Lucian Lucia
Ali Ayoub *Editors*

Polysaccharide-based Fibers and Composites

Chemical and Engineering Fundamentals and Industrial Applications

Springer

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Editors
Lucian Lucia
Department of Forest Biomaterials
North Carolina State University
Raleigh, NC
USA

Ali Ayoub
Department of Forest Biomaterials
North Carolina State University
Raleigh, NC
USA

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Preface

We are honored to host within this monolith a unique collection of chapters that discuss polysaccharides within the context of their potential uses as fibers in industrial applications. This effort attempts to provide by virtue of the complexity of their synthesis in plants an overview of the highly multidisciplinary nature of polysaccharides' research for fibers, and the very large variety of applications that are pressed to meet global needs, running a gamut, for example, from biotechnology to fabrics to energy. It is an enormous challenge, therefore, to future leaders especially considering persistent overpopulation and economic throes to properly realize the options available to address these needs. Therefore, this book humbly aims to contribute one additional stone to the natural resources landscape from chemical to engineering composites to medical roles of these bio-based products to applications in related and diverse fields. Various questions and answers concerning the optimization of the formulation and development technology for marketing strategy will be offered. Most importantly, fiber-based polysaccharides have replaced many of the conventional metals and/or materials in many applications. The most important advantages of using bio-based polymers are their ease of processing, availability, biodegradability, productivity, and low costs. In this book, we will cover various aspects of polysaccharides-fiber reinforced composites and address some of the basic issues for the development of such composites; types of natural fibers; chemical composition of natural fibers; microstructure of fibers and the modification of fibers through reactive extrusion techniques and how we can improve the stability of these fibers so that they can be used with engineered polymers and further the advantage of polysaccharides.

From insects to trees, many complex multicellular organisms require architectures that support their rigid skeletons, while also allowing for degrees of freedom in flexibility. For example, the biochemical components of insect exoskeletons are proteins, chitin, enzymes, phenols, and polysaccharides. Interestingly, the variety of mechanical and physicochemical properties found in their tissues are ascribed to the cross-linking of proteins and/or polysaccharides. In this book, we intend to focus on the mechanism of this type of chemistry, including the composition and structural characterization of the materials and how we can prepare biomimetic materials such

as fiber-based polysaccharides using technologies from electro-spinning to melting spinning by reactive extrusion. We will investigate the polymer chemistry associated with the matrix to gauge different industrial applications from water treatments to textiles.

It has been and continues to be our goal to provide a text aspiring to high readability and comprehension for the technology-oriented. Our target audience is not just students or practitioners of engineering analysis, but includes those studying fiber science and composites in order to appreciate, understand, and manage materials and technology at an operations management level.

Raleigh, USA

Lucian Lucia
Ali Ayoub

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About the Editors

Lucian Lucia is a professor and a renewable chemist who directs *The Laboratory of Soft Materials and Green Chemistry*. He is affiliated with several universities including Jiangnan University, PR China (Foreign Talent Professor), North Carolina State University (USA), and Qilu University of Technology (Distinguished Professor of Green Chemistry). He has strong interest in fiber sciences and soft materials within the context of the principles of their green chemistry and accompanying transformation and mechanisms, and applications. He works intensively with scientists from the USA, Brazil, and China.

Ali Ayoub is an internationally recognized expert in the biopolymer science and engineering field and has successfully developed groundbreaking inventions in areas relevant to polymeric materials and the biorefinery concept. Currently, he is a senior scientist in the chemical industry and an Adjunct Assistant Professor and Member Associate Graduate Faculty at North Carolina State University, USA. Dr. Ayoub is affiliated to the US Department of Interior, SE Climate Science Center.

Chapter 1
The State of the Art: Introduction to Spinning

Remil Aguda and Ali Ayoub

Abstract This chapter gives a general introduction to the book and describes briefly the context for which the editors established its contents. The characteristics of polysaccharides during fiber processing and several technical challenges are presented alongside opportunities for processing polysaccharide fibers with desired properties. This book is not the first survey dealing with the interest of polysaccharides fibers or materials derived from renewable resources since several monographs have been published in recent years. The common denominator to many of these collective overviews is the biodegradable blends character of the ensuing material. We have attempted to gather in the present volume what we feel is a more comprehensive collection of monographs with the materials science elements as the predominant feature. Of course, the making blends based fiber issues remain essential here, but within the primary focus spelled out in the tittle.

Keywords Fiber spinning · Manufacturing of fibers · Mechanism of spinning

1.1 The Context

Polysaccharides are biomolecules composed of sugar units covalently linked to form polymer chains. Examples of polysaccharides are cellulose, chitosan, starch and cyclodextrin. Polysaccharide fibers are naturally found in the seeds and fruits of plants that are cultivated as sources of food, feed or fiber. Polysaccharide fibers are utilized for the production of materials for a wide range of applications in apparel, furniture, furnishing, weaving, composites, biocompatible materials, biomedical devices and energy storage. Compared to fibers derived from polymers synthesized from petroleum fractions, these polysaccharide fibers are derived from renewable sources such as rotational crops and managed forests. Polysaccharide fibers are also

R. Aguda · A. Ayoub (✉)
Department of Forest Biomaterials, College of Natural Resources,
North Carolina State University, Raleigh, NC, USA
e-mail: info@ayoubsciences.org

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biodegradable, which is an advantage over non-biodegradable petroleum-derived polymer fibers such as polyethylene, polyethylene terephthalate, polypropylene and nylon. The processing of these materials necessitates the understanding of how these fibers are made from the molecular to microscopic to macroscopic scale. There are also expected changes during formation in the macroscopic properties such as viscosity, glass transition temperature, degradation temperature, rigidity, tensile strength and compressive strength.

1.2 Manufacturing of Fibers

During the manufacturing of fibers, three important steps are controlled to obtain a fiber with desired fiber properties (Fig. 1.1). The preparation of the polysaccharide as a raw material can be melting, dissolution in a solvent, formation of a gel or inducing charges. The raw materials are polysaccharides such as cellulose, cellulose esters, chitosan, starch and cyclodextrin, which may be mixed with proteins in fiber composites (Chap. 5). The second step involves the flow within the spinneret channel, exit zone, elongation of the fluid jet and fiber solidification. The third step involves treatment of the fiber with mechanical drawing, chemical additives or heat.

The mechanics of fiber spinning involves four aspects: (1) flow within the spinneret, (2) the exit zone, (3) elongation of the fluid jet and (4) fiber solidification. The flow within the spinneret channel involves the rheological behavior of the spinning fluid. This behavior determines the required pressure and the optimum dimensions of the spinneret channel. Flow within the channel is also closely associated with the phenomena appearing in the exit zone of the capillary. As a rule of thumb, the transit times in fiber spinning are 0.1–100 ms, while the polymer relaxation times are as long as 100–700 ms. Thus relaxation processes play an important role in "spinneret flow". When the spinning fluid emerges from the capillary (exit zone), the character of the flow changes rapidly. The fluid leaves the channel with rigid walls and enters the gaseous or liquid medium, where the free jet is subjected to axial tension. The transition from shear flow within the channel to uniaxial extension in the downstream parts, is accompanied by stress and velocity rearrangement in the exit zone and by change of the fluid diameter. When the fluid jet passes the transition zone (elongation of the fluid jet), the velocity distribution

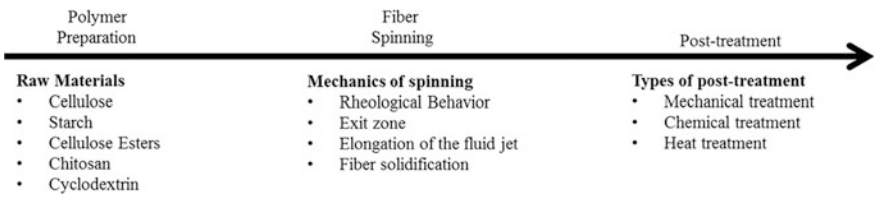

Fig. 1.1 Steps in the manufacture of fibers

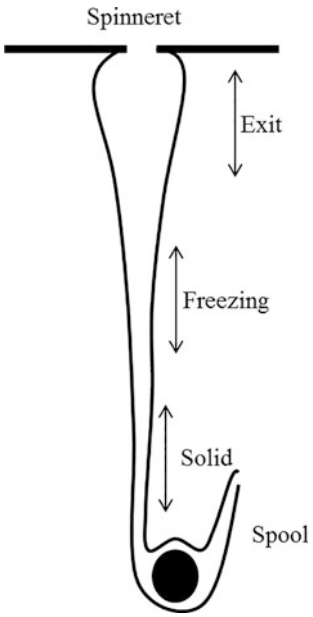

Fig. 1.2 Mechanics of fiber spinning

through its cross section is nearly uniform and normal stress connected with shear flow in the spinneret is practically relaxed. The elongation region extends over some scores of centimeters of the spinning path, molecular orientation develops here and solidification processes take place, thereby making this region the most important step in the technology of the spinning process (Ziabicki 1988).

When the polysaccharide flows into the channel, the velocity, temperature, viscosity and stress are important parameters that control the macroscopic dimensions upon exiting the channel. In the exit zone, relaxation of internal stresses and transformation of the velocity profile occurs. The emerging fluid from the capillary extends to a jet, accompanied by stress and velocity rearrangement. There is a flow transition from uniaxial tension from shear flow. The elongation of the fluid jet involves the passing of a fluid jet through a cross section with a known velocity distribution and normal stress is experienced with shear flow in spinneret. Fiber solidification involves the freezing of the spinning fluid into a solid fiber with simultaneous changes in viscosity, modulus and yield stress, which are measurable physical properties (Brydson 1981a) (Fig. 1.2).

1.3 Types of Fiber Making Processes

Polysaccharides have been made into fiber by spinning methods depending on their thermal, chemical, mechanical or electrical properties. The process description and examples of each type of fiber manufacturing process are shown in Table 1.1.

Table 1.1 Types of fiber making processes

Type of fiber making process	Description of the fiber making process	Solidification process of the fiber	Polysaccharides manufactured using this type of process	References
Melt Spinning	An undiluted polymer melt extruded into a cooling chamber with air or non-volatile, non-reactive liquid	A solid fiber is formed from a temperature drop and volume contraction, resulting in fibers which are cylindrical in shape	Cellulose acetate butyrate (Eastman Chemical Company) with Cellulose Nanocrystals	
Dry Spinning	Polymer dissolved in a volatile solvent liquid. The fiber is formed by the evaporation of the liquid during spinning, resulting in a fiber with specific surface area	Solvent evaporation creates a solid fiber in one direction by diffusion of the solvent from filament that contract. Rapid solidification of outer layer creates non cylindrical shapes with well-developed surfaces	Cellulose acetate in acetone	
Wet Spinning	The polymer is precipitated from a liquid bath that does not dissolve the polymer and washed out during fiber formation	A solid fiber is formed by coagulation with relative diffusion rates of solvents and precipitating agents, leading to non-cylindrical shapes	Chitin Chitosan	Rathke and Hudson (1994), Sharma and Pillai (2009)
Gel Spinning	A combination of dry and wet spinning where the polymer is in a partially liquid state	A solid fiber is dried in air, then cooled in a liquid bath	Composities of cellulose or chitosan and lignin	Peretti et al. (2016)
Electrospinning	The polymer is spun using an electric force to draw charged fibers, while can also melt	A solid fiber is created by using charge d surfaces and deposited on an electrical neutral, grounded collector	Composties of cellulose or chitosan and lignin	Peretti et al. (2016)

(continued)

Table 1.1 (continued)

Type of fiber making process	Description of the fiber making process	Solidification process of the fiber	Polysaccharides manufactured using this type of process	References
Dispersion Spinning	Dispersion of polymer with a high melting point in an aqueous solution of another thermally destructible, fiber-forming polymer to form a homogeneous dispersion	Solvent evaporation or coagulation of the polymer creates a fiber. After spinning, a thermal treatment step is applied to destroy the fiber-forming polymer and fuse the actual polymer particles into fibers		
Reaction Spinning	Two prepolymers are mixed in a solution with some additives and are extruded through a spinneret	After exiting the spinneret, the filaments are heated in the presence of nitrogen and solvent and the two prepolymers react to form solidified fibers		

Melt spinning, dry spinning, wet spinning and electrospinning process diagrams are shown in Figs. 1.3, 1.4, 1.5 and 1.6. The structures of the surface, internal core and cross-sectional area are determined by each step of the manufacturing process. The solidification of the fiber spinning fluid forms the structure related to the strength and flexibility of the fiber. However, polysaccharides must be thermally and chemically stable under the conditions of spinning. The flow of the polysaccharide raw material involved in fiber spinning is also important to the material. This rheological behavior is described by mathematical relations between stress in a material subjected to deformation under known measurable conditions (Brydson 1981b). During spinning of fibers, changes in structure are influenced by material characteristics. These characteristics are viscosity, modulus and relaxation time, which are sufficient information for the prediction of flow behavior. Depending on the type of process, polysaccharide phase transitions can be crystallization and precipitation of the fiber from molten material (in melt spinning), solution (in dry and wet spinning) or charged material (in electrospinning). The solidification process involves the freezing of the spinning fluid into a solid fiber, which is one of the most important elements of the spinning process. Although the structure and physical properties of "as spun" fiber often differ from those of finished, drawn, washed and dried ones, the primary structures sets the conditions of further treatment and considerably affects the final properties. Solidification involves a change in many physical properties, such as viscosity, modulus and yield stress. An important structural process observed in some spinning solutions is gelation,

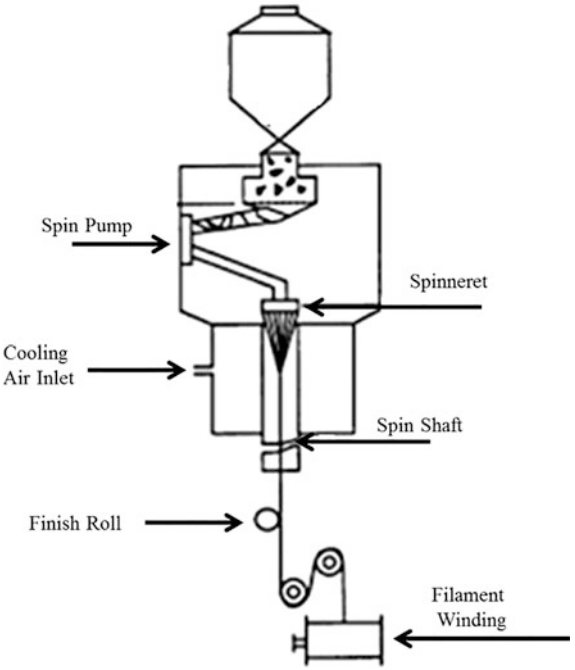

Fig. 1.3 Melt spinning process flowchart (Textile Engineer, Blogspot 2016)

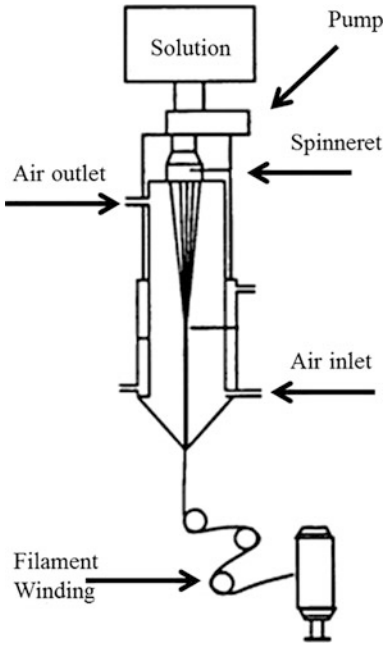

Fig. 1.4 Dry spinning process flowchart (Textile Engineer, Blogspot 2016)

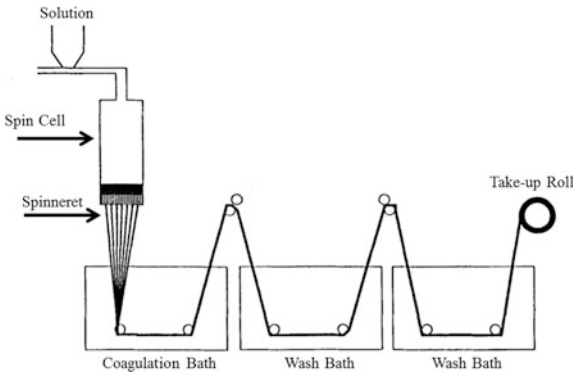

Fig. 1.5 Wet spinning process flowchart (Textile Engineer, Blogspot 2016)

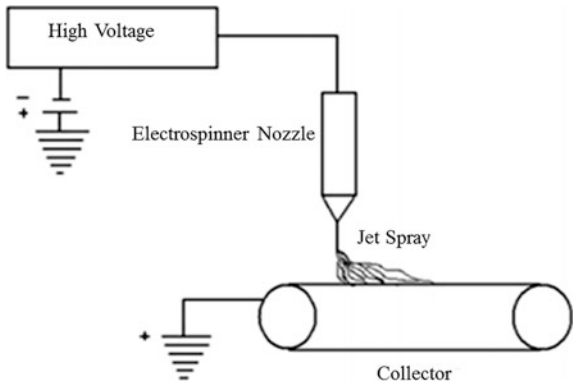

Fig. 1.6 Electrospinning process flowchart (Textile Engineer, Blogspot 2016)

which means transitions of a fluid into a homogeneous elastic gel without any phase separation.

The formation of the fiber structure is based on the nature of the fiber structure, which in turn determines their material properties for desired applications such as textiles, furniture, biocompatible materials and energy storage. Properties are a result of the characteristics of the polysaccharide chemical structure and process parameters during spinning, drawing and post-treatment.

The shape of the fiber cross section is determined mainly by the volume change accompanying the spinning process. Melt-spun fibers, where volume contraction is only about 10%, exhibit as a rule, cylindrical shapes. In dry spinning, one direction diffusion of the solvent from filament leads to large contraction and as a result, of rapid solidification of the outer most layers to non-cylindrical shapes with well-developed specific surfaces. In wet spinning, the volume change is determined by relative diffusion rates of solvent and precipitating agent and high rates of solvent diffusion, leading to non-cylindrical shapes (Zhang 2014). Commonly used

solvents are water, organic acids such as acetic acid and organic solvents such as acetone. These are generally recognized as safe organic solvents by the government regulatory agencies on environmental health, food, and pharmaceuticals.

1.4 Characteristics of Polysaccharides During Fiber Processing

The molecular structure and physical morphology of the natural polysaccharides and their chemically manufactured derivatives are important to know for fiber processing, to control the process parameters that change these molecular and macroscopic properties. Parallelization and extension of structural units as individual macromolecules, crystallites, aggregates, along the fiber axis in the course of spinning are among the most important structural processes in fiber technology. The degree of orientation affects the mechanical, sorptional and optical properties of fibers. It should be noted that the resulting degree of orientation may be unequally distributed between various structural units.

For fibers from various botanical origins, there are differences in the cellulose content and helix angles as shown in Table 1.2. Cellulose chains form microfibrils at a helix formation. Lower helix angles result in higher tensile modulus of the fiber. Another physical property of these natural fibers are their diameters and degree of crystallinity of the cellulose. The diameters of most microfibrils in most natural cellulose fibers are the same although their internal structures exhibit varying degrees of crystallinity. Natural cellulose and manufactured cellulose fibers have different crystalline structures. For example, for cellulose fibers with crystalline and amorphous content, the orientation factor for rigid parts as crystallites may be different from that for elastic, deformable amorphous regions. Crystallinity affects the tensile draw strength, maximum draw ratio, elongation, density, dyeability and other physical properties. These are demonstrated in spinning cellulose and chitosan composite fibers (Peretti et al. 2016).

Cellulose is an abundant polysaccharide, estimated at an annual global biomass production to be 1.5×10^{12} tons. It is considered a renewable source of raw material to meet the demand for sustainable and biocompatible materials and composite products (Fink et al. 2014).

The industrial manufacturing of cellulose fibers can be classified as the direct method or derivative method. In the direct method, special solvents are used without chemical modification of the cellulose. These special solvents are usually composed of two components, one example of which is using NMMO/water (*N*-methylmorpholine-N-oxide/H_2O) to obtain a homogeneous solution of cellulose that is extruded through a spinneret into water to obtain filaments. In the derivative method, cellulose polymer chains are chemically modified to form cellulose derivatives, which then are dissolved and spun into fibers. Production of manufactured cellulose fibers can be made using either the viscose, cuprammonium, and carbamate

Table 1.2 Fibers from plant parts with their respective cellulose content and helix angles

Cellulose fiber	Plant part origin	Content (weight %)	Helix angle (°)
Cotton	Seed	8S–95	20–30
Hemp	Bast	70–32	6.2
Pineapple	Leaf	70–82	6–14
Jute	East	51–84	8.1
Flax	East	60–81	5
Ramie	Bast	6S–75	None
Sisal	Leaf	43–78	10–22
Phomiijrn	Leaf	67	None
Banana	Leaf	60–65	11–12
Abaca	Leaf	61–64	None
Kenaf	Bast.	44–57	None
Coconut coir	Fruit	43–46	39–49
Bagasse	Bast	32–AS	None
Bamboo	Bast	25–43	None
Kapok	Seed	13	None

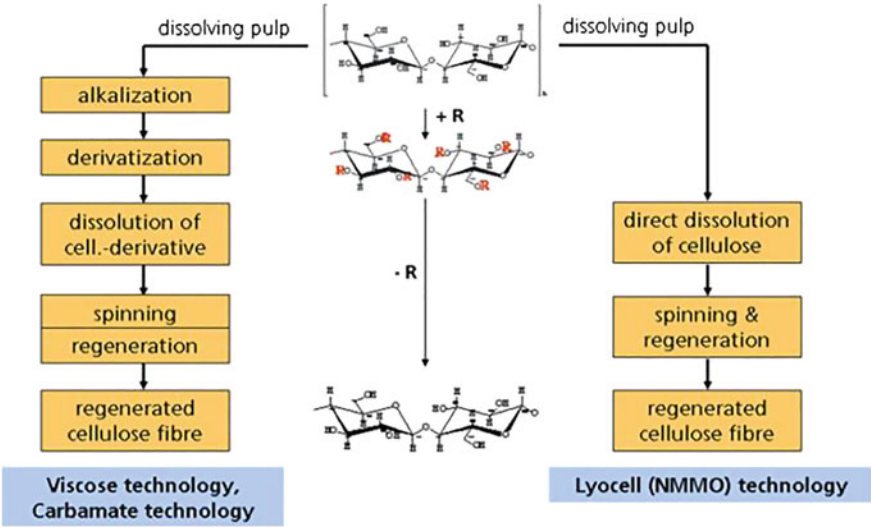

Fig. 1.7 Processes for making cellulose regenerated cellulose fiber technologies (Fink et al. 2014)

process. In these processes, the cellulose is chemically modified, regenerated into cellulose after the extrusion, and called rayon fibers. However, useful fibers can be produced by derivative methods without the regeneration of cellulose. Two important examples are cellulose acetate and cellulose triacetate fibers, which keep their derivative structure in the final forms of the fibers (Fig. 1.7).

1.5 Factors Influencing Polysaccharide Fiber Drawing

Spinning methods can convert polysaccharide melts or solutions into fibers. Different modes of drawing can improve the properties of the fibers by providing large, irreversible elongation to as-spun solid fibers to 20–8000% of their original lengths. This fiber elongation enables extension and parallelization of polymer chains and crystallites along the fiber axial direction, and the molecular orientation developed in drawing often is accompanied by changes in phase structure, such as crystallization or partial destruction of crystallites, and in other structural characteristics. Polysaccharide fiber drawing involves drawing of the initially amorphous filaments, drawing of crystallized filaments and heat treatment after drawing. Drawing changes the molecular orientation and the amorphous and crystalline phases of the filaments. Heat treatment stabilized the fiber dimensions, equilibrate the crystalline structure, improve the mechanical properties and modifies the chemical structure through cross-linking. Heat treatment in a free state is more effective in minimizing the residual shrinkage while the treatment under tension is effective in reducing the strain-at-break (Ziabicki 1988).

1.6 Technical Challenges and Opportunities in Polysaccharide Fiber Processing

Studying the flow properties of the polysaccharides identifies faults in the fiber spinning process. Choosing the polysaccharide and a polymer to form a composite for a specific application is important in understanding the flow properties that result in the structure of the fiber. A specific example is characterizing the flow behavior of molten polymer or polymer melts during extrusion through a capillary by measuring its viscosity and pressure drop across the capillary through commercially available capillary rheometers or parallel plate rheometers. Capillary rheometers are prone to clogging during measurements. Parallel plate rheometers are limited to the spread of the top plate and also does not consider the entrance effects of the spinning fluid during extrusion into a spinneret. During fiber making, an operator would be able to control the processing parameters (temperature and molecular weight of the polymer) to know the resulting properties (such as shape, cross-sectional area, and surface properties), and the amount of polysaccharide or polymer composite (grams per unit time) to meet a desired specified property and denier of fiber. During fiber formation through a pipe or capillary, assumptions are made which include:

(1) There is no velocity at the wall which is known as “no slip” at the surface of the wall;
(2) The velocity profile throughout the pipe is the same (which is assumed as steady state);

(3) The fluid is time independent, meaning that the shear rate is dependent on stress and nothing else;
(4) The flow is isothermal;
(5) The fluid is incompressible and has constant viscosity.

These assumptions must be verified when analyzing the flow through a fiber formation pipe or capillary.

Current opportunities in product development involve using recycled fiber from paper recycling as a source of polysaccharide fibers and demonstrating the formation of fibers from hemicellulose. Fibers from recycled paper (Hubbe et al. 2007) and hemicellulose from the papermaking (Hamaguchi et al. 2013) have been characterized, but these materials have not been spun intro fiber composites. In chitosan and chitin fiber formation, comparative coagulation studies should be performed to investigate the effect of a coagulant to allow polysaccharide regeneration or solidification (Sharma and Pillai 2009).

References

Brydson JA (1981a) Flow properties in flow properties of polymer melts. Van Nostrand Reinhold Company. Chapter 1, pp 1–20

Brydson JA (1981b) Flow through channels of simple cross section in flow properties of polymer melts. Van Nostrand Reinhold Company. Chapter 2:21–34

Fink HP, Ganster J, Lehmann A (2014) Progress in cellulose shaping: 20 years industrial case studies at Fraunhofer IAP. Cellulose 21(1):31–51

Gagov A (2007) Instabilities in elongation flows of polymers at high Deborag Number. PhD Dissertation. University of Akron

Hamaguchi M, Kautto J, Vakkilainen E (2013) Effects of hemicellulose extraction on the kraft mill operation and energy use: review and case study with lignin removal. Chem Eng Res Des 91:1284–1291

Hooshmand S, Aitomaki Y, Skrifvars M, Mathew AP, Oksman K (2014) All-cellulose nanocomposite fibers produced by melt spinning cellulose acetate butyrate and cellulose nanocrystals. Cellulose 21:2665–2678

Hubbe M, Venditti R, Rojas O (2007) What happens to cellulose fibers during papermaking and recycling? A review. Bioresources 2(4):739–788

Peretti SW, Barton R, Mendonca, RT (2016) Lignin as Feedstock for fibers and chemicals in commercializing biobased products: opportunities, challenges, benefits, and risks (pp.): The Royal Society of Chemistry. Chapter 7, pp 132–165

Rathke TD, Hudson SM (1994) Review of chitin and chitosan as fiber and film formers. J Macromol Sci, Part C 34(3):375–437

Sharma CP, Pillai CKS (2009) Chitin and chitosan polymers: chemistry, solubility and fiber formation. Prog Polym Sci 34:641–678

Textile Engineer @ Blogspot http://textileengineerr.blogspot.com/2010/10/types-of-spinning-man-made-fibers.html. Accessed 28 Feb 2016

Zhang X (2014) Fundamentals of fiber science. DEStech Publications, Inc

Ziabicki A (1988) The mechanisms of neck-like deformation in high speed melt Spinning. 1. Rheological and dynamic factors. J Nonnewton Fluid Mech 30:141–155

Chapter 2
One Step Dissolution, Extrusion, and Fiber Spinning of Chitin Using Ionic Liquid Solvents

Chenchen Zhu, Robert M. Richardson, Yuangqiang Song and Sameer Sharad Rahatekar

Abstract In this chapter we will discuss a one-step dissolution and fibre spinning method for chitin using ionic liquid 1-Ethyl-3-Methylimidazolium Acetate (EMImAc) as an environmentally benign solvent. A temperature-sensitive behaviour of chitin/EMImAc solution was observed during the fibre extrusion process. The regenerated chitin fibres were characterised through Fourier Transform Infrared Spectroscopy (FTIR), tensile testing, Scanning Electron Microscopy (SEM) and Wide Angle X-ray Diffraction (WAXD). Both molecular alignment and mechanical properties of chitin fibre increased as the draw ratio increased, confirmed by tensile testing results and the full width at half maximum (FWHM) of WAXD azimuthal scans. The regenerated chitin fibres with well controlled length, and good mechanical properties reported in this work could be potentially useful to explore the second most widely available polymer in nature for engineering and biomedical applications.

Keywords Extrusion · Fiber · Melt Spinning · Chitosan

2.1 Introduction

Chitin is considered to be the most widespread polysaccharide in living organisms (Muzzarelli 1977) and the second most abundant natural polymer in the world after cellulose (Dutkiewicz 2002). Chitin and its derivatives attract wide attention due to

C. Zhu · Y. Song · S.S. Rahatekar (✉)
Advanced Composites Centre for Innovation and Science (ACCIS), Aerospace Engineering, University of Bristol, Bristol BS8 1TR, UK
e-mail: Sameer.Rahatekar@bristol.ac.uk

R.M. Richardson
H H Wills Physics Laboratory, University of Bristol, Bristol BS8 1TR, UK

Y. Song
School of Energy Science and Engineering, University of Electronic Science and Technology of China, Chengdu 610054, China

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their industrial applications, such as in the manufacturing of textile, recovery of metal ions, water purification (Cardenas et al. 2004), food industry (Peter 1995) (value-added food products (Revahmoiseev and Carroad 1981), preservative (Shahid et al. 1999), packaging material (Kittur et al. 1998), etc.), pharmaceutical and cosmetic formulations (Ramos et al. 2003), drug/gene delivery (Sato et al. 2001) immobilisation of enzymes and flocculation (Krajewska 2004), as well as tissue engineering (Singh et al. 2013). Chitin possesses excellent properties including biocompatibility (Krajewka 2004), biodegradability, nontoxicity, physiological inertness, antibacterial activity, hydrophilicity, gel-forming properties, and affinity for protein (Rinaudo 2006). These biological advantages in combination with good mechanical properties also make chitin a good candidate material for wound sutures, one of the most widely used implants in the human body (Yang and Wu 2001). However, due to the inter- and intra-sheet hydrogen bonding involving acetyl amide groups, chitin is insoluble in traditional solvents like water and ethanol (Qin et al. 2010). Most of the traditional dissolution processes of chitin use toxic, corrosive, non-degradable or mutagenic solvents, such as formic acid–dichloroacetic acid (DCA) mixtures (Tokura et al. 1979), methanesulfonic acid (MSA) (Nishi et al. 1979), N,N-dimethylacetamide (DMAc)/lithium chloride (LiCl) (Poirier and Charlet 2002), NaOH- ice mixture (Einbu et al. 2004), and 1,1,1,3,3,3-hexafluoro-2-propanol (HFIP) (Min et al. 2004), which make the manufacturing processes of regenerated chitin products difficult to handle (Jaworska et al. 2012) and scale up (Synowiecki and Al-Khateeb 2003). Hence, despite the abundance of chitin, the lack of an environmentally benign process to manufacture regenerated chitin makes the large scale utilisation of chitin more difficult.

Ionic liquids (ILs) have received much attention as environmentally benign solvents of natural polymers (Zhu et al. 2006; Singh et al. 2014; Fox et al. 2003) for their low toxicity, good chemical and thermal stabilities (Zhu et al. 2006), high decomposition temperatures, low vapour pressure, low flammability (Fox et al. 2003), and recyclability (Hermanutz et al. 2008). The first attempt of the dissolution of chitin at room temperature ILs was conducted by Green's group (Green et al. 2006). A number of other researchers have used ILs for the dissolution of chitin (Singh et al. 2013; Qin et al. 2010; Jaworska et al. 2012; Wu et al. 2008; Wang et al. 2010). Most of their work based on the dissolution of chitin focused on the rheological study (Ding et al. 2012), or the regenerated films (Wang et al. 2010), foam (Singh et al. 2013) and gels (Wu et al. 2008). Recently regenerated chitin fibers were produced by Qin and Rogers's group (Qin et al. 2010). 25 wt% pure chitin, 10 wt% pure grade (PG) chitin and 10 wt% shrimp shell were dissolved in 1-ethyl-3-methylimidazolium acetate (EMImAc), respectively, by oil-bath heating and stirring the solutions at 100 °C for 19 h. However, undissolved chitin residues were found in solutions and needed to be removed by centrifuging after diluting the solutions with DMSO. Rogers's team also reported several studies on the dry-jet wet spinning of regenerated chitin fibers from the chitin/EMImAc solutions prepared by microwave-heating for 2 min and vigorous stirring between every 3 s heating pulses (Qin et al. 2010; Barber et al. 2013). The chitin from different sources was dissolved in EMImAc using this method, however the solution was

required to be removed from the microwave oven for stirring several times during this preparation process. This multiple-step operation is likely to be difficult to scale up for industrial applications.

In the current chapter, a one-step process for the dissolution of chitin prepared by oil-bath heating and magnetic stirring is reported. Furthermore, strong temperature-dependant fiber spinnability (ability to form stable and stretchable fiber from the chitin/EMImAc solution) was observed in the chitin solution prepared using the one-step dissolution method. The relationship the between the fiber winding velocity and the degree of the alignment of chitin fibers was systematically studied using a combination of tensile testing and wide angle X-ray diffraction. This study will be specifically useful for improving the manufacturing process of chitin fibers of well controlled length, diameter and specific mechanical properties using ILs as environmentally benign solvents, for potential medical applications such as tissue, scaffolds and wound sutures.

2.2 Experimental Section

2.2.1 Materials and Methods

The ionic liquid (IL) 1-Ethyl-3-Methylimidazolium Acetate (EMImAc) was purchased from Sigma-Aldrich (Gillingham, UK). The chitin from snow crab with a number-average molecular weight (Mn) of 1,000,000 Da was purchased from Heppe Medical Chitosan GmbH (Heinrich-Damerow-Straße, Germany). A magnetic stirrer hotplate (Fisher scientific, Loughborough, UK) with oil bath was used for the solution preparation. The dissolution process was carried out in a fume hood. 1.2 g chitin (3 wt% with respect to the mass of EMImAc) was added to 40 g EMImAc. The solution was heated at 145 °C for 6 h with stirring at 100 rpm to achieve the dissolution of chitin.

2.2.2 Fiber Spinning of Chitin

Specifically-designed fiber spinning equipment (Rondol, UK), which consists of a vertical ram extruder, a water bath and a haul off unit, was used for the dry-jet wet fiber spinning of chitin (Fig. 2.1).

After complete dissolution, chitin/EMImAc solution was transferred into the removable steel barrel. The solution in the barrel was degassed in a vacuum oven at 80 °C for 16 h to remove bubbles before spinning. The schematic of the fiber spinning process is shown in Fig. 2.1. The chitin/EMImAc solution dope was injected through a 1 mm-diameter nozzle into the water coagulation bath at constant temperature of 60 °C and constant extrusion velocity (V_1) of 0.09 m/s.

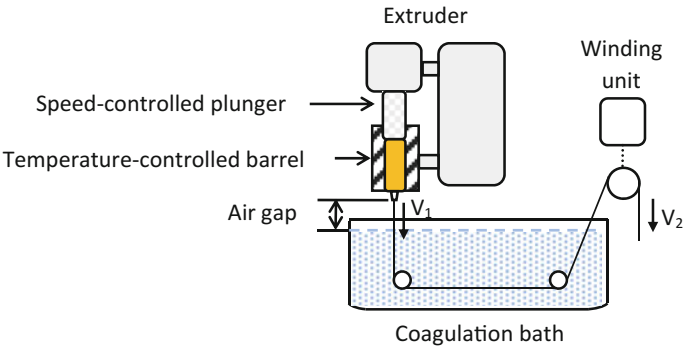

Fig. 2.1 Schematic of dry-jet wet fiber spinning process for chitin with a constant extrusion velocity V_1 = 0.09 m/s and various winding velocities (V_2)

Meanwhile, the winding drum and electric motor were continuously winding the fibers at varying winding velocities (V_2) of 0 m/s (draw ratio = 0), 0.13 m/s (draw ratio = 1.4) and 0.28 m/s (draw ratio = 3.1) downstream, which are hereafter referred to as Fiber set A, B and C, respectively. The air gap between the nozzle and water surface was 1 cm. After spinning, the chitin fibers were immersed in distilled water for two days, with a change of water every 24 h. Then the fibers were rolled and dried in a fume hood for another 48 h.

2.2.3 Characterization of Chitin/EMImAc Solution and Chitin Fibers

The Fourier Transform Infrared Spectroscopy (FTIR) reflection was performed on a Spectrum 100 FTIR spectrometer produced by PerkinElmer (Massachusetts, USA). A total of 4 cumulative scans were taken, with a resolution of 4 cm^{-1}, in the wavenumber range between 4000 and 650 cm^{-1} under the absorbance mode.

The diameter measurements of chitin fibers were carried out using a DMI 3000B microscope under TL-BF method, produced by Leica Microsystems CMS GmbH (Wetzlar, Germany). Three photos on different locations of every fiber sample were taken. For every microscope picture, three different locations' diameters were measured using the ImageJ software package. Thus, for all chitin fiber samples, nine different locations' fiber diameters were measured. The average diameter and the standard deviation of regenerated chitin fibers were calculated.

To observe the cross-sections of chitin fiber, three random picked fiber samples of Fiber set A, B and C were mounted vertically into a cylindrical resin mould, respectively. The resin moulds were composed of PRIME™ 20LV epoxy resin and PRIME™ 20 slow hardener purchased from Gurit (Newport, UK) with a mix ratio (weight) of 100:26, then cured at room temperature for 2 days. The cross-sections

of the resin moulds were polished smoothly using Buehler Beta™ grinder polisher and Vector™ power head (Esslingen am Neckar, Germany). The shapes of the cross-sections of all single fiber samples mounted in resin moulds were lobulated like textile viscose fibers (Fink et al. 2001), observed using ZEISS Axio Imager 2 microscope (Cambridge, UK). The fiber cross-section area was calculated using Eq. (2.1).

$$A = \frac{\pi d^2}{4} \tag{2.1}$$

where A is the fiber cross-section area and d is the fiber diameter. All the measured cross-section area were found to be smaller than the ones calculated using the microscopy diameters. This indicates that, due to the lobulated shapes of cross-sections of chitin fibers, it is not accurate to use the microscopy diameters of chitin fibers in the calculation of cross-section area as well as mechanical property. Thus, the average cross-section area measured from resin mounted filaments were used to calculate the Young's modulus and tensile strength of chitin fibers in tensile testing.

The tensile testing was carried out using a Dia-stron LEX820 single fiber tester (Hampshire, UK), containing a 20 N capacity load cell with a resolution of 0.5 mN. The tensile samples were prepared by mounting single fiber filaments between two plastic tabs on a 20-slot linear plastic cassette with a gauge length of 2 cm. Every single fiber filament was located straight and tightly on the tabs using DYMAX 3193 UV adhesive (Wiesbaden, Germany). The tabs were clamped horizontally between a fixed jaw and a movable jaw. The tensile samples were prepared for each kind of fibers and tested at the same strain rate of 10%/min. The tensile testing was controlled through UvWin PC application. The tensile load and displacement data points were recorded automatically with an interval of 50 ms during the testing. The tensile strength and breaking strain were calculated from the tensile load and displacement after tensile testing using Eqs. (2.2) and (2.3). Due to the bad alignment of chitin chains along the fiber axis and the large fiber diameters, both attributed to the slow spinning velocity, Fiber set A of chitin possessed suboptimal mechanical properties and was therefore excluded from the tensile testing. Twelve samples of Fiber set B and C were tested to failure.

$$\sigma = \frac{F}{A} \tag{2.2}$$

$$\varepsilon = \frac{l}{l_0} \tag{2.3}$$

where σ is the tensile strength, ε is the breaking strain, F is the largest tensile load before breaking, l is the displacement, l_0 is the fiber gauge length before tensile testing, and A is the fiber cross-section area.

All samples for Scanning Electron Microscope (SEM) analysis were prepared using Agar Scientific High Resolution Sputter Coater with 15 nm-thickness silver sputter coating. The fiber samples were stretched and broken manually at room temperature. The outer surfaces and cross-sectional areas of the samples were revealed and further observed by using JEOL IT300.

The Wide Angle X-ray Diffraction (WAXD) patterns of chitin single filaments of Fiber set B and C were obtained, respectively, using a GANESHA 300 XL SAXS system in the School of Physics at University of Bristol. It consists of an x-ray generator producing Cu Kα radiation with a wavelength of 0.154 nm, a sample stage and a detector inside a vacuum chamber, as well as data reduction and analysis software named SAXSGUI.

2.3 Temperature-Sensitive Fiber Spinning Behavior of Chitin/EMImAc Solution

The injection of chitin/EMImAc solution out from a syringe showed a temperature-sensitive behavior (Fig. 2.2). When the chitin/EMImAc solution was heated to 60 °C or higher before injection, the surface of the solution dope was smooth and shining (Fig. 2.2a). When the solution was cooled to room temperature, the surface of the injected solution dope became rough and dull, which severely reduced the ability of the spinning dope to be stretched or drawn in form of a continuous fiber (Fig. 2.2b).

To find the best injection temperature, a series of experiments were conducted by heating chitin/EMImAc solutions to different temperatures before fiber spinning under the same conditions. It was found that when the solution was heated to 60 °C, the draw ratio was the highest, which can give the best chitin molecular alignment along the fiber axis.

