan is a linear water-soluble polysaccharide mainly consisting of maltotriose units connected by α-1,6 glycosidic units. Pullulan was first reported by Bauer in 1938 and is obtained from the fermentation broth of *Aureobasidium pullulans*. Pullulan is produced by a simple fermentation process using a number of feedstocks containing simple sugars (Bernier 1958). Pullulan can be chemically modified to produce a polymer that is either less soluble or even completely insoluble in water. The unique properties of this polysaccharide are due to its characteristic glycosidic linking. Pullulan is easily chemically modified to reduce the water solubility or to develop pH sensitivity, by introducing functional reactive groups, etc. Due to its high water solubility and low viscosity, Pullulan has numerous commercial applications including use as a food additive, a flocculant, a blood plasma substitute, an adhesive, and a film (Zajic and LeDuy 1973). Pullulan can be formed into molding articles which can resemble conventional polymers such as polystyrene in their transparency, strength, and toughness (Leathers 2003).

Pullulan is extensively used in the food industry. It is a slow-digesting macromolecule which is tasteless as well as odorless, hence its application as a low-calorie food additive providing bulk and texture. Pullulan possesses oxygen barrier property (slow oxygen diffusion across a pullulan film) and good moisture retention; it also inhibits fungal growth. These properties make it an excellent material for food preservation; hence, pullulan is used extensively in the food industry. In recent years, pullulan has also been studied for biomedical applications in various aspects, including targeted drug and gene delivery, tissue engineering, wound healing, and even in diagnostic imaging medium. Other emerging markets for pullulan include oral care and formulations of capsules for dietary supplements and pharmaceuticals (Leathers 2003), leading to increased demand for this unique biopolymer.

**Collagen and Gelatin**

Collagen is a major insoluble fibrous protein in the extracellular matrix and in connective tissue. In fact, it is the single most abundant protein in the animal kingdom; all bones contain collagen. There are at least 27 types of collagens, and the structures all serve the same purpose: to help tissues withstand stretching. The most abundant sources of collagen are pig skin, bovine hide, and pork and cattle bones. However, the industrial use of collagen is obtained from nonmammalian species (Gomez-Guille et al. 2011) Gelatin is obtained through the hydrolysis of collagen. The degree of conversion of collagen into gelatin depends on the pretreatment, function of temperature, pH, and extraction time (Johnston-Banks 1990).

Collagen is one of the most useful biomaterials due to its biocompatibility, biodegradability, and weak antigenicity (Maeda et al. 1999). The main application of collagen films in ophthalmology is as drug delivery systems for slow release of incorporated drugs (Rubin et al. 1973). It is also used for tissue engineering including skin replacement, bone substitutes, and artificial blood vessels and valves (Lee et al. 2001).

The classical food, photographic, cosmetic, and pharmaceutical applications of gelatin is based mainly on its gel-forming properties. Recently in the food industry, an increasing number of new applications have been found for gelatin in products in line with the growing trend to replace synthetic agents with more natural ones (Gomez-Guille et al. 2011). These include emulsifiers, foaming agents, colloid stabilizers, biodegradable film-forming materials, and microencapsulating agents.

**Alginates**

Alginate is a linear polysaccharide that is abundant in nature as it is synthesized by brown seaweeds and by soil bacteria (Draget et al. 1997). Sodium alginate is the most commonly used alginate form in the industry since it is the first byproduct of algal purification (Draget et al. 1997). Sodium alginate consists of α-L-guluronic acid residues (G blocks) and ß-D-mannuronic acid residues (M blocks), as well as segments of alternating guluronic and mannuronic acids.

Although alginates are a heterogeneous family of polymers with varying content of G and M blocks depending on the source of extraction, alginates with high G content have far more industrial importance (Siddhesh and Edgar 2012). The acid or alkali treatment processes used to make sodium alginate from brown seaweeds are relatively simple. The difficulties in processing arise mainly from the separation of sodium alginate from slimy residues (Black and Woodward 1954). It is estimated that the annual production of alginates is approximately 38,000 tons worldwide (Helgerud et al. 2009).

Alginates have various industrial uses as viscosifiers, stabilizers, and gel-forming, film-forming, or water-binding agents. These applications range from textile printing and manufacturing of ceramics to production of welding rods and water treatment (Teli and Chiplunkar 1986; Qin et al. 2007; Xie et al. 2001). The polymer is soluble in cold water and forms thermostable gels. These properties are

utilized in the food industry in products such as custard creams and restructured food. Alginates are also used as stabilizers and thickeners in a variety of beverages, ice creams, emulsions, and sauces (Iain et al. 2009).

Alginates are widely used as a gelling agent in pharmaceutical and food applications. Studies into their positive effects on human health have broadened recently with the recognition that they have a number of potentially beneficial physiological effects in the gastrointestinal tract (Peter et al. 2011; Mandel et al. 2000). Alginate-containing wound dressings are commonly used, especially in making hydrophilic gels over wounds which can produce comfortable, localized hydrophilic environments in healing wounds (Onsoyen 1996). Alginates are used in controlled drug delivery, where the rate of drug release depends on the type and molecular weight of alginates used (Alexander et al. 2006). Additionally, dental impressions made with alginates are easy to handle for both the dentist and the patient as they fast set at room temperature and are cost-effective (Onsoyen 1996). Recent studies show that alginates can be effective in treating obesity, and currently, various functional alginates are being evaluated in human clinical trials (Georg et al. 2012).

## 10.4 Current Status and Future Trends

The use of bio-based feedstocks in the chemical sector is not a novel concept. They have been industrially feasible on a large scale at least since the beginning of the twenty-first century. However, the price of oil was so cost-effective, and the development of oil-based products created so many opportunities that bio-based products were not prioritized for a long time. Several factors, such as the limitations and uncertainty in supplies of fossil fuels, environmental considerations, and technological developments, accelerated the advancement of bio-based polymers and products. It took more than a century to evolve the fossil fuel-based chemical industry. However, the bio-based polymer industry is already catching up with fossil fuel-based chemical industry, which has augmented since late 1990s. Thanks to advancements in white biotechnology, the production of bio-based polymers and other chemicals from renewable resources has become a reality. The first-generation technologies mainly focused on food resources such as corn, starch, rice, etc. to produce bio-based polymers. As the food-versus-fuel debate intensified, the focus of technologies changed to cellulose-based feedstocks - focusing on waste from wood and paper, food industries, and even stems and leaves and solid municipal waste streams. More and more of these technologies are already in the pipeline to align with the above-mentioned waste streams; however, it may take a few decades to develop the full spectrum of chemicals based on these technologies (Michael et al. 2011).

Challenges that need to be addressed in the coming years include management of raw materials, performance of bio-based materials, and their cost for production. Economy of scale will be one of the main challenges for production of

bio-based monomers and bio-based polymers from renewable sources. Building large-scale plants can be difficult due to the lack of experience in new technologies and estimation of supply/demand balance. In order to make these technologies economically viable, it is very important to develop (1) logistics for biomass feedstocks, (2) new manufacturing routes by replacing existing methods with high yields, (3) new microbial strains/enzymes, and (4) efficient downstream processing methods for recovery of bio-based products.

The current bio-based industry focus is mainly on making bio-versions of existing monomers and polymers. Performance of these products is well known, and it is relatively easy to replace the existing product with similar performance of bio-versions. Thus, all the polymers mentioned above often display similar properties of current fossil-based polymers. However, many efforts are seen towards introducing new bio-based polymers with higher performance and value. For example, Nature Works LLC has introduced new grades of PLA with improved thermal and mechanical properties. New PLA-tri block copolymers have been reported to behave like thermoplastic elastomer. Many developments are currently underway to develop various polyamides, polyesters, polyhydroxyalkanates, etc. with a high differentiation in their final properties for use in automotive, electronics, and biomedical applications.

The disadvantage of some of the new bio-based polymers is that they cannot be processed in typical processing equipment. There is vast knowledge on additive-based chemistry developed for improving the performance and processing of fossil fuel-based polymers, and this knowledge can be used to develop new additive chemistry to improve the performance and properties of bio-based polymers (Ray and Bousmina 2005). For bio-based polymers like PLA and PHA, additives are being developed to improve their performance, by blending with other polymers or making new copolymers. However, the additive market for bio-based polymers is still very small, which makes it difficult to justify major development efforts according to some key additive supplier companies.

The use of nanoparticles as additives to enhance polymer performance has long been established for petroleum-based polymers. Various nano-reinforcements currently being developed include carbon nanotubes, graphene, nanoclays, 2-D layered materials, and cellulose nanowhiskers. Combining these nanofillers with bio-based polymers could enhance a large number of physical properties, including barrier, flame resistance, thermal stability, solvent uptake, and rate of biodegradability, relative to unmodified polymer resin. These improvements are generally attained at low filler content, and this nano-reinforcement is an attractive route to generate new functional biomaterials for various applications.

Even though new bio-based polymers are produced on an industrial scale, there are still several factors which need to be determined for the long-term viability of these polymers. It is expected that there will be feedstock competition—as global demand for food and energy increases over time. Currently, renewable feedstocks used for manufacturing bio-based monomers and polymers often compete with requirements for food-based products. The expansion of first-generation bio-based fuel production will place unsustainable demands on biomass resources and is

as much a threat to the sustainability of biochemical and biopolymer production as it is to food production (Michael et al. 2011). Indeed, the European commission has altered its targets downwards for first-generation biofuels since October 2012, indicating its preference for non-food sources of sugar for biofuel production (EurActiv.com 2012). Several initiatives are underway to use cellulose-based feedstocks for the production of usable sugars for biofuels, biochemicals, and biopolymers.

