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Chitin and chitosan polymers: Chemistry, solubility and fiber formation

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ABSTRACT

Chitin and chitosan (CS) are biopolymers having immense structural possibilities for chemical and mechanical modifications to generate novel properties, functions and applications especially in biomedical area. Despite its huge availability, the utilization of chitin has been restricted by its intractability and insolubility. The fact that chitin is as an effective material for sutures essentially because of its biocompatibility, biodegradability and non-toxicity together with its antimicrobial activity and low immunogenicity, points to immense potential for future development. This review discusses the various attempts reported on solving this problem from the point of view of the chemistry and the structure of these polymers highlighting the drawbacks and advantages of each method and proposes that based on considerations of structure–property relations, it is possible to obtain chitin fibers with improved strength by making use of their nanostructures and/or mesophase properties of chitin.

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1. Introduction

Chitin and chitosan (CS) polymers are natural aminopolysaccharides having unique structures, multidimensional properties, highly sophisticated functions and wide ranging applications in biomedical and other industrial areas [1–3]. Being considered to be materials of great futuristic potential with immense possibilities for structural modifications to impart desired properties and functions, research and development work on chitin and CS have reached a status of intense activities in many parts of the world [4–6]. The positive attributes of excellent biocompatibility and admirable biodegradability with ecological safety and low toxicity with versatile biological activities such as antimicrobial activity and low immunogenicity have provided ample opportunities for further development [7–12]. It has become of great interest not only as an under-utilized resource but also as a new functional biomaterial of high potential in various fields [13–15].

With data emerging from not less than 20 books, over 300 reviews, over 12,000 publications and innumerable patents, the science and technology of these biopolymers are at a turning point where one needs a very critical look on its potential to deliver the goods [16,17]. Prior to doing so, it is necessary to overview the data emerged on one of the serious problems faced in the utilization of chitin and CS. Despite its huge annual production and easy availability, chitin still remains an under utilized resource primarily because of its intractable molecular structure [10,16]. The non-solubility of chitin in almost all common solvents has been a stumbling block in its appropriate utilization [4,5,6,13]. This review proposes to consolidate and discuss the available data on the work on the chemistry related to the solubilization of chitin and CS and the attempts at fiber formation.

There have been a number of earlier attempts at reviewing the area on chitin and CS fibers covering certain aspects of their importance, properties and applications [18–25]. Rathke and Hudson [18] pointed out that chitin's microfibrillar structure indicated its potential as fiber- and film-former, but as chitin was found to be insoluble in common organic solvents, the N-deacetylated derivative of chitin, CS, was developed. After Rinaudo and coworkers [24] who described the production of chitin and CS fibers by wet spinning method in 2001 and Rajendran and Anand [25] who discussed briefly the properties of chitin and chitin fibers in 2002, there have been no serious attempts at reviewing the production, properties and applications of chitin and CS fibers. Considering the potential applications of chitin and CS fibers, it appears that a consolidation of the data relating the chemistry, solubility and fiber formation of chitin and CS polymers is required. Chitin fibers stand apart from all the other biodegradable natural fibers in many inherent properties such as biocompatibility, non-toxicity, biodegradability, low immunogenicity, non-toxicity, etc. [5,10,11,18]. These properties in combination with good mechanical properties make them good candidate materials for sutures that form the largest groups of material implants used in human body [5,8,26]. It was reported that the chitin suture was absorbed in about 4 months in rat muscles [26]. Application in 132 patients proved satisfactory in terms of tissue reaction and good healing indicating satisfactory biocompatibility. Toxicity tests, including acute toxicity, pyrogenicity, and mutagenicity were negative in all respects. The persistence of the tensile strength of the chitin was better than Dexon™ or catgut in bile, urine and pancreatic juice but weakening occurred early in the presence of gastric juice [26]. Apart from sutures, chitin and CS fibers have been found to be useful in other medical textiles [27,28], wound dressing [2,29–34] and haemostatic materials [35–39] and several other prosthetic devices such as haemostatic clips, vascular and joint prostheses, mesh and knit abdominal thoracic wall replacements and as antimicrobial agents [39–41].

2. Structures of chitin and chitosan

2.1. General remarks

It is now well established that the difficulty in solubilization of chitin results mainly from the highly extended hydrogen bonded semi-crystalline structure of chitin [6,14,42–44]. Chitin is a structural biopolymer, which has a

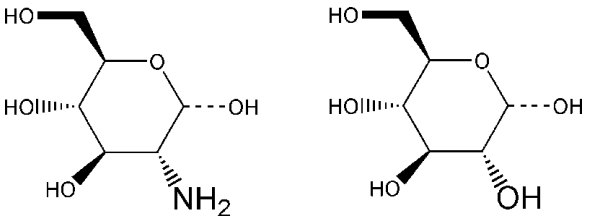

Fig. 1. Structure of glucosamine (monomer of chitosan) and glucose (monomer of cellulose).

role analogous to that of collagen in the higher animals and cellulose in terrestrial plants [43–45]. Plants produce cellulose in their cell walls and insects and crustaceans produce chitin in their shells [42]. Cellulose and chitin are, thus, two important and structurally related polysaccharides that provide structural integrity and protection to plants and animals, respectively [42,46,47]. Chitin occurs in nature as ordered crystalline microfibrils forming structural components in the exoskeleton of arthropods or in the cell walls of fungi and yeast [8,48–49]. In crustaceans, chitin is found to occur as fibrous material embedded in a six stranded protein helix [17]. Chitin may be regarded as cellulose with hydroxyl at position C-2 replaced by an acetamido group [6,46,50]. Both are polymers of monosaccharide made up of β-(1-4)-2-acetamido-2-deoxy-β-D-glucose and β-(1-4)-2-deoxy-β-D-glucopyranose units, respectively (Fig. 1). Thus, chitin is poly (β-(1-4)-N-acetyl-D-glucosamine) [51] (Fig. 2). In fact, as in the case of cellulose, chitin exists in three different polymorphic forms (α, β and γ) [52–55]. Recent studies have reported that the γ form is a variant of α family [56]. The polymorphic forms of chitin differ in the packing and polarities of adjacent chains in successive sheets; in the β-form, all chains are aligned in a parallel manner, which is not the case in α-chitin. The molecular order of chitin depends on the physiological role and tissue characteristics. The grasping spines of *Sagitta* are made of pure α-chitin, because they should be suitably hard to hold a prey, while the centric diatom Thalassiosira contains pure β-chitin. A simple treatment with 20% NaOH followed by washing with water is reported to convert α-chitin to β-chitin [57,58]. In both structures, the chitin chains are organized in sheets where they are tightly held by a number of intra-sheet hydrogen bonds with the α and β chains packed in antiparallel arrangements [8,59–65]. This tight network, dominated by the rather strong C–O–NH hydrogen bonds (Fig. 3), maintains the chains at a distance of about 0.47 nm [60]. Such a feature is not found in the structure of β-chitin, which is therefore more susceptible than α-chitin to intra-crystalline swelling [61,64]. The current model for the crystalline structure of α-chitin indicates that the inter-sheet hydrogen bonds are distributed in two sets with half occupancy in each set [60]. These aspects make evident the insolubility and intractability of chitin [6].

In chitin, the degree of acetylation (DA) is typically 0.90 indicating the presence of some amino groups (as some amount of deacetylation might take place during extraction, chitin may also contain about 5–15% amino groups) [66,67]. So, the degree of N-acetylation, i.e. the ratio of 2-acetamido-2-deoxy-D-glucopyranose to 2-amino-2-deoxy-D-glucopyranose structural units has a striking effect on chitin solubility and solution properties [6,43,67,68]. CS is the N-deacetylated derivative of chitin with a typical DA of less than 0.35. It is, thus, a copolymer composed of glucosamine and N-acetylglucosamine. The physical properties of CS depend on a number of parameters such as the molecular weight (from approximately 10,000 to 1 million Dalton), DD (in the range of 50–95%), sequence of the amino and the acetamido groups and

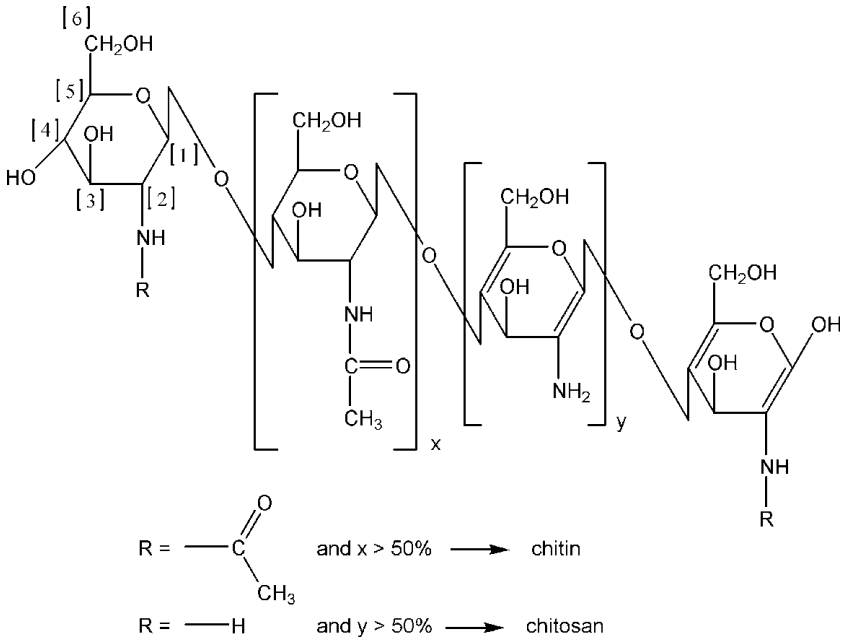

Fig. 2. Structure of chitin and chitosan (reproduced from Ref. [51] by permission of Elsevier Science, Amsterdam).

the purity of the product [8,68–71]. The crustacean shells (crabs, etc.) which are waste products (now byproducts) of food industry are commercially employed for the production of chitin and CS [4]. It is believed that at least 10^{11} tons (10^{13} kg) of chitin are synthesized and degraded, but only over 1,50,000 tons of chitin is made available for commercial use [72].