It was believed that the observed temperature-sensitive behaviour is caused by the variable solubility of crystalline and amorphous zones coexisting in chitin[22]. The amorphous domains of native chitin can be dissolved in ILs. However, the highly packed, compact crystalline domains cannot be completely dissolved, but get dispersed in the form of small particles in the solution[22]. It is further believed that, at high temperature, a higher concentration of chitin can be dissolved and the undissolved chitin crystalline domains disperse well in the low viscosity chitin/EMImAc solutions. On injection, smooth and shining solution surfaces result. However, at low temperature, lower concentration of chitin can be dissolved, the undissolved crystalline domains aggregate more strongly, and the die effect is more obvious in the high viscosity solutions. On injection, rough solution surfaces result (Fig. 2.2b). For this reason, the extruder barrel was heated to a constant 60 °C to prevent the solution temperature dropping before injection when the Fiber set A to Fiber set C were made.

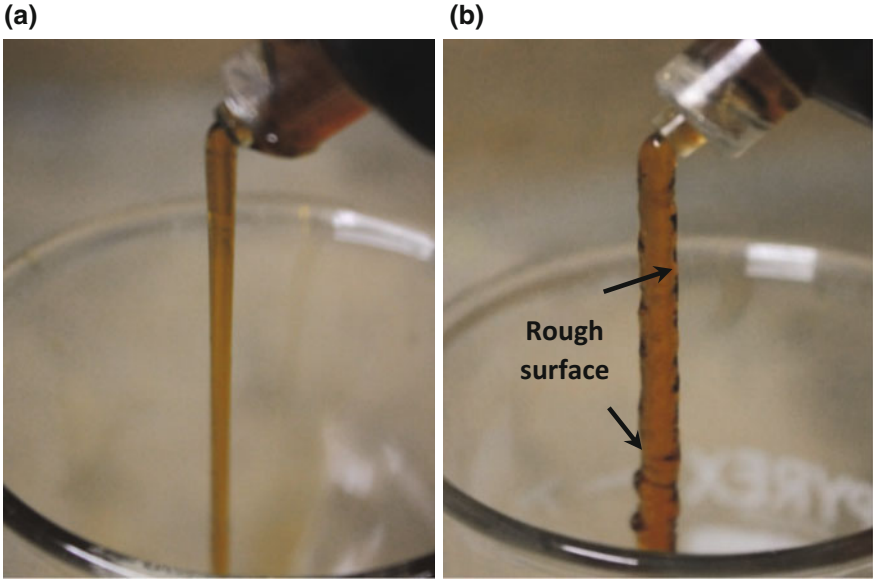

Fig. 2.2 Observation of chitin/EMImAc solution dope **a** heated to 60 °C and **b** cooled to room temperature (before injection). At 60 °C, higher concentration of chitin were dissolved and the undissolved chitin crystalline domains dispersed well in the low viscosity chitin/EMImAc solution, resulting in smooth and shining solution surfaces on injection. At room temperature, lower concentration of chitin were dissolved, the undissolved crystalline domains aggregated more strongly, and the die effect appeared more obvious in the high viscosity solution, resulting in rough solution surfaces on injection

2.4 FTIR Analysis of Chitin Fiber

The FTIR spectra of as-received chitin, regenerated chitin fiber and EMImAc are shown in Fig. 2.3.

The spectrum of chitin fiber is very similar to as-received chitin, indicating their similar structures before and after regeneration (Fig. 2.3a). The typical excitations shown on the spectrum of chitin, such as N-H anti-symmetric stretch (3264, 3261 cm^{-1}), N-H symmetric stretch (3113, 3108 cm^{-1}), C-N stretch (1548, 1557 cm^{-1}), C-H bend (1375, 1376 cm^{-1}), C–O–C anti-symmetric stretch (1155, 1155 cm^{-1}), and C-O stretch (1111, 1114 cm^{-1}) vibrations, are shown in both spectra of chitin fiber and as-received chitin (Fig. 2.3a) (Cardenas et al. 2004).

Both structures of as-received chitin and regenerated chitin fiber were confirmed to be α-chitin through FTIR. There are two absorption peaks in the spectra of regenerated chitin fiber (1647, 1627 cm^{-1}) and as-received chitin (1657, 1621 cm^{-1}), generated by C=O stretching vibration on amide I, which is a distinguishing feature of α-chitin structure instead of only one C=O peak appearing for β–chitin structure (Fig. 2.3b) (Rudall et al. 1963). This difference between α– and β–chitin is caused by the existence of two types of amides (Tanner et al. 1990). In

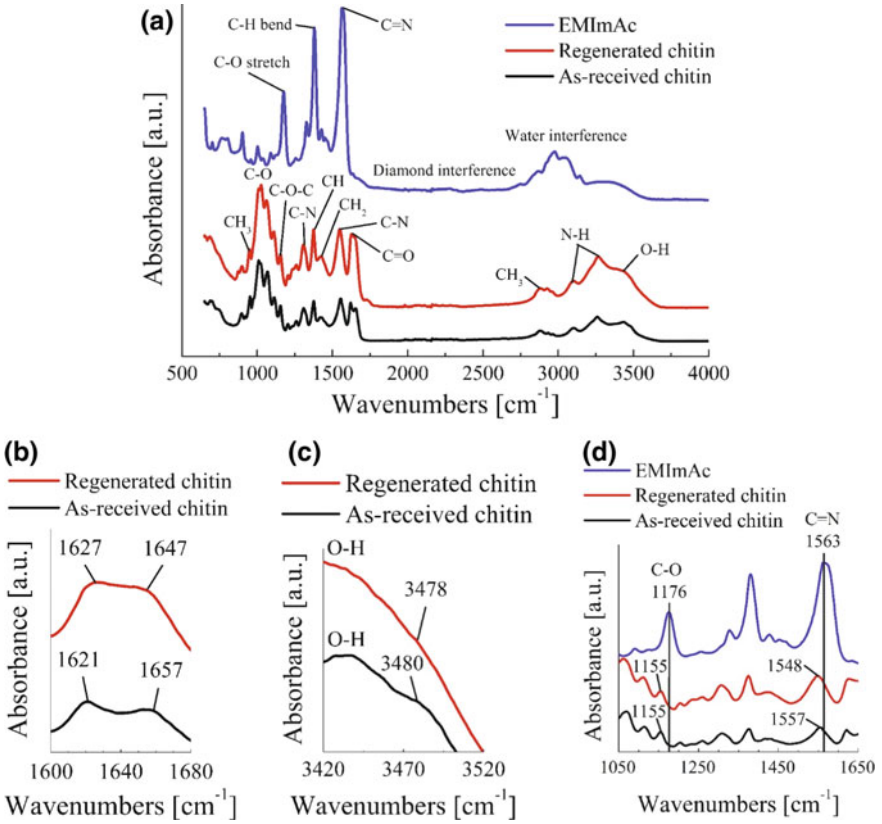

Fig. 2.3 FTIR spectra of **a** as-received chitin, chitin fiber and EMImAc between 650 and 4000 cm^{-1}; **b** as-received chitin and regenerated chitin fiber between 1600 and 1680 cm^{-1} and **c** 3420-3520 cm^{-1}, which show the α-chitin structures of chitin before and after regeneration; **d** as-received chitin, regenerated chitin fiber and EMImAc between 1050-1650 cm^{-1}, which shows the different wavenumbers of the C–O peak in EMImAc and the C-O-C peak in chitin as well as the larger C=N peak in EMImAc than the C-N peak in chitin as the evidence of completed removal of EMImAc from chitin fiber

α-chitin, half of the carbonyl groups generate intra-chain hydrogen bonds with an amino group (C=O···H-N), corresponding to the vibrations at 1647 cm^{-1} in regenerated chitin fiber and 1657 cm^{-1} in as-received chitin; the another half produce inter-chain hydrogen bonds with a primary alcohol group on the side chain, corresponding to the decreasing band at 1627 cm^{-1} in regenerated chitin fiber and 1621 cm^{-1} in as-received chitin (Miya et al. 1980). However, in β-chitin, only the first kind of intra-chain hydrogen bonds exists. The existence of extra inter-chain hydrogen bonds is responsible for the high chemical stability of α-chitin structure. The shoulders appearing in the spectra of both regenerated chitin fiber (3478 cm^{-1}) and as-received chitin (3480 cm^{-1}) also prove their α-chitin structures, which is

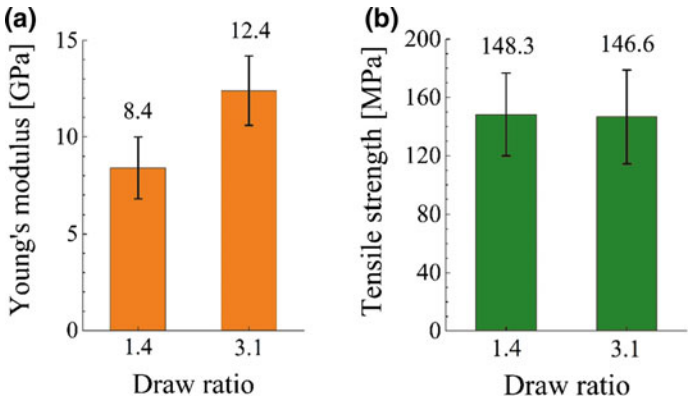

Fig. 2.4 **a** Young's modulus and **b** tensile strength comparision of chitin Fiber set B (draw ratio = 1.4) and Fiber set C (draw ratio = 3.1) spun at a constant extrusion velocity V_1 = 0.09 m/s

attributed to the intramolecular hydrogen bonds involving $O_6H\cdots O_2$'=C on with O_6 as donator absent in β-chitin (Fig. 2.3c) (Cardenas et al. 2004).

Peaks associated with the functional groups of EMImAc, such as the C-O stretch (1176 $cm^{-1)}$, C-H bend (1380 cm^{-1}) and C=N (1563 cm^{-1}) are similar to those in chitin (Fig. 2.3d) (FitzPatrick et al. 2012). However, the C-O peak in EMImAc is attributed to its carboxyl group, while the similar peaks in chitin before and after regeneration are attributed to the C-O-C ring. Therefore, compared with the larger C-O peak at longer wavenumber (1176 cm^{-1}) on the spectrum of EMImAc, exactly the same area of the C-O peak at the same wavenumber (1155 cm^{-1}) for chitin before and after regeneration proved that the EMImAc was removed completely from regenerated fibers (Fig. 2.3d).

2.5 Tensile Testing of Chitin Fibers

The tensile testing results of chitin fibers are shown in Table 2.1 and Fig. 2.4. With a constant extrusion velocity, the Young's modulus and tensile strength of chitin fibers increased as the draw ratio increased (Fig. 2.4 and Table 2.1), while the breaking strain decreased at the same time (Table 2.1).

Table 2.1 The Young's modulus, tensile strength, breaking strain and full width at half maximum (FWHM) of chitin (013) peak results for chitin Fiber set B (draw ratio = 1.4) and Fiber set C (draw ratio = 3.1)

Name	Fiber set B	Fiber set C
Young's modulus (GPa)	8.4 (±1.6)	12.4 (±1.8)
Tensile strength (MPa)	148.3 (±28.5)	146.6 (±32.2)
Breaking strain (%)	4.3 (±1.6)	2.1 (±0.9)
$FWHM_{(013)}$ (°)	31.5	29.8

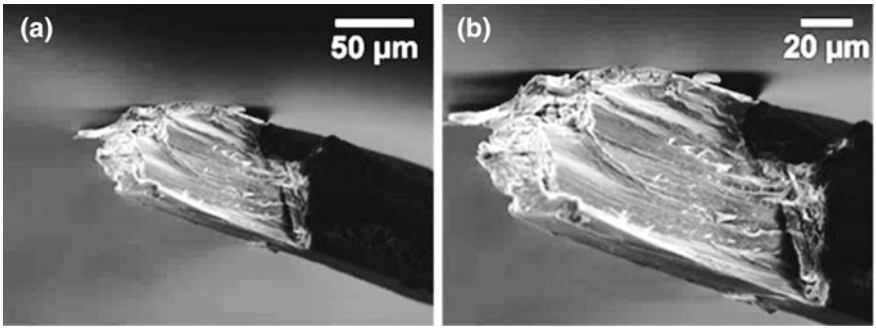

Fig. 2.5 **a**, **b** SEM images of fracturing cross-section of Fiber set B (draw ratio = 3.1) spun at a constant extrusion velocity V_1 = 0.09 m/s

As the draw ratio increased from 1.4 (Fiber set B) to 3.1 (Fiber set C), Young's modulus of chitin fibers increased from 8.4 GPa to 12.4 GPa (Fig. 2.4a), while breaking strain decreased from 4.3% to 2.1% (Table 2.1). This is because higher draw ratio stretches the same amount of injected chitin/EMImAc solution more in fiber-axis direction, resulting in better alignment of chitin molecules. However, the tensile strength of Fiber set B (148.3 MPa) and Fiber set C (146.6 MPa) appeared to be very similar (Table 2.1 and Fig. 2.4b), which might be due to the increasing fiber defects as the draw ratio increased.

2.6 SEM Analysis of Chitin Fibers

The fracturing cross-sections (perpendicular to fiber axis) after tensile testing of chitin Fiber set C (draw ratio = 3.1) were also observed under SEM (Fig. 2.5). It is found that the fibrillating structures of regenerated chitin fibers are apt to lateral splitting (Fig. 2.5b).

2.7 WAXD Analysis of Chitin Fibers

Figure 2.6a, b shows the two dimensional WAXD diffraction patterns of Fiber set B (draw ratio = 1.4) and Fiber set C (draw ratio = 3.1). Corresponding cellulose planes were labelled on the diffraction pattern of Fiber set B (Fig. 2.6a) (Al-Sawalmih et al. 2008; Ogawa et al. 2010). The radial scanning data (intensity against 2θ) of the diffraction patterns of Fiber set B and Fiber set C are shown in Fig. 2.6c and Table 2.2, which are relevant to the crystallinity of chitin fibers[3]. There are a (020) secondary peak at 9.3°, a (021) peak at 12.8°, a (040) shoulder peak at 18°, a (110) main peak at 19.5° and a (013) third peak at 26.7° for both Fiber set B and

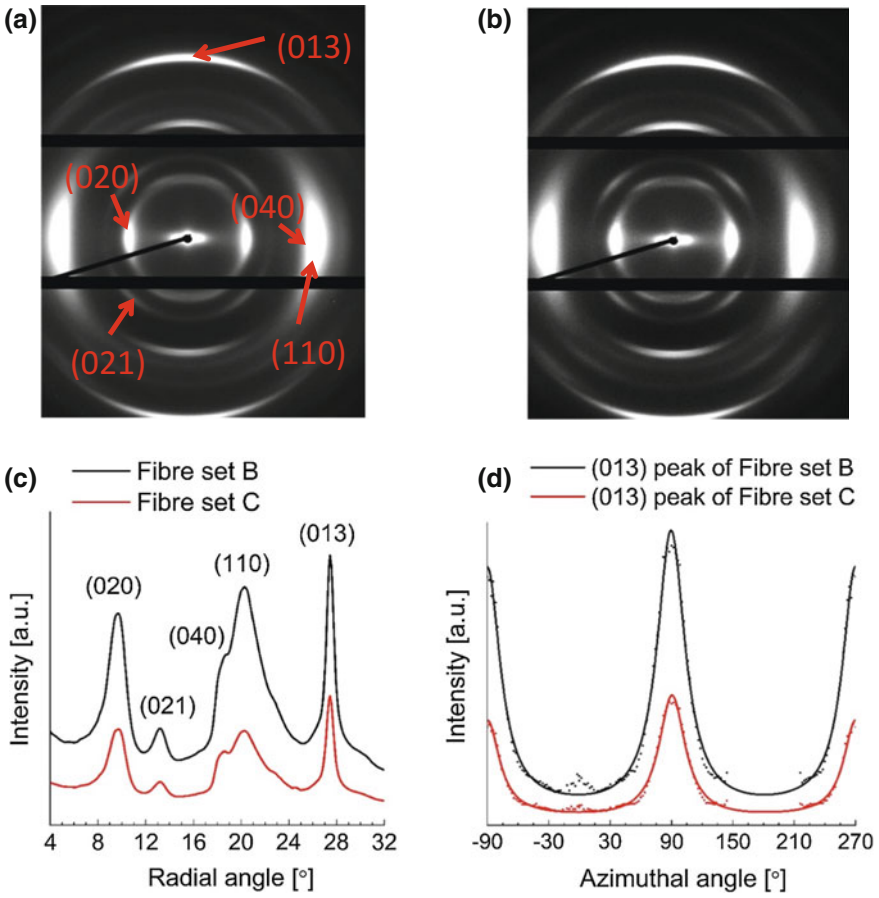

Fig. 2.6 WAXD patterns of single chitin filament for **a** Fiber set B (draw ratio = 1.4), **b** Fiber set C (draw ratio = 3.1), **c** integrated radial scans of Fiber set B (draw ratio = 1.4) and Fiber set C (draw ratio = 3.1) spun at a constant extrusion velocity V_1 = 0.09 m/s, as well as (D) azimuthal scans of the chitin (013) diffraction peaks of Fiber set B (draw ratio = 1.4) and Fiber set C (draw ratio = 3.1) spun at a constant extrusion velocity V_1 = 0.09 m/s

Fiber set C as shown in Fig. 2.6c and Table 2.2, all of which are signature peaks for the α-chitin crystalline structure[38] with similar radial angles compared with those reported by previous researchers (hereafter referred to as reference A-G) (Table 2.2) (Tamura et al. 2006).

In a stretched fiber, the chitin chains have a preferred orientation: with their longitudinal axes parallel to strain direction, which appeared as concentrated intensity at certain azimuthal positions on the diffraction peaks. The intensity became more anisotropic as the draw ratio increased, as shown in Fig. 2.6a, b (Gedde, 1995). The intensities of diffraction peaks of Fiber set B and Fiber set C corresponding to the chitin (013) planes were plotted as a function of azimuthal

Table 2.2 The radial scanning angles of chitin (020), (021), (040), (110), (120), (130) and (013) peaks for Fiber set B (draw ratio = 1.4) and Fiber set C (draw ratio = 3.1) compared with the corresponding angles reported in reference A-G (Tamura et al. 2006)

	Radial scanning angle (°)										
Peak	Fiber set B	Fiber set C	A[38]	B[3]	C[22]			D[28]	E[29]	F[37]	G[39]
(020)	9.3	9.3	9	9.24	9.27	8.97	9.2	9.44	9.4	9.2	9.2
(021)	12.8	12.8	12	12.9	12.66	12.76	12.7	12.83	12.8	–	–
(040)	18	18	–	–	–	–	–	–	–	–	–
(110)	19.5	19.5	18	19.18	19.21	19.37	19.44	19.21	19.3	19	19.4
(013)	26.7	26.7	26	26.14	26.36	26.36	26.42	26.25	26.4	–	26.8

angle and fitted by a Lorentzian function (Fig. 2.6d). The full width at half maximum (FWHM) is the difference in angle across the peak where the intensity is 50% of the maximum value. The FWHM of chitin (013) peaks were calculated as an estimation on the degree of alignment of molecular chains in chitin fibers (Table 2.1). The lower the value of FWHM is, the higher degree of molecular alignment is in chitin fibers (Yudin et al. 2014). As the draw ratio increased from 1.4 (Fiber set B) to 3.1 (Fiber set C), the FWHM decreased from 31.5° to 29.8° for (013) peak (Fig. 2.6 and Table 2.1).

2.8 Discussion

The direct information on chitin structures before and after regeneration as well as the confirmation of complete removal of EMImAc from regenerated chitin fibers were characterized through FT-IR. Cardenas's group applied FTIR on regenerated chitin from different sources to distinguish their α- and β-chitin crystal structures (Cardenas et al. 2004). Both groups of Ogawa and Ding used FTIR to identify the α-chitin structrures of their regenerated chitin (Ding et al. 2012). However, they did not apply FT-IR to confirm the complete removal of solvents after regeneration by comparing the spectra of regenerated chitin with the ones of applied solvents. The investigation on the complete removal of solvents from regenerated chitin is necessary, because it will exclude the possibility of the effect of remaining solvent on subsequent analyses of regenerated chitin fibers. FTIR is the easiest method for this investigation.

After the draw ratio increased to 3.1, the Young's modulus and tensile strength of our chitin fibers increased to 12.4 GPa and 146.6 MPa, while the breaking strain dropped to 2.1%. Qin and his team analysed the mechanical properties of shrimp shell chitin, practical grade chitin (PG-chitin) as well as the reconstituted shrimp shell chitin and reconstituted PG-chitin using ILs[14]. The modulus and strength of all those chitin in his study were lower than results in this study except the reconstituted shrimp shell chitin (modulus = 10 GPa, strength = 237 MPa). The

reconstituted shrimp shell chitin in his study was regenerated by dissolving natural shrimp shell directly in ILs, while the as-received chitin used in this study was extracted from snow crab through an industrial process before dissolving it in EMImAc. The higher molecular weight of chitin attributed to the processing might be the reason for better mechanical performances, which was also given by Qin et al. (2010).

2.9 Conclusion

A one-step dissolution method for chitin and manufacturing of regenerated chitin fibers with well controlled length, specific molecular alignment and mechanical properties using dry-jet wet spinning process was developed. The regenerated fibers shows α-chitin crystal structure, confirmed by FTIR and X-ray. As the draw ratio of chitin fibers increased from 1.4 (Fiber set B) to 3.1 (Fiber set C), their Young's modulus increased from 8.4 GPa to 12.4 GPa, tensile strength decreased slightly from 148.3 MPa to 146.6 MPa, and breaking strain decreased from 4.3% to 2.1%. The fracturing cross-sections of chitin Fiber set C (draw ratio = 3.1) under SEM confirmed that the regenerated chitin fibers have circular cross-sections and lateral splitting structures. The WAXD patterns of single chitin fibers contained the diffraction peaks corresponding to chitin (020), (021), (040), (110) and (013) planes existing in α-chitin structure. As the draw ratio increased from 1.4 (Fiber set B) to 3.1 (Fiber set C), the reductions in FWHM of WAXD azimuthal scans were observed for chitin (013) planes, which confirmed the increase of alignment of chitin chains along the fiber axis. The current work will be a valuable guideline to reduce the complexity in dissolution and regeneration of chitin fiber, thus allowing potential scale up of the process.

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References

Al-Sawalmih A, Li C, Siegel S, Fabritius H, Yi S, Raabe D, Fratzl P, Paris O (2008) Microtexture and chitin/calcite orientation relationship in the mineralized exoskeleton of the American lobster. Adv Funct Mater 18(20):3307–3314

Barber PS, Griggs CS, Bonner JR, Rogers RD (2013) Electrospinning of chitin nanofibers directly from an ionic liquid extract of shrimp shells. Green Chem 15(3):601–607

Cárdenas G, Cabrera G, Taboada E, Miranda SP (2004) Chitin characterization by SEM, FTIR, XRD, and 13C cross polarization/mass angle spinning NMR. J Appl Polym Sci 93(4):1876–1885

Ding BB, Cai J, Huang JC, Zhang LN, Chen Y, Shi XW, Du YM, Kuga S (2012) Facile preparation of robust and biocompatible chitin aerogels. J Mater Chem 22(12):5801–5809
Dutkiewicz JK (2002) Superabsorbent materials from shellfish waste—a review. J Biomed Mater Res 63(3):373–381
Einbu A, Naess SN, Elgsaeter A, Vårum KM (2004) Solution properties of chitin in alkali. Biomacromolecules 5(5):2048–2054
Fink HP, Weigel P, Purz HJ, Ganster J (2001) Structure formation of regenerated cellulose materials from NMMO-solutions. Prog Polym Sci 26(9):1473–1524
FitzPatrick M, Champagne P, Cunningham MF (2012) Quantitative determination of cellulose dissolved in 1-ethyl-3-methylimidazolium acetate using partial least squares regression on FTIR spectra. Carbohyd Polym 87(2):1124–1130
Fox DM, Awad WH, Gilman JW, Maupin, PH, De Long HC, Trulove PC 92003) Flammability, thermal stability, and phase change characteristics of several trialkylimidazolium salts. Green Chem 5(6):724–727
Green JM III, Fox DM, De Long HC, Trulove PC (2006) Using well known methods in unprecedented ways: The dissolution/reconstitution of chitin and chitosan using room temperature ionic liquids. Abstracts of Papers of the American Chemical Society, p 231
Hermanutz F, Gaehr F, Uerdingen E, Meister F, Kosan B (2008) New developments in dissolving and processing of cellulose in ionic liquids. Macromol Symposia 262:23–27
Jaworska MM, Kozlecki T, Gorak A (2012) Review of the application of ionic liquids as solvents for chitin. J Polym Eng 32(2):67–69
Kittur FS, Kumar KR, Tharanathan RN (1998) Functional packaging properties of chitosan films. Zeitschrift Fur Lebensmittel-Untersuchung Und-Forschung a-Food Res Technol 206(1):44–47
Krajewska B (2004) Application of chitin- and chitosan-based materials for enzyme immobilizations: a review. Enzyme Microb Technol 35(2–3):126–139
Min BM, Lee SW, Lim JN, You Y, Lee TS, Kang PH, Park WH (2004) Chitin and chitosan nanofibers: electrospinning of chitin and deacetylation of chitin nanofibers. Polymer 45 (21):7137–7142
Miya M, Iwamoto R, Yoshikawa S, Mima S (1980) I.r. spectroscopic determination of CONH content in highly deacylated chitosan. Int J Biol Macromol 2(5):323–324
Muzzarelli RAA (1977) Chitin. Pergamon Press, Oxford
Nishi N, Noguchi J, Tokura S, Shiota H (1979) Studies on chitin. I. Acetylation of chitin. Polym J 11(1):27–32
Ogawa Y, Kimura S, Wada M, Kuga S (2010) Crystal analysis and high-resolution imaging of microfibrillar α-chitin from Phaeocystis. J Struct Biol 171(1):111–116
Oh DX, Shin S, Lim C, Hwang DS (2013) Dopamine-mediated sclerotization of regenerated chitin in ionic liquid. Materials 6(9):3826–3839
Peter MG (1995) Applications and environmental aspects of chitin and chitosan. J Macromol Sci-Pure Appl Chem A 32(4):629–640
Poirier M, Charlet G (2002) Chitin fractionation and characterization in N N-dimethylacetamide/lithium chloride solvent system. Carbohydr Polym 50(4):363–370
Qin Y, Lu XM, Sun N, Rogers RD (2010) Dissolution or extraction of crustacean shells using ionic liquids to obtain high molecular weight purified chitin and direct production of chitin films and fibers. Green Chem 12(6):968–971
Ramos VM, Heras NM, Rodrı A, Agulló E (2003) Modified chitosan carrying phosphonic and alkyl groups. Carbohyd Polym 51(4):425–429
Revahmoiseev S, Carroad PA (1981) Conversion of the enzymatic hydrolysate of shellfish waste chitin to single-cell protein. Biotechnol Bioeng 23(5):1067–1078
Rinaudo M (2006) Chitin and chitosan: Properties and applications. Prog Polym Sci 31(7):603–632
Rudall KM (1963) The chitin/protein complexes of insect cuticles. In: Beament JWL, Wigglesworth JET, VB (eds) Advances in insect physiology. Academic Press: pp 257–313
Sato T, Ishii T, Okahata Y (2001) In vitro gene delivery mediated by chitosan. Effect of pH, serum, and molecular mass of chitosan on the transfection efficiency. Biomaterials 22(15):2075–2080

Shahidi F, Arachchi JKV, Jeon YJ (1999) Food applications of chitin and chitosans. Trends Food Sci Technol 10(2):37–51

Singh N, Koziol KKK, Chen J, Patil AJ, Gilman JW, Trulove PC, Kafienah W, Rahatekar SS (2013a) Ionic liquids-based processing of electrically conducting chitin nanocomposite scaffolds for stem cell growth. Green Chem 15(5):1192–1202

Singh N, Rahatekar SS, Koziol KKK, Ng TS, Patil AJ, Mann S, Hollander AP, Kafienah W (2013b) Directing chondrogenesis of stem cells with specific blends of cellulose and silk. Biomacromolecules 14(5):1287–98

Synowiecki J, Al-Khateeb NA (2003) Production, properties, and some new applications of chitin and its derivatives. Crit Rev Food Sci Nutr 43(2):145–171

Tanner SF, Chanzy H, Vincendon M, Roux JC, Gaill F (1990) High-resolution solid-state carbon-13 nuclear magnetic resonance study of chitin. Macromolecules 23(15):3576–3583

Tamura H, Nagahama H, Tokura S (2006) Preparation of chitin hydrogel under mild conditions. Cellulose 13(4):357–364

Tokura S, Nishi N, Noguchi J (1979) Studies on chitin. III. Preparation of chitin fibers. Polym J 11 (10):781–786

Wang WT, Zhu J, Wang XL, Huang Y, Wang YZ (2010) Dissolution behavior of chitin in ionic liquids. J Macromol Sci Part B-Phys 49(3):528–541

Wu Y, Sasaki T, Irie S, Sakurai K (2008) A novel biomass-ionic liquid platform for the utilization of native chitin. Polymer 49(9):2321–2327

Yang A, Wu RJ (2001) Mechanical properties and interfacial interaction of a novel bioabsorbable chitin fiber reinforced poly(epsilon-caprolactone) composite. J Mater Sci Lett 20(11):977–979

Yudin VE, Dobrovolskaya IP, Neelov IM, Dresvyanina EN, Popryadukhin PV, Ivan'kova EM, Elokhovskii VY, Kasatkin IA, Okrugin BM, Morganti P (2014) Wet spinning of fibers made of chitosan and chitin nanofibrils. Carbohyd Polym 108:176–182

Zhu SD, Wu YX, Chen QM, Yu ZN, Wang CW, Jin SW, Ding YG, Wu G (2006) Dissolution of cellulose with ionic liquids and its application: a mini-review. Green Chem 8(4):325–327

Chapter 3
Functional Nanofibers Containing Cyclodextrins

Ganesh Narayanan, Ramiz Boy, Bhupender S. Gupta and Alan E. Tonelli

Abstract The process of obtaining nanofibers from polymer solutions has been reported in the literature for the past two decades. However, only in the past few years, have nanofibers containing cyclodextrins (CDs) or their inclusion compounds (ICs) with low or high molecular weight compounds been extensively reported. These nanofibers exhibit superior properties compared to those of their neat polymer nanofibers. It has been observed that with the simple addition of CDs, marked increases in crystallinity, crystallizability, small molecule encapsulation capability, lowered hydrophobicity, and other surface functionalities can be achieved. In this chapter, an in-depth discussion of cyclodextrins, their structures, and inclusion complexes will be provided. Various strategies utilized to obtain those nanofibers functionalized with CDs or their ICs will be discussed. CD based technologies offer green alternatives for designing scaffolds with specific improved properties for growing cells and tissues. For example, increased small molecule encapsulation or release capability can be achieved, as well stronger nanofibers can be produced. Due to their excellent biocompatibility, biodegradability, and abundant availability, CDs and their ICs, offer excellent opportunities for producing functionalized nanofibers, which have not yet been extensively reported. For this reason, much of our focus in this chapter will concentrate on various strategies for future research in nanofibers functionalized with CDs and their ICs.

Keywords Electrospinning · Polymer-cyclodextrin nanofibers · Cyclodextrin nanofibers · Pseudorotaxane nanofibers · Filtration · Wound odor absorbance

G. Narayanan · R. Boy · B.S. Gupta · A.E. Tonelli (✉)
Fiber and Polymer Science Program, North Carolina State University,
Raleigh, NC 27606, USA
e-mail: alan_tonelli@ncsu.edu

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3.1 Introduction

3.1.1 Cyclodextrins

Cyclodextrins (CDs) are naturally occurring substance formed by the enzymatic degradation of the linear component of starch (amylose) (Jeang et al. 2005). CDs contain six or more (α-1,4)-linked glucopyranose units, and the most easily formed and widely used CDs are, alpha (α-CD), beta (β-CD), and gamma (γ-CD), containing six, seven, and eight glucopyranose units, respectively (Loftsson and Brewster 1996). Due to the chair conformation of their glucopyranose units, CDs adopt a truncated cone, instead of a cylinder like structure (Szejtli 1988). Their different number of glucopyranose units result in different molecular weights, cavity diameters, and water solubilities (Del Valle 2004). Amongst the three native CDs, α-CD has the smallest cavity size (5.7 Å), followed by β-CD (7.8 Å), and finally, γ-CD (0.95 Å). Schematic representations of these most widely used CDs are shown in Fig. 3.1.

The inner cavity of the CDs are lined with CH and CH_2 carbons, and ether oxygens, while their outer rims are lined with hydroxyl groups resulting in hydrophilic outer surfaces and inner cavities that are largely hydrophobic (Li and Purdy 1992). Although β-CD is the most widely available and has a slightly larger cavity size compared to α-CD, compared to both α- and γ-CDs, it has the lowest solubility in water (Narayanan 2014). This phenomenon has been attributed to the intermolecular hydrogen bonding between β-CDs in aqueous solution (Williamson 2010). To overcome the low aqueous solubility of β-CD, variety of chemical

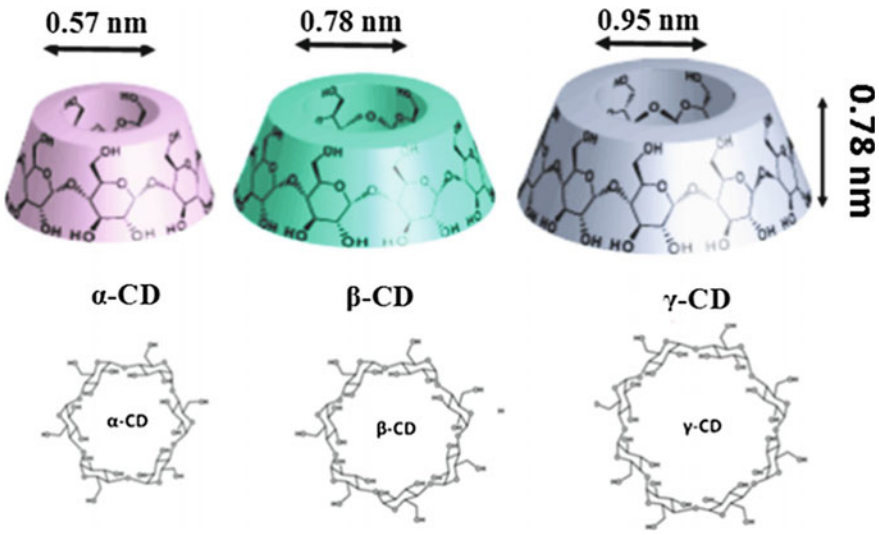

Fig. 3.1 Schematic representations of the native cyclodextrins (α-, β-, and γ -CDs) (Narayanan 2014)

modifications have been performed to obtain modified β-CD derivatives with improved aqueous solubility (Cui et al. 2010; Loftsson et al. 2015). Among the many modified β-CDs reported, the most widely used are randomly methylated (RAM-β-CD) and 2-hydroxypropyl β-CD (HP-β-CD) (Cui et al. 2010). A particular RAM-β-CD, heptakis(2,6-di-O-methyl)-β-CD (DIMEB) was once touted to be an excellent modified β-CD, owing to its excellent water solubility (at lower temperatures) and insolubility (at higher temperatures), which is favorable for easy separation. But unfortunately, due to its high cost and toxic preparation steps, it has fallen out of favor, and instead other RAM-β-CDs are being used. At lower substitutions, these RAM-β-CDs, although more hydrophobic than native β-CD, have higher water solubility, which is credited to their amorphous nature. HP-β-CD, on the other hand, owing to its hydrophilic nature, on complexation with cholesterol, does not result in the formation of cholesterol-HP-β-CD-IC complex crystals in the kidneys; hence it is not nephrotoxic (Li and Purdy 1992).

3.1.2 CD Inclusion Complexation

In their natural states, cavities of both native as well as modified CDs are occupied by water molecules. Because the water molecules reside inside a relatively apolar cavity, they are in an energetically unfavorable environment, which is readily stabilized by the replacement of the cavity water by less polar guest molecules (Rafati et al. 2005). Apart from apolar-apolar interaction between guest and the cavity, other effects may also play vital roles in complexation, including the reduced strain in the CD rings and van der waals interactions and hydrogen bonds between CD hosts and included guests (Astray et al. 2009). Depending on the size of the "guest" molecule, one, two or three CD molecules can be included/entrapped the guest molecules, which forms the essence of molecular encapsulation. CD-ICs thus formed generally precipitate, and can then be easily removed. Apart from a few inorganic compounds, especially inorganic salts, a wide variety of compounds including oligomers and polymers have been complexed, including those found in pharma formulations (Li and Purdy 1992).

In the case of the formation of polymer-CD-ICs, guest polymer is typically initially dissolved in organic solvents, such as acetone or formic acid, and the host CDs in water. Once both the guest and host are completely dissolved, either the CD: water solution or polymer:organic solvent solution is added in a drop by drop fashion accompanied by stirring and/or sonication to the other solution to avoid precipitation of the guest polymer or host CD. Once mixed, they are allowed to stir for about 48 h, by which time, complete precipitation of the polymer-CD-IC is observed. The precipitate is then washed several times with the solvents used for complexation, filtered and finally dried (See Fig. 3.2) (Wei et al. 2002).

Non-stoichiometric ICs are prepared when the stoichiometric molar ratios of CD: polymer are less than that required for full coverage of the guest polymers by the host CDs. Non-stoichiometric ICs are also called poly-pseudorotaxanes, and a

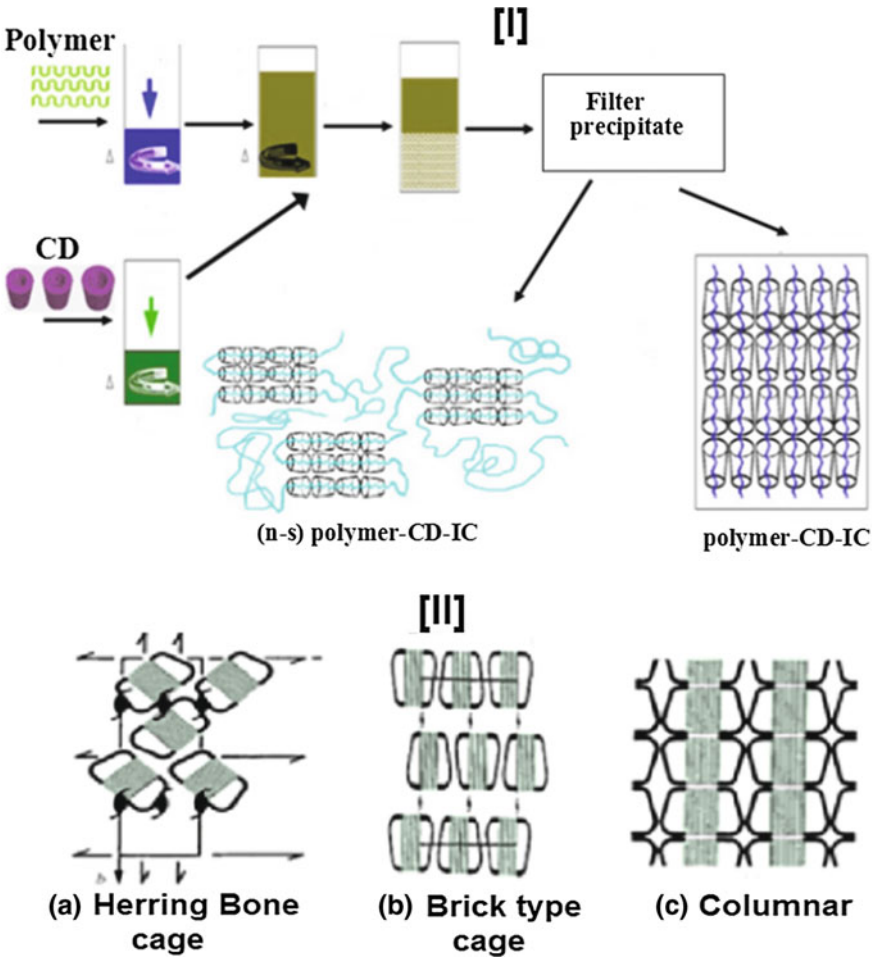

Fig. 3.2 Schematic of (i) polymer-CD-IC formation and (ii) crystal structures of CD-inclusion complexes (As an example of forming ICs, a schematic illustrating various steps typically undertaken to prepare polymer-CD-ICs are shown in Fig. 3.2I. Initially, polymer is dissolved in an organic solvent, and CDs are dissolved in water. Once clear solutions form, CD solution is added in a drop-by-drop fashion, forming a precipitate, which progressively settles at the bottom of the solutions. Once the reaction is complete, the precipitate is filtered and dried. As the polymer (or other long molecule guests) thread through the CD cavity, native crystal structure of CDs (herring or brick type cage) undergoes transformation into a columnar structure (Fig. 2IIC), which can be easily characterized by wide angle x-ray diffraction) (Wei et al. 2002)

permanent molecular necklace can be formed when both ends of the polymer chains are capped by bulky groups, such that the polymer chains cannot slip out of the CD cavities. Movement of the host CDs is then restricted to sliding along the axes of their permanently included and threaded guest polymer chains (Williamson and Tonelli 2012).

3.1.3 Applications of CDs

CDs are employed as IC hosts for guest molecules that need to be protected from sunlight, oxygen, chemical reaction, and to reduce their volatility. Apart from protecting the guest molecules, CDs are also used to enhance the solubility, control the release, and deliver the flavor of the guest molecules. Relatedly, CDs are also employed to form ICs and mask objectionable odors and bitter or strong flavors (Marques 2010). Based on these capabilities, it is quite obvious that CDs can be employed for a variety of applications. Some of the diverse sectors where CDs are employed include pharmaceutical, biological, food, pesticide, textiles, and analytical chemistry.

In the food and beverage industries, CDs are utilized to increase the shelf life of products containing sensitive ingredients. Several studies, both accelerated as well as long term, have indicated that CD containing products lasted longer, compared to traditional products (Linde et al. 2011). Utilizing CDs is also advantageous in cases where reactive ingredients are to be used in a product. CDs, in effect, prevent the mixing of two ingredients, thereby, protecting both ingredients from each other (Szejtli 2003). Flavorful compounds, such as essential oils and spice oils that are highly volatile, upon inclusion complexation, can be converted into microcrystalline products, making them easy to store, process and transport (Szejtli et al. 1979). This process also inhibits their biological and moisture absorption activities. Under enzymatic action, processed juices often turn brown, and this can be avoided by complexation with CDs. Food components that are bitter and/or sour, as found in fish oils and vitamins, can be made palatable by forming ICs with CDs, and their susceptibility to degrade upon exposure to air and heat also can be reduced (Na et al. 2011). CDs are also widely used in food packaging to avoid the deleterious effects of microbes (Ayala-Zavala et al. 2008).