Overall, it is definitely possible for plastic production to meet the demands of green chemistry for lean and clean production: solvent-free processes with efficient use of resources, no byproduct formation, no waste, exploitation of renewable resources are in principle within our reach. Will we take advantage of the possibility? As Abraham Maslow once said, "One's only failure is failing to live up to one's own possibilities." Let's not fail!

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# Chapter 11
# Economic Impacts of Natural Polymers

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## 11.1 Introduction

This chapter is a multidisciplinary discourse and exposition on the economic impacts of natural polymers. The goal is to report, as much as possible, the cost–benefit utility of natural polymers as a versatile natural resource with diverse applications resulting from advances in science, technology, innovation, research and development. This entails the value chain in their development, production, distribution and consumption; involving people, intellectual and patent rights, industry, investment and market for natural polymer-based goods and services. Opportunities and challenges associated with natural polymer economy from raw materials to finished products are being reported from the original works of different authorities.

The perspectives employed in this chapter is a careful and objective attempt to share knowledge on exactly how and why natural polymers may have economic impacts and what constitutes it. Here, the author elucidates the concept, i.e. what we mean by the term natural polymers with overview of the broader spectrum of polymers, such as, synthetic and biodegradable polymers; biopolymers and biomaterials. It considers the context, i.e. the sources, types, properties and potentials of natural polymers. And presents the content, i.e. the applications or uses of, demand and value of natural polymers to man.

The author relies on the arguments from reputable journals, books and reports on natural polymers and the issues represented in this chapter are intended to promote a general understanding on what natural polymers are; their classification,

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O. Olatunji (ed.), *Natural Polymers*, DOI 10.1007/978-3-319-26414-1_11

relationship, sources, importance, demand, application, as well as the value they add as food, medicine, healthcare or pharmaceuticals, cosmetics, textiles, packaging and other industrial products, to national and global economy.

There are several natural polymers known to man. Natural polymers such as collagen, elastin and fibrinogen make up much of the body's native extracellular matrix (ECM) (Bowlin et al. 2010). Protein, enzymes, muscle fibres, polysaccharides and gummy exudates are the natural polymers being used effectively in formulating the variety of pharmaceutical products. The well-known natural polymers used in pharmacy and other fields are chitosan, carrageenan, ispaghula, acacia, agar, gelatin, shellac, guar gum and gum karaya. These natural polymers are widely used in pharmaceutical industry as emulsifying agent, adjuvant and adhesive in packaging; and also well suited for pharmaceutical and cosmetic product development (Shanmugam et al. 2005).

With the availability of variety of natural polymers, the manufacturers today have achieved a great success in developing the most and promising therapeutic systems, namely drug delivery systems, which provides an effective therapy to the patients for prolonged periods (Shanmugam et al. 2005). Biodegradable polymers are widely being studied as potential materials for site-specific drug delivery because of its non-toxic, biocompatible nature. Natural polysaccharides have been investigated for drug delivery applications as well as in biomedical fields. Modified polymer has found its application as a support material for gene delivery, cell culture and tissue engineering (Jana et al. 2011). The structural similarity of some natural polymers with the components of the extracellular matrix (ECM) makes them interesting candidates as biomaterials. The natural polymers with relevance in the biomedical area can be divided into three major classes: polysaccharides (alginate, hyaluronan, dextran, starch, cellulose derivatives, chitin derivatives), protein (collagen, gelatin, fibrin, elastin, silk fibroin, soy protein) and bacterial polyesters (polyhydroxyalkanoates) (Azevedo et al. 2008).

Extracellular matrix (ECM) provides structure and mechanical integrity to tissues, as well as communicating with the cellular components it supports to help facilitate and regulate daily cellular processes and wound healing. An ideal tissue engineering scaffold would not only replicate the structure of this ECM, but would also replicate many functions that ECM performs (Bowlin et al. 2010).

A polymer is a large molecule (macromolecule) composed of repeating structural units. These subunits are typically connected by covalent chemical bonds. Both synthetic and natural polymers are available but the use of natural polymers for pharmaceutical applications is attractive because they are economical, readily available and non-toxic. They are capable of chemical modifications, potentially biodegradable and with few exceptions, also biocompatible (Kulkarni et al. 2012).

According to the Webster's New World College Dictionary, Fourth Edition, a polymer is a naturally occurring or synthetic substance consisting of giant molecules formed from polymerization.[1] Natural polymers or biopolymers are polymers that occur naturally or are produced by living organisms (such as cellulose,

[1] http://www.yourdictionary.com/polymer.

silk, chitin, protein and DNA). By a wider definition, natural polymers can be man-made out of raw materials that are found in nature.[2] Natural polymers include RNA and DNA that are so important in genes and life processes (Thomas 2013). The DNA is transcribed to RNA and the trio of mRNA, tRNA and rRNA play very crucial role in protein synthesis through the formation of polypeptides. Enzymes are the protein-based catalyst that make metabolism possible inside living cells and other polypeptides such as collagen and keratin make up the components of skin, hair and nails. Natural rubber is a good example of natural polymer. Natural polymers are the polymers derived from natural sources. Their effectiveness has long been established, and they have been in use for decades. One such natural polymer, chitosan, has been explored in every aspect of the medical field, e.g. drug delivery, tissue engineering, gene delivery, etc. Further, alginates have been reported to form gels, microparticles, nanoparticles, etc. To make natural polymers more suitable for site-specific drug delivery, their properties have been tailored (Galaev and Mattiasson 2008). Natural polymers constitute a wide class of important polymers with many commercial applications, including food packaging, fibres, fuel, coatings, automobile components, adhesives and genetic engineering materials among others. The main categories of natural polymers are polysaccharides (starch, chitin, chitosan, cellulose and their derivatives), proteins (amino acids, enzymes and peptides) and polynucleotides (polyesters of phosphoric acid and nucleosides). Others include rubber, lignin, humus, coal, kerogen, asphaltenes, shellac and amber. With many diversified applications, natural polymers have attracted a lot of research interests, particularly in biochemistry and material science engineering (Pielichowski and Njuguna 2005).

## 11.2 Natural and Synthetic Polymers in the Industries

There are two types of polymers: synthetic and natural. Synthetic polymers are derived from petroleum oil and made by scientists and engineers. Examples of synthetic polymers include: nylon, polyethylene, polyester, Teflon and epoxy. Natural polymers occur in nature and can be extracted. They are often water based. Examples of naturally occurring polymers are silk, wool, DNA, cellulose and protein.[3]

### *11.2.1 Comparing Natural and Synthetic Rubber*

Vulcanized rubber is a synthetic (man-made) polymer. Rubber can be found in nature and harvested as latex (milky liquid) from several types of trees. Natural rubber coming from tree latex is essentially a polymer made from isoprene units

[2] http://www.polymersolutions.com/blog/green-and-natural-polymers-on-the-rise.

[3] http://www.cmu.edu/gelfand/k12-teachers/polymers/natural-synthetic-polymers/index.html.

with a small percentage of impurities in it. Rubber can also be made (synthesized) by man. Synthetic rubber can be made from the polymerization of a variety of monomers, including isoprene.

Natural rubber does not handle easily (it is sticky), nor does it have very good properties or durability (it rots). It is usually vulcanized, a process by which the rubber is heated in the presence of sulphur, to improve its resilience, elasticity and durability. Synthetic rubber is preferable because different monomers can be mixed in various proportions resulting in a wide range of physical, mechanical and chemical properties. The monomers can be produced pure and addition of impurities or additives can be controlled by design to give optimal properties.[4]

Why Natural Polymers?

In developing countries, environmental pollution by synthetic polymers has assumed dangerous proportions. Petroleum-derived plastics are not readily biodegradable and because of their resistance to microbial degradation, they accumulate in the environment. In addition, in recent times, oil prices have increased markedly. These facts have helped to stimulate interests in biodegradable polymers. Biodegradable plastics and polymers were first introduced in the 1980s. Polymers from renewable resources have attracted an increasing amount of attention over the last two decades, predominantly due to two major reasons: first environmental concerns, and second the realization that our petroleum resources are finite. There are many sources of biodegradable plastics, from synthetic to natural polymers. Natural polymers are available in large quantities from renewable sources, while synthetic polymers are produced from non-renewable petroleum resources. Biodegradation of polymeric biomaterials involves cleavage of hydrolytically or enzymatically sensitive bonds in the polymer leading to polymer erosion. A vast number of biodegradable polymers have been synthesized recently and some microorganisms and enzymes capable of degrading them have been identified (Babak and Hadi 2013).

### *11.2.2 Some Natural Polymers of Economic Importance*

The biodegradable polymers can be classified according to their chemical composition, origin and synthesis method, processing method, economic importance, application, etc. In this reference, biodegradable polymers are classified according to their origin into two groups: natural polymers which are obtained from natural resources and synthetic polymers which are produced from oil. An overview of these categories is given in Fig. 11.1, while Fig. 11.2 shows the world production capacity of some biopolymers in 2010 (Imre and Pukanszky 2013).

[4]http://www.cmu.edu/gelfand/k12-teachers/polymers/natural-synthetic-polymers/index.html.