2.2. Chemical modifications

Chitin and CS are interesting polysaccharides because of the presence of the amino functionality, which could be suitably modified to impart desired properties and distinctive biological functions including solubility [6,43,44,66,73–76]. Apart from the amino groups, they have two hydroxyl functionalities for effecting appropriate chemical modifications to enhance solubility [46]. The possible reaction sites for chitin and CS are illustrated in Fig. 4. As with cellulose [46], chitin and CS can undergo many of the reactions such as etherification [76–78], esterification [76,78,79], cross-linking [71], graft copolymerization [80,81], etc. Muzzarelli [43] and Hon [82] have summarized the possible chemical modification reactions. A number of authors have reviewed the area emphasizing various aspects of chemical modification of CS [3,4,6,7,9–16,76,80–87]. The amino functionality gives rise to chemical reactions such as acetylation, quaternization, reactions with aldehydes and ketones (to give Schiff's base) alkylation, grafting, chelation of metals, etc. to provide a variety of products with properties such as such as antibacterial, anti-fungal, anti-viral, anti-acid, anti-ulcer, non-toxic, non-allergenic, total biocompatibility and biodegradability, etc. The hydroxyl functional groups also give various reactions such as o-acetylation, H-bonding with polar atoms, grafting, etc. Due to the intractability and insolubility of chitin [6,42,43], attention has been given to CS with regard to developing derivatives with well-defined molecular architectures having advanced properties and functions. The trends are to design the macromolecule to meet certain functions such as receptor-mediated gene delivery [88–91], cell penetration enhancer [92], site specific tracking [91,93], etc. to cite a few examples. Specific examples of modifications effected on chitin and CS to enhance solubility will be discussed under Section 4.12.

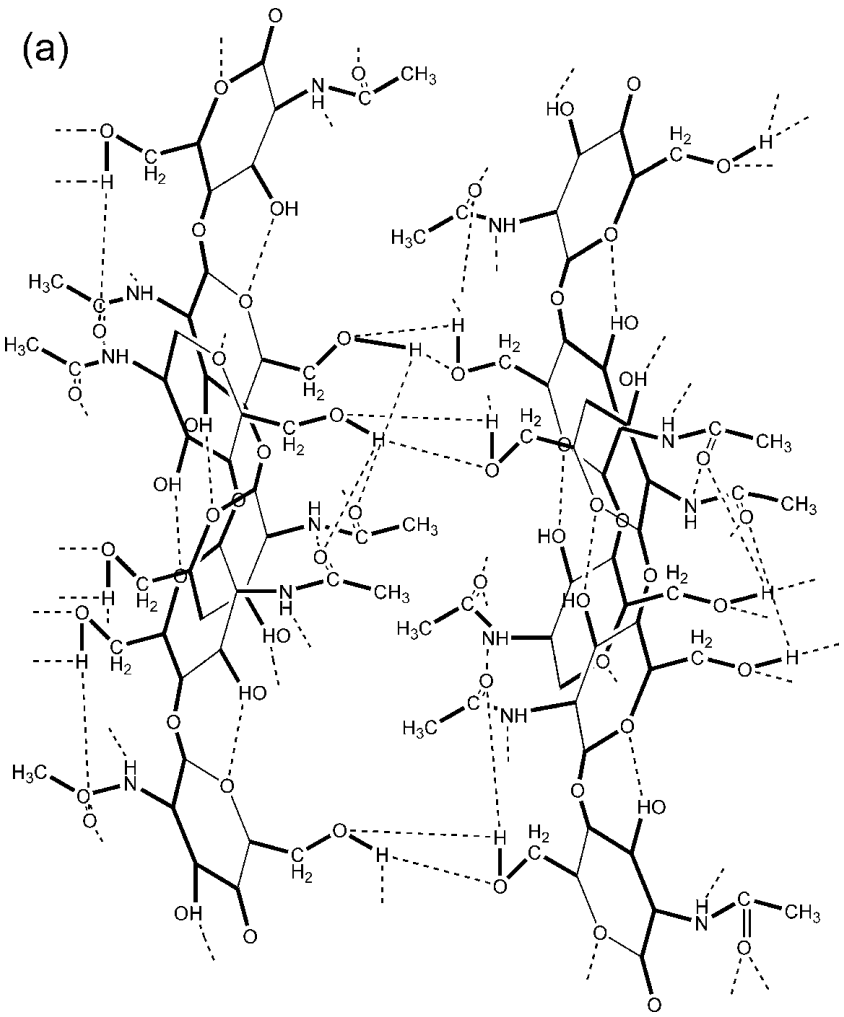

Fig. 3. Molecular structure and hydrogen bonding in (a) α-chitin and (b) β-chitin (reproduced from Ref. [51] by permission of Elsevier Science, Amsterdam).

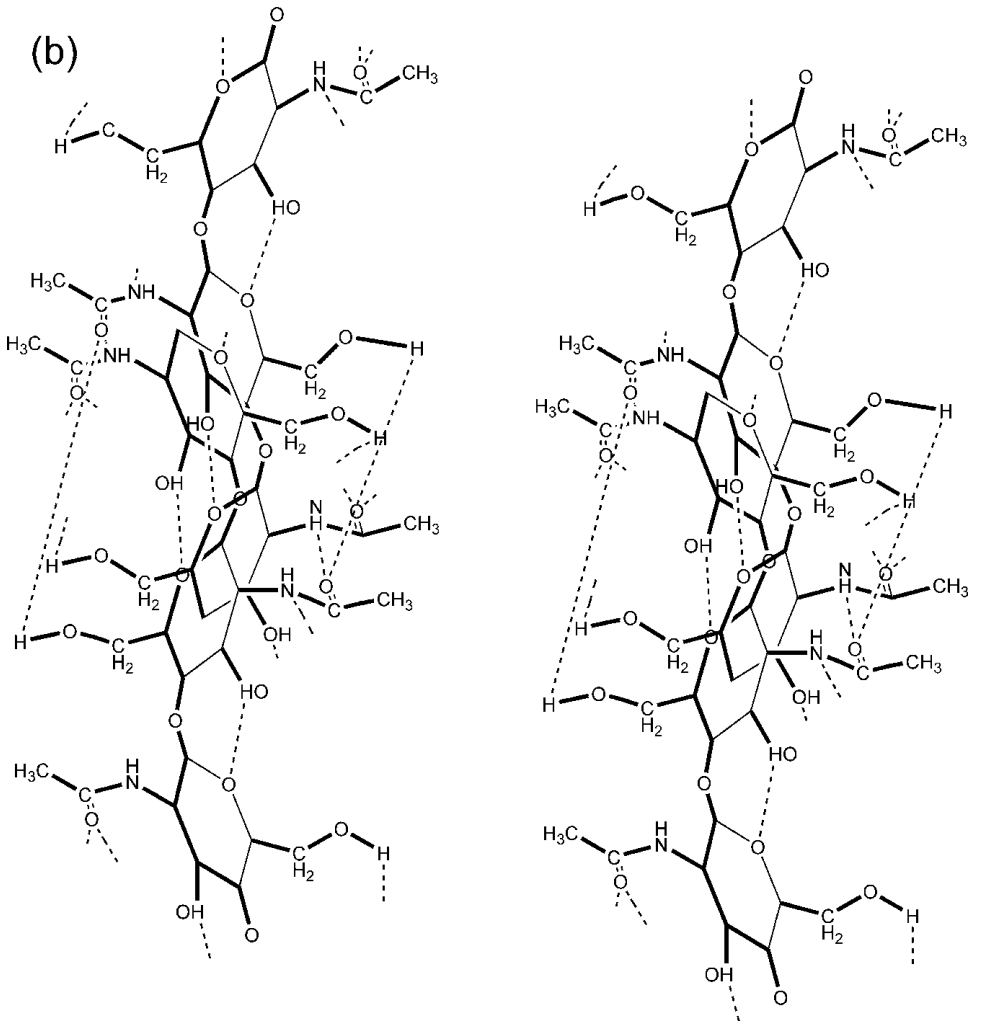

Fig. 3. (*Continued*)

3. Criteria for polymer solubility

Owing to the semi-crystalline structure of chitin with extensive hydrogen bonding, the cohesive energy density and hence the solubility parameter will be very high and so it will be insoluble in all the usual solvents [6,44,50,94–98]. The solubility parameter of chitin and CS was determined by group contribution methods (GCM) and the values were compared with the values determined from maximum intrinsic viscosity, surface tension, the Flory–Huggins interaction parameter and dielectric constant values [94]. The values, thus, obtained were confirmed by values obtained from GCM. The solubility parameters of CS determined by these methods are more or less equal and the average is approximately 41 $J^{1/2}/cm^{3/2}$ [94]. The solubility of chitin can be enhanced by treatment with strong aqueous HCl whereby a solid-state transformation of β-chitin into α-chitin occurs [99]. β-Chitin is reported to be more reactive than the α-form, an important property in regard to enzymatic and chemical transformations of chitin [6,100–102].

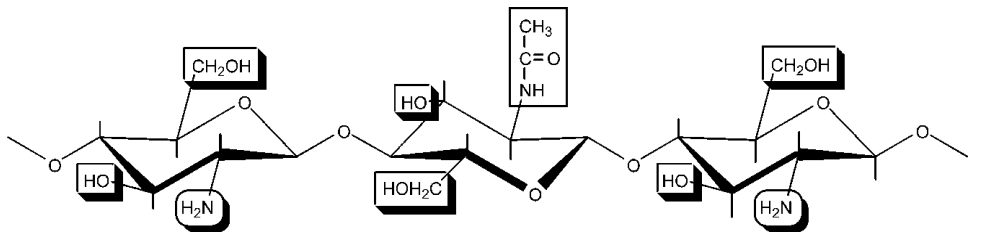

Fig. 4. Illustration of the possible reaction sites in chitin and chitosan.

Aiba demonstrated that the distribution of acetyl groups influenced the solution properties and showed that the distribution of acetyl groups must be random to achieve the higher water solubility around 50% acetylation [103].

The structural similarity of chitin to cellulose has induced many authors to try the solvents used for cellulose [104–106]. As in the case of cellulose, the existence of both intra- and intermolecular hydrogen bonds for chitin in the solid state strongly resists dissolution [107–109]. But, many of these solvents are toxic, corrosive or degradative or mutagenic and hence cannot be used in medicinal application and also have difficulties in scaling up for industrial production. For each solvent system, a number of parameters such as polymer concentration, pH, counter ion concentration, temperature effects, DA, molecular weights, etc. are known to influence the dissolution process and solution viscosity. The dissolution may involve several days of penetration, swelling prior to going into solution. In many cases, the solvents are strong acids, fluoroalcohols, chloroalcohols and certain hydrotropic salt solutions, which degrade the chitin or are inconvenient to use [8,18,110–112].