Inclusion complexation was originally intended for pharma applications, which is evidenced by the number of publications in this field. Because of the low quantities used in pharma formulations, the volume of CDs used in pharma are only a distant second ($\sim$20% of total CDs), when compared to their food applications (Szejtli 1997). Complexation of drugs with CDs is considered under certain conditions where there is no alternative way to deliver the drug efficiently, for example, for drugs with poor solubility (Stegemann et al. 2007). When drug solubility is low, their bioavailability is poor, and injectable solutions cannot be prepared (Strickley 2004). Furthermore, some drugs are bitter, or exhibit poor stability on exposure to light, air, etc., and need protection from these elements (Szejtli and Szente 2005).

Even with these advantages, unfortunately, not all drugs can be complexed with CDs. Some of the reasons for their inability to complex or be utilized include: mismatch in molar mass (either too small or too large) (Arun et al. 2008), high hydrophilicity (Liu and Guo 1999), and extremely high complexed stability, rendering reduced bioavailability. Furthermore, their high molar mass and large number of hydrogen donors and acceptors restrict the ability of CDs to permeate biological barriers (Irie and Uekama 1998). In addition, toxicological evaluations

indicated β-CD not to be suitable for parenteral applications, as was α-CD, while γ-CD based formulations were deemed suitable. For oral applications, practically all drug-CD-ICs are non-toxic due to their poor adsorption by the gastrointestinal tract, with the exception of methylated β-CD, which exhibited some adsorption (ca. 10%). Currently, two modified CDs: 2-Hydroxypropyl-β-CD and sulfobutylether-β-CD are observed to possess excellent capabilities for drug delivery applications (Gould and Scott 2005; Rajewski et al. 1995). Some of the CD formulations currently used in pharma applications can be obtained from Loftsson and Brewster (2010).

In the cosmetic industry, similar to pharma applications, CDs are used to avoid destruction of flavors and vitamins associated with their formulation. Moreover, most of the ingredients used are unstable and degrade or lose their potential upon exposure to light, air, heat, etc. By incorporating them inside the CD cavities, they can be efficiently protected, and can thus provide long lasting fragrances and other properties (Numanoglu et al. 2007). In addition, most ingredients are lipophilic and/or acidic. Without complexation, they cause skin irritation and or tissue inflammation, which can be avoided by complexation with CDs, and when complexed they are able to penetrate the skin more efficiently (Loftsson 2000). Because most cosmetic ingredients exist as liquids, it is also convenient to process them as solid CD-ICs (Gal-Fuzy et al 1984). Essential oils, such as tea tree oil, which has excellent antimicrobial and antibacterial properties degrade in the presence of light and oxygen forming skin irritating terpenes (Chemie et al. 2015). However, when they are complexed with CDs, their stability is increased along with maintaining their cosmetic properties. Similar effects have also been seen for hydroquinone and kojic acid, which are used in cosmetic formulations as whitening agents (Petit and Pierard 2003). Kojic acid, similar to fruit juices, degrades upon exposure to light and turns yellow. This can be prevented by complexation with CDs (Kim et al. 2003).

In addition, cosmetic formulations consist of wide ranges of components, such as essential oils, animal and vegetable fats, vitamins, and hormones. Unfortunately most of these components are insoluble in water. As a result, by complexing with CDs, their solubilities can be substantially enhanced. For instance, salicylic acid, a skin cleansing agent used in topical formulations, is insoluble in water. As an acidic substance, direct application of salicylic acid causes irritation. However, when complexed with CDs, possible skin irritation due to acidity can be avoided (Thau 2005). Likewise, triclosan, a commonly used antiseptic and a common disinfectant used in hospital settings, is insoluble in water. Upon complexation, a polymeric derivative of Triclosan forms a clear solution, which can then be applied (Jug et al. 2011).

In the textile industry, CDs are primarily used in the dyeing process. The applications of CDs, especially β-CDs, have been observed to result in decreased dye loss during the washing process. Furthermore, utilizing dyes in complexed form have been observed to result in improved color intensity. CDs are also used, similar to the food and cosmetic industries, in masking obnoxious odor from sweat or to deliver perfumes upon contact with sweat, simultaneously complexing with sweat and masking the odor (Bhaskara-Amrit et al. 2011). The guest odor molecules

complexed in the CD cavities can then be unloaded in the washing process and new fragrance molecules loaded into the CD cavities during the drying cycle (Martel et al. 2002). A type of β-CD named, monochlorotriazinyl-β-CD, is a widely used derivative for textile applications, especially for anti-microbial applications (Reuscher and Hirsenkorn 1996). Over the years, based on the type of textile fiber and the particular CD, various strategies to incorporate the CDs have been established. Some of the widely used techniques include: spraying, printing, coating, impregnation, cross-linking, and grafting (Voncina and Marechal Le 2005). For permanent fixation, cross-linking and grafting are the most suitable techniques, and these studies demonstrate the diverse applications of CDs.

3.2 Electrospinning

3.2.1 Techniques

Various techniques for preparing nanofibers, such as template synthesis, self-assembly, phase separation, freeze-drying, and electrospinning have been reported. Amongst these techniques, electrospinning is the most widely studied due to its simple setup, low cost, and versatility, with potential for industrial scalability (Agarwal et al. 2008). Although conceptualized and rudimentary experiments were performed more than a century ago, the process of electrospinning was first demonstrated in a patent filed by A. Formhals in 1934 (Anton 1934). There was no further interest in electrospinning of solutions or melts until the 1980s, when Larrondo and Manley attempted to electrospin from a polymer melt (Larrondo and John Manley 1981). During the 1990s, Reneker's group at the University of Akron revived interest in electrospinning technology, when they extensively reported electrospinning from a wide variety of polymer solutions (Doshi and Reneker 1995). Ever since, electrospinning has become one of the most widely studied techniques to prepare fibers with submicron diameters.

A typical electrospinning setup is illustrated in Fig. 3.3 and consists of a syringe with a nozzle, a collector, either stationary or rotating, a pump to deliver the solution at a precise rate, and a source for generating an electric potential difference between the nozzle and the collector (Narayanan et al. 2017). As the solution is pumped at a set rate, the electrical potential difference between the electrodes causes the droplet to undergo deformation to form a cone-like structure, commonly known as a Taylor-cone (Yarin et al. 2001). When the surface tension of the liquid cone is overcome by the electric potential difference, the cone becomes further stretched and undergoes a bending instability (Reneker and Chun 1996). With the appropriate polymer concentration, and thus solution viscosity, the polymer solution jet does not collapse, enabling further stretching and bending of the jet, resulting in the accumulation of polymer in the form of nanofibers (Wong et al. 2008). Electrospinning, thus depends critically on both material properties of the

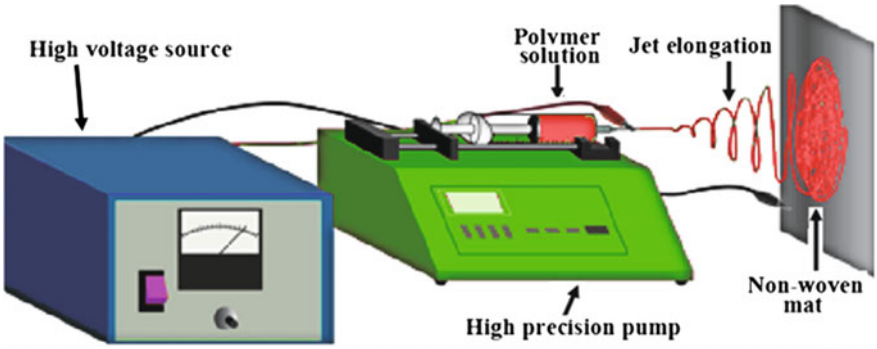

Fig. 3.3 Schematic representation of cyclodextrin containing nanofibers obtained by electrospinning process. A schematic representation of typically used electrospinning apparatus containing high voltage source, high precision pump, and a collector. In this process, solutions of polymer or small molecules in a suitable solvent is held in a syringe, which is then pumped using a high precision pump. While the polymer solution is extruded, a high potential difference is applied between the syringe and a collector causing the polymer solution to undergo elongation resulting in the final product being considerably smaller than the initial jet (Narayanan et al. 2017)

spinning solution as well as processing conditions (You et al. 2006). Various solution properties critical for electrospinning include viscosity (dependent on concentration and molecular weight of polymer) and surface tension and conductivity (Son et al. 2004). Electrospun materials typically have a surface tension low enough to be overcome by the electric field, and viscosity high enough but not too high so it does not prevent stretching of the polymer solution jet, and conductivity high enough to induce stretching of the polymer solution jet by the electric field (Tiwari and Venkataraman 2012).

Various studies have been reported in the recent past that correlate the effects of one or more of these processing factors on the resulting fiber diameter and the morphology of the non-woven mat. Since chemically different materials behave differently, there exists no one recipe for successful electrospinning. Apart from material characteristics, processing variables such as potential difference, tip to collector distance, feed rate, needle or nozzle size, and type of collector can play pivotal roles in the electrospinning process (Deitzel et al. 2001). Typically, increasing voltage avoids bead formation, as an increase in voltage produces additional stretching (Jia et al. 2006). Similar effects can also sometimes be achieved by increasing the tip to collector distance (Hekmati et al. 2013). In addition, fiber diameters can be drastically decreased by utilizing a rotational mandrel. The rotating mandrel causes drawing of the fibers, similar to the conventional fiber manufacturing process, resulting in a drastic reduction in electrospun fiber diameters.

Similar to conventional fiber processing, circular, elliptical, triangular, hexagonal, kidney bean and trilobal fibers can be made through electrospinning. Also, fiber structures, such as hollow, core-sheath, and islands-in the sea are also possible using electrospinning (Liu et al. 2010). In addition, electrospun fibers can also have,

by judicious selection of solvents, porous structure on their surfaces. Further post-processing of the electrospun fibers can enhance the suitability of those fibers for particular applications. Such efforts have been significantly devoted to the filtration and tissue engineering fields. Electrospun nanofibers can be collected using a stationary collector, parallel plates, conveyor, and rotating discs (Ali et al. 2011). The electrospinning process has been applied successfully to several hundreds of polymers, both synthetic as well as natural, using different strategies. Among polymers successfully electrospun were some natural polymers that are typically not possible to spin into fibers using conventional strategies. By utilizing high speed rotating or parallel plate collectors, highly aligned nanofibers can be obtained, and are found suitable for applications in tissue engineering and filtration. Some unique strategies for the electrospinning process found in the literature include: utilizing salts to improve conductivity, utilizing highly volatile solvents, resulting in porous structures, using a solvent with high boiling point to enable post processing enhancements, and employing readily electrospinnable polymers to facilitate the process (Yao et al. 2014; Celebioglu and Uyar 2011).

3.2.2 Tissue Engineering and Drug Delivery Applications

Electrospun nanofibers have immense potential in tissue engineering (bone, skin, neural, cartilage, vascular and muscle), filtration, reinforcements for composites, drug delivery, small molecule delivery, regenerative medicine, antimicrobials, and magnetic nanocomposites (Narayanan et al. 2016a). In tissue engineering and regenerative medicine, nanofibers are advantageous since they mimic the geometrical extracellular environment present in the body. To enhance the suitability of the electrospun nanofibers, post processing by plasma treatment, UV or γ-irradiation crosslinking, conjugation of biomolecules or cell adhesive peptides, or simple adsorption of these molecules are not uncommon (Yan et al. 2013). For instance, there have been many reports on biodegradable polymers, such as poly (ε-caprolactone), poly (lactic-*co*-glycolic acid), and poly (lactic-*co*-caprolactone) being surface modified with cell adhesive molecules, such as fibronectin, heparin, arginylglycylaspartic acid sequences or covalently bonding collagen to plasma treated scaffold (Kim and Park 2006). In summary, there is no one particular technique that appears to be ideal for all nanofibrous systems.

In tissue engineering (TE) applications, some tissues, in particular, those found in heart, ligaments, and cartilage, have limited vascularization potential, and current options, such as allo or autografts, have their own drawbacks, such as donor site morbidity, additional surgeries, etc. With appropriate scaffold construction (geometry, pore size, fiber diameter) along with cell type, it is predicted that electrospun scaffolds will soon replace conventional treatment options (Ghasemi-Mobarakeh et al. 2008). For example, in bone tissue engineering, addition of hydroxyapatite (HA) and or bone morphogenetic protein-2 (BMP-2), a key component found in native bone tissues, have been, in animal models, observed to cause alkaline

phosphatase activity and osteocalcin expression, key markers for bone regeneration (Zhang et al. 2008; Lee et al. 2013).

Nanofibers can be efficiently employed for drug delivery in TE applications. Depending on the material type and geometry of the construction, the drug delivery mechanism can vary, and typically differ due to several reasons, including diffusion of the drug or matrix erosion (Nagai et al. 2006; Grassi and Grassi 2005). Thus it is obvious that drug release rates and sensitivity can be controlled by choosing appropriate carriers for the drug type, polymer type, their compatibility, nanofiber diameter, morphology, geometry, and degradation mechanism. For drug delivery applications, various loading mechanisms have been reported, such as adding dissolved drug (in a separate solvent) into a polymer solution prior to electrospinning, or adding drug after the polymers were dissolved (same solvent), or co-axially electrospinning the polymer and the drug, or emulsion electrospinning, or absorbing the drug into an already electrospun mat (Pillay et al. 2013). Some of the drug types that have been embedded into polymeric nanofibers are listed in Table 3.1.

Table 3.1 Some examples of polymeric nanofibers embedded with drugs

Polymer	Solvent(s)	Drug(s)	References
PCL	Chloroform/Acetone (7:3)	Ibuprofen, Carvedilol	Potrč et al. (2015)
	Dichloromethane/methanol (7:3)	Heparin	Luong-Van et al. (2006)
	Dichloromethane or chloroform	Diclonofac sodium	Kanawung et al. (2007)
	Chloroform/ethanol (3:1)	Resveratrol, gentamycin sulphate	Huang et al. (2006)
	Chloroform/Dimethyl formamide (3:7)	Biteral	Bolgen et al. (2007)
	Chloroform	Ketoprofen	Kenawy et al. (2009)
PVA	Water	Iodine (in ethanol)	Matuseviciute et al. (2012)
	Water	Riboflavin, caffeine	Li et al. (2013)
	Water	Bovine serum albumin	Zeng et al. (2005)
	Water	Meloxicam	Ngawhirunpat et al. (2009)
	Water	Diclonofac sodium,Naproxen, Indomethacin, sodium salicylate	Taepaiboon et al. (2006)
	Water	Raspberry Ketone	Yang et al. (2007)

(continued)

Table 3.1 (continued)

Polymer	Solvent(s)	Drug(s)	References
CA	Acetone/DMAc (2:1)	Vitamin-A acid, α-Tocopherol,	Taepaiboon et al. (2007)
	Acetone/DMAc/Ethanol (4:1:1)	Ketoprofen	Yu et al. (2012)
	Acetone/DMAc/Ethanol (4:1:1)	Naproxen	Wu et al. (2010)
	Acetone/DMAc	Indomethacin, naproxen, ibuprofen, sulindac	Tungprapa et al. (2007)
PEO-PCL	Chloroform/DMSO	Lysozyme	Kim et al. (2007)
PLLA	Chloroform	Cytochrome-C	Maretschek et al. (2008)
	Chloroform	Danarubicin	Chen et al. (2007)
	Chloroform/acetone	Captopril	Wei et al. (2012)
	Chloroform/acetic acid-FCS	BMP-2	Schofer et al. (2011)
	Chloroform/acetone (2:1)	Timosaponin B-II	Huo et al. (2015)
PEG-PLA	Chloroform	Doxorubicin-HCl	Xu et al. (2009)
	Chloroform	Paclitaxel	Xu et al. (2009)
	Chloroform	Tetracycline hydrochloride	Xu et al. (2010)
PLGA	Tetrahydrofuran/Acetone	Tetracycline hydrochloride	Qi et al. (2013)
	Tetrahydrofuran/Dimethyl formamide	Tetracycline	Yan et al. (2012)
	Dichloromethane/Dimethyl formamide	Camptothecin	Amna et al. (2012)
	Tetrahydrofuran/Dimethyl formamide	Amoxicillin	Wang et al. (2012)

3.2.3 Air and Water Filtration

Another major application of nanofibers is in water and air filtration. With advancements in the science and technology and widespread use of micro and nanoparticles, it becomes even more important to keep the water and air pure and safe from contaminants. In one study, Sundararajan et al. succinctly summarized the advantages and potential of electrospun nanofibers compared to the current activated charcoal and fiberglass-based filter (Sundarrajan et al. 2014). In addition, it has also been noted that nanofibers in conjunction with microfibers typically yield higher efficiency for trapping fine particulates (Wang et al. 2012). But despite their

advantages, making higher efficiency and long lasting nanofiber-based filters predominantly rests on the properties of the polymer used. For example, Matulevicius et al. studied the efficacy of nanofiber-based filtration media fabricated from various polymers. Even with contrasting differences in their morphologies, the authors observed that both polyvinyl acetate and polyacrylonitrile (beaded and irregular *vs* smooth and continuous) elicited higher efficiencies in trapping 100 and 300 nm particles. Furthermore, they observed that stacking layers of non-woven mats did not enhance the filtration efficacy. In fact, in some cases, a sharp drop in efficiency was observed (Matulevicius et al. 2016). Another disadvantage with nanofiber based filtration media has been their incapability to control the pressure drop, especially when the fibers are very thin. To avoid this, thin nanofibers are occasionally utilized in conjunction with microfibers (Leung et al. 2012; Mei et al. 2013). These examples illustrate the capability of electrospun nanofibers in filtration applications, especially, when a suitable polymer is chosen to remove an appropriate waste material. However, when the electrospinning process is combined with a material like cyclodextrins, there exist a plethora of additional opportunities that tap into the advantages of both the electrospinning process and complexing characteristics of CDs.

3.3 Electrospinning Nanofibers Containing Cyclodextrins

Nanofibers containing CDs, based on their purpose, role, and carrier can be classified into four types, namely: polymer/CD nanofibers, carrier-free CD nanofibers, polymer/CD-IC nanofibers, and polymer/polymer-CD-IC nanofibers. Kaur and co-workers first reported the electrospinning of modified CDs with PMMA as a carrier for organic waste treatment (Kaur et al. 2006). After this seminal work, several research groups reported fabrication of polymer-CD nanofibers for use in water and air filtration, drug delivery, antimicrobials, and tissue engineering applications. An extensive list of nanofibers containing polymers and CDs is summarized in Table 3.2.

Most reported polymer-CD combinations are typically prepared by dissolving guest polymer and host CD in a common solvent (mostly water, DMF) and then subsequently electrospun to form composite structures. This strategy allows fabrication of polymeric nanofibers containing CDs, with the exception of aliphatic polyesters that have no common solvents with CDs. To overcome this issue, our group first reported electrospinning PCL and α- and γ-CDs using binary solvent mixtures (chloroform/DMF). α- and γ-CDs were chosen for the experiment as they both can form inclusion complexes with PCL. We observed that using a combination of solvents resulted in nanofibers with CDs homogenously distributed and without forming any polymer-CD-ICs. This was further corroborated by analytical techniques (XRD and TGA) and by the absorption of phenolphthalein by both α- and γ-CD containing PCL nanofibers. In a subsequent study, the efficacy of PCL/β-CDs in absorbing simulated wound fluid containing odorous butyric and propionic

Table 3.2 Electrospun polymer-CD nanofibers reported in the literature

Polymer-CD type	Fiber diameter	Study	Reference
PMMA/PC or APC-CD	900 nm	FTIR and XPS analysis indicated the presence of CDs on the nanofiber surfaces. Nanofibers effectively capture the phenolphthalein from the solution	Kaur et al. (2006)
PMMA/α-β-γ-CDs	675–1025 nm	Polymer concentration played a crucial role in fiber morphology. FTIR and XPS analysis indicated the presence of CDs on the nanofiber surfaces	Uyar et al. (2009)
PS/β-CD	900–2000 nm	At lower polymer concentrations, bead free fibers were obtained at higher CD concentration. Similarly, at lower polymer concentrations, bead free fibers were obtained at lower CD concentrations. XPS indicated presence of CDs on the surface	Tamer et al. (2009)
PS/β-CD	1100–2000 nm	Fiber diameters and % CD loading depended on the polymer concentration. Higher CD loading caused higher adsorption of phenolphthalein	Uyar et al. (2009)
PEO/α-β-γ-CDs	690–1100 nm	Due to higher electrical conductivity, bead-free nanofibers were obtained at lower polymer and higher CD concentrations. In addition, CDs were observed to be distributed homogeneously on the PEO surface	Uyar et al. (2009)
PS/α-β-γ-CDs	1000–2000 nm	Direct pyrolysis-mass spectroscopy indicated PS-α-CD had higher binding strength to phenolphthalein compared to PS-β-CD and PS-γ-CD. UV-Vis experiments further showed PS-α-CD had higher encapsulation capability compared to other systems	Uyar et al. (2010a)
PMMA/β-CD	600–1000 nm	Fiber diameter depended on both polymer as well as CD concentration. PMMA-CD nanofibers were capable of removing toxins (aniline, toluene, and styrene) from the environment	Uyar et al. (2010b)
PVA/β-CD	150–350 nm	Small increases in fiber diameter were observed with increases in CD loading. Electrochemical measurements indicated rapid encapsulation of small molecules into the CD cavities	Zhang et al. (2011)
PVP-βCD	250–350 nm	Marginal increase in fiber diameter was observed with the addition of β-CD, and further fiber diameter increase was observed with additional with HDMI crosslinking. The crosslinked nanofibers elicited binding selectivity with naringin	Ma et al. (2011)

(continued)

Table 3.2 (continued)

Polymer-CD type	Fiber diameter	Study	Reference
Zein/α-β-γ-CDs	100–400 nm	Spinnability improved with the addition of CDs. Lower polymer concentration required higher CD concentration and vice-versa. XPS indicated some of the CDs were available on the surface. Thermal stability was slightly enhanced with addition of CDs	Kayaci and Uyar (2012)
PET/α-β-γ-CDs	900–1300 nm	To prevent leaching of CDs, they were immobilized and crosslinked by citric acid onto PET. PET/CD systems showed higher efficiencies in removing polycyclic aromatic hydrocarbons from water	Kayaci et al. (2013)
PCL/α- and γ-CD	400–600 nm	Higher PCL concentration (14%) resulted in thicker fibers, but reduction in PCL concentration (12%) resulted in thinner fibers and higher CD loading. Addition of CDs improved the PCL crystallinity, and crystallization rates. In addition, both α- and γ-CDs encapsulated phenolphthalein from ethanol solution	Narayanan et al. (2014)
PET/α-,β-, and γ-CDs	360–800 nm	CD loading of up to 25% was possible without bead formation. IC formation with aniline was more pronounced in PET/γ-CD than PET/α-CD	Kayaci et al. (2013)
PCL/β-CD	400–600 nm	Similar to previous study with α- and γ-CDs, PCL did not form inclusion with CDs. Also, addition of CDs caused decrease (>25º) in hydrophobicity of the composite mats. In addition, PCL/β-CD system encapsulated wound odor simulants eliciting potential to be used in wound care	Narayanan et al. (2015)
PU/β-CD	400–800 nm	CD loading of up to 30% was possible without bead formation and the fibers were homogenous in size. In addition, thermal stability of PU enhanced by the addition of CDs. Phenolphthalein absorption depended on fiber diameter (lower polymer concentration)	Akçakoca et al. (2014)
Chitosan/HP-βCD	Not reported	Electrospinning of chitosan was possible in wide variety of concentrations facilitated by the addition of HP-CDs. In addition, chitosan formed inclusion complexation with HPCDs evidenced from NMR and FTIR	Burns et al. (2015)

(continued)

Table 3.2 (continued)

Polymer-CD type	Fiber diameter	Study	Reference
Nylon/α-,β-, and γ-CD	100–150 nm	CDs caused drastic improvements (twofold) in adsorbing toluene compared to neat nylon nanofibers. Between α-, β-, and γ-CDs, β-CD was found to most suitable for adsorbing toluene	Kayaci et al. (2015)
PAN/α-,β-, and γ-CDs	Not reported	Gradual increase of fiber diameters observed with increasing CD concentration (values not reported). With increase in adsorption time, increase in Cu ion adsorption was observed	Li et al. (2014)

acids was found. Through XPS and TGA, we showed that with β-CDs predominantly on the nanofibrous surface, these foul odors can be absorbed, thereby demonstrating the potential of these composite fibers for wound care applications.

Fiber diameters play a significant role, for example, in tissue engineering, controlled drug delivery, and air/water filtration applications. The effect of CD addition on fiber diameters have not been observed to be homogenous or follow a linear path. For example, our research group and several other groups mentioned in Table 3.2 indicated increases in fiber diameter with the addition of CDs, especially at higher CD loadings. However, in the case of polyurethane (PU)/β-CD composites, addition of CD caused not only a small increase in fiber diameters, but also made them more homogenous, which was not observed in the neat electrospun PU nanofibers (Akcakoca et al. 2014). A similar effect was observed with chitosan and zein, wherein successful electrospinning was possible only with the addition of CDs (Burns et al. 2015). This phenomenon was attributed to the increased entanglements and/or electrical conductivity with the addition of CDs to these polymeric solutions. These studies demonstrate that both the type and choice of polymer and CDs are crucial for successful electrospinning. They further demonstrated the variety of interactions that take place between the CD and polymer, which can either enhance or retard electrospinnability. In most polymer-CD systems, polymer and CD concentrations cumulatively have a strong influence on the resultant fiber diameters.

Despite the advantages possessed by polymer-CD electrospun nanowebs, major drawbacks include: (i) possibility of leaching CDs from the polymer surface due to solubility of CDs in water, (ii) incapability of the CDs to encapsulate longer molecules due to their narrow pore size (D < 10 Å, see Fig. 3.1), and (iii) possibility of forming inclusion complexation with the polymer itself. A few studies attempted to explore a variety of ways to avoid the leaching of CDs. One commonly reported method is by tethering the CDs to the polymer surface by covalent bonding with citric acid, glutaraldehyde, or by using azide crosslinking chemistry (Xiao et al. 2014; Kang et al. 2015; Celebioglu et al. 2014). However, these

cross-linking chemistries may not be suitable for biomedical applications, as they are known cyto-toxic materials. To date, however, such a system has not been examined. In addition, as neat solid CDs adopt cage form crystals, they are unable to accommodate longer molecules, such as valeric acid found in wound odors. To overcome such an issue, Kayacki et al. demonstrated a facile strategy of polymerizing β-CDs onto PET surfaces (Kayaci et al. 2013). Although they specifically did not analyze the capability for filtration of longer chain molecules, we hypothesize such a construct would be able to encapsulate longer chain molecules.

A major hindrance in filtration applications using polymer-CD systems has been their potential to form inclusion complexes with guest polymers, thereby rendering the CD cavities occupied with polymers. For example, Burns et al. 2015 observed that chitosan forms ICs with CDs. Similarly, we have observed that with α-CD, PCL, to an extent forms an IC causing poor encapsulation of phenolphthalein. We further observed γ-CD, rather than α-CD, to be more conducive for encapsulation of small molecule guests, as was reported previously by Uyar's group on other polymer-CD systems. It has been hypothesized that this phenomenon was due to more facile IC formation of α-CD with PCL, which was corroborated by TGA and XRD analyses.

3.4 Electrospinning Polymers Containing Cyclodextrin-Inclusion Complexes

When CDs are present on the nanofiber surface with their cavities devoid of any small molecule or polymer guests, they are most suited for adsorbing and removing small molecules, such as wound odors or environmental toxins, present in air and water. Instead of using a neat CD, CD-ICs (of small molecules) have also been electrospun with polymers to form composite fibers for a variety of different applications. For example, many research groups investigated delivery of small molecule guests in the form of their CD-ICs using a polymer carrier for potential applications in controlled release of drugs and antibiotics, food packaging, odor control, and fragrance release. Most of the encapsulated guest molecules were unstable to heat, oxygen and are prone to degradation in their neat states. In addition, encapsulated drugs have poor penetration into the cell membrane, thus using their CD-ICs allows a controlled release of these substances. For example, Canbolat et al. showed that naproxen when encapsulated in CD embedded in PCL nanofibers demonstrated a controlled and superior release rate (2-fold higher) when compared with naproxen in native form Canbolat et al. (2014). Likewise, Aytac et al. (2015), showed superior controlled release of sulfisoxale enclosed in CD-IC cavities that were embedded in hydroxypropyl cellulose (HPC) nanofibers. Similarly, controlled release of ketoprofen was reported from β-CD grafted onto chitosan scaffolds by Prabaharan and Jayakumar (2009).

They observed that encapsulated ketoprofen had a larger initial burst followed by a more sustained release [13]. In contrast to these reports, Manasco et al. reported a rapidly degrading construct comprised of PVA/HPC/β-CD nanofibers and ketoprofen. They further showed that a higher loading of the CD, produced the possibility of modulating the release of drugs (Manasco et al. 2014).

Controlling drug release is even more crucial in the case of anti-cancer drugs, as they have been shown to cause deleterious side effects. Encapsulating anti-cancer drugs in CD cavities offers a direct and simple approach to counter their side-effects. For instance, Luo et al. demonstrated modulation and improved anti-tumor activities of hydroxycampothecin (HCPT) (>20 times) by embedding HPCT-HP/CD-IC in electrospun nanowebs. Further they showed in an animal model, higher necrosis and apoptosis of the cancerous tissue when exposed to HCPT contained in HP/CD-IC and embedded in nanowebs (Luo et al. 2012). These studies demonstrate the versatility of such ICs in a variety of applications that require rapid delivery of small molecules.

On the other hand, such fast release rates are actually undesirable for many applications, such as release of fragrances, antibiotics, antioxidants, and antimicrobial substances. A slow release improves the shelf life and long lasting effects in these applications. For instance, Aytac et al. demonstrated a slow long lasting release of allyl isothiocyanate (AITC) from β-CD-ICs compared to neat fibers containing AITC (Fig. 3.4I).

In addition, when nanofibers containing AITC-β-CD-IC were exposed to *S. aureus* and *E. coli,* a superior growth inhibition rate (>99%) was observed compared to a modest rate observed in fibers containing neat AITC (32%) (Fig. 3.4 II–III). Likewise, when they studied the release of Triclosan from its CD-IC, they observed a sustained release, with a higher growth inhibition rate (Kayaci et al. 2013). The same authors demonstrated an increased stability of Quercetin, an antioxidant, encapsulated in β-CD and embedded in electrospun polyacrylic acid nanofibers. In addition, they reported the cumulative release and photostability of Quercetin from those systems to be higher compared to the neat system (Aytac et al. 2016).

A major advantage with CDs has been their capability to release encapsulated molecules in a controlled manner when an appropriate stimulus is provided. This is especially advantageous in controlled release systems of molecules such as fragrances. Combining the electrospinning process with these small molecule-CD-ICs permits creation of an interesting array of substances for various applications. For instance, Uyar et al. reported encapsulation of menthol, a highly temperature unstable compound in α-CD-ICs embedded in a PMMA matrix. They showed that vaporization of menthol took place only at considerably elevated temperatures (100–350 °C), and in addition, they showed γ-CD to be more appropriate for encapsulating menthol (Tamer et al. 2009). In a subsequent study, they observed a similar trend of γ-CD performing better than α- and β-CD in encapsulating menthol carried in a PS matrix (Uyar et al. 2009). Moreover, another study indicated a longer shelf-life of menthol encapsulated in CD-IC cavities. Due to its temperature sensitive nature, it was observed to vaporize rapidly upon neat storage (Uyar et al. 2011). Similar effects

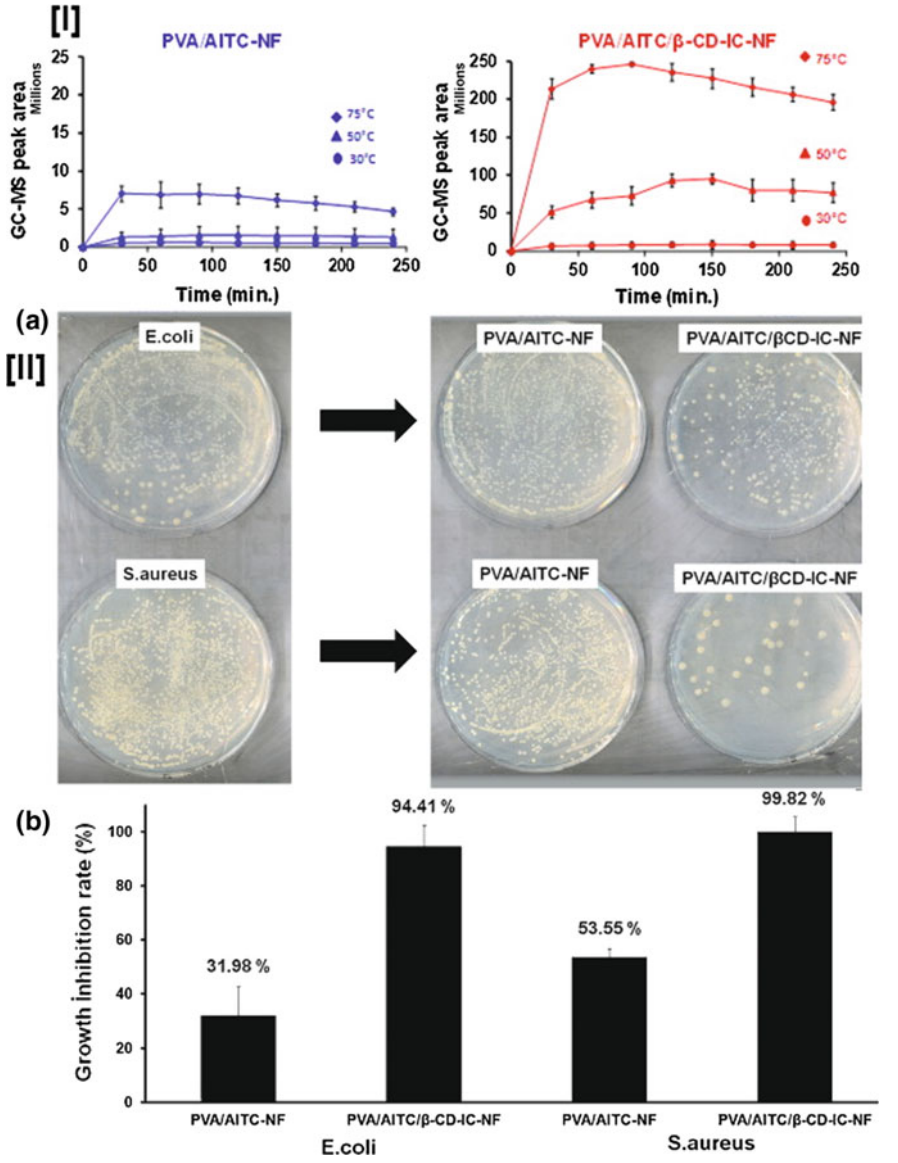

Fig. 3.4 Release (I) and antibacterial activity (II) of electrospun poly vinyl alcohol nanofibers containing allyl isothiocyanate (AITC) and AITC-βCD-ICs were examined. When evaluated for release of AITC from the nanofiber, AITC included within the β-CD cavity showed larger release volume, especially at higher temperatures. Also, when PVA, PVA/AITC, and PVA/AITC-β-CD-IC nanofibers were evaluated for antibacterial activity, higher growth inhibition was observed in AITC/β-CD-IC encapsulated in PVA nanofibers. Adapted with permission from (Aytac et al. 2014)

were also seen with eugenol, a fragrant molecule possessing antibacterial/antimicrobial properties; and vanillin, a fragrant molecule used in the food industry (Kayaci and Uyar 2012a, b). Likewise, in tissue regeneration applications, the presence and availability of oxygen is a necessity for avoiding cell death (Amini and Nukavarapu 2014). To prevent such undesired cell death, Tierney and co-workers fabricated PCL and poly (carbonate urethane) nanofibers embedded with CD-ICs containing guest perfluorohydroxyphenanthrene. Their study demonstrated superior and consistent delivery of oxygen to the cells over a 14-day incubation period (Deluzio et al. 2014). These studies cumulatively demonstrate the capabilities and advantages of modulating delivery of small molecules by utilizing their CD-ICs, compared to simple polymer-neat small molecule systems.

3.5 Crosslinking and Facilitation of Nanoparticle Incorporation in Nanofibers Using Cyclodextrins

Some applications, such as scaffolds for tissue engineering and aerospace applications, typically require superior mechanical properties. Nanofibers, due to their random architecture and higher porosities, generally have low mechanical strength. In addition, in situ or synthesis of nanoparticles in a post-processing step in these matrices lead to poor control of their architectures. To avoid this, a reducing agent, such as hydroxyl containing ethanol and glycol or a stabilizing agent, is typically needed (Wang et al. 2000). As CD molecules possess numerous hydroxyl groups on their outer rims (See Fig. 3.1), they can be used as an alternative and "greener" reducing option. In addition, other advantages include the stability of the formed nanoparticles through interaction with the OH-groups on the CD outer rims (Jaiswal et al. 2010).

Using a similar principle, CDs can also crosslink polymeric nanofibers or aid in doping of inorganic materials onto the polymeric surface, thereby enhancing their potential in several applications. For example, Teng et al. developed a composite nanofiber system using an elaborate technique comprised of PVA doped with SiO_2 modified in a β-CD system (silylated monochlorotriazibyl-β-CD). Further they showed rapid separation of indigo carmine dye from a simulated waste water system. Field emission scanning electron microscopy (FE-SEM) measurements indicated separation of these nano-particles and high roughness on the nanofiber surfaces (Teng et al. 2011). In another study, utilizing a similar mechanism, Xiuling and coworkers fabricated poly (vinyl butyral) (PVB) nanofibers doped with nano-silica particles bonded together by β-CD. When observed by SEM, the homogeneity of the silica phase was more obvious in the doped fibers containing β-CD (Ma et al. 2013). Similarly, Wang et al. reported a single step preparation of Ag nanoparticles containing poly (N-vinylpyrrolidone) (PVP) nanofibers. They observed uniformly distributed Ag nanoparticles in the PVP nanofiber matrix. As nanoparticles based on Ag have significant potential in antibacterial applications,

they tested antibacterial properties of stable Ag nanoparticle containing nanofibers and they observed them to have superior antibacterial activity (Wang et al. 2012). A similar study was undertaken by Celebioglu et al. who studied fabrication of Ag nanoparticles with or without the presence of HP-β-CD in electrospun PVA nanofibers from a silver salt ($AgNO_3$). Without HP-β-CD, nanoparticle sizes were ∼8 nm with occasional agglomeration, while, in the presence of HPβ-CD, particle size not only decreased drastically to ∼2 nm, but were also without any agglomeration and homogenously distributed in the nanofibers (Celebioglu et al. 2014).

By using CDs, most of the drawbacks associated with simple addition to electrospun polymer nanofibers, including heterogeneous distribution and agglomeration of nanoparticles, in addition to bead structure formation, can be avoided. However, to further improve their homogenous distribution, post electrospinning reduction of nanoparticle precursors have also been extensively investigated. For example, one study demonstrated fabrication of homogenously dispersed gold nanoparticles (∼12 nm) in a PVP matrix after electrospinning PVP solutions containing β-CD and chloroauric acid (precursor for gold nanoparticles). Using FTIR analysis, they showed that addition of CDs caused initial stability of the nanoparticles formed, and the presence of PVP further improved their stability (Bai et al. 2008). A similar study was conducted by Wang et al. to synthesize silver nanoparticles in PAN nanofibers via post-electrospinning. In that study, β-CD acted as a secondary reducing and stabilizing agent for Ag nanoparticle synthesis. The composite non-woven membrane further elicited a broad range of antibacterial activity to both *S. aureus* and *E. coli*. (Wang et al. 2012). Similar to Ag and Au nanoparticles, Cu nanoparticles with uniform distribution were fabricated by Xu et al. 2014. They further showed a significant decrease in the nanoparticle size with β-CD mediated reduction and stabilization. They also demonstrated that these small nanoparticles imparted superior antibacterial activity against both *S. aureus* and *E. coli.*

In all the above discussed post electrospun preparations of nanoparticles, the nanoparticle precursors were dispersed in the polymer/CD solution and electrospun. Unlike these studies, Kim et al. demonstrated fabrication of multiple nanoparticles comprised of MWNTs and Au. Although these multifunctional nanocomposites demonstrated suitability for biocatalysis and sensor applications, their particle sizes were in the micron range (Tae-Gyung et al. 2010). These studies cumulatively demonstrate addition of CDs can enhance the reduction and stabilization of nanoparticles, and can act as a secondary agent provided the chosen polymer acts as a primary reduction and or stabilization agent. In addition, significant improvements in their antibacterial effects compared to nanofibers without CDs were evident.

3.6 Polymer-Free Electrospinning of Cyclodextrin Nanofibers

For successful electrospinning processes, materials of higher molecular weight (typically polymers) at higher concentrations, above their critical entanglement concentration, are generally required to withstand the electrostatic forces and whipping instabilities that occur (Gupta et al. 2005). To overcome the necessity of a high molecular weight material, it is customary to electrospin low molecular weight materials with a polymer carrier, as was discussed with polymer-CD systems (Saquing et al. 2013). However, some small molecules possess inter-molecular interactions, such as hydrogen bonding, that offers the potential to electrospin low molecular weight materials. In this regard, several small molecules, such as phospholipids, gemini surfactants, and sodium alginate have been electrospun at relatively higher concentration (McKee et al. 2006; Cashion et al. 2010; Fang et al. 2011). Taking cues from these studies, several CDs including native and modified CDs have been electrospun without a polymer carrier. The first such work was carried out on Mβ-CD by Celebioglu et al. who showed the feasibility of electrospinning M-β-CD from both DMF and water without any bead formation. They attributed the feasibility of electrospinning M-β-CDs to the hydrogen bonding between them, which was disrupted by the addition of urea and prevented their electrospinning (Celebioglu and Uyar 2010).