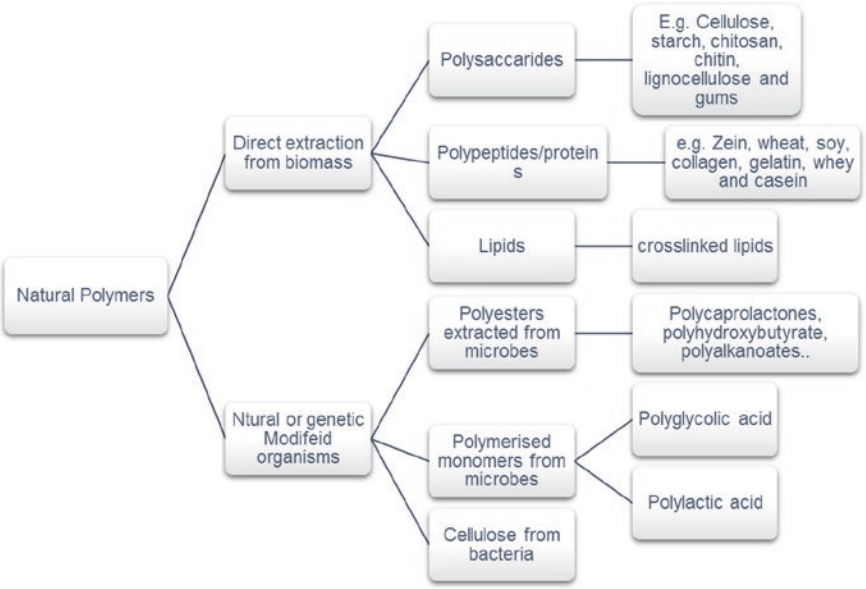


**Fig. 11.1** Schematic presentation of bio-based polymers based on their origin and method of production

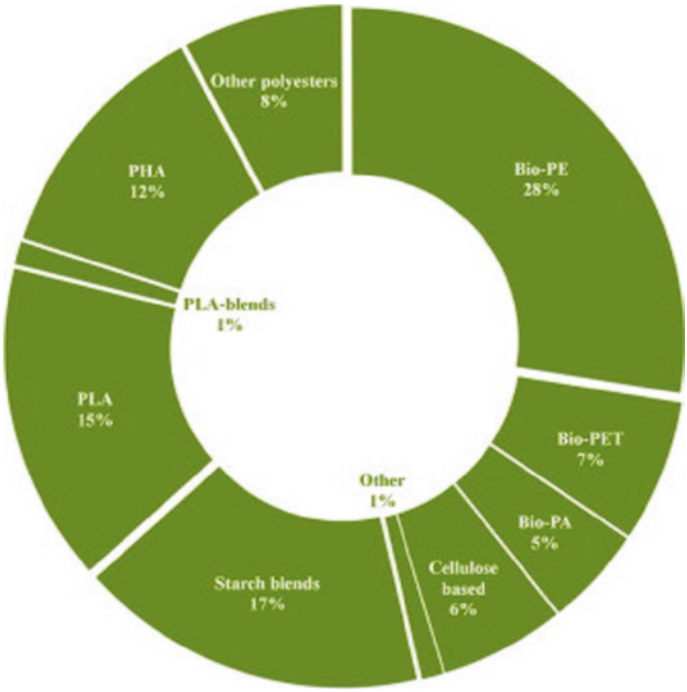


**Fig. 11.2** World production capacities of biopolymers as of 2010 (reproduced from Imre and Pukanszky (2013) under creative commons license)

### *11.2.3 Natural Biodegradable Polymers in the Industry*

Biopolymers are polymers formed in nature during the growth cycles of all organisms; hence, they are also referred to as natural polymers. Their synthesis generally involves enzyme-catalyzed, chain growth polymerization reactions of activated monomers, which are typically formed within cells by complex metabolic processes (Babak and Hadi 2013).

#### 11.2.3.1 Biopolymers Directly Extracted from Biomass

Polysaccharides

For materials applications, the principal polysaccharides of interest are cellulose and starch, but increasing attention is being given to the more complex carbohydrate polymers produced by bacteria and fungi, especially to polysaccharides such as xanthan, curdlan, pullulan and hyaluronic acid. These latter polymers generally contain more than one type of carbohydrate unit, and in many cases these polymers have regularly arranged branched structures. Because of this difference, enzymes that catalyze hydrolysis reactions during the biodegradation of each kind of polysaccharides are different and are not interchangeable.

Thermoplastic starch

Starch is the major polysaccharide reserve material of photosynthetic tissues and of many types of plant storage organs such as seeds and swollen stems. The principal crops used for its production include potatoes, corn and rice. In all of these plants, starch is produced in the form of granules, which vary in size and somewhat in composition from plant to plant (Chandra and Rustgi 1998). The starch granule is essentially composed of two main polysaccharides, amylose and amylopectin with some minor components such as lipids and proteins.

Cellulose and its derivatives

At present, cellulose is the most abundant polymer available worldwide with an estimated annual natural production of $1.5 \times 10^{12}$ tons and considered as an almost inexhaustible source of raw materials. Figure 11.2 shows the world production of biopolymers with cellulose-based biopolymers being 6 %.

Fibres (Lignocellulosic complex)

Plant fibres include bast (or stem of soft sclerenchyma) fibres, leaf or hard fibres, seed, fruit, wood, cereal straw and other grass fibres. All these plant-based natural fibres are lignocellulosic in nature and are composed of cellulose, hemicelluloses, lignin, pectin and waxy substances. Lignocellulosic biomass comprises approximately 50 % of the global biomass and is by far the most abundant renewable organic resource on earth. This woody material is comprised of 30–50 % cellulose, 20–50 % hemicellulose and 15– 35 % lignin, dependent upon the plant species and environmental (growing) conditions.

Chitin and Chitosan

Chitin is a polysaccharide found in the shells of crabs, lobsters, shrimps and insects or can be generated via fungal fermentation processes. Chitosan is the deacylated derivative of chitin and forms the exoskeleton of arthropod.

Gums

Gums are a group of polysaccharides that can form gels in solution upon the introduction of counterions. The degree of cross-linking is dependent on various factors such as pH, type of counterion and the functional charge density of these polymers (Chandra and Rustgi 1998).

Polypeptides (Proteins)

Proteins can be defined as natural polymers able to form amorphous three-dimensional structures stabilized mainly by non-covalent interactions. The functional properties of these materials are highly dependent on structural heterogeneity, thermal sensitivity and hydrophilic behaviour of proteins. Numerous vegetable and animal proteins are commonly used as biodegradable polymers.

Corn zein

Zein comprises a group of alcohol-soluble proteins (prolamins) found in corn endosperm. It accounts for 50 % or more of total endosperm protein, and its only known role is the storage of nitrogen for the germinating embryo (Gennadios 2002). It can be extracted with aqueous alcohol and dried to a granular powder.

Wheat gluten

Whereas dry wheat flour comprises 9–13 % protein and 75–80 % starch, wheat gluten consists mainly of wheat storage protein (70–80 %, dry matter basis) with traces of starch and non-starch polysaccharides (10–14 %), lipids (6–8 %) and minerals (0.8–1.4 %). Osborne distinguished four wheat protein classes based on their solubility in different solvents, namely, albumins, globulins, gliadins and glutenins.

Soy protein

The major use of soybean in the food industry is as a source of oil, while soy protein concentrate and isolate are readily available as co-products of the oil processing industry. Soy protein is a complex mixture of proteins with widely different molecular properties. The major soybean proteins have molecular weights ranging from 200 to 600 kDa.

Collagen and gelatin

Collagen is an abundant protein constituent of connective tissue in vertebrate (about 50 % of total human protein) and invertebrate animals. Similar to cellulose in plants, collagen molecules support mechanical stresses transferred to them by a low-modulus matrix (Gennadios 2002).

Casein and caseinates

Casein is the main protein of milk, representing 80 % of the total milk proteins. It is a phosphoprotein that may be separate into various electrophoretic fractions, $\alpha_{s1}$-casein, $\alpha_{s2}$-casein, β-casein and κ-casein, which differ in primary, secondary and tertiary structure and molecular weight. These four different types of casein are found in bovine milk in the approximate ratio of 4:1:4:1, respectively. Casein exists in the form of micelles containing all four casein species complexed with colloidal calcium phosphate. The casein micelles are stable to most common milk processes such as heating, compacting and homogenization. Micellar integrity is preserved by extensive electrostatic and hydrogen bonding, and hydrophobic interactions (Gennadios 2002).

Whey proteins

Whey proteins are those proteins that remain in milk serum after pH/rennet coagulation of casein during cheese or casein manufacture (Gennadios 2002). Whey protein, which represents approximately 20 % of total milk proteins, is a mixture of proteins with diverse functional properties. The five main proteins are α-lactalbumins, β-lactoglobulins, bovine serum albumin, immunoglobulins and preteose peptones.

Other proteins

There are other proteins, which have potential to use as biopolymeric materials for different applications. Most important of them includes elastin (a major protein component of vascular and lung tissue), egg albumins, fish myofibrillar protein and wood keratin (Gennadios 2002).

#### 11.2.3.2 Biopolymers Produced Directly by Natural or Genetically Modified Organisms

Microbial polyesters

The microbial polyesters are produced by biosynthetic function of a microorganism and readily biodegraded by microorganisms and within the body of higher animals, including humans. In the field of medicine, they can be used as implanting material and a drug carrier.