The first systematic study on the solubility of chitin and CS was carried out by Austin who introduced the solubility parameters for chitin in various solvents [113,114]. The choice of solvent in a particular situation involves many more factors such as presence of solubilizing chemical entities, solution viscosity, etc. [115,116].

4. Chitin and chitosan solubility

4.1. General remarks

The general properties of chitin and CS are provided in Table 1.

While chitin is insoluble in most organic solvents, CS is readily soluble in dilute acidic solutions below pH 6.0. This is because CS can be considered a strong base as it possesses primary amino groups with a pKa value of 6.3. The presence of the amino groups indicates that pH substantially alters the charged state and properties of CS [12]. At low pH, these amines get protonated and become positively charged and that makes CS a water-soluble cationic polyelectrolyte. On the other hand, as the pH increases above 6, CS's amines become deprotonated and the polymer loses its charge and becomes insoluble. The soluble–insoluble transition occurs at its pKa value around pH between 6 and 6.5. As the pKa value is highly dependent on the degree of N-acetylation, the solubility of CS is dependent on the DD and the method of deacetylation used [117]. The degree of ionization depends on the pH and the pK of the acid with respect to studies based on the role of the protonation of CS in the presence of acetic acid and hydrochloric acid [118,119]. The following salts, among others, are water-soluble: formate, acetate, lactate, malate, citrate, glyoxylate, pyruvate, glycolate, and ascorbate.

Table 1
General properties of chitin and CS.

Property	Chitin	CS
Mol. wt.	$(1–1.03)\times10^6$ to 2.5×10^6	10^5 to 5×10^3
DD	~10%	60–90
Viscosity of 1% soln. in 1% acetic acid, cps	–	200–2000
Moisture content		6–7
Solubility	DMAc–LiCl/TCA–MC	Dilute acids TCA–MC

The dissolution constant K_a of the amine group is obtained from the equilibrium:

$$-NH_2 + H_2O \leftrightarrow -NH_3^+ + OH^-$$

$$K_a = [-NH_2][H_3O_-]/[NH_3^+] \quad \text{and} \quad pKa = -\log Ka.$$

For polyelectrolytes, the dissociation constant is not a constant, but depends on the degree of dissociation at which it is determined. The variation of pKa can be calculated using Kachalsky's equation [44].

$$pKa = pH + \log\left(\frac{1-\alpha}{\alpha}\right) = pKo - \frac{\varepsilon\Delta\psi(\alpha)}{k_T}$$

where $\Delta\psi$ is the difference in electrostatic potential between the surface of polyion and the reference, α is the degree of dissociation, k_T is the Boltsman constant and ε is the electron charge. Extrapolation of the pKa value to $\alpha = 1$, where the polymer becomes uncharged and the electrostatic charge becomes zero enables the value of intrinsic dissociation constant of the ionizable groups pKo to be estimated. This value is ~6.5. The intrinsic pKo value of the ionizable groups ~6.5 is independent of the degree of N-acetylation whereas the pKa value is highly dependent. pKo is called the intrinsic pKa of CS.

CS can easily form quaternary nitrogen salts at low pH values. So, organic acids such as acetic, formic, and lactic acids can dissolve CS [118,120]. The best solvent for CS was found to be formic acid, where solutions are obtained in aqueous systems containing 0.2–100% of formic acid (FA) [121]. The most commonly used solvent is 1% acetic acid (as a reference) at about pH 4.0. CS is also soluble in 1% hydrochloric acid and dilute nitric acid but insoluble in sulfuric and phosphoric acids. But concentrated acetic acid solutions at high temperature can cause depolymerization of CS [118,119]. Solubilization of CS with a low DA occurs for an average degree of ionization α of CS around 0.5; in HCl, when $\alpha = 0{:}5$, it corresponds to a pH of 4.5–5. It is reported that at higher pH, precipitation or gelation tends to occur and the CS solution tends to form gels with anionic hydrocolloids [14]. The concentration of the acid plays a great importance to impart desired functionality [122]. Solubility also depends on the ionic concentration and a salting-out effect was observed in excess of HCl (1 M HCl), making it possible to prepare the chlorhydrate form of CS. When the chlorhydrate and acetate forms of CS are isolated, they are directly soluble in water giving an acidic solution with $pKo = 6 \pm 0.1$ [119] in agreement with previous data [123] and corresponding to the extrapolation of pK for a degree of $\alpha = 0$. Thus, CS, as stated above, is soluble at pH below 6. It is known that the amount of acid needed depends on the quantity of CS to be dissolved [118]. The concentration of protons needed is at least equal to the concentration of $-NH_2$ units involved. The solubility is thus a very dif-

ficult parameter to control as it involves a complex array of controlling factors [6]. CS is not soluble in any organic solvents such as dimethylformamide and dimethyl sulfoxide. Its solubility in acidified polyol is substantially good. There are several critical factors that contribute to CS solubility. They may include factors such as temperature and time of deacetylation, alkali concentration, prior treatments applied to chitin isolation, ratio of chitin to alkali solution, particle size, etc. A study on intrinsic viscosity, FTIR, and powder X-ray diffraction (XRD) showed that the molecular weight and DD are collectively responsible for the solubility in the condition of random deacetylation of acetyl groups, which resulted from the intermolecular force [124]. The solution properties of CS, thus, depend not only on its average DA but also on the distribution of the acetyl groups along the main chain in addition of the molecular weight [102,125–128]. Apart from the DD, the molecular weight is also an important parameter that controls significantly the solubility and other properties [129–132,127,133–138]. Both the DD and the molecular weight are reported to affect the properties of electrospun CS nanofibers [139]. The acid-soluble CSs with >95% solubility in 1% acetic acid at a 0.5% concentration could be obtained by treatment of the original chitin with 45–50% NaOH for 10–30 min [140–142]. It is reported that [143] a reaction time of 5 min with 45% NaOH may not be enough for chitin particles to be sufficiently swollen. A study on the thermodynamic aspects of deacetylation concludes that the amount of water present in the system chitin/soda/water/sodium acetate controls the complex equilibriums governing the reaction [144]. Further, the microstructure of the polymer is said to have a role in the dissolution [102]. It is also reported that the crystallinity index decreases on treating chitin with HCl, NaOH, etc. [145]. Apart from acids and alkalies, polyols such as polyethyleneglycol (PEG) and glycerol-2-phosphate are reported to aid the preparation of water-soluble CS at neutral pH [115,146–148].

CS becomes soluble with the entire pH range with increasing substitution of the amino groups by carboxylic groups, which became negatively charged above pH 6.0. The solubility of the partially deacetylated chitins has a close relationship with their crystal structure, crystallinity, and crystal imperfection as well as the glucosamine content. For example, chitin with ca. 28% DD is reported to retain the crystal structure of α-chitin with significantly reduced crystallinity [110,149]. As the DD increases to ca. 49%, chitin has a new crystal structure similar to that of β-chitin rather than either α-chitin or CS, suggesting that the homogeneous deacetylation transformed the crystal structure of chitin from the α- to the β-form [117] and it is water-soluble. Further discussion on water-soluble CS is presented elsewhere.

4.2. Dissolution by inorganic chemicals

There were several attempts at dissolution of chitin using inorganic bases such as sodium hydroxide and inorganic salts [102,145,150,151]. Kunike was reported to have kept chitin in 5% caustic soda at 60 °C for 14 days and got a deacetylated product soluble in acetic acid [150]. Weimarn used inorganic salts such as LiCNS, $Ca(CNS)_2$, CaI_2, $CaBr_2$, $CaCl_2$, etc. capable of strong hydration to dissolve chitin [151]. Clark and Smith dissolved chitin in presaturated solution of lithium thiocyanate at 95 °C, but it was difficult to remove the solvent even at 200 °C [152]. Threads extruded from lithium thiocyanate with tension applied during their formation were said to develop orientation, but an X-ray pattern of a chitin sheet supported on a glass plate reprecipitated from lithium thiocyanate solution, showed only the broad diffuse nodes of a strained, noncrystalline material [152]. Vincendon noted a decrease in the viscosity and molecular weight with time on dissolving chitin in concentrated phosphoric acid at room temperature and reported the nuclear magnetic resonance (NMR) spectra of chitin dissolved in a fresh saturated solution of lithium thiocyanate [153].

Varum and coworkers studied the solution properties of α-chitin dissolved in NaOH and obtained second virial coefficients in the range $(1–2) \times 10^{-3}$ mL mol g^{-2} indicating that 2.77 M NaOH is a good solvent for chitin molecule [140]. They proposed a random-coil structure having a Kuhn length in the range 23–26 nm for the chitin molecules in alkaline conditions. Danilov and coworkers tried repeated freezing and thawing in alkali solution for several attempts and thought that chitin structure becomes friable [154]. Kennedy and coworkers showed that addition of urea enhances solubility of chitin with 8 wt% NaOH and 4 wt% urea concentrations at −20 °C [155]. In addition, the rheological properties suggested that chitin aqueous solution in high concentration behaved as a pseudoplastic fluid whereas in low concentrations it exhibited Newtonian fluid character [155]. The NaOH–urea system was earlier used by Zheng et al. to dissolve regenerated cellulose/chitin blend films [156]. Using Fourier transform infra-red (FTIR) spectroscopy, scanning electron microscopy (SEM), ultraviolet–visible (UV–vis) spectroscopy, XRD, tensile test, and differential scanning colorimetry (DSC), they showed that the blends were miscible when the content of chitin was lower than 40 wt% and the mechanical properties of chitin films containing 10–50 wt% chitin were significantly improved due possibly to strong interaction between cellulose and chitin molecules caused by intermolecular hydrogen bonding.