In their subsequent study, these authors studied the electrospinning of HP-β-CD and HP-β-CD-triclosan ICs. In this and the former study, they chose modified CDs (M-βCD and HP-β-CD) over native CDs, as they have superior aqueous solubilities. Intermolecular hydrogen bonding in HP-β-CDs and HP-β-CD-ICs allowed successful electrospinning without any beads. However, urea addition (20% by wt of HPβ-CD) caused disruption of their intermolecular bonding, preventing fiber formation. However, at lower wt%s of urea (up to 10%), fiber formation was still possible (Celebioglu and Uyar 2011). In a subsequent study, they further demonstrated the possibility of electrospinning these modified CDs (HP-β-CD, HP-γ-CD) not only from water, but also DMF and DMAc. In addition, they observed a linear relationship between wt% of CDs and increases in viscosity due to their intermolecular hydrogen bonding that facilitated successful electrospinning (Celebioglu and Uyar 2012). Although up until that point, only intermolecular hydrogen bonding was postulated to play a key role in successful electrospinning of these low molecular weight CDs, Manasco et al. showed the possibility of impure chloride ions present in HP-CDs to also play a key role in successful electrospinning (Manasco et al. 2012).

In addition to modified CDs, Celebioglu et al. studied the possibility of electrospinning native CD (γ-CD) from DMSO/water. γ-CD was chosen instead of β- and α-CDs as it has a higher water solubility. As with the modified CDs, successful electrospinning depended on the concentration of the native CDs, which in turn caused an increase in the spinning solution viscosity. In addition, similar to polymer-CD systems, γ-CD nanofibers were able to capture aniline and toluene vapors demonstrating the potential of these nanofibers for air filtration applications.

As mentioned before, low solubility of native CDs cause significant challenges for successful electrospinning. One way to overcome the low solubility was by electrospinning highly concentrated basic solutions of CDs. As CDs are stable under alkaline conditions, this strategy demonstrates the potential to electrospin native CDs and possibly similar systems. An alternative to basic solutions was put forth by Ahn et al. who studied the electrospinning of native β-CD solutions from a combination of an ionic liquid (1-ethyl-3- methylimidazolium acetate) and DMF (Ahn et al. 2013). These CD nanofibers have been tested for UV-responsive behavior and inclusion of gold nanoparticles and were found to be suitable for a variety of applications (Chen et al. 2013; Celebioglu et al. 2013). But a major disadvantage, as with polymer-CD systems, have been the leaching and thus destruction of nanofiber structure. With significant advancements in safe and efficient crosslinking of these CD nanofibers, a variety of applications for these supramolecular materials is anticipated.

3.7 Electrospinning of Polymer-Cyclodextrin-Inclusion Complexes

Supramolecular hydrogels based on cyclodextrins are well known for their ability to control the release of drugs and proteins (Chee et al. 2014). Some of the drugs that have been incorporated into these hydrogels include ibuprofen, melatonin, triamcinolone acetonide, and prednisolone (Hoare and Kohane 2008; Woldum et al. 2008). Similar to hydrogels, and as mentioned before, nanofibers fabricated via electrospinning have also been increasingly reported for controlling drug delivery. In addition, nanofibers mimic the extracellular nature of tissues, thereby making them even more attractive for tissue regeneration applications. Stable, polymer-CD nanofibers or polymer-CD nanofibers contained in a polymeric matrix offer promising potential applications in various aspects of tissue engineering. For example, it has been well established that polymer-CD-ICs can act as an excellent nucleating agent for the bulk polymer resulting in enhanced mechanical properties which is a prerequisite for many tissue engineering applications (for instance, bone growth) (Vogel et al. 2006). In addition, electrospinning polymer-CD-ICs without a carrier would similarly lead to fabrication of a wide array of devices for applications in modulating surface properties (for instance, enhancing cell-material interaction); pH, moisture, and heat sensitive drug delivery, and immobilization of growth factors and proteins.

In this regard, initial work was conducted by Pellerin's research group who investigated electrospinning of polymer-urea-ICs (Liu and Pellerin 2006). Although, these ICs were made with urea (U) as a host molecule, their report spurred interests in electrospinning such supramolecular materials with both urea and CD as host molecules. Uyar et al. first reported successful preparation of PEO nanofibers containing PEG-U pseudorotaxane crystals. Using elaborate characterization techniques (WAXD, rheology, SEM, and TEM), they showed the PEG-U pseudorotaxane crystals remained intact in the nanofiber structure (Figs. 3.5 I–II).

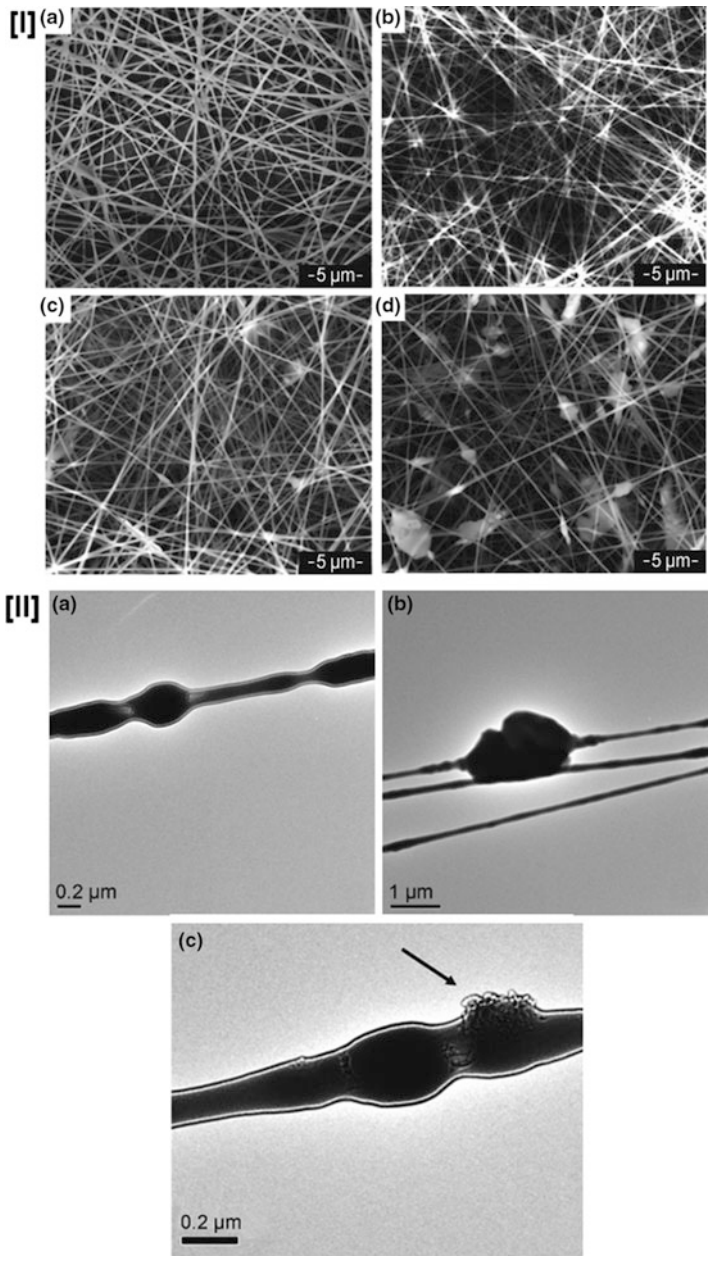

Fig. 3.5 The electron micrographs of electrospun poly ethylene oxide nanofibers containing α-CD/poly (ethylene glycol) (PEG) pseudorotaxanes (PRs) at various concentrations. At lower concentrations of PRs, the nanofibers resembled control PEO nanofibers, albeit with fibers showing non-uniform sizes. Whereas as the concentration of the PRs increases, beaded fibers were obtained, and due to poor extension of the jet, highly heterogeneous fibers with varying diameters were obtained (Fig. 3.5II). Adapted with permission from (Uyar et al 2008), Copyright, Wiley-VCH Verlag GmbH & Co 2008

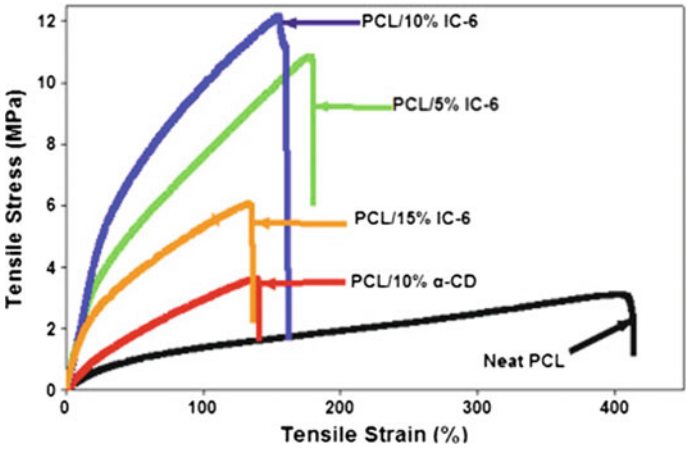

Fig. 3.6 Stress–strain plots of Neat PCL, PCL reinforced with α-CD, and PCL/(n-s)-PCL-α-CD-IC nucleated PCL composites. The neat PCL, which is a flexible polymer showed low modulus with high extensibility. When nucleated with pure α-CD, although the modulus increased only slightly, a rapid decrease in extension was observed. However, upon addition of the (n-s)-PCL-α-CD-IC, modulus increased several fold with concomitant decrease in the extension, demonstrating increases in the stiffness of the composites. Adapted with permission from (Narayanan et al. 2015)

Even though, their report was the first to show pseudorotaxane crystals embedded in a PEO matrix, the PEG used was of low molecular weight (Mn ∼ 2000). Our group demonstrated the feasibility of electrospinning large molecular weight non-stoichiometric (n-s)-PCL-α-CD-ICs, with only partially included guest PCL chains, embedded in a PCL matrix (Narayanan et al. 2016a). Our group further showed significant improvements in the crystallinity of the bulk PCL, along with improvements in crystallization rates and mechanical properties. Our results indicated 3 to fourfold increases in modulus and tensile strengths with marked reduction in elongation (∼50%), indicating significant improvements in the stiffness of the composites (Fig. 3.6).

Finally, TGA and DSC measurements indicated the (n-s)-PCL-α-CD-ICs remained intact in the composites (Narayanan et al. 2015). Through further detailed investigation, we observed that all the non-woven electrospun nanomats had similar porosities and nanofiber alignments, and we attributed such improvements solely to the presence of the (n-s)-PCL-α-CD-ICs, which facilitated enhanced interactions between the bulk and partially included PCL chains, and thus improved mechanical properties (Narayanan et al. 2015). With improved mechanical properties, we anticipate the suitability of these scaffolds for tissue engineering, particularly bone tissue engineering.

Apart from enhanced mechanical properties, scaffolds for tissue engineering also require sites for cell-material interaction. In addition to cell-material interaction sites, biomaterials are also required to facilitate interactions between the cells and

growth factors promoting tissue morphogenesis. In both cases, biomaterials are expected to possess surface epitopes such as hydroxyl, carbonyl, and amine groups to facilitate the process (Narayanan et al. 2016b). Unfortunately, frequently used biomaterials such as poly (lactic acid) and PCL do not possess such epitopes. But as cyclodextrins possess numerous accessible hydroxyls, having these polymers at least partially encapsulated in cyclodextrins is expected to facilitate the cell-material interaction process. In addition, by having such a configuration, immobilization of growth factors with temporal and spatial control may also be possible.

In this regard, Zhan et al. and Oster et al. attempted to fabricate nanofibers of PCL-α-CD-IC from CFM/DMF, but Oster et al. reported successful fabrication of nanofibers with intact IC structure only from a star polymer, not with a linear polymer (Oster et al. 2015). On the other hand, Zhan et al. 2012 reported successful fabrication of PCL-α-CD-IC nanofibers. However, our group recently demonstrated fabrication of PCL-α-CD-IC nanofibers from CFM. We further reported that, the presence of DMF in the solvent mixture caused de-threading of PCL from PCL-α-CD-IC, which the unsuccessful fabrication of these fibers by Zhan et al. and Oster et al. can be attributed to (Narayanan et al. 2016b). Our hypothesis was further corroborated by rheological experiments that showed a ten-fold increase in zero shear viscosity values for (n-s)-PCL-α-CD-ICs compared to neat and de-threaded solutions. In addition, quasi static mechanical tests revealed a fourfold improvement in tensile modulus and strength values.

To further investigate the reasons why these IC nanofibers elicit significantly higher mechanical properties, we conducted selected area electron diffraction pattern (SAED) and 2D-wide angle X-ray diffraction pattern measurements, which unexpectedly indicated an absence of molecular orientation in the (n-s)-PCL-α-CD-ICs (Narayanan et al. 2016c). The neat (PCL) nanofibers elicited much lower levels of crystallinity, which was to an extent expected as PCL is a semi crystalline material. Other factors, such as fiber alignment and porosities that could also potentially contribute to improving mechanical properties, were found to be insignificant, as all the nanofiber webs showed identical characteristics. Thus, we attributed enhancements in mechanical properties solely to the interaction between the PCL chain portions protruding from the (n-s)-α-CD-IC cavities and the adjacent un-included PCL chains (Narayanan et al. 2016b).

Finally, in a subsequent proof-of-concept study we investigated bio-conjugation of type-I collagen molecules onto the hydrophilic OH-groups present on the CDs. We observed a linear relationship between the stoichiometry (CD: PCL ratio) and the amount of collagen on the nanowebs. As more PCL chains were covered by α-CDs, higher loading of collagen was feasible. These studies illustrate the diverse applications of nanofibers containing ICs. We chose collagen as a biomacromolecule to illustrate the feasibility of bio-activation using these nanofibers. Conversely, in tissue engineering, there is a significant need for a biomaterial to be immobilized and to sequester growth factors and other proteins. However, these needs have not as yet, been addressed with nanofibers. With recent developments in our quest to enrich our knowledge and develop strategies, we anticipate there will soon be significant interests in utilizing CD based nanofibers for a variety of applications.

3.8 Conclusions

Cyclodextrins are an exciting class of materials that are biodegradable/bioabsorbable and do not elicit any unfavorable reactions in vivo. They are currently used widely in the food, pharma, agricultural, chemical, personal cosmetics, adhesives, and coatings industries. Significant advancements in nanofabrication techniques, such as electrospinning, has increased the use of CD based materials in filtration, healthcare, and other industries. In this chapter, the discussion began with the formation of inclusion compounds between CD hosts and various guest molecules, followed by classic examples where CDs are currently used. A brief introduction to the electrospinning process followed, and their emerging applications were then discussed. Although, some of the currently reported studies had deficiencies, for example, leaching or formation of ICs with guest polymers, suggestions have been provided that could alleviate some of these concerns. Finally, the combination of the electrospinning process conducted with the introduction of CDs in various ways to create interesting supramolecular materials for potential applications in air and water filtration, and tissue engineering were reported.

References

Agarwal S, Wendorff JH, Greiner A (2008) Use of electrospinning technique for biomedical applications. Polymer 49:5603–5621

Ahn Y, Kang Y, Ku M, Yang Y-H, Jung S, Kim H (2013) Preparation of [small beta]-cyclodextrin fiber using electrospinning. RSC Adv 3:14983–14987

Akçakoca Kumbasar EP, Akduman Ç, Çay A (2014) Effects of β-cyclodextrin on selected properties of electrospun thermoplastic polyurethane nanofibres. Carbohyd Polym 104:42–49

Ali U, Zhou Y, Wang X, Lin T (2011) Electrospinning of continuous nanofiber bundles and twisted nanofiber yarns. Nanofibers–Production, Properties and Functional Applications:153

Amini AR, Nukavarapu SP (2014) Oxygen-tension controlled matrices for enhanced osteogenic cell survival and performance. Ann Biomed Eng 42:1261–1270

Amna T, Hassan MS, Nam K-T, Bing YY, Barakat NAM, Khil M-S (2012) Preparation, characterization, and cytotoxicity of CPT/Fe(2)O(3)-embedded PLGA ultrafine composite fibers: a synergistic approach to develop promising anticancer material. Int J Nanomed 7:1659–1670

Anton F (1934) Process and apparatus for preparing artificial threads. US Patent 1975504

Arun R, Ashok Kumar CK, Sravanthi V (2008) Cyclodextrins as drug carrier molecule: a review. Sci Pharm 76:567–598

Astray G, Gonzalez-Barreiro C, Mejuto JC, Rial-Otero R, Simal-Gándara J (2009) A review on the use of cyclodextrins in foods. Food Hydrocolloids 23:1631–1640

Ayala-Zavala JF, Del-Toro-Sanchez L, Alvarez-Parrilla E, Gonzalez-Aguilar GA (2008) High relative humidity in-package of fresh-cut fruits and vegetables: advantage or disadvantage considering microbiological problems and antimicrobial delivering systems? J Food Sci 73:41–47

Aytac Z, Dogan SY, Tekinay T, Uyar T (2014) Release and antibacterial activity of allyl isothiocyanate/β-cyclodextrin complex encapsulated in electrospun nanofibers. Colloids Surf, B 120:125–131

Aytac Z, Sen HS, Durgun E, Uyar T (2015) Sulfisoxazole/cyclodextrin inclusion complex incorporated in electrospun hydroxypropyl cellulose nanofibers as drug delivery system. Colloids Surf B: Biointerface 128:331–338

Aytac Z, Kusku SI, Durgun E, Uyar T (2016) Quercetin/β-cyclodextrin inclusion complex embedded nanofibres: slow release and high solubility. Food Chem (197), Part A:864–871
Bai J, Yang Q, Li M, Wang S, Zhang C, Li Y (2008) Preparation of composite nanofibers containing gold nanoparticles by using poly(N-vinylpyrrolidone) and β- cyclodextrin. Mater Chem Phys 111:205–208
Bhaskara-Amrit UR, Agrawal PB, Warmoeskerken M (2011) Applications of β-cyclodextrins in textiles. Autex Res J. 11:94–101
Bolgen N, Vargel I, Korkusuz P, Menceloglu YZ, Piskin E (2007) In vivo performance of antibiotic embedded electrospun PCL membranes for prevention of abdominal adhesions. J Biomed Mater Res B Appl Biomater 81:530–543
Burns NA, Burroughs MC, Gracz H, Pritchard CQ, Brozena AH, Willoughby (2015) Cyclodextrin facilitated electrospun chitosan nanofibers. RSC Advances 5:7131–7137
Canbolat MF, Celebioglu A, Uyar T (2014) Drug delivery system based on cyclodextrin-naproxen inclusion complex incorporated in electrospun polycaprolactone nanofibers. Colloids Surf, B 115:15–21
Cashion MP, Li X, Geng Y, Hunley MT, Long TE (2010) Gemini surfactant electrospun membranes. Langmui 26:678–683
Celebioglu A, Uyar T (2010) Cyclodextrin nanofibers by electrospinning. Chem Commun 46:6903–6905
Celebioglu A, Uyar T (2011a) Electrospun porous cellulose acetate fibers from volatile solvent mixture. Mater Lett 65:2291–2294
Celebioglu A, Uyar T (2011b) Electrospinning of polymer-free nanofibers from cyclodextrin inclusion complexes. Langmuir 27:6218–6226
Celebioglu A, Uyar T (2012) Electrospinning of nanofibers from non-polymeric systems: polymer-free nanofibers from cyclodextrin derivatives. Nanoscale 4:621–631
Celebioglu A, Uyar T (2013a) Electrospun gamma-cyclodextrin ([gamma]-CD) nanofibers for the entrapment of volatile organic compounds. RSC Adv 3:22891–22895
Celebioglu A, Uyar T (2013b) Electrospinning of nanofibers from non-polymeric systems: Electrospun nanofibers from native cyclodextrins. J Colloid Interface Sci 404:1–7
Celebioglu A, Uyar T (2013c) Green and one-step synthesis of gold nanoparticles incorporated into electrospun cyclodextrin nanofibers. RSC Adv 3:10197–10201
Celebioglu A, Umu OCO, Tekinay T, Uyar T (2013) Antibacterial electrospun nanofibers from triclosan/cyclodextrin inclusion complexes. Colloids Surf, B 116:612–619
Celebioglu A, Demirci S, Uyar T (2014a) Cyclodextrin-grafted electrospun cellulose acetate nanofibers via "Click" reaction for removal of phenanthrene. Appl Surf Sci 305:581–588
Celebioglu A, Aytac Z, Umu OCO, Dana A, Tekinay T, Uyar T (2014b) One-step synthesis of size-tunable Ag nanoparticles incorporated in electrospun PVA/cyclodextrin nanofibers. Carbohyd Polym 99:808–816
Chee PL, Prasad A, Fang X, Owh C, Yeo VJJ, Loh XJ (2014) Supramolecular cyclodextrin pseudorotaxane hydrogels: A candidate for sustained release? Mater Sci Eng, C 39:6–12
Chemie W et al (2015) Cavamax® and Cavasol® Cyclodextrins-Theinnovators molecule
Chen C, Gang L, Chao P, Min S, Chunhui W, Dadong G (2007) Poly(lactic acid) (PLA) based nanocomposites—a novel way of drug-releasing. Biomed Mater:2
Chen M, Nielsen SR, Uyar T, Zhang S, Zafar A, Dong M (2013) Electrospun UV-responsive supramolecular nanofibers from a cyclodextrin-azobenzene inclusion complex. J Mater Chem C 1:850–855
Cui Y, Wang C, Mao J, Yu Y (2010) A facile and practical approach to randomly methylated β-cyclodextrin. J Chem Technol Biotechnol 85:248–251
Deitzel J, Kleinmeyer J, Harris D, Tan NB (2001) The effect of processing variables on the morphology of electrospun nanofibers and textiles. Polymer 42:261–272
Del Valle EMM (2004) Cyclodextrins and their uses: a review. Process Biochem 39:1033–1046
Deluzio TGB, Penev KI, Mequanint K (2014) Cyclodextrin inclusion complexes as potential oxygen delivery vehicles in tissue engineering. J Biomater Tissue Eng 4:957–966

Doshi J, Reneker DH (1995) Electrospinning process and applications of electrospun fibers. J Electrostat 35:151–160

Fang D, Liu Y, Jiang S, Nie J, Ma G (2011) Effect of intermolecular interaction on electrospinning of sodium alginate. Carbohyd Polym 85:276–279

Gal-Fuzy M, Szente L, Szejtli J, Harangi J (1984) Cyclodextrin-stabilized volatile substances for inhalation therapy. Pharmazie 39:558–559

Ghasemi-Mobarakeh L, Prabhakaran MP, Morshed M, Nasr-Esfahani M-H, Ramakrishna S (2008) Electrospun poly(ε-caprolactone)/gelatin nanofibrous scaffolds for nerve tissue engineering. Biomaterials 29:4532–4539

Gould S, Scott RC (2005) 2-Hydroxypropyl-beta-cyclodextrin (HP-beta-CD): a toxicology review. Food and chemical toxicology: an international journal published for the British Industrial Biological Research Association. 43:1451–1459

Grassi M, Grassi G (2005) Mathematical modelling and controlled drug delivery: matrix systems. Curr Drug Deliv (2):97–116

Gupta P, Elkins C, Long TE, Wilkes GL (2005) Electrospinning of linear homopolymers of poly (methyl methacrylate): exploring relationships between fiber formation, viscosity, molecular weight and concentration in a good solvent. Polymer 46:4799–4810

Hekmati AH, Rashidi A, Ghazisaeidi R, Drean J-Y (2013) Effect of needle length, electrospinning distance, and solution concentration on morphological properties of polyamide-6 electrospun nanowebs. Text Res J 84:2045–2055

Hoare TR, Kohane DS (2008) Hydrogels in drug delivery: Progress and challenges. Polymer 49:1993–2007

Huang Z-M, He C-L, Yang A, Zhang Y, Han X-J, Yin J (2006) Encapsulating drugs in biodegradable ultrafine fibers through co-axial electrospinning. J Biomed Mater Res, Part A 77A:169–179

Huo Z, Qiu Y, Chu Z, Yin P, Lu W, Yan Y (2015) Electrospinning preparation of Timosaponin B-II-loaded plla nanofibers and their antitumor recurrence activities in vivo. J Nanomater 9

Irie T, Uekama K (1998) Pharmaceutical applications of cyclodextrins. III. Toxicological issues and safety evaluation. J Pharm Sci 86:147–162

Jaiswal S, Duffy B, Jaiswal AK, Stobie N, McHale P (2010) Enhancement of the antibacterial properties of silver nanoparticles using β-cyclodextrin as a capping agent. Int J Antimicrob Agents 36:280–283

Jeang CL, Lin DG, Hsieh SH (2005) Characterization of cyclodextrin glycosyltransferase of the same gene expressed from Bacillus macerans, Bacillus subtilis, and Escherichia coli. J Agric Food Chem 53:6301–6304

Jia Y-T, Kim H-Y, Gong J, Lee D-R (2006) Electrospun nanofibers of block copolymer of trimethylene carbonate and ϵ-caprolactone. J Appl Polym Sci 99:1462–1470

Jug M, Kosalec I, Maestrelli F, Mura P (2011) Analysis of triclosan inclusion complexes with beta-cyclodextrin and its water-soluble polymeric derivative. J Pharm Biomed Anal 54:1030–1039

Kanawung K, Panitchanapan K, S-o Puangmalee, Utok W, Kreua-ongarjnukool N, Rangkupan R (2007) Preparation and characterization of polycaprolactone/diclofenac sodium and poly(vinyl alcohol)/tetracycline hydrochloride fiber mats and their release of the model drug. Polymer 39:369–378

Kang Y, Choi YK, Kim HJ, Song Y, Kim H (2015) Preparation of anti-bacterial cellulose fiber via electrospinning and crosslinking with β-cyclodextrin. Fashion Textiles 2:1–10

Kaur S, Kotaki M, Ma Z, Gopal R, Ramakrishna S (2006) Oligosaccharide functionalized nanofibrous membrane. Int J Nanosci 5:1–11

Kayaci F, Uyar T (2012a) Electrospun zein nanofibers incorporating cyclodextrins. Carbohyd Polym 90:558–568

Kayaci F, Uyar T (2012b) Encapsulation of vanillin/cyclodextrin inclusion complex in electrospun polyvinyl alcohol (PVA) nanowebs: prolonged shelf-life and high temperature stability of vanillin. Food Chem 133:641–649

Kayaci F, Uyar T (2014) Electrospun polyester/cyclodextrin nanofibers for entrapment of volatile organic compounds. Polym Eng Sci 54:2970–2978

Kayaci F, Aytac Z, Uyar T (2013a) Surface modification of electrospun polyester nanofibers with cyclodextrin polymer for the removal of phenanthrene from aqueous solution. J Hazard Mater 261:286–294

Kayaci F, Umu OCO, Tekinay T, Uyar T (2013b) Antibacterial electrospun poly(lactic acid) (PLA) nanofibrous webs incorporating triclosan/cyclodextrin inclusion complexes. J Agric Food Chem 61:3901–3908

Kayaci F, Ertas Y, Uyar T (2013c) Enhanced thermal stability of eugenol by cyclodextrin inclusion complex encapsulated in electrospun polymeric nanofibers. J Agric Food Chem 61:8156–8165

Kayaci F, Sen HS, Durgun E, Uyar T (2015) Electrospun nylon 6,6 nanofibers functionalized with cyclodextrins for removal of toluene vapor. J Appl Polym Sci 132

Kenawy E-R, Abdel-Hay FI, El-Newehy MH, Wnek GE (2009) Processing of polymer nanofibers through electrospinning as drug delivery systems. Mater Chem Phys 113:296–302

Khalil AS, Xie AW, Murphy WL (2014) Context clues: the importance of stem cell-material interactions. ACS Chem Biol 9:45–56

Kim TG, Park TG (2006) Biomimicking extracellular matrix: cell adhesive RGD peptide modified electrospun poly (D, L-lactic-co-glycolic acid) nanofiber mesh. Tissue Eng 12:221–233

Kim JW, Kang HH, Suh KD, Oh SG (2003) Stabilization of water-soluble antioxidant in water-in-oil-in-water double emulsions. J Dispersion Sci Technol 24:833–839

Kim TG, Lee DS, Park TG (2007) Controlled protein release from electrospun biodegradable fiber mesh composed of poly(ε-caprolactone) and poly(ethylene oxide). Int J Pharm 338:276–283

Larrondo L, St John Manley R (1981) Electrostatic fiber spinning from polymer melts. I. Experimental observations on fiber formation and properties. J Polym Sci: Polymer Phys Ed 19:909–920

Lee SS, Huang BJ, Kaltz SR, Sur S, Newcomb CJ, Stock SR (2013) Bone regeneration with low dose BMP-2 amplified by biomimetic supramolecular nanofibers within collagen scaffolds. Biomaterials 34:452–459

Leung WW-F, Hung C-H (2012) Skin effect in nanofiber filtration of submicron aerosols. Sep Purif Technol 92:174–180

Li S, Purdy WC (1992) Cyclodextrins and their applications in analytical chemistry. Chem Rev 92:1457–1470

Li X, Kanjwal MA, Lin L, Chronakis IS (2013) Electrospun polyvinyl-alcohol nanofibers as oral fast-dissolving delivery system of caffeine and riboflavin. Colloids Surf, B 103:182–188

Li H, Li C, Bai J, Xu T, Sun W, Xu W (2014) Synthesis of α-, β- and γ-cyclodextrin/poly (Acrylonitrile) composite nanofibers and their applications to Cu(II) ion adsorption. Polymer-Plastics Technol Eng 53:513–519

Linde GA, Laverde A Jr, Colauto NB (2011) Changes to taste perception in the food industry: use of cyclodextrins. Handbook of behavior, food and nutrition. Springer, New York, pp 99–118

Liu L, Guo Q-X (1999) Novel prediction for the driving force and guest orientation in the complexation of α- and β-cyclodextrin with benzene derivatives. J Phys Chem B 103:3461–3467

Liu Y, Pellerin C (2006) Highly oriented electrospun fibers of self-assembled inclusion complexes of poly(ethylene oxide) and urea. Macromolecules 39:8886–8888

Liu R, Cai N, Yang W, Chen W, Liu H (2010) Sea-island polyurethane/polycarbonate composite nanofiber fabricated through electrospinning. J Appl Polym Sci 116:1313–1321

Loftsson T (2000) Cyclodextrins in skin delivery. Cosmet Toilet 115:59–66

Loftsson T, Brewster ME (1996) Pharmaceutical applications of cyclodextrins. 1. Drug solubilization and stabilization. J Pharm Sci 85:1017–1025

Loftsson T, Brewster ME (2010) Pharmaceutical applications of cyclodextrins: basic science and product development. J Pharm Pharmacol 62:1607–1621

Loftsson T, Moya-Ortega MD, Alvarez-Lorenzo C, Concheiro A (2015) Pharmacokinetics of cyclodextrins and drugs after oral and parenteral administration of drug/cyclodextrin complexes. J Pharm Pharmacol 68:544–555

Luo X, Xie C, Wang H, Liu C, Yan S, Li X (2012) Antitumor activities of emulsion electrospun fibers with core loading of hydroxycamptothecin via intratumoral implantation. Int J Pharm 425:19–28

Luong-Van E, Grøndahl L, Chua KN, Leong KW, Nurcombe V, Cool SM (2006) Controlled release of heparin from poly(ε-caprolactone) electrospun fibers. Biomaterials 27:2042–2050

Ma X, Chen Z, Chen X, Chen R, Zheng X (2011) Preparation of imprinted PVB/β-CD nanofiber by electrospinning technique and its selective binding abilities for naringin. Chin J Chem 29:1753–1758

Ma XL, Wu ZY, Chen Z, Chen S (2013) Preparation of PVB/β-CD/silica nanofibers using electrospinning techniques. Adv Mater Res: Trans Tech Publ:2187–2190

Manasco JL, Saquing CD, Tang C, Khan SA (2012) Cyclodextrin fibers via polymer-free electrospinning. RSC Adv 2:3778–3784

Manasco JL, Tang C, Burns NA, Saquing CD, Khan SA (2014) Rapidly dissolving poly(vinyl alcohol)/cyclodextrin electrospun nanofibrous membranes. RSC Adv 4:13274–13279

Maretschek S, Greiner A, Kissel T (2008) Electrospun biodegradable nanofiber nonwovens for controlled release of proteins. J Controlled Release 127:180–187

Marques HMC (2010) A review on cyclodextrin encapsulation of essential oils and volatiles. Flavour Fragrance J 25:313–326

Martel B, Morcellet M, Ruffin D, Vinet F, Weltrowski L (2002) Capture and controlled release of fragrances by CD finished textiles. J Incl Phenom Macrocycl Chem 44:439–442

Matulevicius J, Kliucininkas L, Prasauskas T, Buivydiene D, Martuzevicius D (2016) The comparative study of aerosol filtration by electrospun polyamide, polyvinyl acetate, polyacrylonitrile and cellulose acetate nanofiber media. J Aerosol Sci 92:27–37

Matuseviciute A, Butkiene A, Stanys S, Adomaviciute E (2012) Formation of PVA Nanofibres with Iodine by Electrospinning. Fibres & Textiles in Eastern Europe:21–25

McKee MG, Layman JM, Cashion MP, Long TE (2006) Phospholipid nonwoven electrospun membranes. Science 311:353–355

Mei Y, Wang Z, Li X (2013) Improving filtration performance of electrospun nanofiber mats by a bimodal method. J Appl Polym Sci 128:1089–1094

Na H-S, Kim J-N, Kim J-M, Lee K-Y (2011) Encapsulation of fish oil using cyclodextrin and whey protein concentrate. Biotechnol Bioproc E. 16:1077–1082

Nagai Y, Unsworth LD, Koutsopoulos S, Zhang S (2006) Slow release of molecules in self-assembling peptide nanofiber scaffold. J Controlled Release 115:18–25

Narayanan G (2014) Electrospinning of poly (epsilon-caprolactone) fibers functionalized with cyclodextrins and their inclusion complexes. North Carolina State University, Raleigh, NC, USA

Narayanan G, Gupta BS, Tonelli AE (2014) Poly(ε-caprolactone) nanowebs functionalized with α- and γ-cyclodextrins. Biomacromol 15:4122–4133

Narayanan G, Ormond BR, Gupta BS, Tonelli AE (2015a) Efficient wound odor removal by β-cyclodextrin functionalized poly (ε-caprolactone) nanofibers. J Appl Polym Sci 132:42782

Narayanan G, Gupta BS, Tonelli AE (2015b) Enhanced mechanical properties of poly (ε-caprolactone) nanofibers produced by the addition of non-stoichiometric inclusion complexes of poly (ε-caprolactone) and α-cyclodextrin. Polymer 76:321–330

Narayanan G, Vernekar VN, Kuyinu EL, Laurencin CT (2016a) Poly (lactic acid)-based biomaterials for orthopaedic regenerative engineering. Adv Drug Deliver Rev 107:247–276

Narayanan G, Tekbudak MY, Caydamli Y, Dong J, Krause WE (2017) Accuracy of electrospun fiber diameters: The importance of sampling and person-to-person variation. Polym Test 61:240–248

Narayanan G, Aguda R, Hartman M, Chung C-C, Boy R, Gupta BS (2016b) Fabrication and characterization of Poly(ε-caprolactone)/α-cyclodextrin pseudorotaxane nanofibers. Biomacromol 17:271–279

Narayanan G, Chung C-C, Aguda R, Boy R, Hartman M, Mehraban N, et al (2016c) Correlation of the stoichiometries of poly(ε-caprolactone) and α-cyclodextrin pseudorotaxanes with their solution rheology and the molecular orientation, crystallite size, and thermomechanical properties of their nanofibers. RSC Adv 6:111326–111336

Ngawhirunpat T, Opanasopit P, Rojanarata T, Akkaramongkolporn P, Ruktanonchai U, Supaphol P (2009) Development of meloxicam-loaded electrospun polyvinyl alcohol mats as a transdermal therapeutic agent. Pharm Dev Technol 14:70–79

Numanoglu U, Sen T, Tarimci N, Kartal M, Koo OM, Onyuksel H (2007) Use of cyclodextrins as a cosmetic delivery system for fragrance materials: linalool and benzyl acetate. AAPS PharmSciTech 8:85

Oster M, Hébraud A, Gallet S, Lapp A, Pollet E, Avérous L (2015) Star-pseudopolyrotaxane organized in nanoplatelets for poly(ε-caprolactone)-based nanofibrous scaffolds with enhanced surface reactivity. Macromol Rapid Commun 36:292–297

Petit L, Pierard GE (2003) Analytic quantification of solar lentigines lightening by a 2% hydroquinone-cyclodextrin formulation. J Eur Acad Dermatol Venereol 17:546–549

Pillay V, Dott C, Choonara YE, Tyagi C, Tomar L, Kumar P (2013) A review of the effect of processing variables on the fabrication of electrospun nanofibers for drug delivery applications. J Nanomater

Potrč T, Baumgartner S, Roškar R, Planinšek O, Lavrič Z, Kristl J (2015) Electrospun polycaprolactone nanofibers as a potential oromucosal delivery system for poorly water-soluble drugs. Eur J Pharm Sci 75:101–113

Prabaharan M, Jayakumar R (2009) Chitosan-graft-β-cyclodextrin scaffolds with controlled drug release capability for tissue engineering applications. Int J Biol Macromol 44:320–325

Qi R, Guo R, Zheng F, Liu H, Yu J, Shi X (2013) Controlled release and antibacterial activity of antibiotic-loaded electrospun halloysite/poly(lactic-co-glycolic acid) composite nanofibers. Colloids Surf, B 110:148–155

Rafati AA, Bagheri A, Iloukhani H, Zarinehzad M (2005) Study of inclusion complex formation between a homologous series of n-alkyltrimethylammonium bromides and β-cyclodextrin, using conductometric technique. J Mol Liq 116:37–41

Rajewski RA, Traiger G, Bresnahan J, Jaberaboansar P, Stella VJ, Thompson DO (1995) Preliminary safety evaluation of parenterally administered sulfoalkyl ether β-cyclodextrin derivatives. J Pharm Sci 84:927–932

Reneker DH, Chun I (1996) Nanometre diameter fibres of polymer, produced by electrospinning. Nanotechnology 7:216

Reuscher H, Hirsenkorn R (1996) New ways in surface modification. J Incl Phenom Mol Recognit Chem 25:191–196

Saquing CD, Tang C, Monian B, Bonino CA, Manasco JL, Alsberg E (2013) Alginate-polyethylene oxide blend nanofibers and the role of the carrier polymer in electrospinning. Ind Eng Chem Res 52:8692–8704

Schofer MD, Roessler PP,Schaefer J, Theisen C, Schlimme S, Heverhagen JT et al (2011) Electrospun PLLA nanofiber scaffolds and theiruse in combination with BMP-2 for reconstruction of bone defects. PLoS ONE 6:e25462

Son WK, Youk JH, Lee TS, Park WH (2004) The effects of solution properties and polyelectrolyte on electrospinning of ultrafine poly (ethylene oxide) fibers. Polymer 45:2959–2966

Stegemann S, Leveiller F, Franchi D, de Jong H, Lindén H (2007) When poor solubility becomes an issue: from early stage to proof of concept. Eur J Pharm Sci 31:249–261

Strickley RG (2004) Solubilizing excipients in oral and injectable formulations. Pharm Res 21:201–230

Sundarrajan S, Tan KL, Lim SH, Ramakrishna S (2014) Electrospun nanofibers for air filtration applications. Procedia Eng 75:159–163

Szejtli J (1988) Cyclodextrins. Springer, Cyclodextrin technology, pp 1–78

Szejtli J (1997) Utilization of cyclodextrins in industrial products and processes. J Mater Chem 7:575–587

Szejtli J (2003) Cyclodextrins in the textile industry. Starch/Stärke 55:191–196

Szejtli J, Szente L (2005) Elimination of bitter, disgusting tastes of drugs and foods by cyclodextrins. Eur J Pharm Biopharm 61:115–125

Szejtli J, Szente L, Bankyelod E (1979) Molecular encapsulation of volatile, easily oxidizable labile flavor substances by cyclodextrins. Acta Chimica Academiae Scientarium Hungaricae 101:27–46

Tae-Gyung K, Dhanusuraman R, Anantha Iyengar G, Kwang-Pill L (2010) Electrospun carbon nanotubes–gold nanoparticles embedded nanowebs: prosperous multi-functional nanomaterials. Nanotechnology 21:134021

Taepaiboon P, Rungsardthong U, Supaphol P (2006) Drug-loaded electrospun mats of poly (vinyl alcohol) fibres and their release characteristics of four model drugs. Nanotechnology 17:2317

Taepaiboon P, Rungsardthong U, Supaphol P (2007) Vitamin-loaded electrospun cellulose acetate nanofiber mats as transdermal and dermal therapeutic agents of vitamin A acid and vitamin E. Eur J Pharm Biopharm 67:387–397

Tamer U, Rasmus H, Jale H, Xingfei Z, Flemming B, Peter K (2009a) The formation and characterization of cyclodextrin functionalized polystyrene nanofibers produced by electrospinning. Nanotechnology 20:125605

Tamer U, Yusuf N, Jale H, Flemming B (2009b) Electrospinning of functional poly(methyl methacrylate) nanofibers containing cyclodextrin-menthol inclusion complexes. Nanotechnology 20:125703

Teng M, Li F, Zhang B, Taha AA (2011) Electrospun cyclodextrin-functionalized mesoporous polyvinyl alcohol/SiO2 nanofiber membranes as a highly efficient adsorbent for indigo carmine dye. Colloids Surf, A 385:229–234

Thau P (2005) Controlled delivery and enhancement of topical activity of salicylic acid. In: Rosen MR (ed) delivery system handbook for personal care and cosmetic products. William Andrew Publishing, Norwich, NY, pp 873–879

Tiwari SK, Venkatraman SS (2012) Importance of viscosity parameters in electrospinning: of monolithic and core–shell fibers (2012). Mater Sci Eng C (32):1037–1042

Tungprapa S, Jangchud I, Supaphol P (2007) Release characteristics of four model drugs from drug-loaded electrospun cellulose acetate fiber mats. Polymer 48:5030–5041

Uyar T, Besenbacher F (2009) Electrospinning of cyclodextrin functionalized polyethylene oxide (PEO) nanofibers. Eur Polymer J 45:1032–1037

Uyar T, Kingshott P, Besenbacher F (2008) Electrospinning of cyclodextrin-pseudopolyrotaxane nanofibers. Angew Chem Int Ed 47:9108–9111