Polyhydroxyalkanoates (PHAs)

Polyhydroxyalkanoates (PHAs) are a family of intracellular biopolymers synthesized by many bacteria as intracellular carbon and energy storage granules.

Poly-3-hydroxybutyrate (PHB)

Among the PHA family, poly-3-hydroxybutyrate (PHB) is the most common member; it belongs to the short chain length PHA with its monomers containing 4–5 carbon atoms.

Poly (Hydroxybutyrate-Hydroxyvalerate) (PHB/HV)

Blends of PHB family are usually compatible and co-crystallization is enhanced.

Poly-ε-Caprolactones (PCL)

Poly (ε-Caprolactone) (PCL) is aliphatic polyester and is of great interest as it can be obtained by the ring opening polymerization of a relatively cheap monomeric unit 'ε-Caprolactone'. This polyester is highly processible as it is soluble in a wide range of organic solvents (Nair and Laurencin 2007).

Bacterial Cellulose (BC)

Bacterial cellulose (BC) belongs to specific products of primary metabolism and is mainly a protective coating, whereas plant cellulose (PC) plays a structural role. Cellulose is synthesized by bacteria belonging to the genera *Acetobacter, Rhizobium, Agrobacterium and Sarcina*. Its most efficient producers are Gram-negative, acetic acid bacteria *Acetobacter xylinum* (reclassified as *Gluconacetobacter xylinus*), which have been applied as model microorganisms for basic and applied studies on cellulose.

Biopolymers (Polyesters) synthesized from bio-derived monomers

This category of biopolymers belongs to biodegradable polyesters and produced by polycondensation or ring-opening polymerization of biologically derived monomers.

Polylactic Acid or polylactide (PLA)

Among the family of biodegradable polyesters, polylactides (i.e. PLA) have been the focus of much attention because they are produced from renewable resources such as starch, they are biodegradable and compostable, and they have very low or no toxicity and high mechanical performance, comparable to those of commercial polymers.

Polyglycolic Acid (PGA)

Polyglycolide or Polyglycolic acid (PGA) is a biodegradable, thermoplastic polymer and the simplest linear, aliphatic polyester. PGA has been known since 1954 as a tough fibre-forming polymer (Pachence et al. 2007) (Tables 11.1 and 11.2).

**Table 11.1** List of common natural polymers (Thomas and John 2012)

| Natural polymer | Examples |
|---|---|
| Polysaccharides | Starch, cellulose, chitin |
| Proteins | Collagen/gelatin, casein, albumin, fibrinogen, silks |
| Polyesters | Poly(hydroxyalkanoates) |
| Other polymers | Lignin, lipids, shellac, natural rubber |

**Table 11.2** List of important natural fibres (Thomas and John 2012)

| Fibre source | Species | Origin |
|---|---|---|
| Abaca | *Musa textilis* | Leaf |
| Agave | *Agave americana* | Leaf |
| Alfa | *Stippa tenacissima* | Grass |
| Bagasse | – | Grass |
| Bamboo | (>1250 species) | Grass |
| Banana | *Musa indica* | Leaf |
| Broom root | *Muhlenbergia macroura* | Root |
| Cantala | *Agave cantala* | Leaf |
| Caroa | *Neoglaziovia variegata* | Leaf |
| China jute | *Abutilon theophrasti* | Stem |
| Coir | *Cocos nucifera* | Fruit |
| Cotton | *Gossypium spp.* | Seed |
| Curaua | *Ananas erectifolius* | Leaf |
| Date palm | *Phoenix dactylifera* | Leaf |
| Flax | *Linum usitatissimum* | Stem |
| Hemp | *Cannabis sativa* | Stem |
| Henequen | *Agave fourcroydes* | Leaf |
| Isora | *Helicteres isora* | Stem |
| Istle | *Samuela carnerosana* | Leaf |
| Jute | *Corchorus capsularis* | Stem |
| Kapok | *Ceiba pentranda* | Fruit |
| Kenaf | *Hibiscus cannabinus* | Stem |
| Kudzu | *Pueraria thunbergiana* | Stem |
| Mauritius hemp | *Furcraea gigantea* | Leaf |
| Nettle | *Urtica dioica* | Stem |
| Oil palm | *Elaeis guineensis* | Fruit |
| Piassava | *Attalea funifera* | Leaf |
| Pineapple | *Ananas comosus* | Leaf |
| Phormium | *Phormium tenas* | Leaf |
| Roselle | *Hibiscus sabdariffa* | Stem |
| Ramie | *Boehmeria nivea* | Stem |
| Sansevieria (bowstring hemp) | *Sansevieria* | Leaf |
| Sisal | *Agave sisalana* | Leaf |
| Sponge gourd | *Luffa cylindrica* | Fruit |
| Straw (cereal) | – | Stalk |
| Sun hemp | *Crorolaria juncea* | Stem |
| Cadillo/urena | *Urena lobata* | Stem |
| Wood | (>10,000 species) | Stem |

### 11.2.4 Industrial and Economic Importance of Natural Polymers

Depending on the starch source and processing conditions, a thermoplastic material may be obtained with different properties suitable for various applications. Starch has been widely used as a raw material in film production because of increasing prices and decreasing availability of conventional film-forming resins (Chandra and Rustgi 1998). Potential applications of starch films include production of disposable food service ware, food packaging, purchase bag, composting bag and loose fill products. Starch is also used in hygiene and cosmetics. Moreover, starch has been used for many years as an additive to plastic for various purposes. Starch was added as filler to various resin systems to make films that are impermeable to water but permeable to water vapour.

Starch is also useful for making agricultural mulch films because it degrades into harmless products when placed in contact with soil microorganisms. Starch is also used in medical applications. For example, starch-based thermoplastic hydrogels for use as bone cements or drug delivery carriers have been developed through blending starch with cellulose acetate.

Important properties of thermoplastic starch-based materials include:

- compostable in accordance with DIN 54900
- high water vapour permeability
- good oxygen barrier
- not electrostatically chargeable
- low thermal stability

In general, the low resistance to water and the variations in mechanical properties under humid conditions affect the use of starch for various applications. As water has a plasticizing power, the material behaviour changes according to the relative humidity of the air. Strong hydrophilic character (water sensitivity) and poor mechanical properties compared to conventional synthetic polymers are the most important disadvantages of starch.

Cellulose has received more attention than any other polymer since it is attacked by a wide variety of microorganisms. The biodegradation of cellulose is complicated, because cellulose exits together with lignin; however, it is fortunate that pure cellulose does decompose readily (Chandra and Rustgi 1998). Fermentation of cellulose has been suggested as a source of chemical such as ethanol and acetic acid, but this has not achieved any commercial importance to date.

The most significant cellulosic applications are in the paper, wood product, textile, film and fibre industries, but recently it has also attracted significant interest as a source of biofuel product. The natural cellulosic carbon skeleton can be utilized in two major applications on an industrial scale. The first is as regenerated or mercerized cellulose (cellulose II, Rayon), which is not moldable and is used only for film and fibre production. The second represents a broader class of applications, which employs chemically modified celluloses, principally the cellulose esters (Chandra and Rustgi 1998).

Lignocellulosic materials have the potential to be utilized as a feedstock for the production of a wide variety of industrial and commodity products, ranging from paper, lumber and platform chemicals to a variety of fuels and advanced materials, including biodegradable polymers (Smith 2005). Plasticized blends of citrus pectin and high amylase starch give strong, flexible films, which are thermally stable up to 180 °C. Pectin is miscible with poly(vinyl alcohol) in all proportions. Potential commercial uses for such films are water-soluble pouches for detergents and insecticides, flushable liners and bags and medical delivery systems and devices.

Chitin is insoluble in its native form, but chitosan is water soluble. Chitosan has been found to be non-toxic after oral administration in humans and is an FDA approved food additive (Nair and Laurencin 2007). These biopolymers are biocompatible and have antimicrobial activities as well as the ability to absorb heavy metal ions. They also find applications in the cosmetic industry because of their water-retaining and moisturizing properties (Chandra and Rustgi 1998). Chitosan has been formed into membranes and matrices suitable for several tissue engineering applications. Chitin derivatives can also be used as drug carriers. Chitosan was used to develop injectable thermosensitive carrier material for biomedical applications. Due to the mild gelling conditions, the hydrogel has been found to be a potential delivery vehicle for growth factors, small molecular weight drugs and cells for localized therapy. The high chemical reactivity of chitosan has also led to several chitosan–drug conjugates for cancer therapy. Chitosan gels, powders, films and fibres have been formed and tested for many applications such as encapsulation, membrane barriers, contact lens materials, cell culture and inhibitors of blood coagulations (Pachence et al. 2007). Chitosan has good film-forming properties and therefore can be used as a food packaging material.

A common type of gum is alginic acid which is present within the cell walls and intracellular spaces of brown algae and has a structural role in giving flexibility and strength to marine plants. Due to its non-toxicity, alginate has been extensively used as a food additive and a thickener in salad dressings and ice creams (Nair and Laurencin 2007). Alginate gels have been used widely in controlled-release drug delivery systems. Alginates have been used to encapsulate various herbicides, microorganisms and cells. Even though alginates have been extensively investigated as biomaterials, one of the main disadvantages of using alginate-based material is their inability to undergo enzymatic degradation by mammals.