4.3. Chitin dissolution by strong acids and polar solvents

Strong polar protic solvents such as trichloroacetic acid (TCA), dichloroacetic acid (DCA), etc. have been found to dissolve chitin. In 1975, Brine and Austin dissolved chitin in TCA as a solvent [157,158] after pulverization with two parts by weight of chitin added to 87 parts by weight of a solvent mixture containing 40% TCA, 40% chloral hydrate (CH) and 20% dichloromethane (MC). Kifune and co-workers tried dissolving chitin in TCA containing chlorinated hydrocarbons such as MC and 1,1,2-trichloroethane [159,160]. A number of similar patents have also been reported wherein a mixture of water and DCA [161] and mixtures of TCA/MC or TCA/CH/MC solvent system [162–164] have been used. Tokura et al. used a combination of FA, DCA and diisopropyl ether as a solvent system [165]. But, TCA and DCA are corrosive and degrade the polymer lowering the molecular weight to such levels where the strength of the fibers

will get affected. Although dry tenacities of above 3 g/d were obtained, the low wet tenacities were still undesirable. In addition, chlorohydrocarbons are solvents that are increasingly becoming environmentally unacceptable. Austin and Brine [166] describe high tensile strength chitin fibers are obtained when chitin dope prepared by dissolving chitin in a TCA containing solution followed by wet spinning and cold stretching. The chitin fibers obtained, however, are very thick. Filaments having a tensile strength of 63 kg/mm^2 were obtained. This value corresponds to 5 g/d when calculated assuming that the density is 1.4. Although it is apparent that high tensile strength chitin fibers can be obtained, the diameter thereof is 0.25 mm. When calculated with the density as 1.4, it corresponds to 618 denier. When chitin was dissolved in DCA to prepare a chitin dope solution, the fibers obatined after wet-spinned and stretching gave only low tensile strength [167]. It is described that 3.0–3.5 denier of chitin fibers were obtained, but that the tensile strength was 1.2–1.5 g/d (a knot tensile strength of 0.6–0.7 g/d).

4.4. Highly polar fluorinated solvents

Solubilization of chitin has also been reported using highly polar solvents such as hexafluoroisopropyl alcohol (HFP), hexafluoracetone sesquihydrate (HFAS), methane sulfonic acid [168–170]. Capozza used HFP or HFAS as solvents for chitin and the resulting solution could be wet spun or dry spun into fiber, filaments, or cast into films or solid articles, which may be used as absorbable surgical sutures, or other absorbable surgical elements. As chitin is enzymatically degradable in living tissue, and is resistant to hydrolytic degradation, surgical elements prepared from this polymer have good storage characteristics under a wide variety of conditions. Although fluorinated solvents solvents are reported to be toxic, there is an increasing trend to use them in electrospinning of CS (see Section 8 for details).

4.5. The xanthate process

In analogy to the spinning of cellulose to form rayon, chitin fibers were spun by a xanthate process by various groups [171–176]. Thor and Henderson described the preparation of regenerated chitin films having a tensile strength of 9.49 kg/mm^2 (dry) and 1.75 kg/mm^2 (wet) spun from a chitin xanthate solution [173]. Somewhat later, Thor described the preparation of chitin xanthate for regenerating chitin films and fibers [174]. The patent mentions the stretching of filaments in the gel state to improve physical properties, but not the drawing of solid chitin, required for fiber orientation. Thor in another patent disclosed some further details of his efforts to produce commercially useful films and fibers from chitin, but covers only homogeneous mixtures of chitin and cellulose coprecipitated from the mixed xanthates [175]. Regenerated chitin films were said to possess good strength in the dry state, but became soft and slimy on wetting, implying a lack of toughness when wet. He got a tensile strength of 9.1–9.49 kg/mm^2 for the regenerated chitin in comparison to 58 of natural chitin (151), 35 regenerated chitin (151), 36.6 of silk [176], 25 of viscose rayon (151), 14.5 of wool [177]. This process is used to make chitin–CS fiber materials, knits and textiles, non-woven fabrics, miscellaneous daily goods or foam materials having an improved dyeability, bio-compatibility, antimicrobial activity, good bio-degradative property, and being effective for deodorizing uses, growth enhancing uses for plants and medical uses, and having antimicrobial effect. However, this process was later considered of giving fibers of low strength [178,179]. In another work, Joffe and Hepburn [180] obtained values as high as 9.31×10^7 Nm^2 (6.3×10^3 pounds/in.^{2}) for the strength of films of regenerated chitin, from a chitin xanthate dispersion. Chitin and CS polymers are initially treated with NaOH followed by carbon disulfide treatment for fiber spinning [18]. On blending with cellulose xanthate, the blend solution showed excellent filtering property as an ordinary cellulose viscose [181]. The dry and wet strength and density of blend fibers decrease with increasing chitin content. The fiber exhibited bacteriostatic effects on *Staphylococcus aureus*, *Escherchia coli*, etc., the bacteriostastic rate increasing with increasing chitin content [181]. Nousiainen et al. prepared blends of microcrystalline CS (MCCS) with cellulose xanthate alkaline solutions and noted that the properties of the spinning solution were mainly dependent on the concentration of MCCS in the aqueous gel-like dispersion and finally it got mixed with the cellulose xanthate solution [182]. The yield of MCCS in the resulting fibers was dependent on the molecular mass, and varied between 73 and 82%. The strength, elongation, and color of the resulting hybrid fibers were only slightly changed.

4.6. Lithium complexation and dissolution in strong polar solvents

The major breakthrough for solvent systems that dissolve chitin samples came in 1976 when Austin and Rutherford found that lithium chloride–tertiary amide solvent systems would yield at least 5% chitin solutions [68,158,183]. LiCl (which is coordinated with the acetyl carbonyl group) forms a complex with chitin that is soluble in dimethylacetamide (DMAc) and in N-methyl-2-pyrrolidone (NMP). It should be noted that the same solvents and especially, LiCl/DMAc mixtures, are also solvents for cellulose [184,185]. In addition, Austin also used formic, dichloroacetic and trichloroacetic acids for dissolution of chitin chains. The most frequent solvents used to make a 5–7% (w/v) lithium chloride solution are DMAc, N,N-dimethylpropionamide, NMP and 1,3-dimethyl-2-imidazolldinone. It is also possible to dissolve chitin in a narrow range of carboxylic and sulfonic acids. Austin introduced the solubility parameters for chitin in various solvents [68,113,158]. Thus, the discovery of non-degrading solvent systems has permitted the spinning of filaments, for example, for use as surgical sutures [68,69]. Following this discovery, a number of similar studies have been reported [186–192]. Although this LiCl-polar aprotic solvent system was greatly useful in characterizing the chitin polymer, the fiber formed had always contaminated with traces of LiCl [189]. This method has been used to prepare chitin–cellulose blend fibers with adequate strength properties [185,186,188,190,191].

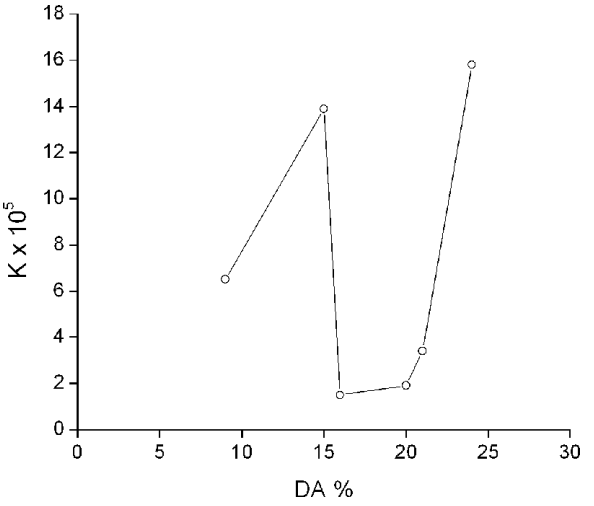

Fig. 5. Plot of *K* values of Table 3 of the paper of Kasai et al. with degree of acetylation (table data collected from Table 3 of Ref. [196] with permission from John Wiley & Sons, Inc.).

4.7. Solubility and molecular weight

The selection of the solvent is also important when molecular weight has to be calculated from intrinsic viscosity using the Mark–Houwink relation ($\eta = KM^{\alpha}$ where η is the intrinsic viscosity, M is the molecular weight, K and α are constants.). The values of the parameters K depend on the nature of the solvent and polymer. For example, one solvent system first proposed (0.1 M AcOH/0.2 M NaCl) for molecular weight characterization was shown to promote aggregation and the values of molecular weights calculated were overestimated [193,194]. Rinaudo et al. proposed that 0.3 M acetic acid/0.2 M sodium acetate (pH 4.5) as a solvent can be used to overcome the problem of aggregation as there was no evidence for aggregation in this mixture [195]. Using acid-soluble CSs of DA varying from 0.02 to 0.61, they concluded that the stiffness of the chain was nearly independent of the DA and demonstrated that the various parameters depended only slightly on the DA [195]. In contrast to this proposition, Kasaai et al. indicate that a and K are inversely related and that they are influenced by DA, and pH and ionic strength of the solvent [196]. They studied the intrinsic viscosity–molecular weight relationship for CS in 0.25 M acetic acid/0.25 M sodium acetate. CS samples with a DA between 20 and 26% were prepared from shrimp-shell CS by acid hydrolysis (HCl) and oxidative fragmentation ($NaNO_2$). Absolute molecular weights were measured by light scattering and membrane osmometry. Size exclusion chromatography was used to determine average molecular weights and polydispersity. The data of K determined by various authors (refer Table 3 of Ref. [196]) can be plotted against DA as shown in Fig. 5 which indicates that there cannot be any relationship between DA and K value (Kasaai has since modified his work [197]).

As the values of K and α differ, it is pointed that it would always be better to follow those values where the authors have used a standard reference for comparing the molecular weights and a standard method such as light scattering or gel permeation chromatography [198,199] to determine the absolute molecular weights. The relatively high values for the parameter α are in agreement with the semirigid character of CS. On the other hand, Varum and coworkers proposed that Mark–Houwink–Sakurada equation can be written as $[\eta] = 0.10\,M_w^{0.68}$ (mL g^{-1}) and the relationship between the z-average radius of gyration (R_g) and the weight-average molecular weight (M_w) was determined to be and $R_g = 0.17\,M_w^{0.46}$ (nm), suggesting a random-coil structure for the chitin molecules in alkali conditions [140]. The charged nature of CS in acid solvents and CS's propensity to form aggregation complexes require care when applying these constants [114]. The weight-average molecular weight of chitin is 1.03×10^6 to 2.5×10^6, but the N-deacetylation reaction reduces this to 1×10^5 to 5×10^5 [68].

4.8. The calcium chloride–MeOH system

Tamura reports that $CaCl_2$–MeOH system acts as a good solvent combination for chitin [200]. Both the amount of water and the number of calcium ions are main factors affecting the dissolution of chitin in calcium chloride dihydrate-saturated methanol (calcium solvent). The higher degree of N-acetylation of the chitin was also indicated by its higher solubility in calcium solvent [200–203]. Calcium gets coordinated to chitin and the complex gets dissolved in MeOH. This is good a solvent as lithium is toxic and calcium is not, but high viscosities might hinder scale up operations during large scale production. Investigations on the crystalline structure of chitin and CS showed pronounced differences in the by XRD patterns for specimens with DA values between 44.2 and 52.2% [204]. It was proposed that the crystalline structure changed from an anhydrous-type CS to a α-chitin type without any additives. The dissolution behavior of chitin was investigated by using ternary phase diagram [205–207]. It was further noted that while CaC_2–MeOH is a good solvent for chitin, it is a poor solvent for CS and that it can regulate the distribution of N-acetyl glucosamine and glucosamine between amorphous and crystalline regions [204].