Uyar T, Balan A, Toppare L, Besenbacher F (2009a) Electrospinning of cyclodextrin functionalized poly(methyl methacrylate) (PMMA) nanofibers. Polymer 50:475–480

Uyar T, Havelund R, Nur Y, Hacaloglu J, Besenbacher F, Kingshott P (2009b) Molecular filters based on cyclodextrin functionalized electrospun fibers. J Membr Sci 332:129–137

Uyar T, Hacaloglu J, Besenbacher F (2009c) Electrospun polystyrene fibers containing high temperature stable volatile fragrance/flavor facilitated by cyclodextrin inclusion complexes. React Funct Polym 69:145–150

Uyar T, Havelund R, Hacaloglu J, Besenbacher F, Kingshott P (2010a) Functional electrospun polystyrene nanofibers incorporating α-, β-, and γ-cyclodextrins: comparison of molecular filter performance. ACS Nano 4:5121–5130

Uyar T, Havelund R, Nur Y, Balan A, Hacaloglu J, Toppare L (2010b) Cyclodextrin functionalized poly(methyl methacrylate) (PMMA) electrospun nanofibers for organic vapors waste treatment. J Membr Sci 365:409–417

Uyar T, Hacaloglu J, Besenbacher F (2011) Electrospun Polyethylene Oxide (PEO) nanofibers containing cyclodextrin inclusion complex. J Nanosci Nanotechnol 11:3949–3958

Vogel R, Tändler B, Häussler L, Jehnichen D, Brünig H (2006) Melt spinning of poly (3-hydroxybutyrate) fibers for tissue engineering using α-cyclodextrin/polymer inclusion complexes as the nucleation agent. Macromol Biosci 6:730–736

Voncina B, Le Marechal AM (2005) Grafting of cotton with β-cyclodextrin via poly(carboxylic acid). J Appl Polym Sci 96:1323–1328

Wang Y, Ren J, Deng K, Gui L, Tang Y (2000) Preparation of tractable platinum, rhodium, and ruthenium nanoclusters with small particle size in organic media. Chem Mater 12:1622–1627

Wang S, Zheng F, Huang Y, Fang Y, Shen M, Zhu M (2012a) Encapsulation of amoxicillin within laponite-doped poly(lactic-co-glycolic acid) nanofibers: preparation, characterization, and antibacterial activity. ACS Appl Mater Interfaces 4:6393–6401

Wang N, Wang X, Ding B, Yu J, Sun G (2012b) Tunable fabrication of three-dimensional polyamide-66 nano-fiber/nets for high efficiency fine particulate filtration. J Mater Chem 22:1445–1452

Wang S, Bai J, Li C, Zhang Y, Zhang J (2012c) Ag nanoparticle-embedded one-dimensional β-CD/PVP composite nanofibers prepared via electrospinning for use in antibacterial material. Colloid Polym Sci 290:667–672

Wang S, Bai J, Li C, Zhang J (2012d) Functionalization of electrospun β-cyclodextrin/polyacrylonitrile (PAN) with silver nanoparticles: Broad-spectrum antibacterial property. Appl Surf Sci 261:499–503

Wei M, Davis W, Urban B, Song Y, Porbeni FE, Wang X (2002) Manipulation of Nylon-6 crystal structures with its α-cyclodextrin inclusion complex. Macromolecules 35:8039–8044

Wei A, Wang J, Wang X, Hou D, Wei Q (2012) Morphology and surface properties of poly (L-lactic acid)/captopril composite nanofiber membranes. J Eng Fabrics Fibers 7

Williamson B, Tonelli A (2012) Constrained polymer chain behavior observed in their non-stoichiometric cyclodextrin inclusion complexes. J Incl Phenom Macrocycl Chem 72:71–78

Woldum HS, Larsen KL, Madsen F (2008) Cyclodextrin controlled release of poorly water-soluble drugs from hydrogels. Drug Deliv 15:69–80

Wong S-C, Baji A, Leng S (2008) Effect of fiber diameter on tensile properties of electrospun poly (ε-caprolactone). Polymer 49:4713–4722

Xiao N, Wen Q, Liu Q, Yang Q, Li Y (2014) Electrospinning preparation of β-cyclodextrin/glutaraldehyde crosslinked PVP nanofibrous membranes to adsorb dye in aqueous solution. Chem Res Chin Univ 30:1057–1062

Wu X-M , Branford-White C, Zhu L-M , Chatterton N, D-g Yu (2010) Ester prodrug-loaded electrospun cellulose acetate fiber mats as transdermal drug delivery systems. J Mater Sci Mater Med 21:2403–2411

Xu X, Chen X, Wang Z, Jing X (2009) Ultrafine PEG–PLA fibers loaded with both paclitaxel and doxorubicin hydrochloride and their in vitro cytotoxicity. Eur J Pharm Biopharm 72:18–25

Xu X, Zhong W, Zhou S, Trajtman A, Alfa M (2010) Electrospun PEG–PLA nanofibrous membrane for sustained release of hydrophilic antibiotics. J Appl Polym Sci 118:588–595

Xu T, Li C, Li H, Bai J, Qin H, Sun W (2014) Synthesis and characterization of Cu nanoparticles embedded in PAN/β-cyclodextrin (β-CD) composite nanofiber films. Part Sci Technol 32:306–310

Yan N, Zhang X, Cai Q, Yang X, Zhou X, Wang B (2012) The effects of lactidyl/glycolidyl ratio and molecular weight of poly(D, L -Lactide-co-Glycolide) on the tetracycline entrapment and release kinetics of drug-loaded nanofibers. J Biomater Sci Polym Ed 23:1005–1019

Yan D, Jones J, Yuan XY, Xu XH, Sheng J, Lee JCM (2013) Plasma treatment of electrospun PCL random nanofiber meshes (NFMs) for biological property improvement. J Biomed Mater Res, Part A 101A:963–972

Yang D, Li Y, Nie J (2007) Preparation of gelatin/PVA nanofibers and their potential application in controlled release of drugs. Carbohyd Polym 69:538–543

Yao J, Bastiaansen CW, Peijs T (2014) High strength and high modulus electrospun nanofibers. Fibers 2:158–186

Yarin AL, Koombhongse S, Reneker DH (2001) Taylor cone and jetting from liquid droplets in electrospinning of nanofibers. J Appl Phys 90:4836–4846

You Y, Lee SJ, Min B-M, Park WH (2006) Effect of solution properties on nanofibrous structure of electrospun poly(lactic-co-glycolic acid). J Appl Polym Sci 99:1214–1221

Yu D-G, Yu J-H, Chen L, Williams GR, Wang X (2012) Modified coaxial electrospinning for the preparation of high-quality ketoprofen-loaded cellulose acetate nanofibers. Carbohyd Polym 90:1016–1023

Zeng J, Aigner A, Czubayko F, Kissel T, Wendorff JH, Greiner A (2005) Poly(vinyl alcohol) nanofibers by electrospinning as a protein delivery system and the retardation of enzyme release by additional polymer coatings. Biomacromol 6:1484–1488

Zhan J, Singh A, Zhang Z, Huang L, Elisseeff JH (2012) Multifunctional aliphatic polyester nanofibers for tissue engineering. Biomatter. 2:202–212

Zhang Y, Venugopal JR, El-Turki A, Ramakrishna S, Su B (2008) Lim CT (2008) Electrospun biomimetic nanocomposite nanofibers of hydroxyapatite/chitosan for bone tissue engineering. Biomaterials 29:4314–4322

Zhang W, Chen M, Diao G (2011) Electrospinning β-cyclodextrin/poly(vinyl alcohol) nanofibrous membrane for molecular capture. Carbohyd Polym 86:1410–1416

Chapter 4
Recent Advances in Cationic and Anionic Polysaccharides Fibers

Ramakrishnan Krishnaswamy and Ali Ayoub

Abstract This chapter will discuss the recent advances on the cationic and anionic polysaccharides fiber and the effect on the paper properties.

Keywords Starch · Ionic fiber · Starch fiber

4.1 Introduction

Starch is used widely in the food, papermaking, cosmetics, chemical and pharmaceutical industries (Whistler 1984). In the paper-making industry, starch is the most commonly used in applications such as surface sizing agent, retention agent, strength increasing agent and as a binder in paper coatings. Native starch is a blend of two polysaccharides, amylose, which is a linear polymer and amylopectin, a branched polymer. In a study that looked at adsorption of amylose and amylopectin, it was found that amylose preferentially adsorbed on fibers (Shirazi et al. 2003). In reference to the paper industry, the papermaking fibers are classified as short and long fibers. The fibers ranging from one to two mm in length and originating from hardwoods and pulped through the sulphite process are classified as short fibers while the fibers from softwoods ranging from 2.5 to 5 mm are classified as long fibers (Nachtergaele 1989). With regard to forming fibrous assemblies from cationically and anionically charged fibers, the prior art is described in U.S Patent by Lyness et al. 1976. It describes a method for forming fibrous assemblies of short fibers having the strength of long fibers. It also describes the agents used to bind the fibers together and categorizes these as anionic and cationic, which is caused by presence of polarizable functional groups. A common difficulty known in the art with adding these agents is their agglomeration with each other, thereby preventing their interaction with the fibers, which imparts functionality to the fibers. A method

R. Krishnaswamy · A. Ayoub (✉)
Department of Forest Biomaterials, College of Natural Resources,
North Carolina State University, Raleigh, NC, USA
e-mail: info@ayoubsciences.org

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for obtaining uniform fiber distribution through the use of high yield stress fluid fraction is demonstrated by Lyness et al. 1976. This invention discusses the properties of the product such as strength, toughness, ductility and flexibility that results on having a uniform distribution.

4.1.1 Cationic Polysaccharide

Polymers containing positive charge or synthesized in the presence of cations are called cationic polymers (Sennett and Olivier 1965). One such example is the cationic polysaccharide, Dextran, which is an FDA approved water soluble polysaccharide. Its solubility in water is independent of pH. Cationic cellulose fiber derivatives are another example of polysaccharides having functional properties such as hydrophilicity, biodegradability and anti-bacterial properties (Samal et al. 2012, Song et al. 2011 and Xu et al. 2009). Homogeneous quaternization of fiber cellulose in aqueous solution was first reported that by Song and others, also they extended the work to obtain hydrophobically modified quarternized cellulose (HMCO) for therapeutic applications such as delivery of poorly water soluble drugs (Samal et al. 2012). However, quaternized cellulose fiber derivatives have not been widely reported due to the lack of solubility in water of cellulose.

The benefits provided by using cationic starches for applications such as surface sizing of paper, are manifold, such as better mechanical properties, quicker drainage and reduction of pollution due to waste water and better retention of fillers. Cationic starch is absorbed mainly by finer fraction and fillers which are characterized by their high surface area. Of the cationic, the most tenacious and strongly absorbed are polymeric cations such as polyacrylamides and starches (Nachtergaele 1989). There are many models to explain the rather complex interactions between the cationic starch and the surface of the fiber. One such model explains the formation of a two-part electrical layer at the interface of the solid and liquid (Lyness et al. 1976). Of these two parts, one comprises of a thin layer of ions adjoining the solid surface, and of opposite charge while the other is a diffuse layer, comprising of ions of opposite charge to that of the solid, which extends to the bulk of the liquid. An important parameter that influences the retention of ionic wet-end chemicals and governs many processes involved in making a functional paper is Zeta Potential (Nachtergaele 1989). Using cationic starch has multiple benefits such as presence of multiple complex interactions not limited to electrostatic and hydrogen bonds resulting in flocculation, which leads to better mechanical properties, better retention of fillers and improved drainage (Nachtergaele 1989).

Villiers in 1891 was the first to discover cyclodextrins. They were named cellulosine because they behaved similar to cellulose, i.e., resistant to hydrolysis. This crystalline product was isolated after bacterial digestion of potato starch and is regarded as the first published record of cyclodextrin (Fayazpour et al. 2006). Years later, Schardinger discovered two crystalline polysaccharides, while investigating food spoilage, that were named ‘crystalline dextrin a’ and ‘crystalline dextrin b.’

(Villiers 1891). Freudenberg and Jacobi developed a method to purify a, ß and.-dextrin and studied the chemical composition of these molecules (Freudenberg and Jacobi 1935). A series of studies published in the 1930s led to the confirmation of the cyclic structures of these starches. Now, it is common knowledge that cyclodextrins are annular molecules. Cyclodextrins have hydroxyl groups that are primary and secondary and are attached on one rim or the other (Schardinger 1911). The hydroxyl groups, and more importantly their positioning (outside the cavity on both rims), leads to many structural features and complexation behaviors that are unique to cyclodextrins. The glucopyranose unit, hinders bond rotation and leads to the truncated cone shape of the cyclodextrins. This coupled with the hydrophilic exterior/hydrophobic core and cyclodextrins' bio-degradable, bio-absorbable nature makes their utility unique for drug delivery. However there are certain issues with using cyclodextrins. For example, amongst the cyclodextrins, due to asymmetry among the odd number of glucose units and the low solubility in water, ß-CD behaves differently from α-and γ-CDs, so its oral administration/absorption is not that effective, and parenteral administration is the preferred route of drug delivery (Brewster and Loftsson 2007). The main advantages of using Cyclodextrins are their monodisperse ring structure, ease of making specific chemical modification such as monochlorotriazine-β-Cyclodextrin (MCT-β-CD) (Hebesih and El-Hilw 2001), the ability to fix β-CD to cellulose by the use of epichlorohydrin (Gonzalez et al. 1999). Other advantages of cationic cyclodextrins include the availability of multiple sites for the introduction of moieties and to bind to nucleotides and the ability to be incorporated in dentric and polycationic systems. Chitosan is another example of cationic polymer being used for applications such as hydrogels, drug release systems and polyelectrolyte complex (Sennett and Olivier 1965). Ma and coworkers prepared chitosan microspheres loaded with proteins by the combination of application of high voltage electric field and ionotropic gelation method for their sustained delivery (Ma and Liu 2010). Electrospun cationic fibers containing chitosan and polycaprolactone have been used for biomedical applications such as tissue engineering, drug delivery and such (Sennett and Olivier 1965).

In another study, cationic complexes synthesized by Zhang and others were found to be effective in protecting from degradation in the gastrointestinal tract due to the complexation of β-CD with insulin and the subsequent encapsulation into alginate/chitosan nanospheres (Zhang et al. 2010). Also, a localized controlled release hydrogel system composed of cationic gelatin and chitosan has been reported to deliver an antisense oligonucleotide targeting murine TNF-α for the treatment of endotoxin induced osteolysis (Dong et al. 2010).

Davis and others investigated the effectiveness of using cyclodextrin in an electrostatic complex with cationic polymers such as polyaminothiourea by polycondensation reaction. They found that the electrostatic complexation of the CD and cationic polymers capable of binding to DNA had in vitro cell transfection efficiency comparable to that of Lipofectamine™ or PEI (Davis et al. 2010). Diaz-Moscosco and others designed a polycationic CD based facial ampiphiles whose architecture allowed the fine-tuning of the density and flexibility of cationic groups apart from functionalizing the polymer in terms of additional hydrogen

bonding (Diaz-Moscoso et al. 2009). A further extension of this study was the development of polycationic β-CD that could form complex with homogeneous DNA nanoparticles. Cationic CD has also been used to separate anionic pharmaceuticals by capillary electrophoresis (Tang and Ng 2007). Figure 4.2 shows examples of nano-fiber electrospun mats.

4.1.2 Anionic Polysaccharides

Anionic polysaccharides include examples such as pectin, xanthan gum, alginic acid, gum Arabic and other materials (Wen and Oh 2014). Alginate is an example of anionic polysaccharide copolymer comprising blocks of (1,4)-linked β-D-mannuronic acid (M) and α-L-guluronic acid (G) that is obtained from brown seaweed (Lee et al. 2009). Alginate based nanomaterials being biocompatible, is a good candidate for variety of biomedical applications such as tissue engineering, with the underlying hypothesis being that the biopolymer nanofibers can best mimic the extra cellular matrix (ECM). Additionally, it was found that polymer viscosity, which can be manipulated by a number of ways, such as addition of a hydrophilic polymer or surfactant and varying the molecular weight of the polysaccharide. Since the viscosity of the polymer solution and its structure are changeable with time owing to external variables, it is important to control the same in order to retain the structural identity of the scaffold in vivo for a stipulated period of time. In this context, it is relevant to utilize crosslinking approaches to accomplish the same (Lee et al. 2009).

Another approach is the synthesis of anionic copolymers by modifying the terminal end group of the polysaccharide by using one of the standard grafting methods viz 'grafting from' or 'grafting to' (Wen and Oh 2014).

4.2 Ionic Polysaccharide Nanofibers and Applications

Nanofibers are an exceptional class of material structures that are rapidly gaining traction for myriad applications such as water and air filtration, tissue regeneration, and drug delivery, to name a few (Narayanan et al. 2014). Unlike electrospinning of other materials from natural origin such as cyclodextrins with several variants, either with or without a polymer carrier, that have been studied extensively in the last 5 years, electrospinning of polysaccharide nanofibers has not developed many applications due to various factors such as poor solubility and high surface tension. These problems could be overcome in the future by using mixed solvent systems, synthesizing polysaccharide derivatives, developing core-shell type structures, and micro-nano fiber composites (Wen and Oh 2014). Promising new applications such as tumor targeting drug delivery require multiple stimuli responsive degradation from the polysaccharide based nanomaterials. Another rmethod that is being explored is the mini-emulsion technique, however a drawback associated with this

is that the removal of residual oil soluble surfactant requires harsh treatment. Alternate methods that could be explored for nanogels with narrow size distribution include the temperature driven self-assembly and crosslinking (Lee et al. 2009).

4.3 Recent Advances in Nano and Micropariclesfrom Protein-Polysaccharide Complexes

Functionalized protein-polysaccharide complexes formed by heat-setting are being used for myriad applications such as fat mimetics, lightening agents, texture modifying agents and encapsulation and drug delivery systems (Jones et al. 2010). The behavior of both anionic (chitosan) and cationic (high methoxy pectin, carrageenan, low methoxy pectin) polysaccharides have been preliminarily studied and, further investigation in this area is needed to conclusively establish the relationship between the polysaccharide molecular structure and the resultant properties of the complex. Of the two methods commonly used, one involves heating globular proteins above their denaturation temperature and complexing them with ionic polysaccharides. In this method, the properties of the particles are influenced more by the electrical properties of the polysaccharide and the light scattering and atomic force microscopy images are used to propose a core-shell structure whereby the protein particles get encapsulated by the polysaccharide shell. The second method involves heating a solution of protein-polysaccharide complexes at a specific pH above the denaturation temperature of the protein and the properties that result were markedly different suggesting that this method resulted in a higher surface coverage with pectin, thereby reducing the tendency of the particles to aggregate (Jones et al. 2010). Microparticle addition has been shown to be effective, after a sufficient amount of cationic additive -that shifts the net charge of the system to positive- have been added as the microparticles have a negative surface charge and this facilitates rapid complexation between the microparticles and cationic polymer. In contrast, excess amount of DCS has been shown to adversely affect performance of microparticle addition (Wackerberg et al. 1994).

4.4 Influence on Paper Properties

Cationic chitosan acetate and its blends have been utilized to modify the anionic cellulose fibers and improve the properties of the paper due to possible ionic interactions. Addition of low weight fraction of poly vinyl alcohol and gelated starch give the optimum mechanical strength (Mucha and Miśkiewicz 2000). The tensile strength of paper is influenced most profoundly by the individual fiber strength and also the strength of the joints and thus improving the fiber joint would be a logical way increase paper strength. Use of polyacrylic acid and polyallylamine hydrochloride to form a polyelectrolyte multilayer has been shown to improve the

fiber joint strength in paper by increasing the number of fiber joints, also increasing the degree of contact between the fibers and increasing the covalent bonding degree in the molecular contact area between the fibers (Eriksson et al. 2006).

Chemical additives and the machines themselves can vary depending upon the state of the art of the technology used. Paper making, in general, needs to consider both microscopic and macroscopic scales to optimize the settings especially when very high mass polyelectrolytes are used for the process. In the future technological development could lead to more success in retention of fine particles, while also improving uniformity.

4.5 Multilayered Polysaccharide Biofilms

Hseih and others demonstrated that Multiple Bilayered polysaccharide Biofilms consisting of alternate deposition of cationic chitosan and anionic Dextran sulfate onto partially hydrolysed cellulose acetate fibers and ultra fine cellulose. Thus it was demonstrated that long chained Polysaccharides can be self-assembled as nano bilayers fine cellulose fibers giving a fully Polysaccharide based fiber architecture with superior chemical reactivity, structural flexibility and advantageous electrolytic nature. This technique is in contrast with the more conventional Langmuir-Blodgett technique where a self assembled monolayer in water is deposited on the solid surface containing hydrophilic heads and hydrophobic tails. The main goal of the study by study was to elucidate the surface effects of cellulose fibers on layer by layer deposition of polysaccharides, thereby establishing multiple bilayers on ultrathin fibers, and the characterization of the fibers that result. An earlier approach of electrospinning Cellulose acetate that was developed was used for the purpose of the cellulose substrate, owing to the robust and versatile nature of the fibers that result. Nucleophilic substitution of acetyl groups by hydroxyl groups as a means of improving the hydrophilicity of the substrate was employed. Among the factors critical for layer by layer deposition of polysaccharides was the surface hydrophilicity which improved the uniformity of the deposition and surface charge which increased the thickness of the layer by layer deposition. Thus, the flexibility offered by the wide ranging structure of the cellulose fiber template coupled with the ability to control the number of fibers deposited layer by layer and their packing density demonstrate the wide ranging applications of these bilayers such as in delivery and administration of biologically relevant molecules in vivo, of polysaccharide scaffolds and such.

4.6 Complex Coacervation

Reaction and bonding of positively charged cationic polyacrylamide with anionic sulfonated kraft lignin for paper making applications was demonstrated by Vanerek and others, who investigated the formation of polyelectrolyte complexes between

cationic 'retention aids' and model anionic compounds, in order to elucidate the mechanisms by which cationic aids operate in presence of dissolved and colloidal substances. They demonstrated the formation of complex coecervates increase with the molecular weight of the cationic polyacrylamide. In general, the efficiency of the retention aids used in the paper making industry is reduced due to the presence of Dissolved and colloidal substances (DCS) such as Dissolved Lignin, Hemicellulose, colloidal wood resin and such. The reaction stoichiometry of such reactions have been shown to depend upon the flexibility of the polymer chains, and branching, with rigid chains and chains that are branched forming more non stoichiometric complexes and branched chains (Vanerek and Van de ven 2006). Bundenberg and others were the first to study Polyelectrolyte complexes in solution (Bunderberg et al. 1949). The use of these 'retention aids' is in maintaining the fine particle sizes at high efficiency and in economy. Studies have shown that when such cationic retention aids are employed, the retention performance can be significantly enhanced by pre treating with something strongly cationic. This was found to occur because the cationic agent, on absorption, provides sites for the anionic agent to attach (Allen and Yaraskavitch 1989).

The DCS in the water used in wet processing of paper making has been shown to interfere with various phenomena such as fine particle retention, retardation of water drainage from the wet web thereby hindering the intended functions of the polyelectrolytes. Hubbe and others reviewed the literature in the area that tried to characterize the nature and affects of various paper fractions and the ways to overcome some of the challenges associated with the same. They defined DCS as the net addition of the poly electrolytes, minute suspended particles and other dissolved substances present in the process water used in paper making.

Anionic is a term often associated with DCS since substances that are released from wood during process oftentimes contain carboxylic acid groups which dissociate to their negatively charged form at the pH and other conditions encountered in a paper mill. Ongoing research continues to reveal various mean by which the individual components of DCS contribute to effects observed during paper production. A reliable method to separate DCS from a fiber suspension, say for further evaluation, would be centrifugation. Evaluation using Gas chromatography have been used to further determine the composition of Pectins, hemicelluloses, wood pitch, ligands, lignin fragments and such.

Surface charge on a wet surface arises when dissociation of small ions such as H^+ dissociate, thus giving rise to a multi ion system which can be monomers, polyelectrolytes, colloidal particles or larger particles such as cellulosic fibers or cellulosic fines. Among these, the size of colloidal particles causes the interaction between surfaces to play a dominant role in determining the property those results. In this scenario, a net neutral surface is defined as one that has a zeta potential of zero at the end point of the titration, where zeta potential is defined as the electrical potential measured in millivolts at the hydrodynamic slip plane that is close to the surface of the material being investigated. An important distinction between the measurement of zeta potential and net charge demand is that while for zeta potential

measurement does not take into account the measurement of sample size, colloidal charge demand by its very definition takes into account the amount of polyelectrolyte titrant it takes to neutralize the charge of a given amount of sample (Hubbe et al. 2012). Polyelectrolyte solution behavior is key to understand their interaction with other charged surfaces, For example research has shown that there exists a threshold concentration above which formation of polyelectrolyte complexes is prevented. Theoretically, flocculation of a charge stabilized system is possible by using same charged polyelectrolyte, the polyelectrolyte concentration and its adsorption on non-porous surfaces play a role in the phenomenon. On interacting with polyelectrolyte of the opposite charge, multivalent ions form coacervate system the formation of which is favoured both by a reduction in enthalpy (caused by electrostatic attraction between the charges) and entropy which is disorderliness caused by freeing up of counter ions. Studies have also shown that PEC particles can exist in a stable suspension since they contain an outer layer that contains large quantities of whichever polyelectrolyte is present in excess. (Hubbe et al. 2012). The molecular mass dependence of the cationic polymers have been shown.

Studies have shown a strong molecular mass dependency of cationic demand, the strongest evidence of which comes from studies performed by Liu and others by using enzymes to cleave macromolecules, which show a drastic fall in cationic demand owing to enzyme treatment which results in a fall in the net molecular mass of the polymer (Liu et al. 2010). Peroxide bleaching has also been shown to increase cationic demand of mechanical pulp.

Among the factors that influence the formation of PEC is molecular size, level of addition and net ionic charge. Also, the adsorption of polyelectrolyte from solution to suspended material depends on heat generation and entropic contribution to free energy. The effects of poly electrolyte addition on colloidal stability is influenced by charge density, molecular mass and level of addition." The charged patch" model has been developed to elucidate the effect of molecular mass changes on retention and drainage enhancement A defining feature of this model is that the poly electrolyte adsorbs to one surface with a relatively flat conformation, the patch that results can thus attract the exposed areas of other suspended particulate matter (Hubbe et al. 2012).

Whether a system recoagulates readily on being knocked apart by hydrodynamic shear can be used to infer if it has been coagulated either by a charged patch or charge neutralization (Tripattharanan et al. 2004) Polyelectrolyte complexes also form gels as reported by Miao and others.

Although the cellulose fibers cannot be considered DCS, their contribution to cationic demand cannot be overlooked. For instance Strom and others performed charge related tests both in the presence and absence of fibers and demonstrated this. Due to the presence of carboxylic acid and sulfonic acid groups, cellulosic fiber surfaces usually contribute to the anionic charge of paper making systems. The net amount of charge accessible to the fiber surface is important from the processing stand point. In practical terms if one were to increase a certain state of cationic demand then the amount of highly charged additive has to be increased. Studies have shown that the adsorption capacity of highly cationic polyelectrolytes of high

and low molecular mass can be used to estimate the ratio of surface carboxyl groups to the total number of carboxyl groups present. The dissociation of one surface carboxyl group thus influences the dissociation of other groups possibly due to their proximity to each other. Different classes of cellulosic fibers have different densities and anionic charges at their surface Herington et al. demonstrated that the density of carboxylic acid groups varied to a great extent depending upon the origin type and treatment of cellulosic fiber. The amount of negatively charged groups present at the fiber surface is shown to increase with peroxide bleaching. The extraction of spruce TMP with hexane before separating the fractions was shown to result in higher surface charge as determined by titration. This implied that the polysaccharide component of the fiber had higher charge density than that of the extractives. Increased refining has been found to increase the amount of surface refining. This is attributed to the correlation between the surface area of the fibers and cationic demand. The technical definition of 'fines' fraction of papermaking furnish is any solid particle small enough to pass through a 72 μm opening according to T261 standard test, which in practical terms means that fines are solid particles small enough to pass through the openings in the forming fabric of a paper machine. Studies have shown that the fines take up from two to ten times more cationic additives per unit mass than the fibers. However the time required to saturate the surface of the fines is also a lot lesser than that of fibers owing to the fine size of the pores of fines. Structural and chemical differences between fibers and fines also lead to differential adsorption or cationic demand. Research shows that shape of the fines also impacts its properties. For instance, fibrillar fines in mechanical pulp are more likely to have cellulose and hemicelluloses on their surface while flakes of fines are more likely to contain pectic acid, lignin, thus giving them a more negative charge density. Although certain level of salt is needed to facilitate PEC formation, increased salt concentration can cause the material to inflame more with water, due to weaker interactions between the oppositely charged polymers (Schindler and Nordmeier 1994).

Electrostatic interactions dominate the interactions between DCS, polymeric additives, fibers, fillers and water. Increased recycling, dominated by deinking and washing can provide cleaner future stocks. Also biorefineries activities would mean cleaner raw materials on account of removal of DCS components for other productive uses and chemical reactions. Expansion of paper making activity to drier geographies would mean greater increases in ionic strength of paper stock as much more closure of paper machine water circuits. Development of Biomimetic systems which depend upon polymer-polymer interaction would lead to salty media. Much of the current understanding of the physical chemistry of ionic polysaccharides comes from model systems that are in ideal condition as opposed to the practical scenarios that may lead to magnified and complex affects. Placing the charge demand interactions under the larger context of a holistic range of molecular interactions as opposed to only charge base interactions being considered would provide a more realistic picture (Hubbe et al. 2012).

4.7 Recycling of Paper and the Use of Scavenger Additives

Large fluctuations in charge demand are reported in the incoming material in recycling operations due to variability in the size of the material. One of the main motivation in controlling the colloidal charge is to maintain stability and quality of the recycled product with time. Studies have shown that materials such as palmitic acid salts that are used in deinking of the incoming materials have been found in the pulp after washing. Also, DCS released during the bleaching of secondary fiber and charged additives such as cationic starch have been found in most samples of recovered fibers. The term Scavenger describes the cationic polyelectrolytes of high charged density that is used to neutralize negative colloidal charges that are present in excess in paper making. The use of scavengers, which are basically inexpensive and mass produced is in improving the performance of retention aids and cause significant improvement in drainage rates (Hubbe et al. 2012).

4.8 Fiber Porosity and Its Effects on Polyelectrolyte Permeation and Surface Charge

A consequence of the mesoporous nature of cellulose fibers is that low mass cationic polymers tend to adsorb in greater quantity than their high mass counterparts. Zeta potential values however of cellulosic fiber structures tend to revert to their original levels on treatment with low levels of cationic polyelectrolyte. Studies have also reported the effect of time on polyelectrolyte complexation. Van de ven and others reported the time effects on poly electrolyte complexation. Other studies have also showed that the low charged polymers show a greater tendency to diffuse into the mesopore structure than high charged ones possibly owing to the repulsion of like charge(high) macromolecules by the approaching high charged ones (Hubbe et al. 2012).

4.9 Anionic Polysaccharide Hydrogels and Their Properties

Study of smart materials such as biopolymers used in drug release has been gaining ground lately Such materials possess advantages such as improved effectiveness, uniform drug delivery lower frequency of dosage administration and minimization of side effects (Brazel and Peppas 1999) Microparticles of anionic polysaccharide such as cross linked carboxymethyl pullulun that have been chemically modified by the introduction of hydrophobic thermosensitive poloxamer group exhibit both amphiphilic and thermosensitive properties besides ionic character. It is shown that the retention and release of the bio molecules is influenced by electrostatic,

hydrophobic forces and the presence of thermosensitive groups. Hydrogel is defined as three dimensional, physically or chemically cross linked hydrophylic network that is able to retain large amount of water base system or biological fluids (Peppas et al. 2000). Hydrogels find the following applications controlled and sustained drug delivery, biosensors and bioseparations (Masteikova et al. 2003).

Hydrogels containing pendent anionic and cationic groups are pH sensitive in that they change protons when the pH changes (Mocanu et al. 2011). The swelling and/or shrinking of the hydrogel thus depends upon pH, presence of counter ions and ionic strength which in turn depends on the presence of ionizable groups in the polymer change. For example, hydrogels that contain weak acidic group are swollen in the basic pH and shrink in the acidic pH, this can find applications in drug delivery since the hydrogel would remain shrunk in the stomach acid and swell in the GI track leading to the ionization of the carboxyl group. Anionic hydrogels find use in site specific drug delivery in the large intestine whereas cationic hydrogels are used when drug delivery is decided in the stomach such as for treating H pylori. Mocanu and others studied the synthesis, characterization and crosslinking of microparticles of carboxymethylpullulun modified by poloxomer chains. Studies have shown that these poloxomer block copolymers lead to improved delivery of variety of vaccines. The retention of biologically active proteins by the microparticles is found to increase with molecular weight of the biocompounds. For instance, the lower molecular weight lysozyme is retained mainly by ionic interactions while Tetanus Anatoxin is retained only on account of its high molecular weight (Mocanu et al. 2011).

References

Allen LH, Yaraskavitch I (1989) Dual Polymer retention aids—a review. TAPPI retention and drainage short course notes. TAPPI Press, Atlanta, pp 59–63

Brazel CS, Peppas NA (1999) Mechanism of solute and drug transport in relaxing swellables hydrophilic glassy polymers. Polymer 40:3383–3398

Brewster ME, Loftsson T (2007) Cyclodextrins as pharmaceutical solubilizers. Adv Drug Deliv Rev 59:645–666

Davis ME, Zuckerman JE, Choi CHJ, Seligson D, Tolcher A, Alabi CA (2010) Evidence of RNAi in humans from systemically administered siRNA via targeted nanoparticles. Nature 464:1067–1070

Díaz-Moscoso A, Le Gourriérec L, Gómez-García M, Benito JM, Balbuena P, Ortega-Caballero F (2009) Polycationic amphiphilic cyclodextrins for gene delivery: synthesis and effect of structural modifications on plasmid DNA complex stability, cytotoxicity, and gene expression. Chemistry—A. Eur J 15:12871–12888

Ding B, Du J, Hsieh Y-L (2011) Tubular multi bilayer polysaccharide biofilms on ultra thin cellulose fibers. J Appl Polym Sci 121:2526–2534

Dong L, Huang Z, Cai X, Xiang J, Zhu Y-A, Wang R (2010) Localized delivery of antisense oligonucleotides by cationic hydrogel suppresses TNF-α expression and endotoxin-induced osteolysis. Pharm Res 28:1349–1356

Eriksson M, Torgnysdotter A, Wågberg L (2006) Surface modification of wood fibers using the polyelectrolyte multilayer technique: effects on fiber joint and paper strength properties. Ind Eng Chem Res 45:5279–5286

Fayazpour F, Lucas B, Alvarez-Lorenzo C, Sanders NN, Demeester J, De Smedt SC (2006) Physicochemical and transfection properties of cationic hydroxyethylcellulose/DNA nanoparticles. Biomacromolecules 7:2856–2862

Freudenberg K, Jacobi R (1935) Über Schardingers Dextrine aus Stärke. Justus Liebigs Annalen der Chemie 518:102–108

Gonzalez H, Hwang SJ, Davis ME (1999) New class of polymers for the delivery of macromolecular therapeutics. Bioconjug Chem 10:1068–1074

Hebeish A, El-Hilw Z (2001) Chemical finishing of cotton using reactive cyclodextrin. Color Technol 117:104–110

Hubbe MA, Sundberg A, Mocchiutti P, Ni Y, Pelton R (2012) Dissolved and colloidal susbstances and the charge demand of papermaking process waters and suspensions: a review. Bioresources 7(4):6109–6193

Jones OG, Decker EA, McClements DJ (2010) Comparison of protein–polysaccharide nanoparticle fabrication methods: impact of biopolymer complexation before or after particle formation. J Colloid Interface Sci 344:21–29

Lee KY, Jeong L, Kang YO, Lee SJ, Park WH (2009) Electrospinning of polysaccharides for regenerative medicine. Adv Drug Deliv Rev 61:1020–1032

Liu K, Li X-F, Li X-M, He BH, Zhao GL (2010) Lowering the cationic demand caused by PGA in papermaking by solute adsorption and immobilized pectinase on Chitosan beads. Carbohydr Polym 82(3):648–652

Lyness WI, Gloss RA, Bates NA (1976) Fibrous assemblies from cationically and anionically charged fibers. US Patent 3998690

Ma L, Liu C (2010) Preparation of chitosan microspheres by ionotropic gelation under a high voltage electrostatic field for protein delivery. Colloids Surf, B 75:448–453

Masteikova R, Chalupova Z, Sklubalova Z (2003) Stimuli-sensitive hydrogels in controlled and sustained drug release. Medicina 39(2):19–24

Mocanu G, Mihai D, Dulong V, Picton L, Le Cerf D, Moscovici M (2011) Anionic polysaccharide hydrogels with thermosensitive properties. Carbohyd Polym 83:52–59

Mucha M, Miśkiewicz D (2000) Chitosan blends as fillers for paper. J Appl Polym Sci 77:3210–3215

Nachtergaele W (1989) The benefits of cationic starches for the paper industry. Starch 41:27–31

Narayanan G, Gupta BS, Tonelli AE (2014) Poly(ε-caprolactone) Nanowebs Functionalized with α- and γ-Cyclodextrins. Biomacromolecules 15:4122–4133

Peppas NA, Bures P, Leobangdung W, Ichikawa H (2000) Hydrogel in pharmaceutical formulations. Eur J Pharm Biopharm (50):27–46

Samal SK, Dash M, Van Vlierberghe S, Kaplan DL, Chiellini E, van Blitterswijk C (2012) Cationic polymers and their therapeutic potential. Chem Soc Rev 41:7147–7194

Schardinger F (1911) Bildung kristallisierter polysaccharide (dextrine) aus stärkekleister durch microben. Zentralbl Bakteriol Parasitenk Abt II 29:188–197

Schindler T, Nordmeier E (1994) Studies on the formation and aggregation of polyelectrolyte complexes formed between Poly (styrenesulfonic acid). Polymer J. 26(10):1124–1131

Sennett P, Olivier JP (1965) Colloidal dispersions electrokinetic effects and the concepet of zeta potential. Ind Eng Chem 57:32–50

Shirazi M, van de Ven TGM, Garnier G (2003) Adsorption of modified starches on pulp fibers. Langmuir 19:10835–10842

Song Y, Zhang L, Gan W, Zhou J, Zhang L (2011) Self-assembled micelles based on hydrophobically modified quaternized cellulose for drug delivery. Colloids Surf, B 83:313–20

Tang W, Ng S-C (2007) Synthesis of cationic single-isomer cyclodextrins for the chiral separation of amino acids and anionic pharmaceuticals. Nat Protocols 2:3195–3200

Tripattharanan T, Hubbe MA, Heitmann JA, Venditti RA (2004) Effect of idealized flow conditions on retention aid performance,Part 2 Polymer bridging, charged patches, and charge neutralisation. Appitta J 57(6):448–454

Vanerek A, Van de ven TGM (2006) Coacervate complex formation between cationic polyacrylamide and anionic sulfonated kraft lignin. Colloids Surf. A-Physicochem Aspects 273(1–3):55-62

Villiers A (1891) Sur la fermentation de la fécule par l'action du ferment butyrique. Compt Rend Acad Sci. 112:536–538

Wackerberg E, Johansson K, Wallin S (1994) Microparticle technology in clay filled groundwood specialty printing grades produced under neutral or alkaline conditions. Pulp Pap Can 95 (7):44–48

Wen Y, Oh JK (2014) Recent strategies to develop polysaccharide-based nanomaterials for biomedical applications. Macromol Rapid Commun 35:1819–1832

Whistler RL (1984) Chapter I. History and future expectation of starch use. Starch: chemistry and technology, 2nd edn. Academic Press, San Diego, pp 1–9

Xu FJ, Ping Y, Ma J, Tang GP, Yang WT, Li J (2009) Comb-shaped copolymers composed of hydroxypropyl cellulose backbones and cationic poly((2-dimethyl amino)ethyl methacrylate) side chains for gene delivery. Bioconjug Chem 20:1449–1458

Zhang N, Li J, Jiang W, Ren C, Li J, Xin J (2010) Effective protection and controlled release of insulin by cationic β-cyclodextrin polymers from alginate/chitosan nanoparticles. Int J Pharm 393:213–219

Chapter 5
Formation of Cellulose and Protein Blend Biofibers

Ramiz Boy, Ganesh Narayanan and Richard Kotek

Abstract Cellulose and proteins are potential polymers for developing biodegradable materials for high value-added applications. A combination with these natural polymers could be useful to enhance the properties of final materials and to extend their application areas. In particular, blend biofibers that are degradable and sustainable can be engineered from a mixture of cellulose and proteins, such as soy protein, silk fibroin, collagen, etc. In a binary polymeric blend, the compatibility of cellulose and proteins is influenced by the characteristics of each polymer in the employed solvent system as well as processing conditions. Therefore, utilizing solvents that can dissolve cellulose and proteins, and coagulants that are non-solvents for both polymers is of importance. In this book chapter, the formation and characteristics of blend biofibers from these polymers will be discussed.

Keywords Cellulose · Protein · Biofibers · Blend

5.1 Introduction

Materials developed from synthetic polymers are widely utilized in the form of films, membranes, coatings and fibers for a myriad of applications. Synthetic materials have a broad array of attractive properties because they can be more easily processed into a particular form and as a result can have good performance for specific applications. On the other hand, the utilization of materials from renewable resources, i.e. cellulose and proteins, is not broadly adopted. These polymers' main drawbacks are a relatively limited range of performance properties which are only appropriate for some applications and narrower processing windows than for synthetic materials. In particular, the combination and modification of these natural

R. Boy · G. Narayanan · R. Kotek (✉)
Fiber and Polymer Science Program, North Carolina State University,
Raleigh, NC 27606, USA
e-mail: rkotek@ncsu.edu

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polymers could be useful to enhance the characteristics of the final materials and to extend their application areas (Kelly et al. 2008; Narayanan 2014; Narayanan et al. 2014, 2015a, b, c, 2016a, b, c).