The film-forming properties of zein have been recognized for decades, and they are the basis for its commercial utilization. Coating films are formed on hard surfaces by covering them with zein solutions and allowing the solvent to evaporate off. The dried zein residues forms hard and glossy, scuff proof, protective coatings that also are resistant to microbial attack. Zein coatings are used as oxygen, lipid and moisture barriers for nuts, candies, confectionery products and other foods. Rice fortified with vitamins and minerals has been coated with zein/stearic acid/wood resin mixtures to prevent vitamin and mineral losses during washing in cold water. Pharmaceutical tablets are zein-coated for controlled ingredient release and protection (Gennadios 2002). Use of zein-based coatings has been suggested

for reducing oil uptake by deep fat fried foods, for protecting active ingredients in chewing gum, for achieving controlled release of active ingredients in pharmaceutical tablets and for masking the taste of orally administered drugs (Gennadios 2002).

Wheat gluten is suitable for numerous food and non-food uses. Its main application is in the bakery industry, where it is used to strengthen weak flours rendering them suitable for bread baking (Gennadios 2002). The other potential applications of gluten are very diverse: windows in envelopes, surface coatings on paper, biodegradable plastic films for agricultural uses, water-soluble bags with fertilizers, detergents, cosmetics, cigarette filters and additives and moulded objects (Cuq et al. 1998). Wheat gluten-based materials are homogenous, transparent, mechanically strong and relatively water resistant. They are biodegradable and a priori biocompatible, apart from some wheat gluten-specific characteristics such as allergenicity.

Soy protein is an abundant and relatively cheap ingredient source for various food applications. The functional properties that make soy protein useful in foods include cohesiveness, adhesiveness, emulsification, dough and fibre formation, whippability, solubility, and foaming (Gennadios 2002). Soy protein also is used in infant formulas and in baked meat, and dairy products. The use of soy protein as a film-forming agent can add value to soybeans by creating new channels for marketing soy protein. Soy protein is a viable and renewable resource for producing edible and environmentally friendly biodegradable films. Soy protein films are flexible, smooth, transparent and clear compared to other films from plant proteins. These films have good mechanical properties but they are generally slightly water resistant (Cuq et al. 1998). Soy protein films are typically prepared by drying thin layers of cast film-forming solutions (Gennadios 2002). Biodegradable plastics were also produced from soy isolate and concentrate by a thermomolding process.

The major sources of collagen currently used for industrial applications are bovine or porcine skin or bovine or equine Achilles tendons (Pachence et al. 2007). Thermal or chemical dissociation of collagen polypeptide chains forms product known as gelatin. The properties of collagen and gelatin are of great interest to various fields, such as surgery (implantations; wound dressings), leather chemistry (tanning), pharmacy (capsule production; tablet binding) and food science (gels; edible films). Reportedly, about 65 % of gelatin manufactured worldwide is used in foods, 20 % in photographic applications, 10 % in pharmaceutical products and 5 % in other specialized and industrial applications. Collagen has been extensively investigated for the localized delivery of low molecular weight drugs including antibiotics. Collagen films have traditionally been used for preparing edible sausage casing. Gelatin has been successfully used to form films that are transparent, flexible, water resistant and impermeable to oxygen. These films were made by cooling and drying an aqueous film-forming solution based on gelatin. Gelatin is also used as a raw material for photographic films, and to microencapsulate aromas, vitamins and sweeteners.

Its relative simple isolation and the useful properties of casein as an industrial material and food ingredient have led to commercial production of casein and caseinates since the nineteenth century. Casein and caseinates are suitable for numerous food and non-food uses such as in industrial applications (especially in glues, paper coatings, paints, leather finishing, textile fibres and plastics), and in various food products. The end-users of casein and caseinates have gradually shifted from industrial to food applications. About 70–80 % of the casein produced worldwide is used as a food ingredient (Gennadios 2002). Film-forming properties of caseins have been used to improve the appearance of numerous foods, to produce water-soluble bags and to produce origin or quality identification labels inserted under pre-cut cheeses, to ensure the surface retention of additives on intermediate moisture foods and to encapsulate polyunsaturated lipids for animal feeds (Cuq et al. 1998). Casein-based edible films are attractive for food applications due to their high nutritional quality, excellent sensory properties and potential to adequately protect food products from their surrounding environment. The mechanical properties of casein and caseinate films, being neither too tough nor too fragile, also make them suitable for edible purposes. Though more permeable to water vapour than plastic films, they are capable of retarding moisture transfer to some degree. Casein and caseinate films dissolve nearly instantaneously in water and this is desirable for many food applications.

Whey protein, a by-product of cheese industry, has excellent nutritional and functional properties and the potential to be used for human food and animal feed. The film-forming properties of whey proteins have been used to produce transparent, flexible, colourless and odourless films, such as those produced from caseins (Cuq et al. 1998). The use of whey proteins to make edible packaging film material brings several environmental advantages because of the film's biodegradability and its capacity to control moisture, carbon dioxide, oxygen, lipid, flavour and aroma transfer. These properties offer the potential to extend the shelf life of many food products, avoiding quality deterioration.

Other proteins have been also used for various purposes, including proteins from rye, pea, barley, sorghum, rice, sunflower, pistachio and peanut (Gennadios 2002).

### *11.2.5 Demand for Natural Polymers in the United States*

The United States is the world's largest economy with a Gross Domestic Product, GDP, of US $16.768 trillion[5]. According to a study on the market for natural polymers—Natural Polymers to 2016; US demand for natural polymers is forecast to expand 6.9 % annually to US $4.6 billion in 2016. Cellulose ethers, led by methyl cellulose, will remain the largest product segment. Exudate and vegetable gums

[5]http://www.data.worldbank.org/data-catalog/GDP-ranking-table.

will enjoy the most rapid gains in demand. The oilfield market will grow the fastest, driven by rising demand for guar gum in hydraulic fracturing fluids. This study analyses the US $3.3 billion US natural polymer industry. It presents historical demand data for the years 2001, 2006 and 2011, and forecasts for 2016 and 2021 by market (e.g. food and beverages, medical, oilfield, cosmetics and toiletries, paint and inks, construction, adhesives) and product (e.g. cellulose ethers, starch and fermentation polymers, exudates and vegetable gums, protein-based polymers, marine polymers). The study also considers market environment factors, details industry structure, evaluates company market share and profiles 39 industry players such as Ashland, Dow Chemical and CP Kelco US.[6]

Another report by Transparency Market Research which focused on the natural polymer market in the United States, estimates that in 2012, the demand for natural polymers was US $4.95 billion, and will grow at a Compound Annual Growth Rate, CAGR, of 6.2 % from 2012 to 2018, by which year it will stand at US $7.12 billion. The report was titled: Natural Polymers—U.S. Industry Analysis, Size, Share, Growth. The report finds that natural polymers are finding widespread applications in the shipment of non-durable good, pharmaceuticals, as well as food and beverages. As the shipments of all these products continue to show an upward graph, the demand for natural polymers in the United States is slated to exhibit an increase too. The study focuses on key applications such as food and beverages, medical, oilfield, as well as other applications such as cosmetics, toiletries and packaging classified under a segment called ‘others’.

An extensive analysis of all these segments reveals that in U.S. natural polymers market, medical applications trumped all others, with a 25.6 % share of the total revenue generated as of 2012. Also, the most extensively consumed type of natural polymer in U.S. natural polymers market was cellulose ether; it constituted 36.5 % of all recorded consumption volumes as of 2012 Fig. 11.3.[7]

The demand for pharmaceuticals is increasing, and as a result, this application area will also witness higher growth. This growth in pharma applications will have a cascading effect wherein the demand for fermentation products and starch will also spike. Cellulose ethers—derived from photosynthesis of wood pulp, cotton and certain other plant types—are used in a variety of markets like medical, food and beverages, and oilfield operations. Some of the most commonly used types of cellulose ethers include: methyl cellulose (MC), carboxymethyl cellulose (CMC), hydroxyethyl cellulose (HEC) and microcrystalline cellulose (MCC). According to the estimates of the market study, by 2018, the demand for starch and fermentation products will likely rise to 479.3 kilotons, exhibiting a CAGR of 12 % between 2012 and 2018.

The study also discusses the important end-user industries within the U.S. natural polymers market. These end-user industries include: Adhesives and sealant, toiletries, packaging, leather tanning, construction, paint and inks and textiles.

[6] http://www.freedoniagroup.com/Natural-Polymers.html.

[7] http://www.transparencymarketresearch.com/pressrelease/natural-polymers-market.htm.