4.9. Dibutyryl chitin

Another major development for chitin dissolution was the synthesis of alkyl derivatives of chitin whereby butyryl chitin was found to be soluble in normal solvents as reported by Szosland [208–211]. Chitin has been known to form microfibrillar arrangements in living organisms [212]. These fibrils are usually embedded in a protein matrix and have diameters from 2.5 to 2.8 nm. Crustacean cuticles possess chitin microfibrils with diameters as large as 25 nm. The presence of microfibrils suggests that chitin has characteristics, which make it a good candidate for fiber spinning. To spin chitin or CS fibers, the raw polymer must be suitably redissolved. This was resolved through alkyl chitin route [208,212,213,214–218].

DBCH was obtained from native krill chitin by its esterification with butyric anhydride in the presence of perchloric acid [213,217–219]. DBCH fibers were manufactured from a polymer solution in ethyl alcohol by extrusion [220,221]

as shown in Fig. 6. Because a dry–wet formation method was applied, the fibers obtained had a porous core [222]. Alkaline treatment was adopted to improve upon the properties. The microporous DBCH fibers were then treated with aqueous KOH solutions [223–227] whose SEM micrograph is as shown in Fig. 7. The wet spinning of a 14.5% solution in dimethylformamide created DBCH filaments, which were treated with an alkali solution for chitin regeneration. Fiber samples with different degrees of chitin restoration were obtained. The restoration of the chitin structure resulted in a gradual increase in the degree of crystallinity, the density of the structured area, the tensile strength, and the average elongation at rupture and in a decrease in the diameter of the fibers. Structural analysis and the physico-chemical properties of DBCH and its blends were evaluated by several groups [227–229]. The crystallinity degree of fully regenerated chitin, the final product of alkaline hydrolysis, reached a value close to that of native chitin [230–232].

Biological evaluation indicated that DBCH and regenerated chitin have positive influence on the wound healing process [233–236].

The wide-angle X-ray scattering (WAXS) measurements of the krill chitin showed that its supermolecular structure is ordered and has a high degree of crystallinity [226,231].

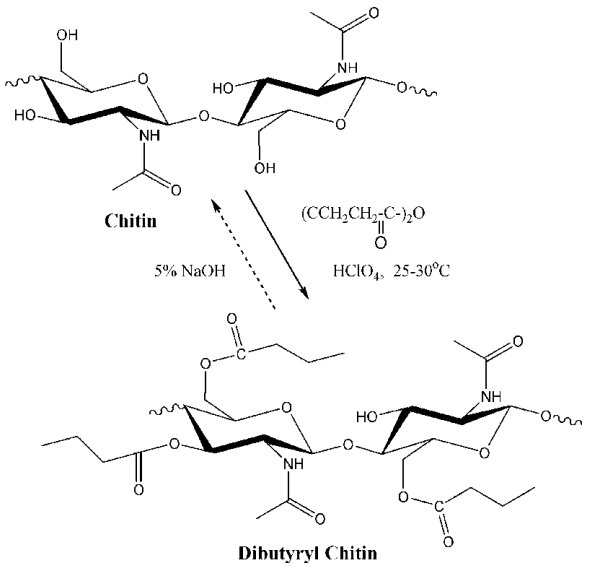

Fig. 6. Synthesis of dibutyrylchitin (reproduced from Ref. [220] with permission of Wiley Interscience).

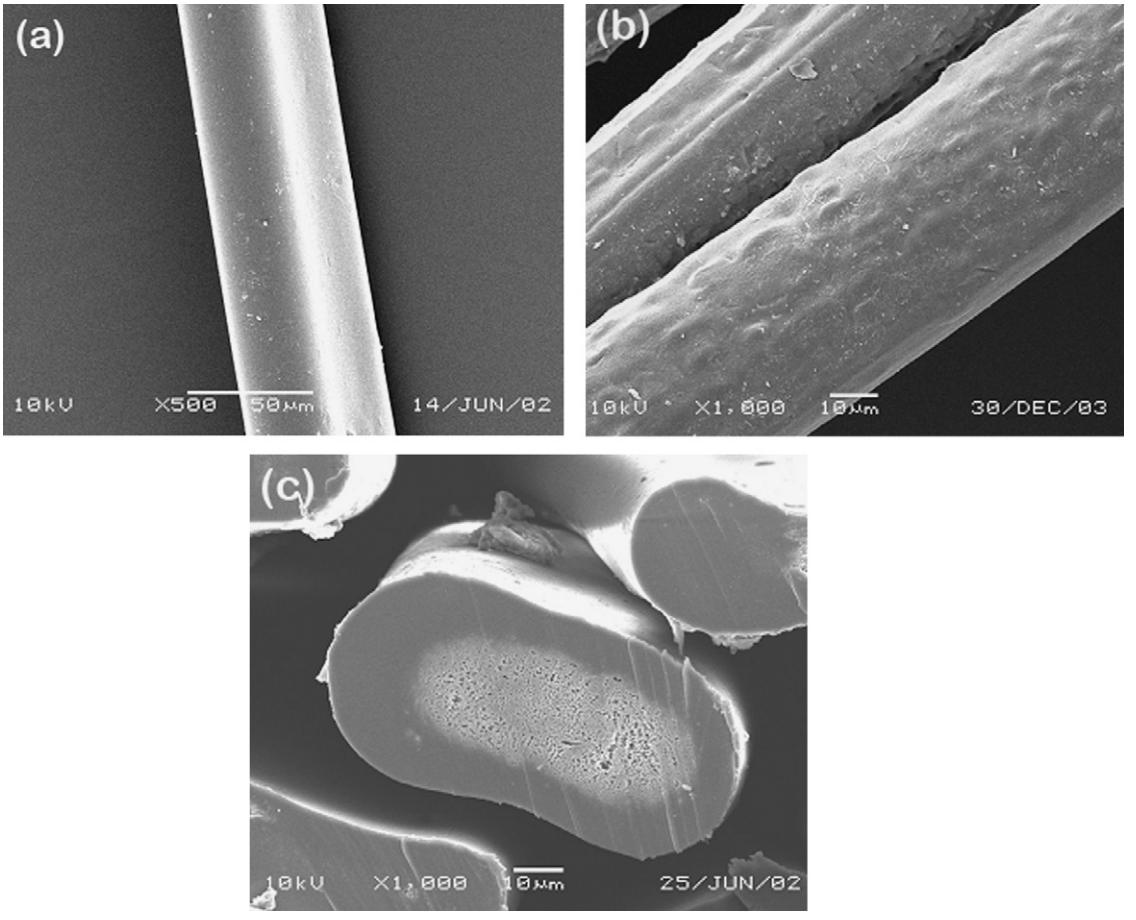

Fig. 7. (a) SEM micrograph of the surface of DBCH fibers (500×), (b) SEM micrograph of the surface of regerated fibers (500×) and (c) SEM micrograph of the cross-section of DBCH fibers (1000×) (reproduced from Ref. [226] with permission from Fibers and Textiles in Eastern EurPoland).

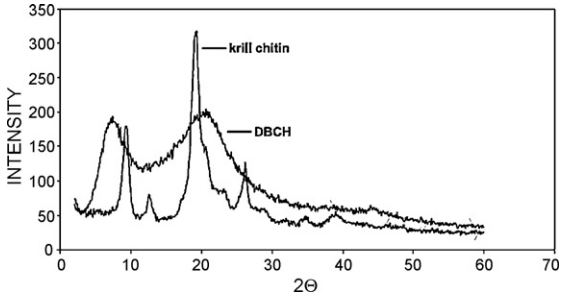

Fig. 8. WAXS diffraction pattern of DBCH and krill chitin fibers (reproduced from Ref. [226] with permission from Fibers and Textiles in Eastern EurPoland).

The butyrylation process leading to DBCH disrupts the supramolecular structure of chitin. The diffraction reflexes in the ordered area disappear followed by a broadening of the remaining reflexes (Fig. 8). DBCH is, thus, characterized by significantly lower crystallinity degree as well as by the smaller size of the crystalline regions, which results from a small structural ordering of the polymer. It was interesting to note that the alkaline treatment of DBCH (5% KOH and at 20 °C-series A, at 50 °C-series B, at 70 °C-series C and at 90 °C-series D) to obtain the regenerated chitin brings about a reverse chemical process in which the supermolecular structure of chitin is gradually being regained and thus the configuration of the polymer macromolecules becomes similar to the crystalline network of the krill chitin [226]. The process as a whole looks to be a case of disruption and reformation of the hydrogen bonded supramolecular structure during butyrylation and debutyrylation, respectively. Spectroscopic examinations carried out using different techniques gave support to these observations. The characteristic changes of amide I band of krill chitin, DBCH and regenerated chitin indicated extensive hydrogen bonds between the C=O and the NH for every second C=O group in chitin [227,231].