Regenerated cellulose fibers have suitable mechanical properties for textiles but regenerated protein fibers lack such properties for that target. This is due in large part to the insufficient information available on how amino acid sequences influence mechanical properties (Vincent et al. 2003).

Cellulose and proteins are potential polymers for developing biodegradable materials for high added-value applications, and blending is a straightforward and efficient method to further improve the performance properties of each polymer in its final applications (Zhou et al. 2008).

5.2 Cellulose

Cellulose is abundantly available in nature as a sustainable organic raw macromolecule; however, it has not yet achieved its true potential in many areas of application. A main challenge is that cellulose must be in a different structure from that found in nature before it can be utilized for numerous final applications. Since cellulose does not melt, the polymer must be dissolved by some means that can lead to its desired final form. An early technique widely adopted by industry focused on chemical modification of cellulose to produce nitrocellulose and cellulose acetate. Based on this premise, a derivative viscose process forming called cellulose xanthogenate was also developed to make cellulose fibers (viscose rayon) and films (cellophane). All chemically modified cellulose materials have been utilized in a wide array of applications from textiles to special technical products. However, this technique includes several stages and creates pollution. Therefore, alternate methods that can facilitate and expedite the dissolution of cellulose have been put forward (Klemm et al. 2005; Turbak et al. 1977; Hudson and Cuculo 1980; Kotek 2002).

As a linear homopolysaccharide, cellulose is composed of β–D–anhydroglucopyranose (often called anhydroglucose or simply glucose) units joined together through β–1,4–glycosidic bonds in the $^4C_1$ chair conformation. Therefore, it is a 1,4–β–D–glucan forming disaccharide cellobiose moieties which constitutes a repeating element of cellulose. Moreover, the thermodynamically favorable $^4C_1$ chair conformation of pyranose rings signifies that hydroxymethyl (–CH_2OH) and hydroxyl (–OH) groups besides the glycosidic bonds are central as regards to the average planes of the rings as shown in Fig. 5.1. Two end groups of cellulose are in a different equilibrium state from one another; one has a normal C_4–OH group (the non-reducing end), while the other having C_1–OH group is in equilibrium with an aldehyde structure (the reducing end) (Klemm et al. 2005; Nevell and Zeronian 1985; Wang et al. 2009; Wertz et al. 2010; Belgacem and Gandini 2011).

This molecular structure delivers characteristic properties, such as significant hydrophilicity and resulting surface energy, chirality, biodegradability, relative thermal stability, and the chemical versatility related to the reactive hydroxyl

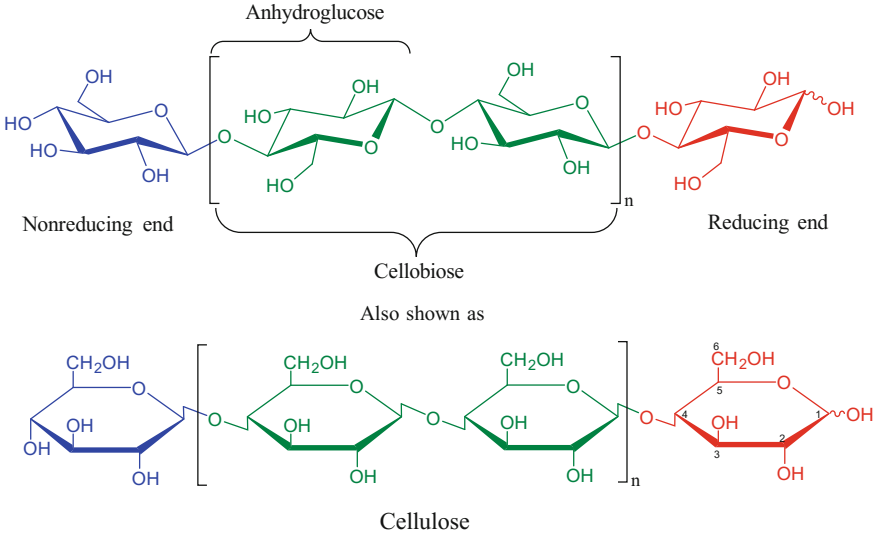

Fig. 5.1 Chemical structure of cellulose: a linear polymer composed of beta (1–4) linked D–glucose (anhydroglucose) units—adapted and redrawn from (Olsson and Wesman 2013); originally published under open access license. Available from: http://www.intechopen.com/books/cellulose-fundamental-aspects/direct-dissolution-of-cellulose-background-means-and-applications {DOI:10.5772/52144} and (http://www.dharmatrading.com/cellulose.html as accessed on February 21, 2016)

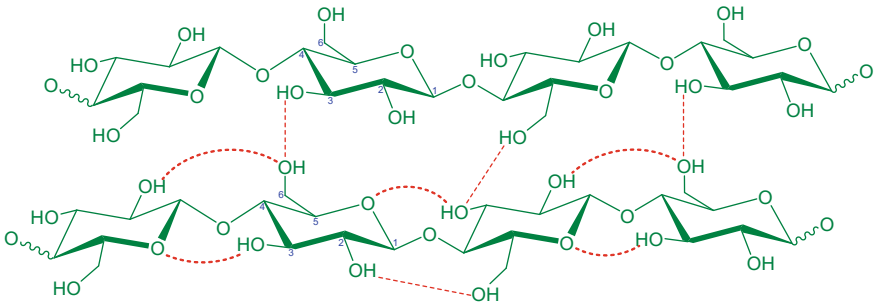

Fig. 5.2 The intra– and intermolecular hydrogen bonds in cellulose. Redrawn with permission from (Pinkert et al. 2009). Copyright 2016, ACS

groups. While other polysaccharides, e.g. starch, chitosan, and alginate have similar properties, cellulose is characterized by strong inter-chain forces. A relatively large network of intra– and intermolecular hydrogen bonds (Fig. 5.2), along with dipole–dipole and van der Waal' interactions, contribute to a partial crystalline structure and morphology of native cellulose with a moderate to low degree of accessibility. As a result, it becomes degraded before it begins to melt (Klemm et al. 2005; Belgacem and Gandini 2011; Rowland and Bertoniere 1985).

The number of component anhydroglucoses determines the degree of polymerization (DP) of cellulose, which changes widely with the source, and the treatment of the raw material. For instance, wood pulp has a DP of 300–1700, flax 36000, cotton and other plant fibers 800–10000, regenerated cellulose fibers 500–1000 (Klemm et al. 2005; Gilbert and Kadla 1998; Winkworth-Smith and Foster 2013).

Native cellulose is perpetually synthesized in a form of fibrils that are long threadlike bundles of cellulose chains. These fibrils are constituted from smaller units. Nearly 36 cellulose chains aggregate to form elementary fibrils (protofibrils). These initial bundles are stacked into nanofibrils that are 2–20 nm in cross-sectional dimension. The nanofibrils, stabilized by hydrogen bonds and van der Waal forces, are then packed into a final form, cellulose fibers. This fibrillar morphology of cellulose provides load-bearing function and structural integrity to plant cell walls. In addition, crystalline and amorphous domains of cellulose can differ in percentage at the large scale of its fiber assembly, but it is apt to prefer the oriented regions towards the nanofibril level. This improves tensile strength and lowers chemical reactivity (Belgacem and Gandini 2011; Winkworth-Smith and Foster 2013; Hon 1994).

The cellulose chains in crystalline domains are compact and oriented due to high density of –OH groups forming hydrogen bonds along and between the polymer chains. In combination with other secondary bonds (mainly van der Waals forces), they are packed into different levels of lateral order varying from ideal dimensional packing to an arbitrary arrangement. This depends on the origin, the isolation and purification method and the treatment of cellulose that generate multiple forms of its polymorphism. There are four major types of reported cellulose polymorphs; cellulose I, II, III, and IV that can easily be identified by X–ray diffraction as graphed in Fig. 5.3 (Winkworth-Smith and Foster 2013; Sangwatanaroj 1995; Isogai 1994).

The crystal structure of native cellulose (wood, bacterial and algal celluloses, cotton, ramie, etc.) is recognized as cellulose I. It displays parallel chain alignment, related to the both reducing and non-reducing ends of cellulose polymer. Although cellulose I is the most abundant form, it is thermodynamically less stable than the others are. Those polymorphic forms are obtained through chemical means or heat treatment of cellulose I. For instance, cellulose II, containing antiparallel chains, is formed by strong alkali treatment (also known as mercerization) or by precipitation of dissolved cellulose (also called regeneration). As discussed earlier, viscose rayon and cellophane are commonly known regenerated forms of cellulose. Both cellulose I and II can be converted to cellulose III_I and III_{II} respectively by processing in liquid ammonia or organic amines (e.g. ethylenediamine), and then removing their corresponding anhydrous residues. In addition, cellulose III is thermodynamically the most stable form. Finally, cellulose IV_I and IV_{II} are produced by heating respective cellulose III_I and III_{II} in glycerol. These forms could be interconverted; however, partials degradation occurs for reversion to cellulose I. (Gilbert and Kadla 1998; Sangwatanaroj 1995; Ciolacu and Popa 2010; French et al. 2002; Aminuddin 1998).

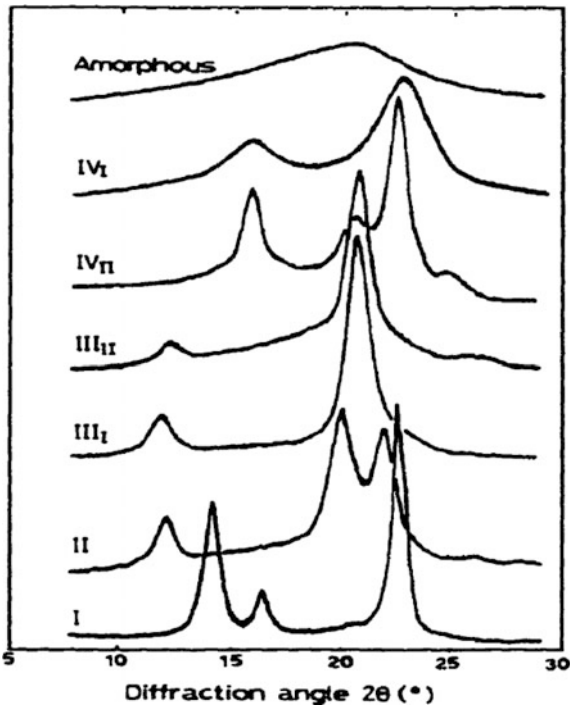

Fig. 5.3 X-ray diffraction patterns of different cellulose polymorphs. Adapted with permission from (Isogai 1994; Isogai et al. 1989). Copyright 2016, ACS and Hanser Publications

5.3 Proteins

Proteins together with polysaccharides and nucleic acids are key macromolecules for living organisms. They enable biological and organic systems to live and propagate. Simply extracted from nature, proteins have been investigated for a long time in aspect of their inherent potential of constituting three-dimensional structures that provide biological functions. Fibroin from silk and spider web, keratin from hair and wool, and all types of enzymes that stimulate bio–reactions in animal bodies are entirely proteins (Butler and McGrath 1998; McMurry 2007).

As natural polymers, proteins have been intuitively utilized in edible packaging and materials, such as soy protein sheets and collagen envelopes. Before synthetic polymers were discovered, plastics from proteins were of interest in terms of finally substituting for cellulose. Molded plastic of casein (milk protein) crosslinked by formaldehyde was developed before the beginning of 20th century to produce articles, for instance, buttons (Saechtling 1995; Kruszewska 1997). Several applications in textile fibers, coatings, resins were made possible by utilizing zein (maize protein), which was patented after 1920. About the same time, formaldehyde was also broadly employed for the same purpose in a mixture of soy protein and blood meal to produce parts, namely, distributor caps for cars (Jane et al. 1994). Furthermore, gelatin was an accessible polymeric material to cast films for

photography, drug shells and foodstuff. Nowadays, there is gaining interest in producing bio-based plastics and materials from proteins as well as other natural polymers. Besides the mentioned ones, there are numerous other proteins, such as gluten from wheat or maize, cottonseed floor, whey proteins, myofibrillar proteins, etc., that could be utilized in various applications (Guilbert and Cuq 2005).

Proteins are much more complex than polysaccharides and are fallen into the class of polyamides with amino acids as their building blocks. Thousands of amino acids can be synthesized in vitro but only 20 amino acids commonly occur in nature and called α-amino acids. The 20 α–amino acids that vary in dimension, form, charge, hydrogen-bonding sites, and chemical reactivity are the basic monomer units of proteins. The structure of every α–amino acid possesses a basic amine group ($–NH_2$), a carboxyl group (–COOH), and a typical side chain, R. The polarity of R groups can classify these α-amino acids into four different groups as shown in Fig. 5.4: nonpolar, polar but neutral, basic, and acidic. The nonpolar side chains are water repellant (hydrophobic), while the others are hydrophilic. The properties of R groups highly affect the nature and behavior of a protein. For instance, many hydrophobic amino acids form the core of protein's globular structure including many other hydrophilic ones at the exterior. Furthermore, half of the 20 α–amino acids are essential for humans in that they are not produced by their metabolic system but a part of their diet (Stevens 1999; Vaz and Cunha 2007; Bettelheim et al. 2012).

Compared to polysaccharides, proteins are monodisperse and made of α-amino acids that are naturally polymerized to constitute an infinite number of sequential arrangements ensuing exceptional molecular diversity. As a condensation polymer, the monomer units (amino acid residues) of proteins are linked by amide bonds (–CO–NH–) which are also called peptide bonds. Two amino acids form a dipeptide, three a tripeptide, and so on. In general, chains with up to 50 α–amino acids are often called polypeptides and larger ones are referred to proteins. In addition to peptide bonds, disulfide bridges (–S–S– bonds formed between two cysteine units) are also possible in proteins (McMurry 2007; Stevens 1999).

A common type of classification of proteins is based on their three dimensional (3D) shapes which are fibrous (scleroproteins) and globular (spheroproteins). Fibrous proteins have elongated thread-like polymers chains that are held strongly together by hydrogen bonds rendering them water–insoluble. As a result, they have structural functions in animal tissues. Collagen (tendons and connective tissue),

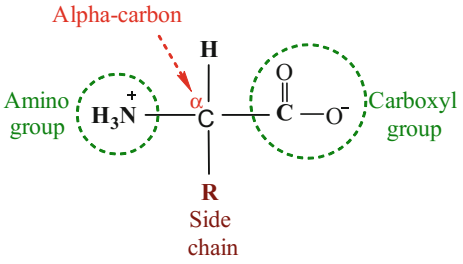

Fig. 5.4 Chemical structure of α-amino acids

myosin (muscles tissue), keratin (skin, hair, feathers, horn), and fibroin (silk) are all examples of fibrous proteins. On the other hand, globular proteins have compact spheroidal structures and are fairly soluble in water. This provides them to be able to move freely in cells. Enzymes and hormones are typical globular proteins of living organisms (McMurry 2007; Stevens 1999).

Figure 5.4 shows the deprotonated carboxyl group (negative charge) and the protonated amino group (positive charge) of an amino acid existing as a dipolar ion, or zwitterion, in an aqueous solution as well as in solid state. Amino acids are therefore ionic compounds incorporating internal salts. This also induces comparable physical properties to a salt, such as water solubility and high melting point. Moreover, amino acids are amphoteric molecules: They can react as acids but also as bases in an aqueous solution with varying pHs. An intermediate pH at which molecules have equal positive and negative net charges is a characteristic of amino acids and is called isoelectric point, *pI* (McMurry 2007; Bettelheim et al. 2012).

The amino acid sequence of a polypeptide chain is referred to primary structure that constitutes three-dimensional structure of a protein. This spatial geometry of proteins invariably occurs due to inter– and intramolecular bonds, such as hydrogen bonds, electrostatic and dipole interactions, etc. While regular folding of the chain determines the secondary structure (Fig. 5.5) of a protein, its overall 3D shape is referred to the tertiary structure. There even a higher degree structure, quaternary, exists due to several polypeptide chains interacting and aggregating into a single protein (McMurry 2007; Bettelheim et al. 2012).

Along the structural hierarchy, the secondary structures are of importance since the chains of most proteins show particularly defined confirmations. α–Helix and *β*–pleated sheet confirmations are the most prevalent ones. α–Helices are formed through creating ample space for large R groups stabilized by hydrogen bonding between N–H and C–O within an amino acid residue. The α–helix is a prevalent secondary structure and is involved with virtually all globular proteins (Fig. 5.5). On the other hand, *β*–pleated sheets are constructed by amino acids with relatively small R groups arranged in a more extended chain conformation than α-helices. These sheets are composed of more than one chain, lying next to each other, forming inter- and intramolecular hydrogen bonding. Furthermore, *β*–sheet or α–helix is rarely found as single structure of a protein. These two structures together just make up a limited percentage of confirmation in many proteins, particularly in globular ones. The remaining percentage consists of random coil. As secondary structures, these three types of confirmation form in different segments of the

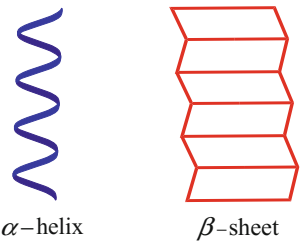

Fig. 5.5 Secondary (α–helix and *β*–sheet) structures of proteins

polymer chains of globular proteins (McMurry 2007; Stevens 1999; Bettelheim et al. 2012).

Keratin is the well-known protein of hair, fingernails, horns and wool. It is a fibrous protein occurring mainly in α–helix form. Particularly in wool, this structure contributes to high extensibility and flexibility. Fibroin, another notable fibrous protein, is extracted from silk. It forms a predominantly β–pleated sheet structure which account for high strength and toughness in spider and silkworm silk. Their mentioned properties are much superior to any synthetic fibers (Bettelheim et al. 2012).

Most proteins do not maintain perfectly uniform confirmations. Some segments of polypeptide chains could interact through side chains (hydrogen bonding), disulfide bridges, salt bridges, hydrophobic interactions, metal ion coordination. Therefore, the overall three-dimensional form of proteins is specified as the tertiary structure. By either or both of chemical and physical treatment, the secondary and tertiary structure can be disturbed to modify the proteins. This method is referred to denaturation of protein. It consequently affects the solubility, water absorbency, intrinsic viscosity, and biological activity of proteins (Stevens 1999; Vaz and Cunha 2007; Bettelheim et al. 2012).

Proteins along with polysaccharides, for instance, cellulose, form the tissue of animals and plants, respectively. The extraction from these sources results in different structures of the natural polymers to be exploited in a myriad of applications. As naturally occurring polymers, they are renewable, biocompatible, biodegradable and immensely common on Earth. Due to their numerous biological functions and significant properties, a mixture of the both classes of polymers could deliver superior properties compared to their individual components in biomedical applications. In addition, blends have already been investigated as conceivable novel materials in fields of research, such as textiles, medicine, food, cosmetics and electronics (Zhou et al. 2008; Sionkowska et al. 2014).

From the perspective of the background and significance including the promising development and utilization of cellulose and proteins, research on developing materials from their combinations shows great potential. In this literature review, the most relevant solvents that dissolve both cellulose and proteins to form fibers, and the solution blending of the two polymers will be elaborated.

5.4 Viscose Process

Viscose (or rayon) process is one of the oldest industrial methods of dissolving wood pulp (Wertz et al. 2010). It includes a derivatizing solvent system, producing a cellulose derivative that can dissolve in water or dilute caustic soda. This process begins with alkali treatment [Cell–OH + NaOH → Cell–O^- Na^+ + H_2O] in order to purify and mercerize the pulp. Then, obtained alkaline cellulose is aged to achieve a certain degree of oxidative degradation to control DP of cellulose. The next major step is the reaction of the cellulose with carbon disulfide (CS_2) resulting

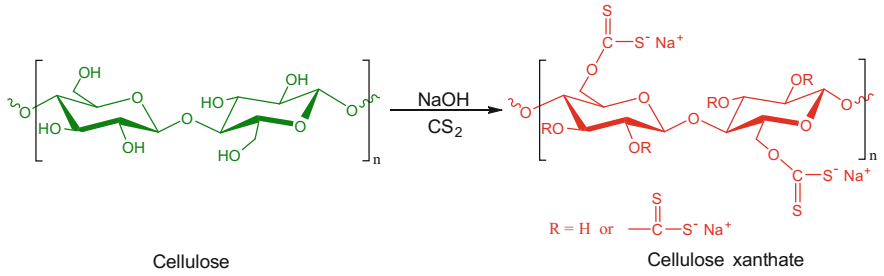

Fig. 5.6 Alkali and carbon disulfide treated cellulose to yield cellulose xanthate. Modified and redrawn with permission from (Libert 2010). Copyright 2016, ACS

in cellulose xanthate [Cell–O^- Na^+ + CS_2 → Cell–OCS_2^- Na^+] (Fig. 5.6). This step renders the process complicated since adding CS_2 induces several reactions at once, yielding by-products, such as H_2S and Na_2CS_3. The latter one discolors the cellulose xanthate and gives its typical orange color (Wertz et al. 2010; French et al. 2002; Aminuddin 1998).

The xanthate is later dissolved in dilute NaOH to form viscose that is a very viscous solution. Subsequently, viscose is left for ripening during which xanthate groups are redistributed and dexanthation takes places, followed by filtration and deaeration. Finally, viscose is spun (or cast) into a coagulation bath, consisting of mainly acid and salt [2Cell–OCS_2^- Na^+ + H_2SO_4 → 2Cell–OCS_2^- H^+ + Na_2SO_4] in order to produce rayon fibers (or films) [Cell–OCS_2^- H^+ → Cell–OH + CS_2]. This final step is invariably combined with washing and drying to stabilize the final form (Wertz et al. 2010; Woodings 2002).

Through viscose processing, the DP of the pulp, as received is around 750–850, drops to about 270–350 due to oxidative depolymerization. In addition, the polymorph of cellulose is transformed from I to II. As an interesting phenomenon, the ballooning effect was first noted on the fibers swollen with alkali and carbon disulfide (Libert 2010; Wilkes and Woodings 2001).

An attempt, as early as 1910, to bring cellulose and proteins together was made by a French scientist H. L. J. Chavassieu. He used viscose process to produce so-called “proteo-cellulosic products”. Proteins from any origin were first treated with alkali, then the resulted alkaline mixture was treated with CS_2 resulting in a protein derivative, so-called “proteid xanthate”. The obtained derivative was mixed with cellulose xanthate. Following the same steps in viscose process, different forms of materials were produced from cellulose/protein mixture. Similarly, a British patent briefly claimed preparing blend solution by adding caustic soda of a protein, such as keratin, fibrin, etc. into cellulose xanthate. More alkali was added to dilute the blend solution before the ripening (Attwater and Heinemann 1926). While earlier patents relied on alkali mixture of proteins and viscose, Esselmann et al. (1936) directly added relatively high molecular weight albuminous substances to viscose solution before or during the deaeration step. Therefore, the decomposition of protein was avoided to provide so-called “animalization” of cellulose fibers

in order to enhance their colorization with acid dyes. To reduce the decomposition of proteins, their dissolution in sodium sulfide (Na_2S) was realized to be efficient to produce blend fibers possessing enhanced mechanical properties (D'Ambrosio and Corbellini 1939). Furthermore, another patent was filed by American Enka Corp. providing details about a method of spinning homogeneous cellulose/protein blend fibers via the viscose process. Mainly, globular proteins, including casein, soy protein, zein, were used. Initially, proteins were decomposed in aqueous solution of NaOH and Na_2SO_3 and reacted with formaldehyde to saturate their free amino groups. Later, the obtained protein solution was mixed with viscose solution to obtain fibers with wool-like characteristics. This means provided homogeneous viscose solution containing 20–25% casein and paved the way for stronger fibers (Koch 1944). The ultimate goal of these early patents was to replace viscose/wool yarn blend with the blend fibers to overcome the dyeability of both components.

Nicoll (1950) of Du Pont patented regenerated cellulose/casein and cellulose/soy protein fibers that can maintain a substantial crimp upon stretching that is similar to wool. The crimps on the fibers could be mechanically removed and restored. Despite non-specified protein loading, relatively high tenacity crimped fibers were reported within a range 2.25–3 g/den for dry and 1.25–2 g/den for wet tenacity. Comparable to Du Pont's, Kanegafuchi Spinning Co. also patented blend fibers with protein derivatives so that rotting and decomposing of protein can be avoided after mixing with viscose. Proteins from milk, corn, and soybean, were derivatized by (a) using a nitrile compound with an attached functional group, e.g. epoxy radicals, halogen atoms, or unsaturated ethylene radical, (b) chemically treating (a), (c) graft-polymerizing with an ethylenic unsaturated monomer. The resulting protein derivatives were utilized to form uniform and stable mixtures with cellulose (Kanegafuchi Spinning 1966).

Mahomed (1966) from Courtaulds Ltd. incorporated 10–40% urea based on 10–40% casein added into the viscose solution at the final stages prior to the extrusion. The resulting fibers aged in formaldehyde, alkali cyanates, and zirconyl salts to prevent protein leaching. This process supposedly helped to produce higher tenacity blend fibers than viscose fiber. However, the results related to the claimed method were not reported. Similarly, Itaya (1969) of Fuji Spinning Corp. employed a grafting agent, epichlorohydrin, in order to form viscose fiber grafted with milk casein. 15 wt% casein solution, prepared from 1% (v/v) NaOH, was reacted with the grafting agent (1–3 wt% of the weight of casein), and then mixed with cellulose xanthate. Casein formed from 13 to 17 wt% of the dope solution of fiber spinning. Compared to viscose rayon, the resulting fiber had some advantages, such as the dyeability with wool dyestuff, better light fastness, higher resistance to burning, heat-retaining property, and resistance against wool-attacking insects, molds and mildews.

Yamazaki (2001a, b) from Daiwabo Rayon filed two (Japanese) patents on making antibacterial viscose rayon and the rayon with modified touch feeling. The author directly incorporated cow's milk (either fresh milk or processed milk powder) into viscose solution. The blend fibers were commercialized under the trade name MILEY (Daiwabo Rayon Co. Ltd. 2016) by the company. The fibers

were emphasized as antibacterial since it combines the two biodegradable polymers and contains no formaldehyde as opposed to the most commercial regenerated protein fibers (Lennox-Kerr 2000).

Yamada et al. (2004) who were also affiliated with Daiwabo Rayon filed a (Japanese) patent describing the blends of cellulose with alkali soluble proteins including keratin, soy protein, and gelatin. The selected protein was first mixed with a water-soluble cross-linking agent, such as formaldehyde, glutaraldehyde, and *N*-methylol compound, in alkali solution. Then, the crosslinked protein was added to viscose solution (Fig. 5.7) that was blended with polyethyleneimine (0.5–5.0 wt% of cellulose). The resulting blend fibers were claimed as cellulose/protein conjugate fibers with modified properties compared to sole viscose rayon. Similar patents on the blend fibers containing keratin were also filed to utilize recovered wool, feathers, hair, etc. as well as to provide higher dye affinity for viscose rayon towards acid dyes (Ikeda and Mukoyama 1997; Saleh 2014).

A recent patent by Yamada and Ohshima (2009) on manufacturing cellulose/gelatin composite viscose rayon explains sufficient details about the mechanical properties of the blend fiber. Applying the same preparation method in their previous patent (Yamada et al. 2004), the authors were able to produce the cellulose/gelatin blend fiber with 16.6% protein content. Gelatin solutions varied in the molecular weight of the polymer were prepared to produce four different blend fibers with the same percentage of protein in addition to the viscose rayon. The blend fibers had tenacity between 1.94 and 2.19 g/den and elongation between 10.5 and 14.2% that were slightly lower than those of the rayon, the tenacity and elongation of which were 2.32 g/den and 18.5%, respectively. The surface of the blend fibers, however, was much smoother and it did not show grooved morphology compared to viscose fiber.

A fabric made of hollow viscose fibers sprayed with casein was used to absorb moisture in order to keep one's body warm. The protein was added to provide smoothness and soft texture to the fabric (Chua 2009).

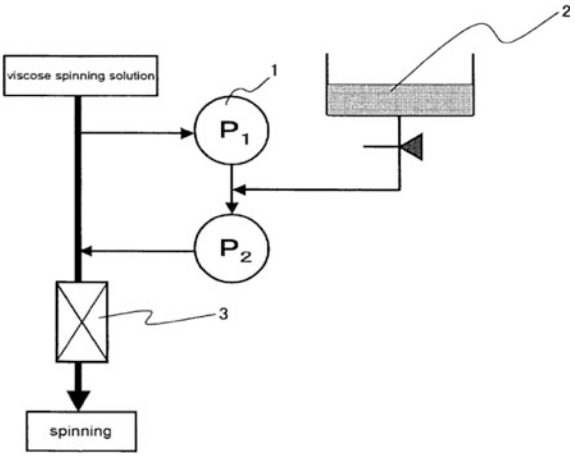

Fig. 5.7 Schematic illustration of mixing method of viscose and protein solution 1. gear pump, 2. protein solution, 3. inline mixer. (From Yamada, M. and Ohshima, K., U.S. Patent 20090166919, July 2, 2009.)

Hirano et al. (2002) briefly included mechanical and morphological properties of cellulose/silk fibroin blend fibers in their report. The linear density of the blend fibers tended to increase with more silk fibroin content. The fiber denier of viscose rayon and the blend fiber (53% protein content) was measured 4.1 and 19.7, respectively. This, however, was on the contrary for the tenacity of fibers. The blend fibers with less than 10% fibroin content showed relatively good mechanical properties. Above 10%, the values drastically reduced. From 2 to 10%, the blend fibers had the tenacity of 1.08–1.20 g/den and the elongation of 29.7–35.0% that were slightly lower than those of the control fiber (100% cellulose or viscose rayon).

Scanning Electron Microscopy (SEM) images of the cellulose/silk fibroin (47/53 w/w) blend fiber (Fig. 5.8) revealed tiny vertical striped patterns on the surface that were similar to those on silk fiber surface. The authors concluded that only weak molecular interactions except some physical entanglements occurred between cellulose and silk fibroin. It was also noted that cellulose behaved as a skeleton and silk fibroin acted as a filling material (Hirano et al. 2002). However, there was no other evidence to support their conclusion. For instance, it was not clear how the entanglements occurred and how the role of the polymers was determined. In addition, Fourier Transform Infrared Spectroscopy (FTIR) results that were briefly mentioned did not have any indication of any sort of interaction.

A recent study regarding the formation of viscose/wool powder fibers showed that acid dye affinity of the blend fibers rises with increasing protein content. It can be observed from Fig. 5.9 that the dye uptake of the fibers with 15 to 20% protein loading exceeds 50% in about 5 min. In comparison with the viscose fiber, the percentage of dye uptake doubled for the fiber with 20% protein. Although acid dyeability of the cellulosic fibers improved, 15% of the both dry and wet tenacity was sacrificed. For instance, the dry tenacity of viscose fibers decreased from 2.70 g/d to 2.29 g/d for the fiber with 15% wool powder (Li et al. 2015).

Zhou et al. (2015) developed a flame retardant viscose rayon by adding a derivative of keratin. The protein was extracted from wool that was treated with

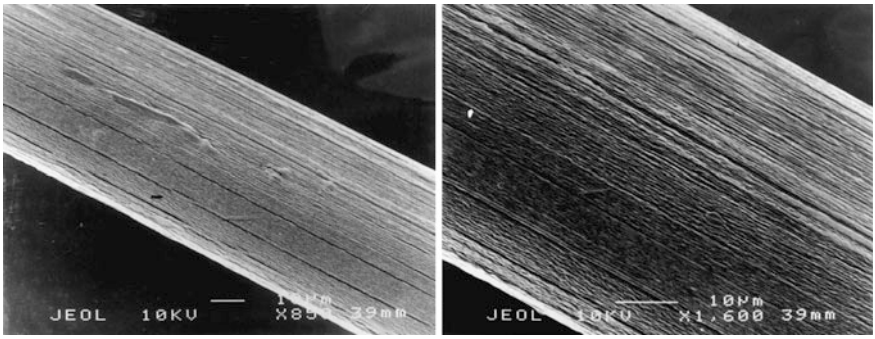

Fig. 5.8 SEM images of the cellulose/protein (53% silk fibroin) fiber (55 μm in diameter). Adapted with permission from (Hirano et al. 2002). Copyright 2016, Elsevier

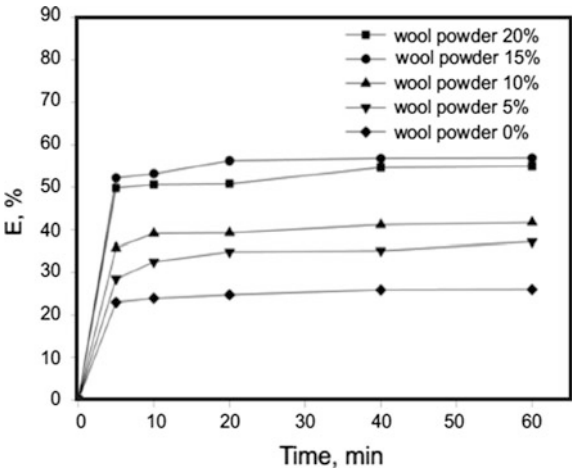

Fig. 5.9 Dye uptake of viscose/wool powder blended fiber with different powder contents. Adapted with permission (Li et al. 2015). Copyright 2016, IBWCh

12% NaOH solution at 70 °C. Then, it was reacted with chlorine atoms of a phosphazene derivative called hexachlorocyclo-triphosphazene to form cyclotriphosphazenekeratin (CCTPK). This protein derivative provided the flame retardancy to the viscose fiber. As a result, the limiting oxygen index (LOI) of the fiber increased from 16.5% to 28.6% by 10% CCTPK loading. After 30 washing cycle, the LOI value decreased to 27.5%. Furthermore, the burning behavior test revealed that while the viscose fiber was decomposed to ashes, flame retardant viscose fiber retained its fiber structure (Fig. 5.10). Similar to the effect of wool powder, CCTPK also lessened the tensile properties of viscose fiber.

Practically any protein, either in solution or in solid state, can be blended with viscose solution (Yamada et al. 2004). Therefore, there have been quite a few blend fibers produced through viscose process. Most of these fibers were found in patent applications and the information about their properties is either very limited or not available. The patents mostly focused on the preparation of blend solutions for extrusion.

In general, introducing proteins into viscose solution weakened the tensile properties of resulting viscose rayon fibers. This is most likely due to a decrease in the viscosity of the solution indicating compatibility issues for the two polymers processed by this system. On the one hand, these combination and modification of viscose rayon with proteins was a good method to increase the functionality of final material. On the other hand, this method consisted of blending alkaline solution of cellulose xanthate and alkaline solutions of the mentioned proteins, which were either decomposed or crosslinked, or grafted onto cellulose xanthate. This approach added more steps to the process of obtaining blend fibers. The viscose process is already multi-stepped, complex, and notorious for releasing CS_2 and H_2S along with other chemicals, which are hazardous, and menace to environment. Their recovery and recycling are difficult and thus raises the cost (Aminuddin 1998). Due to these challenges, many alternative solvent systems have been proposed to dissolve cellulose and some are used as co-solvents for proteins as well.

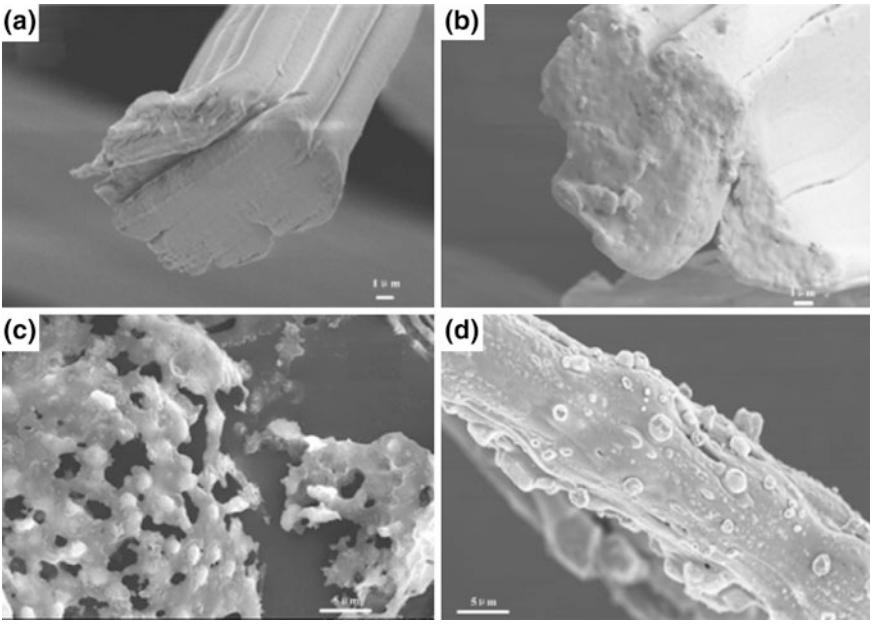

Fig. 5.10 SEM images of the cross sections of **a** viscose fiber and **b** cyclotriphosphazenekeratin/viscose fiber, **c** residues of a and **d** b after burning behavior test. Adapted with permission from (Zhou et al. 2015). Copyright 2016, Springer

5.5 Cuprammonium Process

Cuprammonium hydroxide (tetraamminecopper(II) hydroxide), also known as cuoxam and cuam, was the first solvent discovered by Schweizer (1857) to dissolve natural fibers, such as cotton, linen and silk. It was later recognized as Schweizer reagent. In 1901, E. Thiele made a stride with a stretch spinning along a spinning funnel. It was then commercially used by the Bemberg Rayon Industry to manufacture cuprammonium fiber (or rayon). In this process, copper hydroxide solution is freshly prepared from copper sulfate and sodium hydroxide and transferred into aqueous ammonia to form cuprammonium hydroxide. For effective dissolution, the concentration of copper must be more than 25 g/l and that of ammonia should be in the range of 124–250 g/l (Aminuddin 1998; Browning et al. 1954).

It is commonly acknowledged that cuprammonium ($Cu[NH_3]_4^{+2}$) ions form a complexation with $[OH]^-$ groups of cellulose. It is highly decomposable upon exposure to light. Therefore, freshly made solution should be prepared. This solution is later degassed to avoid oxygen, and then filtered before the extrusion. The formed extrudate is then spun into an alkaline coagulation bath designed as funnel–type where the coagulant cycles down, contracts and solidifies the jet. The rising jet velocity through the funnel induces stretching up to 400%. The process is

finally completed by washing the fibers with 5% H_2SO_4. In addition, cuprammonium fiber is the most closely resembling rayon to silk. These fibers could be hollow to make dialysis membranes, called as cuprophane by Akzo Nobel (Kotek 2002; Aminuddin 1998).

In 1934, a patent on preparing copper-ammonium-fibroin solutions was awarded to Börner et al. The possibilities of regenerating silk from cuprammonium hydroxide into fiber form were discussed by Wakeham et al. (1951). Hori and his coworkers (Howitt 1955) from Japan were able to produce the filaments of silk fibroin dissolved in the same solvent and precipitated in an acid bath. They also explored the commercial aspects of producing fabrics out of these filaments. Similarly, Wormell and Happey (1949) from Courtaulds managed to regenerate the fibers from α–keratin of wool by using the same solvent.

Jayme and Broschinski (1976) experimented a set of metal complex solvent systems with copper and nickel (Ni) as central atoms to dissolve proteins, e.g. casein, gelatin, collagen, zein, and silk fibroin. Their report was a progress of what Schweizer (1857) discovered. A substantial amount of metal complex bound the proteins during dissolution with the solid metal hydroxide contributing to the process. The solution of proteins with only high concentrations could yield intact material coagulated in organic solvents. Using in sulfuric acid for coagulation, the blend of cellulose and protein at 1:1 ratio gave superior properties compared to only protein material. Overall, they developed complex solvent systems to regenerate alkali insoluble proteins and, more importantly, the blends with cellulose.

Two Japanese patents based on cellulose/silk (Akira et al. 2001) and cellulose/keratin (Abe et al. 2002) blends were claimed to utilize cuprammonium process to produce fibers. However, the detailed descriptions on their production and properties cannot be sufficiently interpreted.

Recently, Tomczyńska-Mleko et al. (2015b) produced cellulose/whey protein isolate fibers through cuprammonium process. First, 1g cellulose was dissolved in 30 g of Schweizer's reagent for half an hour and blended with 15 g of 8.5 wt% whey protein isolate (WPI) dispersion (preheated at 80 °C). After complete dissolution, the obtained solution contained about 56% whey protein isolate. The solution was then pumped into a 33% sulfuric acid using a syringe/needle spinning system to form the blend fiber. During coagulation, the acid caused gelation of whey protein into cellulose network. The fiber was then rinsed with distilled water and 5% aqueous ammonia solution and subsequently washed with the water. Applying the same procedure, control fibers from each component was also produced. For instance, the cellulose fiber showed microspores structure and contained significant traces of the solvent indicating incomplete coagulation of all of the reported fibers. According to the authors, 0.156% (53.8 mM) Cu^{2+} left in the blend fiber can be tolerated for daily human consumption. Since some diseases can be treated with copper, it was mentioned that the fibers could be used for medical applications, such as drug release. Furthermore, the transmission electron microscopy (TEM) images revealed phase separated morphology of the blend fiber (Fig. 5.11). In comparison with WPI fiber, protein aggregation was observed in the blend fibers that indicates their composite morphology. Consequently, the infrared

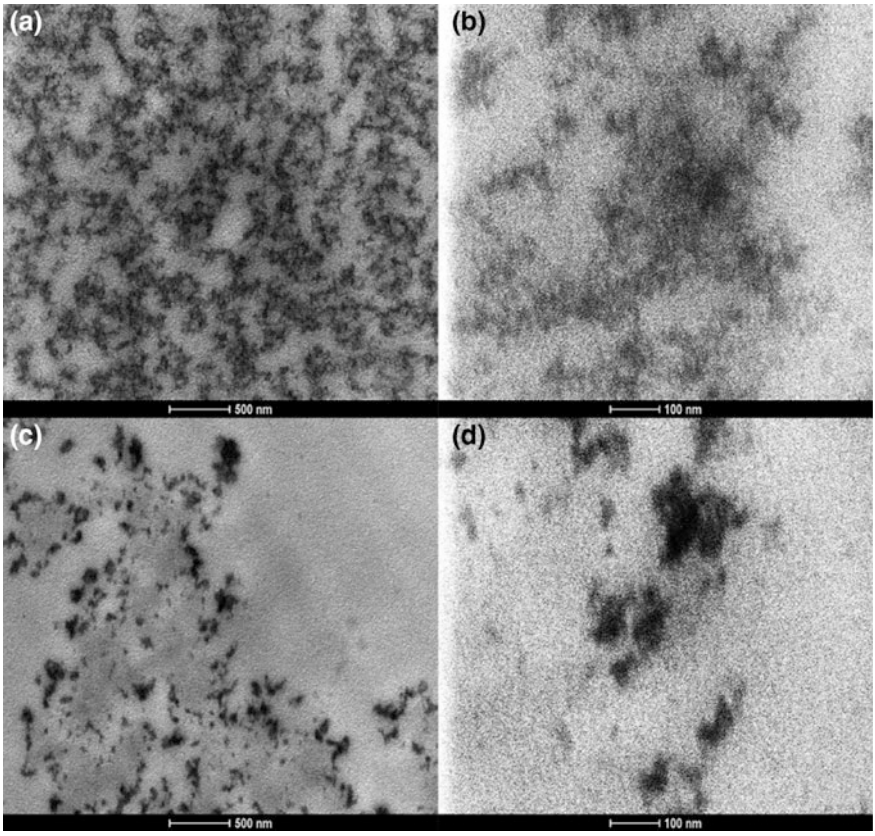

Fig. 5.11 TEM images of **a**, **b** WPI fiber and **c**, **d** cellulose/WPI blend fibers. Adapted with permission from (Tomczyńska-Mleko et al. 2015b). Copyright 2016, Elsevier

spectroscopy of blend fiber did not show distinct peaks relating to the intermolecular interaction between the polymers.