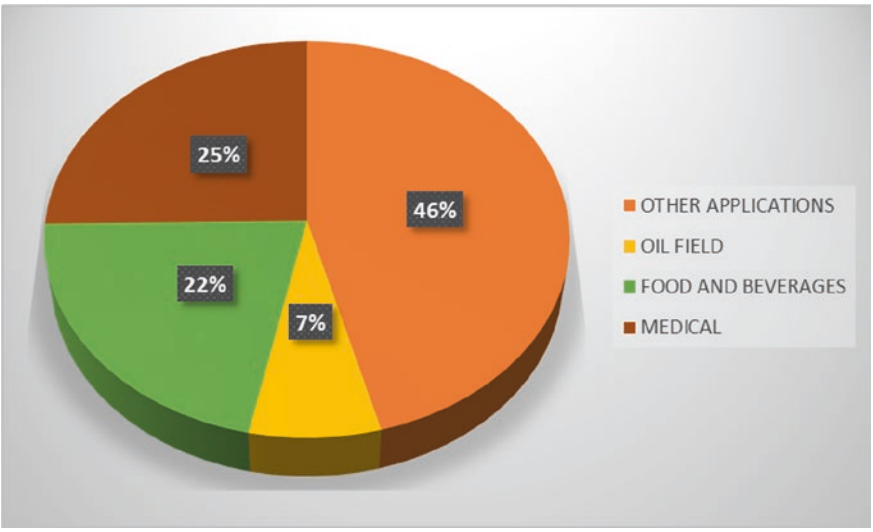


**Fig. 11.3** U.S. Natural Polymer Market Volume Share, by Application in 2011 as reported by transparency market research press release

One of the most important segments that generate considerable revenue for the U.S. natural polymers market is that of packaging. A number of natural polymer-based materials are required for packaging applications. In fact, several players in the U.S. natural polymers market are focused mainly on the packaging segment and conduct extensive research to come up with new and more innovative methods for packaging.

This report also closely profiles the leading players in the U.S. natural polymers market. Some of these names include: Ashland Inc., Economy Polymers & Chemicals, Dow Chemical Company, JM Huber, Archer-Daniels-Midland, Novamont, Plantic Technologies, FMC Corporation, Cargill Inc., Danisco, Cereplast, CP Kelco, Allergan, Croda International Plc., BASF SE and AkzoNobel NV (see Footnote 6).

### *11.2.6 Biomaterials Market in Brazil and Across the Globe*

A biomaterial is a natural or synthetic material suited to replace or treat natural body tissues and organs on interaction with biological systems. It traces its history to more than 2000 years ago, when Romans, Chinese and Aztecs used gold for dental applications. Biomaterials, which are compatible, have since been adapted, improvised and technically enabled to improve body functions and replace damaged tissues. They have evolved to include biodegradable materials that are easily

dissolved in the body. Advances in technology and the emergence of innovative biomaterial products have enhanced their performance and applications.[8]

The Brazil market for biomaterials is expected to reach US $1.7 billion in 2015 from US $550.2 million in 2008 with a CAGR of 19.5 % from 2010 to 2015 (see Footnote 8). Brazil, an emerging market, alongside, China, Russia and India; belong to the group of ten (Pielichowski and Njuguna 2005) richest countries in the world.[9] In 2009, the orthopaedic biomaterial market recorded revenues of US $236.5 million or 37.5 % of the total biomaterials products market. This is mainly because of increasing application areas and introduction of sophisticated technologies in the biomaterials market. However, the orthopaedic biomaterial market is estimated to grow at a CAGR of 17.2 % from 2010 to 2015. Cardiovascular biomaterial products market is the second highest market, contributing 36 % of the total biomaterial products market. Ageing population (population above 60 years was expected to reach 24 million by 2012), higher life expectancy and increase in the incidence of 'lifestyle and chronic diseases' such as cardiovascular diseases has influenced the growth of biomaterial products. According to the World Health Organization, 32 % of the total mortality in Brazil was due to cardiovascular diseases. Such a high incidence of diseases will increase the demand for cardiovascular biomaterial products such as cardiac stents.

The biomaterial products market in Brazil was expected to grow from US $690 million in 2010 to US $1.7 billion in 2015 at an estimated CAGR of 19.5 %. The wound care biomaterial segment was expected to grow at a CAGR of 24.3 % from 2010 to 2015. Of all the application areas of biomaterial in Brazil, surgical appliances and supplies account for the largest share; i.e. 39 % of the total applications of biomaterial. With the technological advancements in orthopaedic and prosthetic applications, there is an increase in demand for biomaterials in surgical appliances and supplies.

The global biomaterial market is estimated to reach US $88.4 billion by 2017 from US $44.0 billion in 2012, growing at a CAGR of 15 %. Increased investments, funding and grants by government bodies worldwide, incessant rise in the number of collaborations, conferences and research-related activities, technological advancements, increasing applications of biomaterials and growing number of elderly people are the major factors propelling the growth of the biomaterial market globally. Immunological and inflammatory reactions, stringent regulatory systems, issue of fracture fatigue and wear and reimbursement concerns are the major deterrents curbing the biomaterial market.

The global biomaterial market witnessed a plethora of growth opportunities. Novel developments of biomaterial for wound healing, plastic surgery, tissue engineering, ophthalmology, and neurology, colossal pool of cardiac patients in Asia, rise of biomaterial market in China and Taiwan, and increased conferences and research-related activities in the Rest of the World (RoW) countries are major

[8] http://www.marketsandmarkets.com/Market-Reports/biomaterials-393.html.

[9] http://www.marketsandmarkets.com/Market-Reports/biomaterials-392.html.

factors influencing the growth of the biomaterial market. The burning issues affecting the growth of biomaterial market are challenges to tissue engineering and effect on suppliers by the Biomaterials Access Assurance Act.

The global biomaterial market is dominated by North America, followed by Europe, Asia and Rest of the World (RoW). North America will continue to lead the biomaterial market in the years to come, followed by Europe. North American market growth is likely to be driven by increasing government investments in biomaterial sector, reimbursements offered by Centres for Medicare and Medicaid Services (CMC) and rising ageing population who are the main consumers of biomaterials. North American biomaterial market is expected to receive a significant push due to phenomenal increase in new products such as botox, botulinum toxins and hyaluronic-based injectibles.

The research report categorizes and analyses the global biomaterial market under two broad segments—type and application. Both of these markets are broken down into segments and sub-segments, providing exhaustive value analysis for the years 2010, 2011, 2012 and forecasts to 2017. Each market was comprehensively analysed at a granular level by geography (North America, Europe, Asia and Rest of the World) to provide an in-depth information on the global scenario. Under the global market segmentation by type, natural biomaterials mentioned include: collagen and gelatin, cellulose, chitin, alginate and hyaluronic acid. The biomaterial market, by type includes materials such as metals, polymers, ceramics and natural biomaterials. Metals and polymers dominate the biomaterial market. The polymers biomaterial market is expected to grow profusely in the coming years; it is anticipated to grow at a CAGR of 22.1 % from 2012 to 2017.

Biomaterial is a combination of four major sciences, namely: basic science, medical science, engineering science and forensic science. Biomaterials have been in use for long in the human body to improve body functions and replace damaged tissues. These biodegradable biomaterials have evolved from biomaterials that do not react with the environment and easily dissolve in the body.[10]

### *11.2.7 Natural Polymers in Nanodrug Delivery*

Natural polymers such as starch, chitosan and gelatin have found use in industries as diverse as food, textiles, cosmetics, plastics, adhesives, paper and pharmaceuticals. The food industry uses these polymers as thickening agents in snacks, meat products, fruit juices. They are also used in the manufacture of disposable items like fast food utensils and containers. From a pharmaceutical standpoint, these polymers have been extensively used in solid oral dosage forms, where they have been used as binders, diluents, disintegrants and matrixing agents. In recent times, nanotechnology has started to make significant advances in biomedical

[10] http://www.marketsandmarkets.com/PressReleases/global-biomaterials-asp.

applications, including newer drug delivery techniques. There has therefore been considerable research into developing biocompatible, biodegradable submicron devices as drug delivery systems using natural polymers; this is because they occur widely in nature, generally biocompatible, biodegradable, safe and non-immunogenic. There are reports of these polymers been made into colloidal particles that act as carriers for both large and small drug molecules, conferring on the drug molecules properties which enhance delivery actively or passively, thereby tuning them for use as controlled, ocular, transdermal or intranasal delivery systems. In more advanced areas of drug delivery, these polymers have also been tested for gene therapy and tissue engineering.

Although the initial properties of nanomaterial studied were for its physical, mechanical, electrical, magnetic, chemical and biological applications, recent attention has been geared towards its pharmaceutical application, especially in the area of drug delivery. This is because of the challenges with the use of large-size materials in drug delivery, some of which include poor bioavailability, in vivo stability, solubility, and intestinal absorption, sustained and targeted delivery to site of action, therapeutic effectiveness, generalized side effects and plasma fluctuations of drugs. Of recent, several publications in nanodrug delivery have been designed to overcome these challenges due to the development and fabrication of nanostructures. It has been reported that nanostructures have the ability to protect drugs from degradation in the gastrointestinal tract; the technology also allows target delivery of drugs to various areas of the body. The technology enables the delivery of drugs that are poorly water soluble and can provide means of bypassing the liver, thereby preventing the first pass metabolism (Anwunobi and Emeje 2011).

Nanotechnology increases oral bioavailability of drugs due to their specialized uptake mechanisms such as absorptive endocytosis and are able to remain in the blood circulation for a longer time, releasing the incorporated drug in a controlled fashion leading to less plasma fluctuations and minimizing side effects. It has been reported that, due to the nano scale size of nanostructures, they are able to penetrate tissues and are taken up by cells, allowing efficient delivery of drugs to the target sites of action with the uptake of nanostructures observed to be 15–250 times greater than that of microparticles in the 1–10 μm range. Nanotechnology improves their performance and acceptability by increasing effectiveness, safety, patient adherence, as well as ultimately reducing healthcare costs. Nanotechnology may also enhance the performance of drugs that are unable to pass clinical trial phases. It definitely promises to serve as drug delivery carriers for the more challenging conventional drugs used for the treatment and management of chronic diseases such as cancer, asthma, hypertension, HIV and diabetes. Despite the great potentials of nanodrug delivery systems in revolutionizing patient treatment, its safety in humans are of great concern (Anwunobi and Emeje 2011).