Studies by fluorescent microscopy have revealed a specific skin-core structure of DBCH fibers, preserved in the whole course of the alkaline treatment [226]. Fig. 9 provides the fluorescent microphotographs of the DBCH fibers and before and after alkali treatment. The fluorescence was intensified by the specific sorption of Rhodamine B used as a dye. As Rhodamine B reveals no affinity to the examined fibers, it is accumulated in microcapillaries of the fibers by adhesion. DBCH fibers in the absence of Rhodamine B revealed a specific greenish fluorescence in UV light when the blue filters are used (Fig. 9a) indicating homogeneity of the fiber surface topography. The fibers are smooth and homogeneous with no impairments or defects. In the photograph of the cross-section of DBCH fibers (Fig. 9b), a

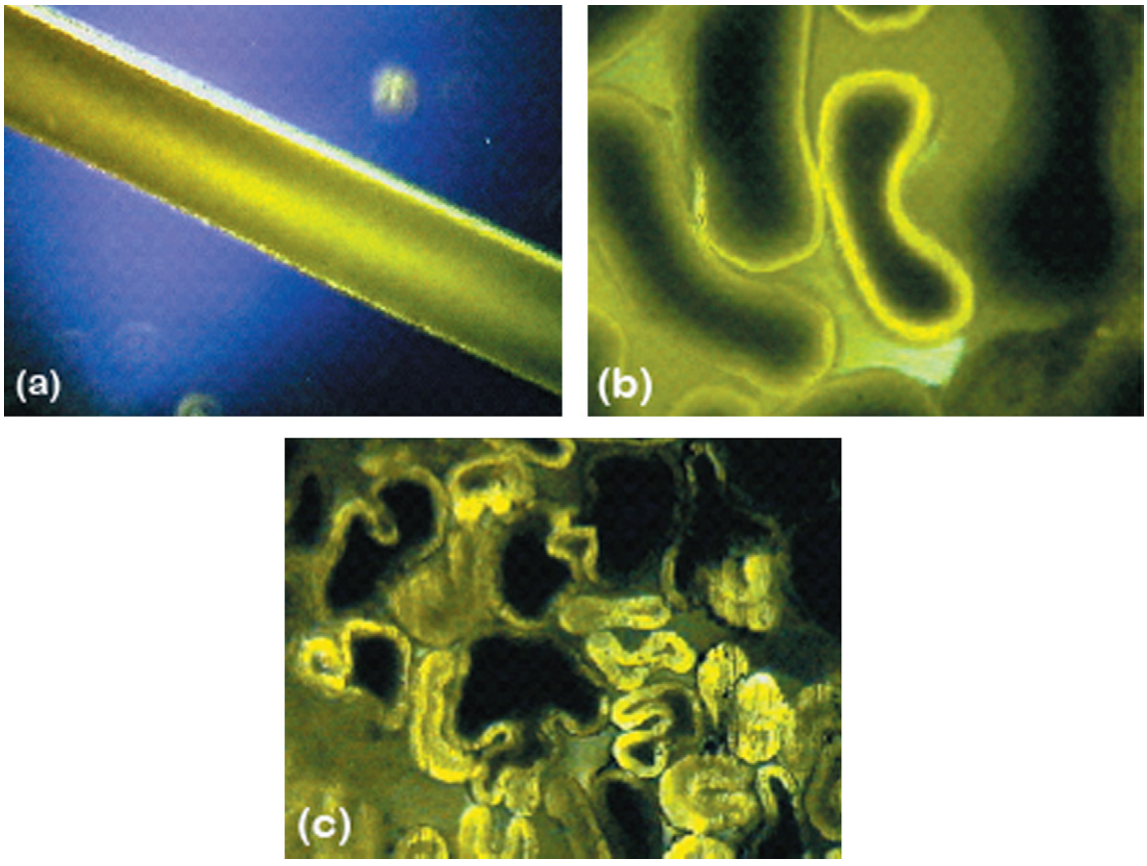

Fig. 9. (a) the surface of DBCH fibers (180×), (b) the cross-section of DBCH fibers (620×) and (c) the cross-section of chitosan fibers (DD = 84) (320×) (reproduced from Ref. [225] with permission from Institute of Biopolymers and Chemical Fibers, Łódź, Poland).

clear fluorescence effect of a thin surface layer of a fiber can be seen. The authors explain this phenomenon as due to the specific supermolecular structure of the fibers formed using a wet–dry spinning method. The fibers were then subjected to the alkaline treatment which resulted in obtaining fibers from the regenerated chitin and finally CS fibers (Fig. 9c). As a result of the partial N-deacetylation, a distinct skin–core structure can be observed. The cytotoxicity of the DBCH was evaluated and no agglutination, vacuolization, and cell membrane lysis was observed [212]. The number of cells separated from the matrix was found to be the same as in the control cultures.

4.10. Water-soluble alkali chitin

Treatment with alkali has been used by many authors to prepare WSC [50,109,237,238]. Alkali is known to deacetylate and degrade chitin. Both these processes are expected to improve solubility. Deacetylation reduces crystallinity and degradation reduces the molecular weight [109]. One gets alkali chitin when reacted with concentrated NaOH. Alkali chitin is highly reactive and can give rise many water/organosoluble derivatives [43,50]. For example, it reacts with 2-chloroethanol to yield *O*-(2-hydroxyethyl) chitin, known as glycol chitin. Alkali chitin with sodium monochloroacetate yields the widely used water-soluble *O*-carboxymethylchitin sodium salt [237]. Liu et al. showed that hydrogen bonds in chitin were weakened by the alkali treatment and the crystallinity of chitin decreased significantly when soaked in higher concentration alkali solutions at room temperature [238]. The molecular weight and DA of chitin decreased significantly at treatment temperatures higher than 20 °C or treatment times longer than 4 h. It was found by Guo et al. that regenerated chitin obtained by a concentrated alkali treatment at a low temperature is water-soluble [239].

In one process, chitin is first dispersed in concentrated NaOH and allowed to stand at 25 °C for 3 h or more; the alkali chitin obtained is dissolved in crushed ice around 0 °C [240]. The resulting chitin is amorphous and under some conditions, it can be dissolved in water, while CS with a lower DA and ordinary chitin are insoluble. Sannan et al. showed that the regenerated chitin with around 50% of deacetylation isolated at low temperature from an alkali chitin solution left at 25 °C for 48–77 h has very good solubility in water at 0 °C. The XRD diagrams showed that these were amorphous, although both chitin with lower DD and CS had crystallinity. The improved solubility of chitin with about 50% of deacetylation would be attributed to the partial deacetylation which probably brought about the destruction of secondary structure and also the increase of the hydrophilic property on account of the increased number of amino groups [141,142]. This phenomenon could also be related to the decrease of molecular weight under alkaline conditions; they confirmed that to get water solubility, the acetyl groups must be regularly dispersed along the chain to prevent packing of chains resulting from the disruption of the secondary structure in the strong alkaline medium. The alkali solubility was used to spun cellulose–chitin–silk fibroin filaments which had 3.9–5.0 deniers for the titer value (for fiber containing less than 43% silk fibroin), 0.70–0.93 g/d for the tenacity value and 20.6–28.6% for the elongation value [241].

4.11. Effect of DD and molecular weight

The relationship between solubility, molecular weight and degree on N-acylation has been established by several groups [126,127,132–134,137,142–145,238–240,242–250]. XRD and deamination analyses suggested that the distribution of N-acetyl groups in the chitin molecule was more random than those in the regenerated chitin [242]. At 50% N-acetylation, CS solubility in water did not show any change with an increase in the molecular weight [136]. However, a notable crystal structure transition from crystal "Form II" with constrained chain conformation to "Form I" having a more extended chain structure to a crystalline form similar to that of chitin was observed on increasing acetyl group [246]. The acetyl group dependent transformation in crystal structure indicates that control of the DA can be used to control solubility. This has led to the preparation of WSC by controlling the DD and molecular weight of chitin through alkaline and ultrasonic treatment [251]. The WSC was found to be more efficient than chitin or CS as a wound-healing accelerator when tested in rats. Homogeneously deacetylated samples were obtained by this alkaline treatment of chitin under dissolved conditions [117,251]. The homogeneity of the deacetylated chitin was later assured by the reacetylation of highly deacetylated CS [252]. The solubility of the partially deacetylated chitins had a close relationship with their crystal structure, crystallinity, and crystal imperfection as well as the glucosamine content [117]. The wide-angle X-ray diffractometry (WAXD) revealed that the chitin with ca. 28% DD retained the crystal structure of α-chitin with significantly reduced crystallinity and perfection of the crystallites. The water-soluble chitin of ca. 49% DD had a new crystal structure similar to that of β-chitin rather than either (-chitin or CS, suggesting that the homogeneous deacetylation transformed the crystal structure of chitin from the (- to the β-form [117]. Physical properties such as crystallinity and polymermorphic forms are reported to be affected by the process conditions of preparation [253–257]. The crystalline state of the samples was said to be the key parameter on which depended the rate constants of both alkaline hydrolysis and deacetylation process [258].

4.12. Enhanced solubility by chemical modification

Chemical modification has been used as means of imparting solubility to chitin and CS by using appropriate chemical entities that enhances solubility [6,12,43,44,50,76,83–85,149,259–262]. Methods such as introducing water-soluble entities, hydrophilic moieties, bulky and hydrocarbon groups, etc. have been generally practised to enhance solubility [3,4,11,14,44,51,76,78,84,149,260,263]. Sashiwa and Aiba have brought out an excellent review on chemical modification of CS [83]. Morimoto et al. have described how chemical modifications can control the properties and functions of chitin and CS [149]. The reactions of CS are considerably more versatile than cellulose due to the

presence of amine ($-NH_2$) groups and hydroxyls (–OH) groups [12,43,82,116,262,264].

Mention was made earlier on the method of N-acylation of chitin and CS to enhance solubility [84,109,110,126,127,246]. Sashiwa and coworkers showed that simple acylations enhanced CS solubility [265,266]. N-Acetylation with acetic anhydride was reported to give an improved method of preparing water-soluble CS [246]. Experiments showed that the amount of acetic anhydride was the most important factor affecting the N-acetylation degree of the CS. The solubility of half N-acetylated CS was not changed with an increase in the molecular weight in water, and the water solubility decreased with increasing molecular weight in the alkaline region [246]. A series of water-soluble chitin were prepared and their properties studied by Tokura et al. [255]. The work of Qin and others showed that solubility in water of half N-acetylated CSs and chitooligomers affected adversely the antimicrobial activity whereas water-insoluble CS in acidic medium exhibited inhibitory effect against microorganisms such as *C. albicans* [267]. The water-insoluble CSs with M_w around 5×10^4 were the optimum for antimicrobial action. On the other hand, Kennedy and his group showed that CS acetate with high solubility retained the structure and antibacterial activity of CS [268]. Long chain fatty acids with a hydrophobic back bone and hydrophilic end groups are known to enhance solubility of polymers. N-Acylation of CS with various fatty acid chlorides increased its hydrophobic character and made important changes in its structural features [269]. The best mechanical characteristics and drug release properties were found for palmitoyl CS (substitution degree 40–50%) tablets with 20% acetaminophen as a tracer suggesting palmitoyl CS excipients as interesting candidates for oral and subdermal pharmaceutical applications [269]. Hirano and others treated CS with n-fatty acid anhydrides in a homogeneous solution in 2 vol% aqueous acetic acid–methanol to obtain water-soluble polymers [270,271].