Tomczyńska-Mleko et al. (2015a) also reported cellulose/egg white protein blend fiber using the same process as they did for cellulose/WPI fiber. In the final solution, the concentration of cellulose was 6.25% and that of egg white isolate (EWI) was 1.875%. The resulting blend fiber showed comparable results to the cellulose/WPI blend fiber. In addition, the authors intended to utilize the blend fibers for biomedical applications. Consequently, they disregarded the tensile properties of fibers in their initial reports. The properties were mentioned to be tailored for textile materials that are resistant to microbial degradation.

The main drawback of cuprammonium process is the recovery of copper, ammonia, and the coagulant that are expensive and not fully achievable (Aminuddin 1998). Despite the disadvantage, the remained copper in cellulose/protein fibers was useful for biomedical applications.

5.6 Lithium Chloride and N,N–Dimethylacetamide

Dawsey and McCormick (1990) developed the mixtures of lithium chloride (LiCl) in *N,N*–dimethylacetamide (DMAc) with which homogenous solutions of cellulose can be prepared. These mixtures had been previously employed to dissolve proteins, polyamides and chitin. As an aprotic solvent, LiCl/DMAc system does not cause any chain degradation or reaction with cellulose. Being a nonderivatizing solvent, it can directly dissolve cellulose in a rapid, facile and reproducible manner. It is also utilized to determine MW distribution of cellulose and other soluble polymers (Dupont 2003).

Dissolution of cellulose by this solvent requires a pretreatment (also referred to activation) step for chain relaxation of the polymer and for the solvent to diffuse into crystalline segments to cause swelling. This contributes to chain unfolding and ease of processing for most polymers. The higher the DP and crystallinity are, the longer the time is required to acquire useful polymer solution. This activation can be achieved by either refluxing cellulose in hot DMAc (close to its boiling point) or a solvent exchange method that is carried out with water later replaced by DMAc (Dupont 2003). The latter is usually preferred because low temperatures do not cause oxidative degradation of cellulose. However, the former takes significantly less time and the related thermal oxidation could be minimized by a constant flow of dry nitrogen (Dawsey and McCormick 1990).

Although the concentration of LiCl in DMAc varies from 8 to 13 wt% in the literature, 8.46 wt% is the highest solubility attained experimentally at 25 °C. In addition, both of the two molecules are so hygroscopic that their mixture can absorb water very easily. Consequently, this could hamper the solvent to form complex with cellulose and to cause aggregation. On the other hand, cellulose solution from LiCl/DMAc is very stable and the polymer does not degrade over a long period of time at ambient temperature (Dupont 2003).

The dissolution is assumed to involve a macrocation $[Li(DMAc)_x]^+$ in the form of an ion–dipole complex (Fig. 5.12). A complexation occurs through a Li^+ cation, residing next to the oxygen of DMAc' carbonyl group, and a Cl^- anion interrupting the hydrogen bonds of cellulose (Striegel 2003).

Pretreatment with DMAc is a facile activation for the dissolution of cellulose. Typically, a given amount of dry cellulose is soaked into a known weight of DMAc. The activation continues at 165 °C by refluxing the mixture for 20–30 min under nitrogen atmosphere. Then, it is chilled to 100 °C and a given amount of LiCl is incorporated into the mixture while stirring. At 80 °C, stirring resumes for 10–40 min to ensure that the dissolution is complete. A maximum concentration of 15 wt% cellulose with the DP of 1130 can be achieved. Above 15 wt%, suspended particles, which are undissolved and swollen fragments of cellulose, are found in the viscous solution (Aminuddin 1998; McCormick et al. 1985).

Besides LiCl/DMAc, some other lithium halide/organic amide solvent systems including lithium bromide (LiBr) and N,N-dimethylformamide (DMF) or *N*-methyl-2-pyrrolidone (NMP) that dissolve cellulose were also reported

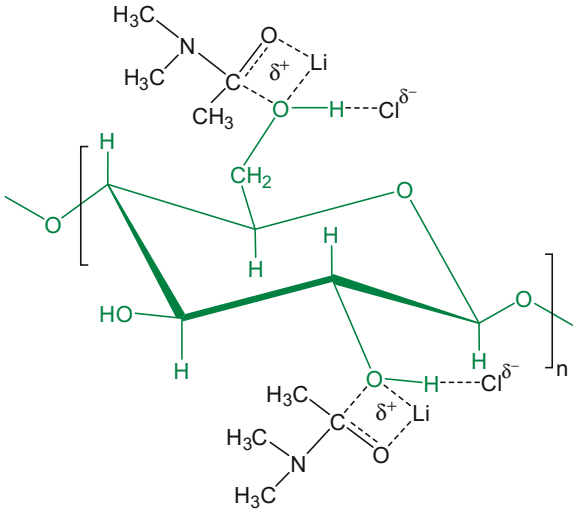

Fig. 5.12 A likely interaction of cellulose with the LiCl/DMAc solvent system. Redrawn with permission from (Tosh et al. 2000). Copyright 2016, Elsevier

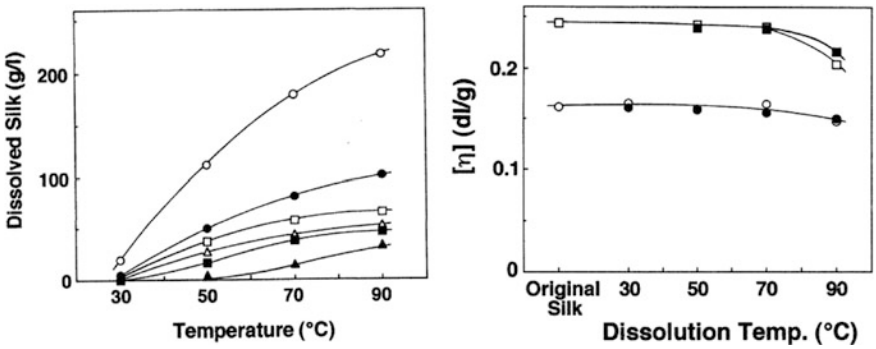

Fig. 5.13 Effect of dissolution temperature on silk fibroin dissolved in lithium halide/organic amide solvent systems: ○, in LiCl/DMAc; ●, in LiBr/DMAc; △, in LiCl/DMF; ▲, in LiBr/DMF; □, in LiCl/NMP; ■, in LiBr/NMP. Dissolved at [LiX] = 1.86 mol/l in 1 h. Adapted with permission from (Furuhata et al. 1994). Copyright 2016, The Japanese Society of Sericultural Science

(Furuhata et al. 1992). This research was also conducted for silk fibroin expecting a comparable dissolution mechanism to cellulose due to its intermolecular hydrogen bonding. By analogy with the dissolution of cellulose in LiCl/DMAc, a calculated amount of degummed silk fibers was pretreated with DMAc at 90 °C under nitrogen for 2 h. Then, the silk fibroin/DMAc mixture is cooled down the dissolution temperature, e.g. 50 °C, and a given amount of LiCl was added. After an hour of stirring, the content was filtered to remove undissolved matter. Finally, the fibroin was regenerated in ethanol. This process is also repeated with other combinations of lithium halide and organic amide. As seen in Fig. 5.13, concentrations

above 20 wt%, which is relatively high, were obtained in LiCl/DMAc solvent at 90 °C. However, temperatures over 70 °C caused degradation that decreased the viscosity. Highly viscous solutions of silk fibroin with LiCl/DMAc and LiCl/DMF were not altered even after one year of storage. Dense but transparent films were cast from these solutions by coagulating in alcohol (ethanol or methanol) bath (Furuhata et al. 1994).

The solubility of silk fibroin in LiCl/DMAc solvent system occurs through the solvent ions interacting with functional groups of the fibroin macromolecules. Comparable to the cellulose dissolution in this system, it is presumed that the hydrogen bonds in the fibroin are disrupted due to the nucleophilic attack by the anion (Dawsey and McCormick 1990). The solvent ions rupture the hydrogen bonds between the polymer chains by interacting with polar and charged groups of pendant chains of fibroin (Sashina et al. 2006). This structural change of fibroin could contribute to formation of novel hydrogen bonding with cellulose in the same solvent system.

Marsano et al. (2007) studied wet and dry-jet wet spinning of the blend solution of cellulose/silk fibroin (CE/SF) in LiCl/DMAc solvent system. The blending ratio of cellulose to silk fibroin was 70/30 (w/w) and the total polymer concentration (C_p) was 5–9 wt%. Using a 100 μm spinneret orifice, the blend solution was pumped into a coagulation bath (25 °C) at an extrusion speed of 7.9 m/min. Monofilaments were spun at draw down ratios (D_r) from 1 to 3 and collected on a set of spools then washed in the selected coagulant for 3–4 days to remove all LiCl salt residue. Water and ethanol were the two coagulants compared in terms of their effect in the resulting blend fiber.

Water had a solubilizing effect for silk fibroin in the spinning dope thus decreased the protein content of the blend fiber. Ethanol, on the other hand, performed better for the blend fibers with almost no loss of protein. As seen on SEM images in Fig. 5.14, the blend fiber coagulated in ethanol possessed a smooth surface, a round-like cross section and no phase separation. Furthermore, C_p = 9 wt% increased the viscosity of the blend solution enough to extrude through an air gap before the coagulation bath

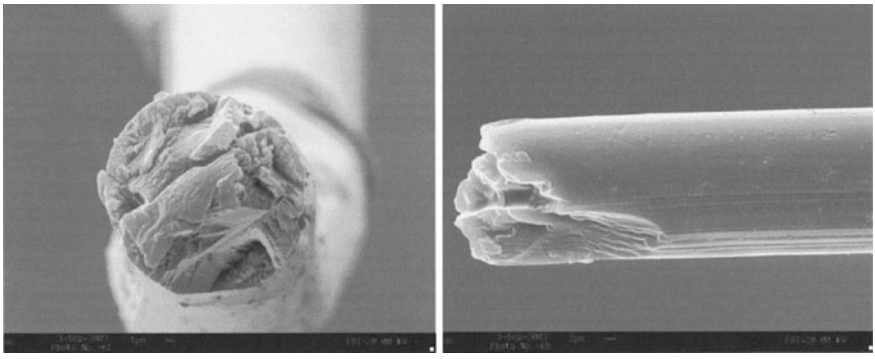

Fig. 5.14 SEM images of the CE/SF blend fiber (C_p = 7 wt% and D_r = 2). Adapted with permission from (Marsano et al. 2007). Copyright 2016, John Wiley and Sons

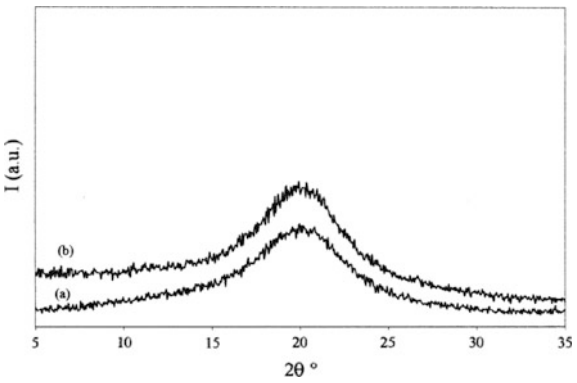

Fig. 5.15 WAXD analysis of (a) CE and (b) CE/SF blend fibers (C_p = 7 wt% and D_r = 2). Adapted with permission from (Marsano et al. 2007). Copyright 2016, John Wiley and Sons

turning the method into dry-jet wet spinning. Therefore, the resulting blend fibers had a perfectly round cross section exhibiting no phase separation, no micro-voids, and no micro-fractures at macroscopic scale (Marsano et al. 2007).

X-ray analysis (Fig. 5.15) of the blend fibers in comparison with the cellulose fiber showed an amorphous structure and suggested a homogeneous distribution of the protein domains into the cellulose matrix (Marsano et al. 2007).

The diameters of the blend fibers with C_p = 9 wt% were between 21.6 and 32.7 μm. Increasing the D_r from 1 to 2 resulted in smaller diameters and adding an air gap (h = 20 mm) at D_r = 1 ended in even further decrease. Even though the elastic modulus of the fibers (∼13 GPa) remained the same, the tenacity and the elongation of the blend fibers significantly improved due to the air gap. This suggested more orientation and less defects in the final fiber structure. It must be also highlighted that the wet-spun blend fibers had nearly the same modulus (∼16 GPa) as the cellulose fibers with lower concentration in similar spinning conditions. The tenacity (179 MPa) and the elongation (3.4%) were, however, lower than that of the cellulose fiber (243 MPa and 13.5%, respectively) (Marsano et al. 2007).

LiCl/DMAc system performed well in blending cellulose and silk fibroin to produce their blend fibers. Compared to viscose process, the miscibility and the compatibility of the two polymers were clearly improved since the system used to dissolve both. No other protein reported to blend with cellulose in this solvent system. Additionally, the pre-activation step and high temperature requirement are the overall disadvantages for this system compared to other direct solvents.

5.7 N–Methylmorpholine N–Oxide and Water

The success of N–Methylmorpholine N–Oxide (NMMO) is based on the strong N–O dipoles forming hydrogen bonds with –OH groups of cellulose (Franks and Varga 1979). It can simply be yielded by oxidizing N–methylmorpholine

(synthesized from ethylene oxide and ammonia) with hydrogen peroxide. Its melting point is 170 °C that is dropped to 74 °C for NMMO monohydrate (13.3 wt % H_2O) to increase its dissolving power. Aqueous solutions of NMMO can dissolve cellulose with no derivatization, complexation or special activation involved (Fink et al. 2001). NMMO–water system simply swells cellulose by diffusing into its fiber matrix. Then, fragmentation into rod like segments occurs through breaking intermolecular hydrogen bonding followed by formation of new ones between NMMO and cellulose chains (Wertz et al. 2010).

Johnson's work (1969) on NMMO was about not only the dissolution of cellulose, but also the solubility of other natural and synthetic polymers that are characterized by intermolecular hydrogen bonding. Such natural polymers including wool, silk, hair, feathers, β–amylose, casein, zein, gelatin, gum arabic, lignin and such synthetic polymers including nylon were all mentioned in his patent. He later filled another one that covers the blending of cellulose in NMMO with other polymers by using a diluent, e.g. dimethyl sulfoxide (DMSO), N–methylpyrrolidone or sulfolane, to decrease the viscosity. These polymers include gelatin, starch, gum arabic, some vinyl polymers and polyanhydroglucoses (Johnson 1970).

NMMO–water system was found to solubilize solely proteins (either fibrous or globular) that could be processed into different final forms, such as fibers, films, membranes, coatings and particles. For instance, 6–30 wt% collagen, a major fibrous protein, was dissolved in NMMO monohydrate in order to use as edible food casing (Gord and Hammer 2006). Silk fibroin, a well-known fibrous protein, was particularly studied by different groups of researchers to obtain concentrations from 6 to 36 wt% in aqueous NMMO. A process that is very similar to the dissolution of cellulose at relatively lower temperatures was successfully applied. It was also suggested that the same forces as in the dissolution mechanism of cellulose drive the dissolution of silk fibroin in NMMO-water system (Freddi et al. 1999; Heinemann and Taeger 2000; Sashina et al. 2003; Xu et al. 2005). Figure 5.16 illustrates the swelling and dissolution of degummed silk fibers (silk fibroin) in NMMO monohydrate. The fibers were swollen at 100 °C and almost completely dissolved at 120 °C with barely visible birefringent silk left. However, a transparent solution of silk fibroin was not achievable and the degradation of silk fibroin was also experimentally observed above 100 °C (Freddi et al. 1999).

Sashina et al. (2003) reported the data in Table 5.1 showing the solubility of silk fibroin in aqueous NMMO with less than 10 wt% water, which is equal to the molar compositions of NMMO·0.8H_2O. The authors obtained clear yellowish solutions of silk fibroin with 5 and higher wt% polymer concentrations. Although a detailed study of the dissolution of silk fibroin in the mixtures of NMMO with organic solvents was also included, the degradation of the polymer at any extent was not investigated.

In contrast to regular silk fibroin obtained by degumming silk fiber, regenerated silk fibroin can easily form homogeneous solutions with NMMO monohydrate. The silk fibroin, regenerated from aqueous LiBr solution in at least one-day processing, was amorphous and thus soluble in NMMO·1.0H_2O at high temperatures. The polymer concentrations between 10 and 25 wt% was attained and spun into fibers

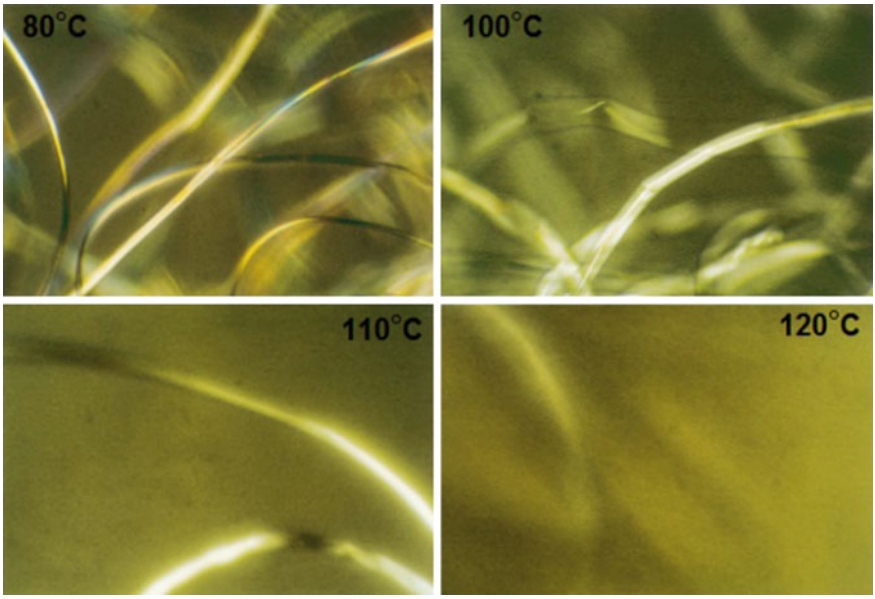

Fig. 5.16 Polarized optical microscopy images (200X) of silk fibroin dissolving in NMMO·1.0H_2O at different temperatures. Adapted with permission from (Freddi et al. 1999). Copyright 2016, Elsevier

Table 5.1 Solubility of silk fibroin in NMMO with varying water content. Adapted with permission from (Sashina et al. 2003). Copyright 2016, Springer

Water content in NMMO (wt%)	Molar composition of the solvent	T_d (°C)	Fibroin concentration in the solvent (wt%)
13.3	NMMO·1.0H_2O		Insoluble
11.5	NMMO·0.85H_2O		Insoluble
10.6	NMMO·0.77H_2O	120	≥ 6
8.4	NMMO·0.6H_2O	>120	≥ 6
4.4	NMMO·0.3H_2O	>120	≥ 6

coagulated in an alcohol bath (Xu et al. 2005; Marsano et al. 2005). Even though the resultant fibers were comparable to the others dissolved in salt containing solvents, the dissolution and processing of silk fibroin became multi-stepped and time consuming.

Solubility of globular proteins in NMMO was pointed out in the patent of Buerger et al. (2004) to produce various shaped articles. Casein, zein and ardein (peanut protein) were optionally used globular proteins that were crosslinked either before by Lewis acids or after by acetylation, aldehyde treatment, etc. Furthermore, proteins along with synthetic polymers, oils, fats, waxes, dyes, etc. that could

contribute functionality to Lyocell fibers by coating were patented by Schuster et al. (2012) at Lenzing AG.

Firgo et al. (1998) at Lenzing AG added gelatin into NMMO-water-cellulose solution in order to decrease and to control the fibrillation properties. Stall and Turbak (1999) at Alfacel S.A. also used gelatin to slow down and to control the rapid precipitation of cellulose from NMMO solution. Weigel et al. (2003) studied NMMO solubility of various proteins that are soluble in different media: Water-soluble proteins (gelatin), acidic media-soluble ones (collagen), ethanol-soluble ones (zein), and alkali soluble ones (soy protein) did not form true solutions but colloidal ones. Nevertheless, the proteins blended with cellulose were able to form homogenous solutions that could be spun. These solutions were used to produce tubular films for food packaging. Similarly, Gord et al. (2004) cast chewable films containing cellulose, a protein (preferably natural globular proteins), and a filler from NMMO monohydrate. In addition, there have been a few reports on cellulose/silk fibroin blends coagulated from an alcohol–water mixture in the form of fibers with improved mechanical and thermal properties compared to the sole cellulose compound (Heinemann and Taeger 2000; Marsano et al. 2008). The compatibility studies by thermal analysis showed strong interactions between the two polymers in their blend from NMMO-water system (Sashina et al. 2007).

A further study by Marsano et al. (2008) focused on the same blend fibers that were spun from the blend solutions prepared from another co-solvent, NMMO-water. As mentioned earlier, regenerated silk fibroin by using LiBr could be easily regenerated again by using NMMO-water system. Therefore, the authors reported fibers from 100% silk fibroin and 100% cellulose as well as the blend solutions at 3 compositions: 75/25, 50/50, and 25/75 CE/SF. C_p was 17 wt% and ethanol was used as the coagulant. The extrusion speed was 4 m/min and the diameter of spinneret was again 100 μm but the height of air gap was 100 mm that was five time longer than the previous setup. The resulting fibers with applied D_r of 1, 3 and 6 were collected on a spool then were kept in ethanol for 3 days to remove residual NMMO.

Compared to the blend fibers from LiCl/DMAc system, the ones from NMMO-water formed a two-phase morphology. The authors explained the two-phase system from the results of FTIR, DSC and WAXD analyses in addition to the SEM images of the blend films. The phase separation observed in the film cross sections was hypothesized for the blend fibers of all composition. It was essentially concluded that the polymers were not miscible in NMMO-water system (Marsano et al. 2008).

Although the polymers were immiscible, their blend solutions were spinnable. Their blend fibers were obtained with different D_r on a dry-jet wet spinning line. The results for the Young's modulus and tenacity of all fibers with applied $D_r = 3$ were graphed in Fig. 5.17 to show the trend in increasing amount of cellulose. Regardless of the miscibility issue, there is a close linear behavior of the mechanical properties between the two polymers. The blend fiber with 25% fibroin content possessed moderately higher tenacity (stress at break) and slightly higher modulus

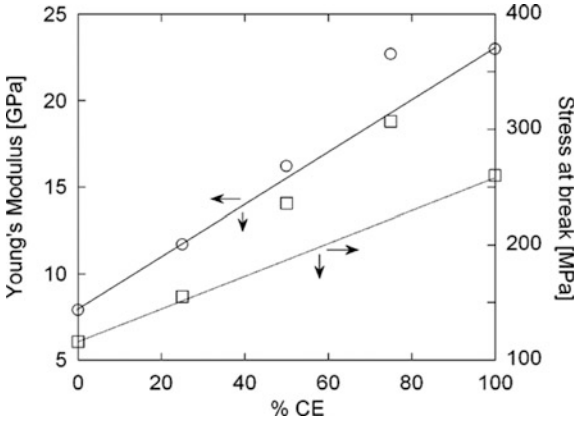

Fig. 5.17 Variation of Young's modulus (○) and stress at break (▲) by increasing CE content for CE/SF blend fibers at $D_r = 3$. Adapted with permission from (Marsano et al. 2008). Copyright 2016, Elsevier

than the cellulose fiber. These results suggest a particular interaction between the two polymer domains indicating a proper compatibility (Marsano et al. 2008).

Heinemann and Taeger (2000) from Thueringisches Inst. Textile Inc. patented similar CE/SF blend fibers in Germany much earlier than the study of Marsano et al. (2008). The English translation of the patent is accessible and describes sufficient details about the preparation of the blend solutions but not the properties of the obtained blend fibers.

Although they are different in the composition of blend solutions and the spinning conditions, the CE/SF blend fibers processed by NMMO/water system showed overall better mechanical properties than those produced from LiCl/DMAc system. On the other hand, cellulose and silk fibroin were not completely miscible in NMMO/water and their compatibility in this system is comparable to LiCl/DMAc.

While NMMO is an excellent direct solvent for cellulose, it appeared that blending with proteins contributed to the fibrillation problem of Lyocell fibers. This approach also facilitated some modifications and enhancements in the blend materials. However, the disadvantages of NMMO, such as demand for high temperature, the high cost, byproducts, and the degradation of the polymers, are the driving force for investigating other solvents for both cellulose and proteins.

5.7.1 Aqueous Alkali and Aqueous Alkali/Urea

Mercerization that causes the change in crystal structure from cellulose I to cellulose II by reforming the hydrogen bonding is an important process that could also be tailored to further modify and to dissolve cellulose. The polymer is only partially solvable in 10% aqueous NaOH and the amount of solubility can vary depending on the molecular weight and the type of crystal structure (Kamida et al. 1984). Using additives, such as urea (Zhang et al. 2001) and/or thiourea (Zhang et al. 2002; Jin et al. 2007) improved the dissolving power of NaOH-water system. The dissolution mechanism of cellulose in aqueous NaOH/urea system was investigated

by analytical techniques, e.g., NMR (^{13}C, ^{15}N, and ^{1}H), FTIR, X-Ray and neutron scattering (Egal et al. 2008; Cai et al. 2008; Qi et al. 2011). The analytical results indicated that the hydrates of NaOH can establish hydrogen bonding with cellulose chain at low temperatures. At the same time, aqueous NaOH/cellulose complex was surrounded by urea molecules shielding it from other cellulose chains in order to prevent polymer aggregation (Olsson and Wesman 2013).

Freeze thawing is the commonly applied method to dissolve cellulose in aqueous solution of 7 wt% NaOH/12 wt% urea system. Cellulose (4 wt%) is mixed with the solvent that is already cooled down to −12 °C at which its dissolution occurs within 2 min (Cai et al. 2008). Subsequently, the resultant polymer solution is precipitated to regenerate cellulose in coagulants, such as diluted acids (acetic acid or H_2SO_4), ethanol, *t*-butanol, acetone, Na_2SO_4, $(NH_4)_2SO_4$, and water (Mao et al. 2006; Yang et al. 2011). This solution, however, is relatively unstable and sensitive to polymer concentration, temperature, and storage time (Libert 2010; Cai and Zhang 2006; Qi et al. 2008). Moreover, potassium hydroxide (KOH) and lithium hydroxide (LiOH) can substitute for NaOH in cellulose dissolution. Addition of urea enhances these systems' dissolving power and makes NaOH/urea much superior than KOH/urea but inferior than LiOH/urea. Overall, aqueous solutions of NaOH and LiOH with the additive induce faster dissolution of cellulose compared to that of KOH (Olsson and Wesman 2013; Cai and Zhang 2005).

A group of researchers from Institute of Biopolymers and Chemical Fibers (IBWCh), Łódź, Poland, studied cellulose-based blends with different proteins that are all soluble in aqueous alkaline solutions. For instance, 6.5 wt% bio-modified cellulose (DP_v = 670) obtained from enzymatically treated cellulose pulp was dissolved in 10 wt% NaOH and blended with regenerated silk fibroin. To enable the dissolution of silk fibroin in aqueous alkali, the polymer was processed for more than 6 days: It was first degummed from silk cocoons, and then dissolved in saturated LiBr solution. It must be recalled that a very similar process was also applied for the dissolution of silk fibroin in NMMO-water system. Later, 10 wt% regenerated silk fibroin is solubilized in 5 wt% NaOH and the blend solutions were prepared at the compositions of cellulose to the fibroin: 98:2, 95:5, 90:10 and 85:15. The increasing fibroin content induced gradual decrease in the dynamic viscosity: 9.950 cP for the cellulose solution dropped down to 8.200 cP with addition of 15% silk-fibroin in the blend solution (Fig. 5.18). The solutions were used to form blend fibers by wet spinning process lined up with a coagulation bath containing sulfuric acid (100 g/dm^3) and ammonium sulfate (450 g/dm^3) (Strobin et al. 2006). It is important to note that the choice of cellulose type and the use of regenerated silk fibroin enabled the polymers to blend in aqueous NaOH. This made the blending process multi-stepped and time-consuming. In addition, the percentage of silk fibroin higher than 15% could not be examined due most likely to the anticipated viscosity decrease.

The blend solutions were extruded at 15 m/min and the resulting fibers were drawn in air at D_r = 30%. The fibers were further washed by water and ethanol to remove the residues of coagulants. The blend fibers were formed with about 10% loss of silk fibroin from the corresponding solutions. This was referred to the

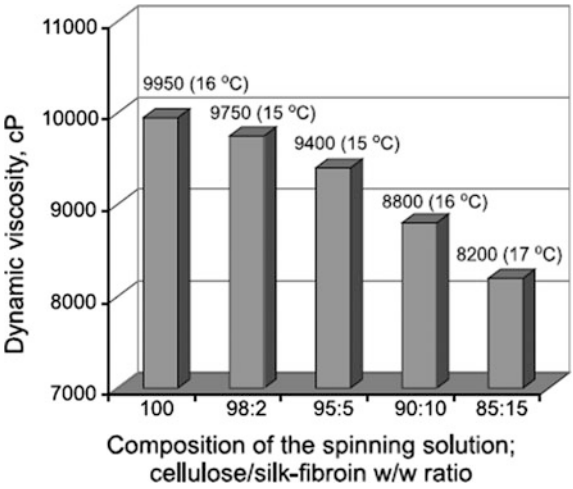

Fig. 5.18 The dynamic viscosity of the spinning dope versus its composition; the temperatures of viscosity measurements are included in the parentheses adjacent to the viscosity values; the C_p of dopes were 6.5 wt% (100:0), 6.63 wt% (98:2), 6.83 wt% (95:5), 7.15 wt% (90:10), and 7.48 wt% (85:15). Adapted with permission from (Strobin et al. 2006). Copyright 2016, IBWCh

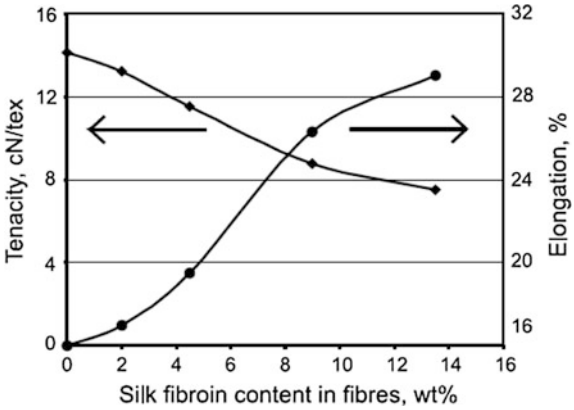

Fig. 5.19 The tenacity and the elongation of CE/SF fibers by increasing silk fibroin content. Adapted with permission from (Strobin et al. 2006). Copyright 2016, IBWCh

peptide fractions due to a partial degradation during the extraction of the fibroin. The SEM images of the blend fibers showed no phase separation and distorted cylindrical cross-sections, which is typical for wet-spun cellulose fibers. However, the authors suggested that the shape of cross-section was a result of the weak coagulation properties of cellulose in ammonium sulfate that was good for silk fibroin. Even though the C_p of the solutions was increased by addition of more silk fibroin, the viscosity decreased gradually as shown in Fig. 5.18. As one can expect, the tenacity of the resulting fibers was also affected correspondingly (Fig. 5.19). Despite decreasing tenacity, the elongation of the fibers was improved by an increasing silk fibroin content. In other words, blending silk fibroin with cellulose made the cellulose fibers more flexible (Strobin et al. 2006).

It can be concluded that the CE/SF blend fibers produced with the aqueous alkali system showed good miscibility and compatibility. Compared to the CE/SF blend fibers by LiCl/DMA and NMMO-water systems, the ones by this system had more elongation by addition of more silk fibroin. Moreover, the blend fibers with 2–9%

silk-fibroin content were characterized by tensile properties suitable for their further processing towards wound dressing materials (Strobin et al. 2006).

Cellulose/keratin biocomposite fibers were also studied in the same research institute as the CE/SF blend fibers from aqueous alkali. Keratin extracted from chicken feathers was first suspended in alkaline solution and then mixed with the bio-modified cellulose solutions at different proportions. Following similar processing conditions to their previous report, cellulose/keratin fibers with up to 48% protein content were formed. As expected, adding the protein suspension resulted in two-phase morphology observed on the cross-section of fibers. Furthermore, these fibers were characterized by their enhanced sorption properties, higher hygroscopy, and a smaller wetting angle than the cellulose fibers. The tensile properties of cellulose fibers lessened by addition of keratin, and yet, applicable fibers were attained as composite fibrous materials from biodegradable polymers. As seen in Fig. 5.20, the total biodegradation of fibers was achieved in 3 weeks (Wrzesniewska-Tosik et al. 2007).

The researchers at the IBWCh also utilized an alkali soluble cellulose (DP_w = 346) pulp (hydrothermally treated at 100–200 °C) that was dissolved in 10.2% NaOH with added zinc oxide (for antibacterial purposes) between 2 and 12 °C. It was later blended with the alkaline solutions of proteins derived from rape and sunflower seeds. The blend solutions containing 5.15–5.82 wt% cellulose, 0.47–1.26 wt% protein, and 7.16–7.74 wt% aqueous NaOH were used to produce fibers. They were successfully wet-spun using coagulation bath with sulfuric acid and sodium sulfate. Due mainly to the varying C_p, the tensile properties of blend fibers did not show any trend by the increasing protein content. While the tenacity of blend fibers was inferior to the cellulose fiber, their elongation was slightly higher. The blend fibers had also somewhat higher water retention values and

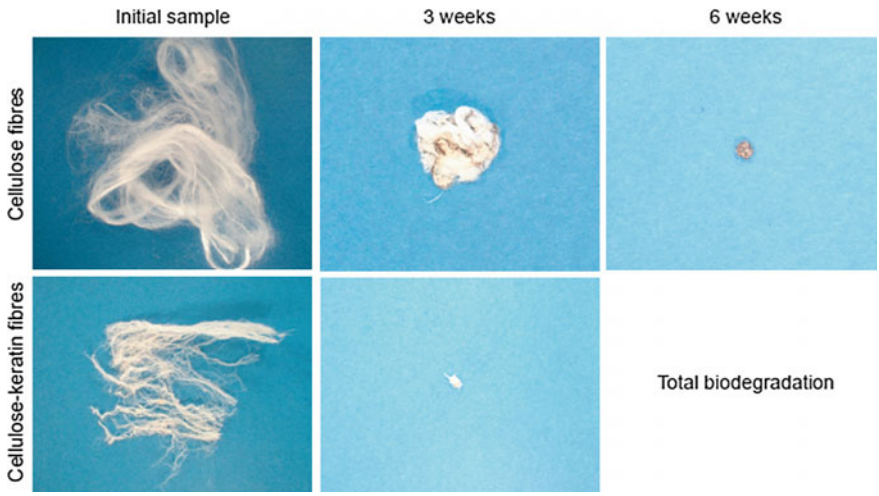

Fig. 5.20 Biodegradation of cellulose and cellulose/keratin composite fibers by composting. Adapted with permission from (Wrzesniewska-Tosik et al. 2007). Copyright 2016, IBWCh

slightly higher LOI then the cellulose fiber. In addition, the zinc content (217.8 mg/kg) in cellulose/sunflower protein fiber showed bacteriostatic activity against Staphylococcus aureus bacteria. On the other hand, proteins were largely agglomerated in the blend fibers and thus extensive defects along the fibers' axes occurred (Wawro and Stęplewski 2010).

Zhang et al. (2011) prepared a solvent from a combination of urea (6.5 wt%), thiourea (8 wt%) and aqueous NaOH (8 wt%) to dissolve 5 wt% cellulose that was blended with soy protein isolate (dissolved in 6 wt% NaOH). On a laboratory-scale wet spinning line, the extrudate was pumped with 0.1 MPa pressure into the coagulating bath containing 10 wt% H_2SO_4 – 12.5 wt% Na_2SO_4 aqueous solution. D_r of 90%, subsequent washing, and 120% post-drawing were applied along the spinning system. The resulting fibers were dried by a heating roller at 65–80 °C and collected on a spool. Although from 10 to 40% protein content was examined in the blend solution, due to high viscosity decrease, only the blend fiber with 10% protein content was successfully spun.

The X-ray analysis showed almost no difference between the cellulose and the blend fibers. Both had the structure of cellulose II. Furthermore, the FTIR spectra in Fig. 5.21 indicated the formation of interactions between the two polymers in their blends. The peaks at 1650 and 1545 cm^{-1} were specific to the blend fiber. This suggested the hydrogen bonding between the amide and carbonyl groups of protein and hydroxyl groups of cellulose (Zhang et al. 2011).

The fiber had a round-like cross section and some irregularities were observed along its axis. However, SPI was fragmented into particles on the surface of the fiber indicating a partial phase separation. The authors also reported some micro-voids based on the cross-sections that cannot be clearly seen on the SEM images. In addition, the tenacity and the elongation of the blend fiber were 2.1 g/den and 12.3%, respectively. The corresponding values for the cellulose fiber were 2.05 g/den and 12%. Considering the reported standard deviations of tensile properties, the blend fiber did not differ from the cellulose fiber. However,

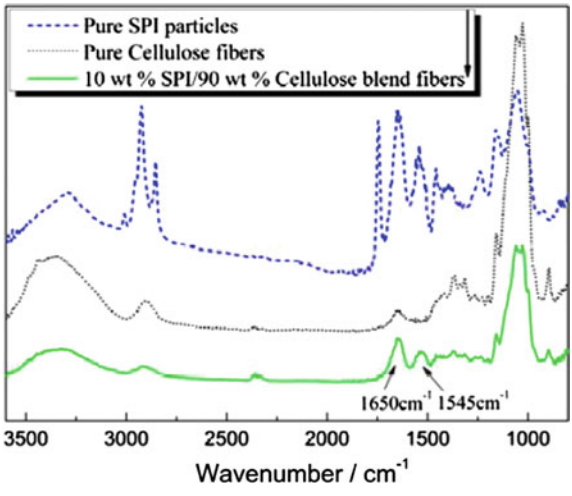

Fig. 5.21 FTIR spectra of raw SPI, cellulose fiber and CE/SPI fibers. "Reproduced courtesy of Journal of Engineered Fibers and Fabrics, P.O. Box 1288, Cary, North Carolina 27512-1288, USA. Tel: (919) 459-3700 Fax: (919) 459–3701 Internet: www.jeffjournal.org." (Zhang et al. 2011)

according to the authors the tensile properties slightly increased by addition of 10% SPI (Zhang et al. 2011).

Compared to the previous solvent systems, alkali/urea system is inexpensive and more ecofriendly (Cai et al. 2004). It allows rapid dissolution of cellulose and its blending with alkali soluble proteins. However, the stability and sensitivity of aqueous alkali/urea solvent system towards polymer concentration, temperature and storage are already major concerns for the solubility of cellulose. The cellulose used in some blend solution was either modified or regenerated to facilitate the dissolution in alkaline solvent. In addition, proteins were separately solubilized with usually a different concentration from the same solvent of cellulose, and then were blended with cellulose. Excessive centrifugation and stirring were necessary. The regeneration of blend solution required modification of the coagulation bath. Due to mentioned drawbacks, a simple way of blending the polymers and their regeneration are pending requirements for the co-solvents.

5.8 Ionic Liquids

Ionic liquids (ILs) represent a broad group of molten organic salts that are in liquid state below 150 °C or most preferably below 100 °C (Holbrey et al. 2005). In 1934, Graenacher prepared a solution of cellulose with *N*–alkylpyridinium salts by heating in a liquid base media containing nitrogen, such as pyridine. The novelty of this study was ignored for a long time since the practical value of ILs as a class of solvents was not recognized until the early 2000s. Swatloski et al. (2002) reported the dissolution of cellulose up to 25 wt% requiring no pretreatment or activation in 1–butyl–3–methylimidazolium chloride ($[C_4MIm]Cl$ or [BMIm]Cl) and other hydrophilic ILs. Its regeneration was simply achieved by addition or extrusion into water.

Swatloski et al. (2002) discussed the effect of the alkyl substituent (R) of the cation and the anion on cellulose dissolution. Their research showed that ILs are nonderivatizing solvents for cellulose. ILs containing anions that have strong hydrogen bonding capacity had the highest dissolving power, particularly elevated by microwave heating. However, ILs incorporating non-coordinating anions, such as BF_4^- and PF_6^-, could not solubilize cellulose. ILs with chloride anions effectively dissolved cellulose, most likely through disrupting and reforming the

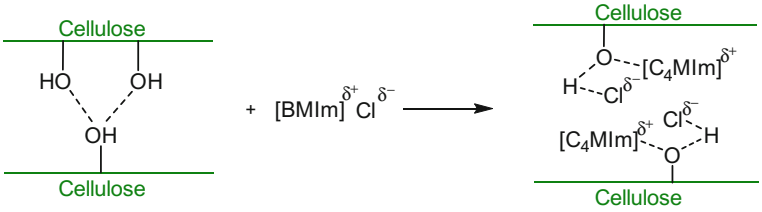

Fig. 5.22 Suggested dissolution process of cellulose in ILs. Redrawn with permission from (Feng and Chen 2008). Copyright 2016, Elsevier

hydrogen bond network (Fig. 5.22). Furthermore, increasing chain length of R reversely affected the solubility of the polymer.