Many other synthetic/semi-synthetic polymers have been extensively utilized and investigated as the preparation materials of microcapsules. Although the synthetic polymers display chemical stability, their unsatisfactory biocompatibility still limits their potential clinical applications. Because the natural polymers always show low/non-toxicity, low immunogenicity and thereafter good biocompatibility,

they have been the preferred polymers in drug delivery systems. Among the natural polymers, alginate has become one of the most common materials used to form microcapsules. Recently, scientists have turned their attention on tuning starch and chitosan for use in nanodrug delivery. One of the ways to avoid the potential hazards of nanodrug delivery may be by using natural polymers. This is because, apart from occurring widely in nature, natural polymers are generally biocompatible, biodegradable, non-immunogenic and safe (Anwunobi and Emeje 2011).

Natural polymers such as starch, gelatin and chitosan are no longer mere traditional excipients for use as binders, disintegrant or diluents, but are now being applied widely as therapeutic drug carriers. The efficiency of delivery and release of bioactive molecules from these systems is influenced by factors such as polymer type, drug loading, polymer breakdown, molecular weight, particle size, interactions between the drug and polymer and several other technological and pharmacotechnical factors. Natural polymers may not for now enjoy the robustness of easy amenability to formulation design as compared to synthetic polymers, but their excellent biocompatibility and safety makes them very important in the preparation of various drug delivery systems with potential to achieve the formulator's desire for target or protected delivery of bioactive agents. However, increasing works need to be done in the near future on these polymers. It is important to note that apart from being safe, natural polymers are relatively very cheap. A major limitation to the use of some of the natural polymers such as starch appears to be its higher sensitivity to acid attack; however, modification has been proved to impart acid resistance to the products. It is therefore important to optimize the process of transition of these polymer granules from their native micro to the artificial submicron level in greater detail and also pay greater attention to the toxicological profiles of the nanoscale polymer derivatives. This is because, although generally regarded as safe, derivatives of these natural polymers and in fact at submicron levels may pose some safety challenges especially as carriers in drug delivery systems. The physicochemical properties of polymers depend largely on their botanical or biological source, therefore, there is a greater need now than ever before for scientists to begin to source for even cheaper polymers from our natural environment; plants, animals and microorganisms alike. If the pharmaceutical industries, governments and donor agencies will take the risk of investing more in natural product research in nanodrug delivery, then the answer to the current 'safety phobia' by regulatory agencies may soon be at hand (Anwunobi and Emeje 2011).

### *11.2.8 Natural Polymers and the Economic Implications of Capital and Technology Dependency on Less Developed Countries*

Advanced applications of natural polymers, including chitosan, alginate, starch, collagen and gelatin, and their utilization in the fabrication of tissue engineering matrices and drug delivery systems have been reported (Ivanova et al. 2014). Sales of

regenerative biomaterials have already exceeded US $240 million per annum, with further growth being expected through the support of newly available and developing technologies, the existing regulatory guidelines and the commercial success of the private sector within the aggregate field comprised of tissue engineering, regenerative medicine and stem cell therapeutics. In regenerative medicine, the genetic engineering of proteins promises to overcome the limitations of traditionally used autografts and allografts, by providing a platform for the on-demand expression of biological components and highly controlled generation of new protein sequences and self-assembling peptides with tunable properties.

Capital resources are rapidly growing and being dispersed to maximize the returns of their owners throughout the world, so too is rapid technological change (mostly in the West) profoundly affecting world trading relationships. One of the most obvious examples of the impact of developed country technological change on developing country export earnings is the development of synthetic substitutes for many traditional primary products. Over the past five decades, synthetic substitutes for such diverse commodities as rubber, wool, cotton, sisal, jute and skins—sources of natural polymers, have been manufactured in increasing quantities. The developing world's market share of these natural products in all cases has fallen steadily. For example, between 1950 and 1980, the share of the natural rubber in total world rubber consumption fell from 62 to 28 %, and cotton's share of total fibre consumption dropped from 41 to 29 % (Todaro and Smith 2003).

Technological substitution, together with the low income and price elasticity of demand for primary products and the rise of agricultural protection in the markets of developed nations, goes a long way towards explaining why uncritical adherence to the theoretical dictates of comparative advantage can be risky and often unrewarding venture for many less developed countries, LDCs. On the other hand, the worldwide availability of new technologies developed in the West has provided many newly industrializing countries, NICs, the opportunity to capitalize on Western research and development expenditures. By first imitating products developed abroad but not on the frontiers of technological research, certain LDCs with sufficient human capital (e.g. the Asian NICs) can follow the product cycle of international trade. Using their relatively lower wages, they move from low-tech to high-tech production, filling manufacturing gaps left vacant by the more industrialized nations. According to the dependency economists, the whole world is divided between two sets of countries; DCs (developed countries) and LDCs (less developed countries). The former are in the centre (Western Europe, Britain and the United States) and the latter are in the periphery (backward countries of Asia, Africa and Latin America). There are unequal centre–periphery relationships whereby LDCs are dependent on DCs in trade, investment, technology, etc. This dependence results in underdevelopment of the periphery because the centre is dominated by the powerful capitalist countries that exploit the former for their benefit. The peripheral LDCs are heavily dependent on the centre for foreign capital. Foreign capital leads to 'external orientation' of LDCs by exporting commodities, importing manufactures and making them dependent for industrialization of their economies. Sunkel posits that it is the stagnation of agriculture, high

concentration of primary commodities for exports, high foreign exchange content of industrialization and growing fiscal deficit in the peripheral countries which necessitate foreign financing for them. The foreign investors exploit LDCs by insisting on the choice of projects, making decisions on pricing, supply of equipment, knowhow and personnel, etc. In fact, they impose a development pattern that is not compatible with local needs. Further, the dependence on foreign capital leads to a much higher outflow in the form of declared profits, royalties, transfer pricing, payment of principal and interest to foreign investors of the centre.

The peripheral countries use excessively capital-intensive technologies imported from the developed countries of the centre. These technologies are inappropriate to the production and consumption needs of LDCs and are sold by multinational corporations (MNCs) of developed countries. The technological dependence of LDCs on DCs arises because of the urgency of importing technologies as they cannot innovate them. They lack information about the availability of appropriate technologies which leads to exploitation of LDCs due to their weak bargaining power. MNCs lead to economic and political distortions in LDCs. Some of the economic distortions created by MNCs are transfer of technologies to LDCs by restricting their right to use or change or transfer according to their discretion or requirements. This leads to their total technological dependence on MNCs. Capital-intensive technologies have limited labour absorption capacity and thus add to unemployment in LDCs. They create social tensions by worsening the distribution of income. There are large wage differentials between workers employed in the branches of MNCs and those engaged in local firms in LDCs. Such wage differentials increase income inequalities and create social tensions which retard the development of LDCs. Both Frank and Santos explain the technological development perpetrated by MNCs. The centre has spread its monopoly to the peripheral countries through technological transfer. For this, LDCs have to borrow from the centre. There is repatriation of profits, royalties, etc., by MNCs to the centre. This worsens balance of payments (BOP) of LDCs. They resort to devaluation and increase in money supply thereby leading to inflation with its resultant adverse effects on the economy. Thus the peripheral countries are caught in a web of dependence structure Jhingan (2005).

## 11.3 Conclusion

The economic impacts of natural polymers to national and global economy have been discussed. Natural polymers have been used for ages to improve the quality of lives of people around the world. Traditionally, a lot of value has been created or derived from the use of various kinds of fibres, especially cotton. Modern improvements have resulted in better value for natural rubber. Natural polymers are, undoubtedly, abundant, universal, diverse, renewable, biodegradable, biocompatible, non-toxic, safe, economical, versatile and indispensable sources of biomaterials. Natural polymers include a wide range of naturally occurring or derived

products classified as polysaccharides, proteins, polynucleotides and certain categories of polyesters. The natural polymer with the highest prevalence, demand and perhaps application is cellulose; a polysaccharide used in a variety of industry. The largest market for natural polymers, as reported, is the United States. Despite the global trends in the development of natural polymers and the growing markets in Latin America, Europe and Asia; Africa is left behind. Substitutes to cotton and natural rubber had dwindled natural polymers' trade revenues for developing countries over several decades and their competitive advantages in global production reduced. Renewed interests in natural polymers are driven by environmental pollution and degradation concerns over the use of non-biodegradable petroleum-based substitutes, the rising cost of petroleum and the realization that petroleum resources are finite and exhaustible. Investments in scientific, engineering and technological research and development efforts by governments and other interests have yielded into various industrial applications for natural polymers. Natural polymers development has impacted the scientific, engineering and technological fields of agriculture, medicine, pharmaceuticals and packaging industry and the economies of countries, mainly in the West; through a wide range of innovative materials employed as food and beverages, healthcare and personal care products. Manpower and technology advancements involving natural polymers have culminated in the novel gene and nanodrug delivery systems, as well as tissue engineering applications.

Although, the natural polymers market, globally, is worth billions of dollars; developing countries, especially in Africa, have not benefitted much because of intellectual, capital, technology, legal and trade constraints.