Introduction of bulky groups has been adopted in general to improve the solubility of insoluble polymers. This idea has been employed in the preparation of butyrylchitin, valeroylchitin, triethyl CS, etc. [208–210,272]. Highly N-triethylated CS chlorides were soluble in water at room temperature [272]. However, if modification is carried out with shorter chain carboxylic acids (as in acetylchitin), the solubility remains poor. By substituting the acetyl residues partially by butyryl residues (mixed ester formation), exclusive use of the bulky carboxylic acids can be avoided and yet good solubility is achieved. These relationships were employed to prepare high molecular weight mixed chitin esters, using methanesulfonic acid as the solvent and catalyst [273]. The mixed chitin esters, varying both in the overall degree of substitution (DS) (1.5–1.9) and the molar ratios of butyryl-to-acetyl residues (1:0.62 to 1:0.72), were characterized by IR spectroscopy, DSC, elemental analysis, and ^1H NMR spectroscopy (in trifluoromethanesulfonic acid); the latter allowed the DS to be determined as well as the molar ratio of butyryl-to-acetyl residues [273]. Another interesting finding concerns the successful use of succinyl group for enhancing water solubility [274–276]. Sashiwa and coworkers used N-succinylations to impart water solubility to otherwise insoluble sialic acid bound CS [277]. Similarly, water-soluble O-succinyl CS has also been reported [278].

The preparation of the highly water-soluble carboxy methyl derivatives of chitin and CS has been a major breakthrough because of their potential for various applications [185,237,279–282,78,283]. The hydrogen bonds are disrupted by the hydrophobic methyl group and the solubility enhanced by the carboxyl group. The carboxymethylation of chitin is done in a way similar to that of cellulose; chitin is treated with monochloroacetic acid in the presence of concentrated sodium hydroxide to get the carboxymethyl (CM) derivative [278–281]. Similarly, hydroxypropylchitin (HPC) used for artificial lachrymal drops is also a water-soluble derivative [283]. Muzzarelli et al. report the preparation and characterization of water-soluble N-carboxymethyl chitiosan (N-CMC) by reacting with glyoxylic acid [284,285]. The film-forming ability of N-CMC assists in imparting a pleasant feeling of smoothness to the skin and in protecting it from adverse environmental conditions and consequences of the use of detergents. N-CMC was found to be superior to hyaluronic acid as far as hydrating effects are concerned [286]. Water-soluble chitins such as N-CM chitin and dihydroxypropyl chitin were also reported to be formed by adopting simple procedures involving freezing and the addition of a detergent such as sodium dodecylsulfate [255]. HPC was prepared by refluxing the chitin and propylene oxide in aqueous alkaline medium [287]. It is soluble in water in ordinary conditions. The water solubility was utilized successfully to graft poly-(DL)-lactide onto HPC backbone by a ring-opening melting polymerization using stannous octoate as catalyst [287]. water-soluble ethylamine hydroxyethyl CS having antibacterial activities was reported to be made by reacting chloroethylamine hydrochloride under alkali condition [288].

With the discovery of the specific recognition of cells, viruses and bacteria by sugar molecules, modification of chitin and CS using cell specific sugars has generally been practiced [83]. Methods adopted include improving the hydrophilicity of CS and introducing certain groups to disrupt the hydrogen bonding between amino groups of CS [289]. Thus, the covalent attachment of a hydrophilic sugar moiety, gluconic acid, through the formation of an amide bond and the N-acetylation of sugar-bearing CS (SBC) improved solubility significantly [289]. The SBCs were further modified by the N-acetylation in an alcoholic aqueous solution. The N-acetylation of SBCs significantly affected the water solubility, for example, the SBCs with the DA, ranging from 29 to 63%, were soluble in the whole range of pH [286]. Another approach was to employ the Maillard-type reaction to prepare the water-soluble CSs using various CSs and saccharides under various operating conditions [290,291]. Results indicated that the solubility of modified CS is significantly greater than that of native CS, and the CS-maltose derivative remained soluble when the pH approached 10. Among CS-saccharide derivatives, the solubility of CS-fructose derivative was highest at 17.1 g/l. Considering yield, solubility and pH stability, the CS-glucosamine derivative was deemed the optimal water-soluble derivative [292]. Sig-

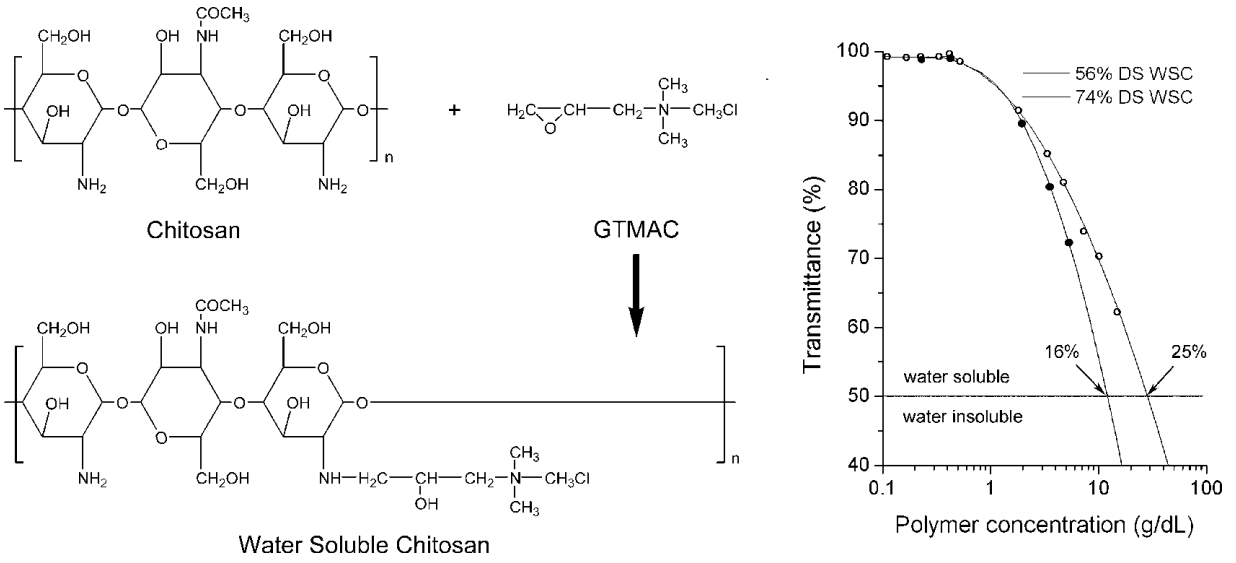

Fig. 10. Preparation of water-soluble chitosan derivative by reacting with epoxy group containing moieties (reproduced from Ref. [251] with permission of Elsevier Science).

nificant improvement in water solubility was observed when disaccharide branches such as maltose, mannose, etc. were introduced [293–296]. Concanavalin A exhibited a specific affinity for the α-mannoside group containing CS [294]. The branched CS also exhibited considerable antimicrobial activity [294]. Introducing galactose sugar or lactose sugar also was reported to give rise to water solubility [297]. Hydrophilic–hydrophobic CS derivatives were obtained through the attachment of lactose and alkyl groups to the amino group of CS with potassium borohydride. These CS polymers had excellent solubility in water [297].

Enzymatic hydrolysis is another method to get water-soluble CSs of low molecular weight [298]. Water-soluble products were obtained when poly(ethyleneglycol) dialdehyde diethyl acetals were used for the cross-linking of partially reacetylated CS via Schiff's reaction and hydrogenation of the aldimines. The products seem to be suitable for medical resorption applications [299]. The solubility of benzyl vs. benzoylchitins was interesting. The solubility of benzylchitins in organic solvents was not so good, because of the low degree of benzylation whereas benzoylchitins were soluble in many organic solvents such as dimethyl sulfoxide, dimethylformamide, benzyl alcohol, etc., in addition to the acidic solvents such as FA [300]. A combination of O- and N-acylation was used in a patented a process to prepare water-soluble, randomly substituted partial N-partial O-acetylated CS with an acetylating agent in the presence of a phase transfer reagent [301]. Another patent introduces dry, free-flowing, water-soluble CS salts formed by the heterogeneous reaction between particulate CS suspended in about 5 to about 50 parts by weight of monohydric alcohol containing an amount of water sufficient to raise the dielectric constant [302]. N-(2-carboxybenzyl) CS, a potential pH-sensitive hydrogel for drug delivery was found to be effective for the release of 5-fluorouracil, a poor water-soluble drug. The water solubility and the easy formation of gel with gluteraldehyde were responsible for this behavior [303].

Introduction of quaternary ammonium groups, phosphonic acid group, etc. is known to enhance solubility of polymers. Thus, N-[(2-hydroxy-3-trimethylammonium) propyl] CS chloride prepared by introducing quaternary ammonium salt groups on the amino groups of CS was found to be water-soluble [304]. Similarly, N-methylenephenyl phosphonic CS and N-methylene phosphonic CS have enhanced solubility [305,306]. But, it is reported that this process, however, reduces the molecular weight [305]. Conjugation with glycidyltrimethylammonium chloride was also reported to impart water solubility [307].

Graft copolymerization has also been cited as a means to achieve solubility [16,76,77,80,81,86]. Grafting of polar monomers onto chitin/CS has been found to give rise to improved solubility [77,80,81,308]. When a non-acrylic monomer, i.e. N-vinyl pyrrolidone, the solubility of CS was markedly reduced either in common organic solvents or in dilute organic or inorganic acids [309]. However, the solubility of the grafted CS substantially improved after adsorption of copper ions, becoming completely soluble in dilute hydrochloric acid. Chitin-*g*-poly(γ-methyl-L-glutamate) copolymers have shown varying degrees of solubility in common polar solvents depending on the side chain length [76,86]. The solubility of the graft copolymers in water was reported to be dependent on the PEG molecular weight, the weight ratio of PEG in the hybrids, DS, and DA [310]. The modification with the higher molecular weight PEG improved water-solubility of CS keeping the main skeleton intact [115]. Sashiwa et al. synthesized a dendronized CS–sialic acid hybrid using convergent grafting of pre-assembled dendrons built on gallic acid and tri(ethyleneglycol) backbone [311]. The water solubility of these novel hybrids was further improved by N-succinylation of the remaining

Table 2
Summary of attempts at fiber formation from chitin.