Since their report, research on the applications of ILs in natural polymers has made an important progress and thus several other ILs have been developed to dissolve cellulose (Heinze et al. 2005; Zhang et al. 2005; Fukaya et al. 2006, 2008) and proteins (Fujita et al. 2005). Silk fibroin (Phillips et al. 2004; Mantz et al. 2007; Goujon et al. 2012; Wang et al. 2012; Goujon et al. 2013), keratin (Xie et al. 2005; Idris et al. 2013, 2014), collagen (Mantz et al. 2007; Meng et al. 2012; Hu et al. 2013), zein (Biswas et al. 2006; Brauer et al. 2009; Choi and Kwon 2010; Tomlinson et al. 2014), gluten (Brauer et al. 2009), soy protein (Wu et al. 2009), and gelatin (Zhang et al. 2012) were proven to dissolve in ILs. Most of these ILs have appeared to effectively dissolve and process the biopolymers without causing degradation and emitting gas. They can also be economically recovered and recycled. Interestingly, one type of IL, for instance, 1–butyl–3–methylimidazolium chloride, could dissolve rather different biopolymers (Wang et al. 2014).

A team of researchers from the US army laboratories worked on the solubility of silk fibroin using [BMIm]Cl, [DMBIm]Cl, and [EMIm]Cl. They first focused on the dissolving power of [BMIm]Cl: Silk fibroin was dissolved in the solvent at 100 °C, and cooled down to 30 °C to analyze crystallinity using wide angle X–ray scattering (WAXS). It was confirmed that [BMIm]Cl disrupted the β–sheet crystalline structure in silk fibroin: Several peaks related to antiparallel β–sheet structure in silk fiber did not appear for so called "amorphous silk/BMIm". This result in combination with optical microscopy observation (which was not reported) of silk fibroin in the solvent agreed in the dissolution of the polymer (Phillips et al. 2004).

This research was expanded to the solubility of several biopolymers including cellulose, chitin, silk, collagen and elastin. The focus though was mainly on the dissolution of silk fibroin in the selected ionic liquids. Based on their ability to disrupt the hydrogen bonds, imidazolium chlorides were useful solvents for the biopolymers. The cation's potential for rupturing the bonds enhanced the dissolution of proteins, which did not occur for polysaccharides. Therefore, the dissolving power of [EMIm]Cl was similar to that of [BMIm]Cl in the solubility of cellulose (Mantz et al. 2007).

Recently, Yao et al. (2015) studied blend fibers from cellulose and silk fibroin both dissolved in [BMIm]Cl. With a C_p of 8 wt%, spinning dopes were prepared at CE/SF 100/0, 80/20 and 60/40 by kneading at 90 °C. The spinning dopes were extruded at 85 °C into ethanol bath (10 °C) passing 5 cm air gap at room temperature. The obtained fibers were strecthed at D_r = 1–5. Before drying, the fibers were further washed in ethanol. Although 100% silk fibroin solution was experimented, its viscosity was not high enough to be used for spinning. Similar to other reported CE/SF solutions, the viscosity decreased by addition of silk fibroin.

The CE/SF fibers possessed lower crystallinity than the cellulose fiber both regenerated by using [BMIm]Cl solvent. Concequently, the blend fibers had lower modulus, tensile strength and elongation compared to the cellulose fiber. The author refferred the changes in the tensile properties to fibrillar structure of the protein continuously dispersed in cellulose network. Because amino acids of proteins have

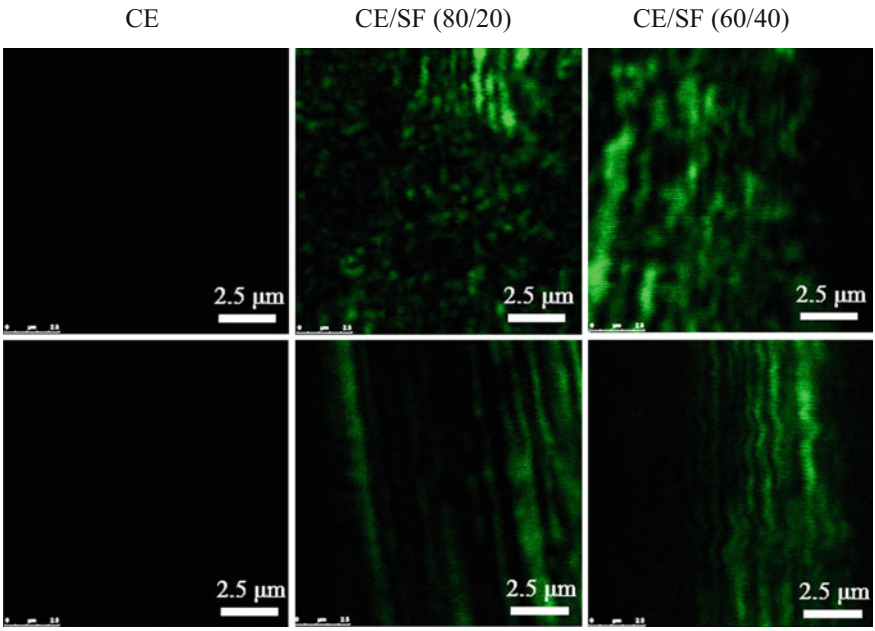

Fig. 5.23 LSCM micrograph of cellulose and CE/SF fibers along the fiber axes (top raw at $D_r = 3.3$, bottom raw at $D_r = 4.3$). Adapted with permission from (Yao et al. 2015). Copyright 2016, Springer

intrinsic flurescence, their phase morphology in the blend fibers (Fig. 5.23) was succesfully analyzed by laser scanning confocal misroscope (LSCM). This technique enabled the researchers to observe the dimension and the distrubition of protein phase of the blend fibers. For instance, the radial size of silk fibroin phase was measured 0.5–1.0 μm. In addition, more protein content and higher draw ratio increased the size of the protein phase and hydrogen bonding was observed between the two phases (Yao et al. 2015).

Ionic liquids are direct solvents for both cellulose and proteins. They are very recently introduced and their cost is too high to develop an economic process and application.

5.9 Cellulose Derivatives/Protein Blend Fibers

Edible nanofibers were produced from blends of cellulose derivative and egg albumen by electrospinning. Cellulose acetate (20 wt%) and egg albumen (12 wt%) were dissolved in 85% acetic acid and 50% formic acid solution, respectively. The polymer solutions were mixed at three compositions: 9, 23, and 34% protein solution with respect to the cellulose acetate solution. Due to insufficient

entanglement and high surface tension of the globular protein in formic acid solution, nanofibers of egg albumen could not be obtained. Incorporation of cellulose acetate and a surfactant (Tween40®) enabled the protein to be spun into nanofibers. SEM images revealed that increased protein resulted in nanofibers with smoother surface. Moreover, FTIR confirmed the interaction of both components in the resulting nanofibers. These nanofibers presumably could be used in food packaging and drug delivery applications (Wongsasulak et al. 2010).

In a similar study to edible nanofibers of cellulose acetate and egg albumen (white), the same group of researchers fabricated bicomponent nanofibers: Their core layer was composed of polyethylene glycol (PEG), amoxicillin (model drug) and soybean oil. Their shell layer consisted of blends of cellulose acetate, gelatin and Tween40®. The resulting fibers had an average diameter of 913 ± 180 nm. The composition of shell layer was increased from 10 to 30% protein decreased the viscosity of its solution and consequently lessened the thickness of the layer. Overall, the fibers were useful for controlled release of the encapsulated drug along the digestive tract (Kiatyongchai et al. 2014).

Amsaveni et al. (2013) studied the formation of blend fibers from collagen of animal skin, a cellulose derivative, hydroxyethyl cellulose (HEC), and bovine serum albumin. The fibers were produced on benchtop equipment including a syringe pump and a 0.5 mm needle attached to a syringe. At a flow rate of 0.5 ml/min, the blend solutions of polymers all dissolved in aqueous acetic acid at different proportions were pumped into a Petri dish containing ethanol and acetone (1:1) solution. The obtained fibers were then transferred into ethyl acetate bath where they were subjected to mild stretching. After drying, the fibers were cross-linked with glutaraldehyde vapor. The blend fibers as shown in Table 5.2 had relatively high linear mass density (fiber denier). The addition of HEC into the protein fibers increased the fiber denier, the tenacity as well as the elongation of the blend fibers. The swelling of blend fibers was also enhanced by more HEC content. In addition, increasing albumen content reduced the surface roughness. Having low tenacity (below 1 g/den), the fibers could find use as bioresorbable materials in wound management and related biomedical applications.

Table 5.2 Tensile properties of collagen (C)/hydroxyethyl cellulose (HEC)/albumin (A) fibers. Adapted with permission from (Amsaveni et al. 2013). Copyright 2016, Springer

Fiber	Fiber denier	Tenacity (g/den)	Elongation (%)
Collagen	12.5 ± 1.1	0.65 ± 0.05	12.6 ± 1.1
2:1 C:A	16.0 ± 1.3	0.69 ± 0.06	11.4 ± 0.8
1:1 C:A	19.0 ± 1.7	0.72 ± 0.05	13.4 ± 1.2
2:1 C:HEC	16.6 ± 1.5	0.84 ± 0.08	17.2 ± 1.2
1:1 C:HEC	22.5 ± 2.1	0.87 ± 0.09	18.5 ± 1.3
2:1:1 C:HEC:A	20.8 ± 1.8	0.73 ± 0.06	13.0 ± 0.9
2:1:2 C:HEC:A	17.3 ± 1.4	0.69 ± 0.05	13.7 ± 1.2
2:2:1 C:HEC:A	21.2 ± 1.9	0.83 ± 0.07	16.2 ± 1.4
1:1:1 C:HEC:A	24.5 ± 2.2	0.84 ± 0.08	18.1 ± 1.6

Although it is less efficient than using cellulose itself, depending on the derivation of cellulose, a co-solvent could be employed to prepare solution blends of cellulose derivative and proteins. Consequently, blending the two polymers could become even more complicated than using cellulose without derivatization. However, utilizing cellulose derivative contributed to the formation of nanofibers from proteins, which is a challenge due to their complex polymer structure. Overall, blend fibers from cellulose derivative/proteins can be produced that are especially aimed for biomedical applications.

5.10 Concluding Remarks

Various blends of cellulose and proteins listed in Table 5.3 was studied using different solvents and processing methods. Except viscose process and cellulose derivatives, all solvent systems used similar blending methods. Depending on the system, the both polymers could be dissolved separately prior to mixing their solutions at varying compositions. Some systems required pretreatment or chemical modification of the polymers. Some dissolved them at different conditions or used the same conditions to facilitate their processing. For instance, Yao et al. (2015) used an ionic liquid (BMImCl) was used for dissolution of cellulose and silk fibroin

Table 5.3 List of cellulose/protein biofibers reported in the literature

Co-solvent	Protein	W_{pro} (wt %)	Spinning method	Application	References
Viscose process	Casein	50	Wet	Fabrics with enhanced properties, such as acid dyeability, permanently crimped, heat-retaining, antimicrobial	Mahomed (1966), Lennox-Kerr (2000), Yamazaki (2001a, b), Chua (2009)
	Soy protein				
	Zein				
	Gelatin	20		Acid dyeable and deodorized fabrics	Yamada and Ohshima (2009)
	Silk fibroin	53		High performance biofiber	Hirano et al. (2002)
	Keratin	20		Acid dyeable, flame retardant	Ikeda and Mukoyama (1997)), Zhou et al. (2015)
Cuprammonium process	Whey protein	56	Wet	Active ingredients release	Tomczyńska-Mleko et al. (2015a)
	Egg albumen	23		Biomedicine	Tomczyńska-Mleko et al. (2015b)
LiCl/DMAc	Silk fibroin	30	Dry-jet wet	High performance biofiber	Marsano et al. (2007)
NMMO/H_2O		75			Marsano et al. (2008)

(continued)

Table 5.3 (continued)

Co-solvent	Protein	W_{pro} (wt %)	Spinning method	Application	References
Aqueous alkali and alkali/urea	Silk fibroin	15	Dry-jet wet	Wound dressing	Strobin et al. (2006)
	Keratin	48	Wet	Biomedical and hygienic	Wrzesniewska-Tosik et al. (2007)
	Rape and sunflower protein	19		Antibacterial	Wawroand Stęplewski (2010)
	Soy protein	10		Biomedicine	Zhang et al. (2011)
Ionic liquid	Silk fibroin	40	Dry-jet wet	High performance biofiber	Yao et al. (2015)
Cellulose derivatives	Egg albumen	34	Electro-spinning	Drug release	Wongsasulak et al. (2010)
	Gelatin	30			Kiatyongchai et al. (2014)
	Collagen	67	Wet	Biomedicine	Amsaveni et al. (2013)

Note W_{pro} is the maximum protein content in the blend solution formed with cellulose

together to prepare blended polymer solutions. In particular, proteins showed similar dissolution mechanism to cellulose in direct solvents.

Producing strong regenerated protein fibers has been a challenge. Therefore, blending proteins with cellulose is found to overcome this issue. The blend fibers with a relatively low protein content possessed comparable tensile strength to the cellulose fibers. However, higher protein content decreased their strength due to the viscosity drop in their blend solutions. In general, the blend fibers showed intermolecular interactions and two-phase morphology. Furthermore, blending cellulose with proteins added some functionalities, such as acid dyeability, flame retardancy, antibacterial activity, shorter biodegradation, and edibility.

References

Abe K, Murate H, Teramoto A, Nagasse Y (2002) Method for producing keratin-cellulose complex regenerated product and method for recycling keratin- containing fiber product. JP Patent 2002167401

Akira H, Eisaku I, Rensuke K, Kenji K (2001) Molecularly composite polymeric material of fibroin/cellulose and process for producing the same. WO Patent 2001036531, 25 May 2001

Aminuddin N (1998) Ammonia/ammonium thiocyanate - cellulose system: dissolution, viscoelastic behavior and fiber formation. Dissertation, North Carolina State University, Raleigh NC

Amsaveni M, Anumary A, Ashokkumar M, Chandrasekaran B, Thanikaivelan P (2013) Green synthesis and characterization of hybrid collagen–cellulose–albumin biofibers from skin waste. Appl Biochem Biotechnol 171(6):1500–1512

Attwater R, Heinemann A (1926) Improved Artificial Textile Fibre and the Process of the Manufacturing of same. GB Patent 255,623, 29 Jul 1926
Belgacem MN, Gandini A (2011) Production, chemistry and properties of cellulose-based materials. In: Plackett D (ed) Biopolymers-new materials for sustainable films and coatings. Wiley, West Sussex, UK, pp 151–178
Bettelheim FA, Brown WH, Campbell MK, Farrell SO, Torres OJ (2012) Introduction to general organic and biochemistry, 10th edn. Brooks/Cole Cengage Learning, Belmont, CA
Biswas A, Shogren RL, Stevenson DG, Willett JL, Bhowmik PK (2006) Ionic liquids as solvents for biopolymers: Acylation of starch and zein protein. Carbohyd Polym 66(4):546–550
Börner K, Rossner E, Mahn H, Irion W (1934) Copper-ammonia-fibroin solutions. US Patent 1,955,221,
Brauer S, Kosan B, Meister F, Bauer RU (2009) Method for producing molded bodies from proteins. US Patent 20090051068, 26 Feb 2009
Browning BL, Sell LO, Abel W (1954) Cellulose solvents for viscosity measurement - The effect of copper and base concentrations in cuprammonium and cupriethylenediamine solutions. TAPPI 37(7):273–283
Buerger H, Taeger E, Eilers M, Berghof K (2004) Protein shaped body and method for the production thereof according to the NMMO method. US Patent 20040046277, 11 Mar 2004
Butler MM, McGrath KP (1998) Protein-based materials. In: Kaplan DL (ed) Biopolymers from renewable resources. Springer, New York, pp 177–194
Cai J, Zhang L (2005) Rapid dissolution of cellulose in LiOH/urea and NaOH/urea aqueous solutions. Macromol Biosci 5(6):539–548
Cai J, Zhang L (2006) Unique gelation behavior of cellulose in NaOH/urea aqueous solution. Biomacromol 7(1):183–189
Cai J, Zhang L, Zhou J, Li H, Chen H, Jin H (2004) Novel fibers prepared from cellulose in NaOH/urea aqueous solution. Macromol Rapid Commun 25(17):1558–1562
Cai J, Zhang L, Liu S, Liu Y, Xu X, Chen X, Chu B, Guo X, Xu J, Cheng H (2008) Dynamic self-assembly induced rapid dissolution of cellulose at low temperatures. Macromolecules 41(23):9345–9351
Chavassieu HLJ (1910) Process of obtaining proteo-cellulosic products. US Patent 950,435, 22 Feb 1910
Choi H-M, Kwon I (2010) Dissolution of zein using protic ionic liquids: N-(2-hydroxyethyl) ammonium formate and N-(2-hydroxyethyl) ammonium acetate. Ind Eng Chem Res 50 (4):2452–2454
Chua JM (2009) Uniqlo's HeatTech Clothing Created Heat From Your Sweat. http://www.ecouterre.com/uniqlos-heattech-clothing-creates-heat-from-yoursweat/. Accessed 17 Jan 2016
Ciolacu D, Popa VI (2010) Cellulose allomorphs: Structure, accessibility and reactivity. Polymer science and technology. Nova Science Publishers, New York
D'Ambrosio A, Corbellini A (1939) Improvements in or relating to the manufacture of artificial spinnable material from mixed solutions of protein and viscose. GB Patent 511,700, 23 Aug 1939
Daiwabo Rayon Co. Ltd. (2016) MILEY "Milk-protein containing viscose rayon". http://www.daiwabo.co.jp/en/products.html?crid=4. Accessed 17 Jan 2016
Dawsey TR, McCormick CL (1990) The lithium chloride/dimethylacetamide solvent for cellulose: a literature review. J Macromol Sci, Rev Macromol Chem Phys 30(3–4):405–440
Dupont A-L (2003) Cellulose in lithium chloride/N, N-dimethylacetamide, optimisation of a dissolution method using paper substrates and stability of the solutions. Polymer 44(15):4117–4126
Egal M, Budtova T, Navard P (2008) The dissolution of microcrystalline cellulose in sodium hydroxide-urea aqueous solutions. Cellulose 15(3):361–370
Esselmann P, Kosslinger K, Bitterfeld WK (1936) Manufacture of artificial silk. US Patent 2,059,632, 3 Nov 1936
Feng L, Z-l Chen (2008) Research progress on dissolution and functional modification of cellulose in ionic liquids. J Mol Liq 142(1):1–5
Fink HP, Weigel P, Purz HJ, Ganster J (2001) Structure formation of regenerated cellulose materials from NMMO-solutions. Prog Polym Sci 26(9):1473–1524

Firgo H, Seidl S, Bartsch P, Koll B, Mulleder E (1998) Cellulose fibre. US Patent 5,795,522, 18 Aug 1998
Franks NE, Varga JK (1979) Process for making precipitated cellulose. US Patent 4,145,532, 20 Mar 1979
Freddi G, Pessina G, Tsukada M (1999) Swelling and dissolution of silk fibroin (bombyx mori) in *N*-methyl morpholine N-oxide. Int J Biol Macromol 24(2):251–263
French AD, Bertoniere NR, Brown RM, Chanzy H, Gray D, Hattori K, Glasser W (2002) Cellulose. In: Mark HF, Kroschwitz JI (eds) Encyclopedia of polymer science and technology, vol 5. 3rd edn. Wiley, Hoboken, NJ, p 473. doi:10.1002/0471440264.pst042
Fujita K, MacFarlane DR, Forsyth M (2005) Protein solubilising and stabilising ionic liquids. Chem Commun 38:4804–4806
Fukaya Y, Sugimoto A, Ohno H (2006) Superior solubility of polysaccharides in low viscosity, polar, and halogen-free 1, 3-dialkylimidazolium formates. Biomacromolecules 7(12):3295–3297
Fukaya Y, Hayashi K, Wada M, Ohno H (2008) Cellulose dissolution with polar ionic liquids under mild conditions: required factors for anions. Green Chem 10(1):44–46
Furuhata K, Okada A, Chen Y, Xu YY, Sakamoto M (1994) Dissolution of silk fibroin in lithium halide/organic amide solvent systems. J Seric Sci Jpn 63(4):315–322
Gilbert RD, Kadla JF (1998) Polysaccharides - Cellulose. In: Kaplan DL (ed) Biopolymers from renewable resources. Springer, New York, pp 47–95
Gord H, Hammer KD, Neeff R, Berghof K, Eilers M, Taeger E, Buerger H (2004) Chewable film containing cellulose. US Patent 20040166209, 26 Aug 2004
Gord H, Hammer KD, Melle J (2006) Collagen-based shaped body. WO Patent 2006131285, 14 Dec 2006
Goujon N, Wang X, Rajkowa R, Byrne N (2012) Regenerated silk fibroin using protic ionic liquids solvents: towards an all-ionic-liquid process for producing silk with tunable properties. Chem Commun 48(9):1278–1280
Goujon N, Rajkhowa R, Wang X, Byrne N (2013) Effect of solvent on ionic liquid dissolved regenerated Antheraea assamensis silk fibroin. J Appl Polym Sci 128(6):4411–4416
Graenacher C (1934) Cellulose solution. US Patent 1,943,176,
Guilbert S, Cuq B (2005) Material formed from proteins. In: Bastioli C (ed) Handbook of biodegradable polymers. Rapra Technology Limited, Shropshire, UK, p 339
Happey F, Wormell RL (1949) Regenerated keratin fibres from wool. J Text Inst Trans 40(12): T855–T869
Heinemann K, Taeger E (2000) Production of solutions of fibrillar proteins, especially silk, comprises dissolving the protein in *N*-methylmorpholine N-oxide. DE Patent 19,841,649, 27 Apr 2000
Heinze T, Schwikal K, Barthel S (2005) Ionic liquids as reaction medium in cellulose functionalization. Macromol Biosci 5(6):520–525
Hirano S, Nakahira T, Zhang M, Nakagawa M, Yoshikawa M, Midorikawa T (2002) Wet-spun blend biofibers of cellulose–silk fibroin and cellulose–chitin–silk fibroin. Carbohyd Polym 47 (2):121–124
Holbrey J, Swatloski R, Chen J, Daly D, Rogers R (2005) Polymer dissolution and blend formation in ionic liquids. US Patent 20050288484, 29 Dec 2005
Hon DNS (1994) Cellulose: a random walk along its historical path. Cellulose 1(1):1–25
Howitt FO (1955) Silk fibroin as a fibrous protein. Text Res J 25:242–246
Hu Y, Liu L, Dan W, Dan N, Gu Z (2013) Evaluation of 1-ethyl-3-methylimidazolium acetate based ionic liquid systems as a suitable solvent for collagen. J Appl Polym Sci 130(4):2245–2256
Hudson SM, Cuculo JA (1980) The solubility of unmodified cellulose: a critique of the literature. J Macromol Sci, Rev Macromol Chem Phys C18(1):1–82
Idris A, Vijayaraghavan R, Rana UA, Fredericks D, Patti AF, MacFarlane DR (2013) Dissolution of feather keratin in ionic liquids. Green Chem 15(2):525–534
Idris A, Vijayaraghavan R, Rana UA, Patti AF, MacFarlane DR (2014) Dissolution and regeneration of wool keratin in ionic liquids. Green Chem 16(5):2857–2864

Ikeda M, Mukoyama H (1997) Regenerated cellulosic fiber excellent in dyeability and its production. JP Patent 09-241920

Isogai A (1994) Allomorphs of cellulose and other polysaccharides. In: Gilbert RD (ed) Cellulosic polymers, blends and composites. Hanser, Munich, Germany, pp 1–24

Isogai A, Usuda M, Kato T, Uryu T, Atalla RH (1989) Solid-state CP/MAS carbon-13 NMR study of cellulose polymorphs. Macromolecules 22(7):3168–3172

Itaya M (1969) Study on the viscose fiber grafted with milk casein. Sen'i Gakkaishi 26(6):286–296

Jane J, Lim S, Paetau I, Spence K, Wang S Biodegradable plastics made from agricultural biopolymers. In: Fishman M, Friedman R, Huang S (eds) Symposium on Polymers from Agricultural Coproducts, at the 206th National Meeting of the American-Chemical-Society, Chicago, IL, 1994. ACS Symposium Series. American Chemical Society, pp 92–100

Jayme G, Broschinski L (1976) Copper and nickel complex solutions as dissolving media for proteins and cellulose. Cell Chem Technol 10(6):655–672

Jin H, Zha C, Gu L (2007) Direct dissolution of cellulose in NaOH/thiourea/urea aqueous solution. Carbohyd Res 342(6):851–858

Johnson DL (1969) Compounds dissolved in cyclic amine oxides. US Patent 3,447,939, 3 Jun 1969

Johnson DL (1970) Method of preparing polymers from a mixture of cyclic amine oxides and polymers. US Patent 3,508,941, 28 Apr 1970

Kamida K, Okajima K, Matsui T, Kowsaka K (1984) Study on the solubility of cellulose in aqueous alkali solution by deuteration IR and 13C NMR. Polym J 16(12):857–866

Kanegafuchi Spinning CL (1966) Method for producing composite protein-cellulose fibres. GB Patent 1,025,798, 14 Apr 1966

Kelly RJ, Ali MA, Roddick-Lanzilotta AD, Worth G, Hassan MM, McLaughlin JR, McKinnon AJ (2008) Composite materials containing keratin. US Patent 7,767,756, 3 Jan 2008

K-i Furuhata, Koganei K, Chang H-S, Aoki N, Sakamoto M (1992) Dissolution of cellulose in lithium bromide-organic solvent systems and homogeneous bromination of cellulose with N-bromosuccinimide-triphenylphosphine in lithium bromide-N N-dimethylacetamide. Carbohyd Res 230(1):165–177

Kiatyongchai T, Wongsasulak S, Yoovidhya T (2014) Coaxial Electrospinning and Release Characteristics of Cellulose Acetate-Gelatin Blend Encapsulating a Model Drug. J Appl Polym Sci 131 (8)

Klemm D, Heublein B, Fink HP, Bohn A (2005) Cellulose: fascinating biopolymer and sustainable raw material. Angew Chem Int Ed Engl 44(22):3358–3393

Koch T (1944) Manufacture of rayon. US Patent 2,345,345, 28 Mar 1944

Kotek R (2002) Regenerated cellulose fibers. In: Lewin M (ed) Handbook of fibre chemistry, vol 16. 3rd edn. CRC Press, Boca Raton, FL, pp 667–771

Kruszewska I (1997) Clean production action report of greenpeace international toxic campaign. Greenpeace, Amsterdam, The Netherlands

Lennox-Kerr P (2000) Milk protein improves rayon. Advances in Textiles Technology, vol October. International Newsletters Ltd, UK

Li W, Ke G, Li G, Xu W (2015) Study on the structure and properties of viscose/wool powder blended fibre. Fibres Text East Eur 23 (1 (109)):26–29

Libert TF (2010) Cellulose solvents-remarkable history, bright future. In: Libert TF, Heinze TJ, Edgar KJ (eds) 235th American-Chemical-Society National Meeting, New Orleans, LA. ACS Symposium Series. American Chemical Society, pp 3–54

Mahomed RS (1966) Improvements in and relating to viscose rayon filaments. GB Patent 1,029,838, 18 May 1966

Mantz RA, Fox DM, Green JM, Fylstra PA, De Long HC, Trulove PC (2007) Dissolution of biopolymers using ionic liquids. Z Naturforsc A 62(5–6):275–280

Mao Y, Zhou J, Cai J, Zhang L (2006) Effects of coagulants on porous structure of membranes prepared from cellulose in NaOH/urea aqueous solution. J Membr Sci 279(1):246–255

Marsano E, Corsini P, Arosio C, Boschi A, Mormino M, Freddi G (2005) Wet spinning of bombyx mori silk fibroin dissolved in *N*-methyl morpholine N-oxide and properties of regenerated fibres. Int J Biol Macromol 37(4):179–188

Marsano E, Canetti M, Conio G, Corsini P, Freddi G (2007) Fibers based on cellulose–silk fibroin blend. J Appl Polym Sci 104(4):2187–2196

Marsano E, Corsini P, Canetti M, Freddi G (2008) Regenerated cellulose-silk fibroin blends fibers. Int J Biol Macromol 43(2):106–114

McCormick CL, Callais PA, Hutchinson BH Jr (1985) Solution studies of cellulose in lithium chloride and N. N-dimethylacetamide. Macromolecules 18(12):2394–2401

McMurry J (2007) Organic Chemistry, 7th edn. Cengage Learning, Belmont, CA

Meng Z, Zheng X, Tang K, Liu J, Ma Z, Zhao Q (2012) Dissolution and regeneration of collagen fibers using ionic liquid. Int J Biol Macromol 51(4):440–448

Narayanan G (2014) Electrospinning of poly (epsilon-caprolactone) fibers functionalized with cyclodextrins and their inclusion complexes. North Carolina State University, Raleigh, NC, USA

Narayanan G, Gupta BS, Tonelli AE (2014) Poly(ε-caprolactone) Nanowebs Functionalized with α- and γ-Cyclodextrins. Biomacromolecules 15(11):4122–4133

Narayanan G, Gupta BS, Tonelli AE (2015a) Enhanced mechanical properties of poly (ε-caprolactone) nanofibers produced by the addition of non-stoichiometric inclusion complexes of poly (ε-caprolactone) and α-cyclodextrin. Polymer 76:321–330

Narayanan G, Gupta BS, Tonelli AE (2015b) Estimation of the poly (ε-caprolactone) [PCL] and α-cyclodextrin [α-CD] stoichiometric ratios in their inclusion complexes [ICs], and evaluation of porosity and fiber alignment in PCL nanofibers containing these ICs. Data in Brief 5:1048–1055

Narayanan G, Ormond BR, Gupta BS, Tonelli AE (2015c) Efficient wound odor removal by β-cyclodextrin functionalized poly (ε-caprolactone) nanofibers. Journal of Applied Polymer Science 132 (45), DOI:10.1002/app.42782

Narayanan G, Aguda R, Hartman M, Chung C-C, Boy R, Gupta BS, Tonelli AE (2016a) Fabrication and characterization of poly(ε-caprolactone)/α-cyclodextrin pseudorotaxane nanofibers. Biomacromolecules 17(1):271–279

Narayanan G, Vernekar VN, Kuyinu EL, Laurencin CT (2016b) Poly (lactic acid)-based biomaterials for orthopaedic regenerative engineering. Adv Drug Deliv Rev. doi:10.1016/j.addr.2016.04.015

Narayanan G, Chung CC, Aguda RM, Boy R, Hartman M, Mehraban N, Gupta BS, Tonelli AE (2016c) Correlation of the stoichiometries of poly (ε-caprolactone) and α-cyclodextrin pseudorotaxanes with their solution rheology and the molecular orientation, crystallite size, and thermomechanical properties of their nanofibers. RSC Adv

Nevell TP, Zeronian SH (1985) Cellulose chemistry fundamentals. In: Nevell TP, Zeronian SH (eds) Cellulose chemistry and its applications. Halsted Press, New York, pp 15–29

Nicoll WD (1950) Process for producing artificial filaments. US Patent 2,515,889, 18 Jul 1950

Olsson C, Wesman G (2013) Direct dissolution of cellulose: background, means and applications. Cellulose - Fundamental aspects, InTech, Online

Phillips DM, Drummy LF, Conrady DG, Fox DM, Naik RR, Stone MO, Trulove PC, De Long HC, Mantz RA (2004) Dissolution and regeneration of bombyx mori silk fibroin using ionic liquids. J Am Chem Soc 126(44):14350–14351

Pinkert A, Marsh KN, Pang S, Staiger MP (2009) Ionic liquids and their interaction with cellulose. Chem Rev 109(12):6712–6728

Qi H, Chang C, Zhang L (2008) Effects of temperature and molecular weight on dissolution of cellulose in NaOH/urea aqueous solution. Cellulose 15(6):779–787

Qi H, Yang Q, Zhang L, Liebert T, Heinze T (2011) The dissolution of cellulose in NaOH-based aqueous system by two-step process. Cellulose 18(2):237–245

Rowland SP, Bertoniere NR (1985) Chemical methods of studying supramolecular structure. In: Nevell TP, Zeronian SH (eds) Cellulose chemistry and its applications. Ellis Horwood Limited, West Sussex, England, pp 112–137

Saechtling H (1995) Saechtling international plastics handbook: For the technologist, engineer, and user, 3rd edn. Hanser, Munich, Germany

Saleh MS (2014) Fibrous protein processing method. US Patent 20140326165, 6 Nov 2014
Sangwatanaroj U (1995) The mechanism of dissolution of cellulose in the ammonia/ammonium thiocyanate solvent. Dissertation/Thesis, North Carolina State University, Raleigh NC
Sashina ES, Novoselov NP, Heinemann K (2003) Dissolution of silk fibroin in *N*-methylmorpholine-N-oxide and its mixtures with organic solvents. Russ J Appl Chem 76(1):128–131
Sashina ES, Bochek AM, Novoselov NP, Kirichenko DA (2006) Structure and solubility of natural silk fibroin. Russ J Appl Chem 79(6):869–876
Sashina ES, Janowska G, Zaborski M, Vnuchkin AV (2007) Compatibility of fibroin/chitosan and fibroin/cellulose blends studied by thermal analysis. J Therm Anal Calorim 89(3):887–891
Schuster KC, Rous MA, Hainbucher KM, Richardt D, Redlinger S, Firgo H, Kroner G (2012) Functionalized molded cellulose body and method for producing the same. US Patent 20120318169, 20 Dec 2012
Schweizer E (1857) Das kupferoxyd-ammoniak, ein auflösungsmittel für die pflanzenfaser. J Prakt Chem 72(1):109–111
Sionkowska A, Lewandowska K, Planecka A, Szarszewska P, Krasinska K, Kaczmarek B, Kozlowska J (2014) Biopolymer blends as potential biomaterials and cosmetic materials. Key Eng Mater 583:95–100
Stall AD, Turbak AF (1999) Slowing and controlling the rapid precipitation of cellulose from tertiary amine oxide solutions by adding a water soluble polymer having a high molecular weight. US Patent 5,951,933, 14 Sep 1999
Stevens MP (1999) Polymer chemistry: An introduction, 3rd edn. Oxford University Press, New York
Striegel AM (2003) Advances in the understanding of the dissolution mechanism of cellulose in DMAc/LiCl. J Chil Chem Soc 48(1):73–77
Strobin G, Wawro D, Stęplewski W, Ciechańska D, Jóźwicka J, Sobczak S, Haga A (2006) Formation of cellulose/silk-fibroin blended fibres. Fibres Text East Eur 14 (4 (58)):32–35
Swatloski RP, Spear SK, Holbrey JD, Rogers RD (2002) Dissolution of cellulose with ionic liquids. J Am Chem Soc 124(18):4974–4975
Tomczyńska-Mleko M, Terpiłowski K, Mleko S (2015a) New product development: Cellulose/egg white protein blend fibers. Carbohyd Poly 126:168–174
Tomczyńska-Mleko M, Terpiłowski K, Mleko S (2015b) Physicochemical properties of cellulose/whey protein fibers as a potential material for active ingredients release. Food Hydrocolloids 49:232–239
Tomlinson SR, Kehr CW, Lopez MS, Schlup JR, Anthony JL (2014) Solubility of the corn protein zein in imidazolium-based ionic liquids. Ind Eng Chem Res 53(6):2293–2298
Tosh B, Saikia CN, Dass NN (2000) Homogeneous esterification of cellulose in the lithium chloride–N, N-dimethylacetamide solvent system: effect of temperature and catalyst. Carbohyd Res 327(3):345–352
Turbak AF, Hammer RB, Davies RE, Portnoy NA (1977) A critical review of cellulose solvent systems. In: Turbak AF (ed) Solvent spun rayon, modified cellulose fibers and derivatives, vol 58. ACS Symposium Series. American Chemical Society, Washington, D.C., pp 12–24
Vaz CM, Cunha AM (2007) Soy-based materials for drug release applications. In: Fakirov S, Bhattacharyya D (eds) Handbook of engineering biopolymers: homopolymers, blends and composites. Hanser, Munich, Germany, p 465
Vincent JFV, Shewry PR, Tatham AS, Bailey AJ (2003) Mechanical applications of elastomeric proteins -A biomimetic approach. In: Shewry PR, Tatham AS, Bailey AJ (eds) Elastomeric proteins: structures, biomechanical properties, and biological roles. Cambridge University Press, New York, pp 352–365
Wakeham H, Toner RK, Jolley HR, Taylor HS (1951) The technical possibilities for a regenerated silk. Text Res J 21(2):110–115
Wang Y, Zhang L, Yu L (2009) Blends and composites based on cellulose and natural polymers. In: Yu L (ed) Biodegradable polymer blends and composites from renewable resources. Wiley, Hoboken, NJ, pp 129–161

Wang Q, Yang Y, Chen X, Shao Z (2012) Investigation of rheological properties and conformation of silk fibroin in the solution of AMImCl. Biomacromolecules 13(6):1875–1881
Wang H, Gurau G, Rogers RD (2014) Dissolution of biomass using ionic liquids. In: Zhang S, Wang J, Lu X, Zhou Q (eds) Structures and interactions of ionic liquids. Springer, Berlin, pp 79–105
Wawro D, Stęplewski W (2010) Producing of continuous cellulose fibres modified with plant proteins. Fibres Text East Eur 18(6):83
Weigel P, Fink HP, Doss M, Beckers S, Hendrikx R (2003) Tubular films formed from cellulose/protein blends. US Patent 20030062648, 3 Apr 2003
Wertz J-L, Bédué O, Mercier JP (2010) Cellulose science and technology. EPFL Press, Lausanne, Switzerland
Wilkes AG, Woodings C (2001) The viscose process. Regenerated cellulose fibres. Woodhead Publishing Limited, Cambridge, England, pp 37–61
Winkworth-Smith C, Foster TJ (2013) General overview of biopolymers: structure, properties, and applications. In: Thomas S, Durand D, Chassenieux C, Jyotishkumar P (eds) Handbook of biopolymer-based materials: from blends and composites to gels and complex networks. Wiley-VCH, Weinheim, Germany, pp 7–36
Wongsasulak S, Patapeejumruswong M, Weiss J, Supaphol P, Yoovidhya T (2010) Electrospinning of food-grade nanofibers from cellulose acetate and egg albumen blends. J Food Eng 98(3):370–376
Woodings C (2002) Cellulose fibers, regenerated. In: Mark HF, Kroschwitz JI (eds) Encyclopedia of polymer science and technology, vol 5. 3rd edn. Wiley, Hoboken. NJ, p 532
Wormell RL, Happey F (1949) Regenerated keratin fibres. Nature 163(4131):18
Wrzesniewska-Tosik K, Wawro D, Ratajska M, Steplewski W (2007) Novel biocomposites with feather keratin. Fibres Text East Eur 15(5–6):157–162
Wu R-L, Wang X-L, Wang Y-Z, Bian X-C, Li F (2009) Cellulose/soy protein isolate blend films prepared via room-temperature ionic liquid. Ind Eng Chem Res 48(15):7132–7136
Xie H, Li S, Zhang S (2005) Ionic liquids as novel solvents for the dissolution and blending of wool keratin fibers. Green Chem 7(8):606–608
Xu Y, Zhang Y, Shao H, Hu X (2005) Solubility and rheological behavior of silk fibroin (bombyx mori) in *N*-methyl morpholine N-oxide. Int J Biol Macromol 35(3):155–161
Yamada M, Ohshima K (2009) Method of manufacturing cellulose-gelatin composite viscose rayon filament. US Patent 20090166919, 2 Jul 2009
Yamada M, Ohshima K, Arimochi M, Nakajima K (2004) Spinning dope for cellulose/protein compound fiber and cellulose/protein compound fiber. JP Patent 2004-149953, 24 May 2004
Yamazaki F (2001a) Antibacterial viscose rayon and its production. JP Patent 2001-003223, 09 Jan 2001
Yamazaki F (2001b) Viscose rayon having modified feeling. JP Patent 2001-003224, 09 Jan 2001
Yang Q, Fukuzumi H, Saito T, Isogai A, Zhang L (2011) Transparent cellulose films with high gas barrier properties fabricated from aqueous alkali/urea solutions. Biomacromolecules 12 (7):2766–2771
Yao Y, Zhang E, Xia X, Yu J, Wu K, Zhang Y, Wang H (2015) Morphology and properties of cellulose/silk fibroin blend fiber prepared with 1-butyl-3-methylimidazolium chloride as solvent. Cellulose 22(1):625–635
Zhang L, Ruan D, Zhou J (2001) Structure and properties of regenerated cellulose films prepared from cotton linters in NaOH/urea aqueous solution. Ind Eng Chem Res 40(25):5923–5928
Zhang L, Ruan D, Gao S (2002) Dissolution and regeneration of cellulose in NaOH/thiourea aqueous solution. J Polym Sci B Polym Phys 40(14):1521–1529
Zhang H, Wu J, Zhang J, He J (2005) 1-Allyl-3-methylimidazolium chloride room temperature ionic liquid: a new and powerful nonderivatizing solvent for cellulose. Macromolecules 38 (20):8272–8277

Zhang SA, Li FX, Yu JY (2011) Novel Cellulose/SPI blend bio-fibers prepared via direct dissolving approach. J Eng Fibers Fabr 6(1):31–37

Zhang L, Qiao C, Ding Y, Cheng J, Li T (2012) Rheological behavior of gelatin/1-allyl-3-methylimidazolium chloride solutions. J Macromol Sci B 51(4):747–755

Zhou Z, Zheng H, Wei M, Huang J, Chen Y (2008) Structure and mechanical properties of cellulose derivatives/soy protein isolate blends. J Appl Polym Sci 107(5):3267–3274

Zhou Z, Weiren B, Youbo D, Jinming D (2015) Preparation and characterization of cyclotriphosphazenekeratin/viscose fibers. Fiber Polym 16(3):560–564