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# Chapter 12
# Future Perspectives

**Ololade Olatunji, Géraldine Savary, Michel Grisel, Céline Picard and Atul Nayak**

## 12.1 Trends and Perspectives of Natural Polymers in Cosmetics Industry

Companies specialized in the raw materials furnishing for cosmetic companies have been recently developing some natural polymer associations, with possible synergies and/or multifunctional benefits. Among the numerous examples, SEPPIC launched a xanthan gum (XG)/acacia gum combination (trade name: Solagum AX®), owing an optimum gums ratio; this system brings improved emulsions stabilizing properties and can be used with cold process. SOLIANCE recently developed a XG/guar gum combination (trade name: Syner-GX®) that allows obtaining gels with good stability versus electrolyte and temperature, and soft touch.

Many commercial examples exist, but due to economic competition only few scientific studies, for physicochemical or sensory aspects, are available for such polymer associations. Recently, Jamshidian et al. (2014) investigated the potential relationship between rheological values and filament stretching property of XG and hydroxypropyl guar (HPG) in pure and mixed aqueous solutions and

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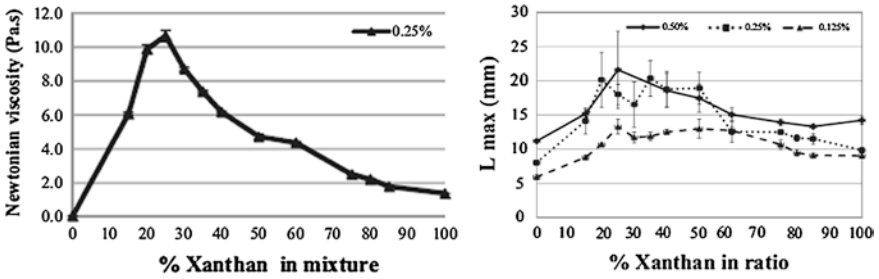


**Fig. 12.1** Viscosity plot of X/HP Guar mixed solutions as a function of xanthan percentage at 0.25 % total polymer concentration and corresponding stretching properties (Jamshidian et al. 2014 reproduced with permission from Elsevier, Licence number 3633661456878)

also in cosmetic emulsions. In pure solution, distinct rheological behaviors were observed between XG and HPG. XG solutions showed higher stretchability values than HPG for concentration below 1 % w/w and then filament stretching properties were close for both polymers at higher concentrations. In mixed solutions, a pronounced synergistic effect was observed for XG/HPG solution at a 25/75 ratio whatever the total concentration tested (below 0.5 % w/w). Noteworthy is the influence of the synergy on the stretching properties since the interaction between XG and HPG results in an enhancement of the maximum filament length as visible in Fig. 12.1.

If considering emulsions, XG demonstrated the major role in viscosity and filament stretching increment. This could be related to interactions between XG and other ingredients present in the emulsion. So more rheological and textural parameters should be investigated in order to understand how XG governs the behaviors of the system and why no interaction was observed with HPG in emulsion.

As described earlier in Chap. 9, many natural polymer derivatives (so-called "artificial polymers") are currently used for cosmetic product elaboration; most were initially issued from widely available polysaccharides such as cellulose, guar, or starch, and many others are also currently available. Nowadays, in relationship with the "multifunctional" tendency and research for new natural-based ingredients, some research projects focus on the modification of some well-developed polysaccharides. As an example, Roy et al. (2014) recently proposed a method for selective and efficient grafting of alkyl residues on xanthan molecules backbone. A series of hydrophobically modified xanthan with tunable grafting density ranging from 0 to 29 % was obtained by coupling reaction onto the carboxylic functions of the biopolymer. The native semi-rigid helix conformation of xanthan was kept intact thus permitting to get high viscosity enhancement related to the native polymer combined with intermolecular associations through alkyl chains. Rheological characterization unambiguously evidence dramatic enhancement of the low shear viscosity as illustrated in Fig. 12.2, but without modifying the well-known shear thinning behavior of the native biopolymer.

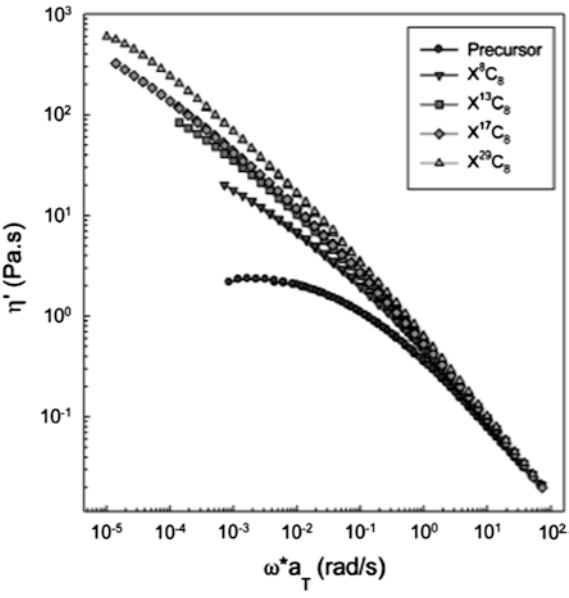


**Fig. 12.2** Master curves of the dynamic viscosity ($\eta'$) as a function of $\omega^* a_T$ with $T_{ref} = 20$ °C at 2 g/L (Roy et al. 2014)

This example shows promising suspending capability of such xanthan derivatives, which is of primary importance when formulating complex mixtures with long-term utilization as required for most cosmetic products.

Other many promising research projects for developing new natural polymeric systems for cosmetic formulation are in course, in both academic and industrial laboratories. Typical examples are extraction and utilization of compounds issued from abundant non alimentary biomass (e.g., proteins) or macroalgae (e.g., polysaccharides), or microalgae and microorganism biotechnology for producing novel polysaccharides or proteins. The future of cosmetic industry largely depends on such innovations.

## 12.2 Future Challenges of Parenteral Devices

In Chap. 10 we discussed microneedles as minimal invasive parenteral devices because the needles are fabricated to penetrate a known depth in skin layers than a hypodermic needle. Natural polymers have the potential to support the sustained release of drugs in the skin and can prove advantageous for the biodegradable class of microneedles. However, the challenge arises to strengthen the microneedles with the result of all microneedles piercing the skin at a reproducible depth. Synthetic biodegradable polymer such as poly(DL-lactic-co-glycolic acid) PLGA and poly(L-lactic acid) (PLLA) possess high mechanical strength

(Ishaug et al. 1994; Leung et al. 2008). The possibility of enhancing the natural polymeric formulation with blended synthetic, polymeric fibers in providing improved mechanical strength properties is one direct solution.

## 12.3 Natural Polymer Bases in Gums in Food Applications

Chewing gums is an example of application of polyisoprenes in food. In the earlier years of their existence, chewing gums were produced from natural gums such as chicle, in addition to gutta and other natural polymer-based materials. As the requirements become more sophisticated and the interests in synthetic polymers grew, more chewing gum producers began to focus on the application of synthetic polymers such as polyethylene, poly vinyl acetate, styrene-butadiene copolymers, and isobutylene-isoprene copolymers to produce chewing gums. In prior invention, a natural polymer-based chewing gum consisted of naturally occurring guayule rubber in combination with hydrogenated vegetable oil and polyvinyl acetate as plasticizers, emulsifying agents, solvent, and inorganic filler (Glass et al. 1983). However, today a large majority of the chewing gum in the commercial market make use of synthetic polymers.

Although synthetic polymers are preferred for the consistency and desired properties achievable, chewing gums based on synthetic polymers are generally hydrophobic causing them to stick to surfaces (Farber et al. 2010). Natural polymers have more hydrophilic options such that non-stick chewing gums using natural bases such as natural rubber could result in non-stick chewing gums. Furthermore, natural polymer-based chewing gums are likely to result in more ingestible chewing gums reducing the health hazards posed by intentional or unintentional swallowing of chewing gums.

Part of the drawbacks from using natural-based polymers such as polyisoprene for food application is the presence of the *trans* and *cis* isomeric forms and the protein residues which could result in allergic reactions. Further developments in processing techniques which can better eliminate these allergens from natural polymers will consequently result in more use food productions.

## 12.4 Nondestructive Testing

Acoustic emissions have recently been employed for nondestructive mechanical characterization. In particular, this method has been applied to natural lignocellulose-based fibers such as jute and flax. Such nondestructive testing could play an important role in cases where in vivo testing of natural polymer-based composites applied in for example food, tissue engineering to test the real-time integrity of a scaffold, or in food to test the mechanical properties of an edible natural polymer-based food packaging after production without destroying the product.

Nondestructive mechanical testing is also important where the natural polymer-based material or the fabrication process is rather expensive (for example hyaluronan sourced from humans).

## 12.5 Addressing Limitations of Natural Polymers Due to Thermomechanical Sensitivity

In processes such as thermal spraying which has been effectively used in the polymer industry for processing of filaments (Rawal and Mukhopadhyay 2014), natural polymers are not commonly applied due to their thermal sensitivity and processibility. This technique generally involves melting and accelerating microparticles toward a substrate unto which they solidify and adhere to form thin layer. Thermal spraying is of different forms, and the melting could be through either a combustion or plasma flame.

The limitation of such methods in natural polymer is due to the weak thermoplasticity of natural polymers compared to synthetic polymers. Such limitations can be addressed either by adapting the processing techniques to suit the thermal tolerance of natural polymers or alternatively or in addition, new blends can be developed with various natural polymers such as their combined effect results in a fully natural polymer-based blend with desirable thermomechanical properties for thermal processing.

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