	Solvent/solvent system	Fiber properties	Remarks	Refs.
1.	N-Deacylation in 5% NaOH–aqueous acetic acid	Tensile breaking load of 35 kg/mm^2 (345 Pa).	Dull lusture good for artificial hair.	[150]
2.	LiCNS,$Ca(CNS)_2$, $CaCl_2$, CaI_2	–	'ropy-plastic' state.	[151]
3.	Repeated freezing and thawing using NaOH	–	Chitin becomes friable.	[153]
4	Alkali	Strength similar to viscose fiber.	–	[340]
5.	Presaturated solutions of lithium thiocyanate at 95 °C	Highly oriented fiber.	Solvent removal not successful.	[152]
6.	Used partially deacetylated chitin dissolved in acetic acid	Film 9000 pound/in.^{2}. The filaments were soft and very tenacious.	Dissolution in acetic acid shows that CS has been formed.	[341]
7.	40% NaOH treatment–Xanthation at −10 15 °C	–	The properties were not good.	[176]
8.	Chloroethanol and sulfuric acid	–	–	[158]
9.	TCA (40%), CH (40%) and MC (20%).	Tensile strength 104 kg/mm (1026 Pa) elongation 44%.	Syringe extrusion employed, strong acid degrades fiber.	[157]
10.	DMAc–5% LiCl. 5% w/v was obtained within 2 h	TS 24–60 kg/mm (236–592 Pa).	Best dry properties, but still poor in wet properties; removal of LiCl is a problem.	[398]
11.	NMP–5% LiCl. 5% w/v was obtained within 2 h	TS 24–60 kg/mm (236–592 Pa).	Removal of LiCl is a problem.	[342]
12.	TCA, a chlorinated solvent and CH	Properties not given.		[166]
13.	Regenerated chitin with 50% N-deacylation. Soluble in water at 0 °C	Data not available.	Deacetylation reduces mol. wt.	[141]
14.	Xanthation of alkali chitin	50% chitin–cellulose–12.3 denier–Tenacity 1.08 g/d.	.	[18,171,341]
15.	Xanthate process	Strength of 9.31×10^7 Nm^2 (6.3×10^3 pounds/in.^{2}) reported.		[172,173,343]
16.	HFP	Good storage characteristics under a wide variety of conditions.		[171]
17.	FA, DCA and diisopropyl ether at −20 °C.	Wet strength < 0.50 g/d, elongation 13%.	DCA is very corrosive and degrades the polymer.	[165]
18.	TCA/MC	Tensile strength 2 g/d and denier 0.5–20.	TCA is very corrosive and degrades the polymer.	[162]
19.	TCA/CH/dichloroethane	Tenacity of 3.2 g/d with an elongation of 20%.	TCA is very corrosive and degrades the polymer, wet strength poor.	[162]
20.	60:40 mixtures of TCA and trichloroethylene.	Not reported.	TCA is very corrosive and degrades the polymer; chlorohydrocarbons are environmentally unacceptable.	[162]
21.	50:50 mixtures of TCA and dichloromethane	Tenacity of 2.65 g/d; denier of 150–175	TCA is very corrosive and degrades the polymer.	[163]
22.	TCA, chloromethane, MC and 1,1,2-trichloroethane below room teperature	Yarn denier of 0.5–20 and a dry tensile strength of 2 g/d or more. TS after treatment with aqueous caustic soda solution for 1 h: 2.25–3.20 g/d with elongations of 19.2–27.3%.	TCA is very corrosive and degrades the polymer.	[159]
23.	FA and DCA	Fineness of 3.0 denier, strength of 1.0 g/denier.	Fibers of *n*-butylchitin and *n*-amylchitin were also made in a similar way. The fibers had a fineness of about 1.0 denier.	[344,345]
24.	TCA, chloromethane, MC and 1,1,2-trichloroethane	Yarn denier of 0.5 to 20 and a dry tensile strength of 2 g/d or more.	Sutures having high tensile strength and flexibility, and good absorption properties could be made.	[346,347]

Table 2 (*Continued*)

	Solvent/solvent system	Fiber properties	Remarks	Refs.
25.	TCA, chloromethane, dichloromethane, and 1,1,2-trichloroethane	A single yarn denier of 0.5–20 and a dry tensile strength of 2 g/d or more obatined.	Strength properties improved by treating filaments formed in a coagulation bath additionally with a coagulation solution in a free state.	[160]
26.	DMAc + 5% LiCl	Composite fibers of chitin and cellulose studied.	Removal of LiCl is a problem.	[348]
27.	TCA/MC	5.5 g/d and moduli at least 150 g/d.	Spun from anisotropic solution which form high strength fibers.	[349]
28	Chitin acetate/formate in a solvent mixture of TCA and MC	Tenacity > 4 g/d, modulus 100 g/den.		[350]
29.	Esterification with butyric anhydride	DBCH fibers had tensile properties similar to or better than those of chitin and some chitin derivatives described in the literature.	Fiber spinning was done in alcohol solution, easily soluble in acetone, alcohols, methylene chloride, and dimethylformamide.	[221]
30.	Tosylation			[350]
31.	Novel chitin–silk fibroin fibers and chitin fibers–14% NaOH			[351]
32.	$CaCl_2$–Methanol	Excellent properties.	High viscosity is a problem.	[199,202]
33.	WSC–N-acetylation of CS	Best values for the dry tensile strength and breaking elongation were obtained when the water-soluble chitin content was 30 wt%.	The wet tensile strength and breaking elongation decreased with the increase of water-soluble chitin content.	[352]

amine functionality. A novel water-soluble photochromic copolymer was prepared by graft copolymerization of 9′-allyloxyindolinospiro-naphthoxazine onto CM chitin. The copolymer was not only soluble in water but also exhibited usual photochromic behavior [312].

Enzymatic grafting is reported to introduce water solubility [313–315]. Tyrosinase converts a wide range of phenolic substrates into electrophilic o-quinones. In slightly acidic media (pH 6), CS could be modified under homogeneous conditions with the natural product chlorogenic acid. The modified CS was soluble under both acid and basic conditions, even when the degree of modification was low [314]. Anionic sidechain-grafting of CS gave water-solubililty having zwitterionic properties [315]. These derivatives were prepared by grafting mono(2-methacryloyl oxyethyl)acid phosphate and vinylsulfonic acid sodium salt onto CS. It is interesting to note that the antimicrobial activity was depended largely on the amount and type of grafted chains as well as changes of pH. Grafting onto CS by various entities has also shown by a number other groups to enhance solubility [316–321]. Chitin-graft-poly(2-methyl-2-oxazoline) showed enhanced solubility and activity of catalase in organic solvent [319]. Another group showed that sonication of chitin enhanced water solubility [320].

Kurita et al. have prepared 6-iodo-chitins that exhibited good solubility in the solvent [322] by tosylation (treatment with excess *p*-toluenesulphonyl chloride) on alkali chitin followed by treatment with sodium iodide in DMSO [323]. Graft copolymerization of γ-methyl-L-glutamate to get chitin-*g*-poly(γ-methyl-L-glutamate) copolymers has shown varying degrees of solubility in common polar solvents depending on the side chain length [324]. PEG which is used as a versatile material in biomedical applications because of its properties such as protein resistance, low toxicity, immunogenicity, etc., has been employed to modify properties of chitin and CS especially the solubility [17,115,310]. For example, glycol CS soluble in water at neutral and acidic pH which was found to be useful as a stabilizer for protein encapsulated into poly(lactide-co-glycolide) microparticle was prepared by the conjugation of CS with ethylene glycol [325].

Chitin was successfully trimethylsilylated with a mixture of hexamethyldisilazane and trimethylsilyl chloride in pyridine [326]. Compared to (-chitin, β-chitin was much more reactive and advantageous as a starting material to prepare fully substituted chitin in a simple manner, though (-chitin also underwent full silylation under appropriate conditions. The resulting silylated chitin was characterized by marked solubility in common organic solvents and by easy desilylation to regenerate hydroxy groups, which enabled clean preparation of chitin films [326]. The solubility of substituted CS samples in neutral and alkaline media increases the possibility of use in cosmetics and pharmaceutical. The hygroscopic capacity of the modified samples could be useful to film formation, to membranes formulated for wound healing and as additive in cosmetics and toiletries. Glycerol was also shown to enhance the water solubility of fish gelatin–CS films [327].

It was shown recently that bipolar membrane electroacidification could be used as a method to solubilize

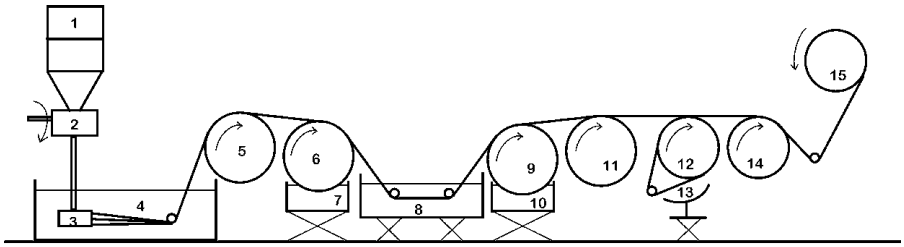

Fig. 11. Schematic depiction of a typical wet-spinning production line (reproduced from Ref. [24] with permission of Wiley InterScience).

CS [328]. Bipolar/anionic configuration and stepwise feeding mode led to CS solubilization yield of 91% in 60 min at 20 mA/cm^2 [328]. Oxidation is known to introduce hydrophylic moieties that enhance water solubility [142]. Oxidization in water with NaClO and catalytic amounts of 2,2,6,6-tetramethylpiperidinyloxy radical and NaBr is employed. Chitin behaved differently. The high crystallinity of the original chitin brought about low reactivity, and the high C-2 amino group content of the N-acetylated CS led to degradations rather than the selective oxidation at the C-6 hydroxyls. The obtained chitouronic acid had low viscosities in water, and clear biodegradability by soil microorganisms [142]. Fig. 10 depicts the preparation of water-soluble CS derivative by reacting with epoxy group containing moieties [251].

5. Chitin fiber formation

5.1. Chitin fiber formation and uses

Sutures are probably the largest groups of material implants used in human body and the suture market is very huge with a total tally exceeding $1.3 billions annually [329]. Physicians have used sutures for the past at least 4000 years [330]. Archaeological records from ancient Egypt and India show use of linen, animal sinew, flax, hair, grass, cotton, silk, pig bristles, and animal gut to close wounds [330,331]. The famed Susruta is reported to have used suture materials of bark, tendon, hair and silk as sutures in surgery [332]. Although chitin fibers could be made into textile materials [25,112,333,334], chitin sutures have remarkable properties over other fibers for biomedical applications [3,5,11,23,26,335–337]. One study reports that chitin fibers have comparable properties to those of collagen and lactide fibers [337]. Chitin sutures resist attack in bile urine and pancreatic juice, which are problem areas with other absorbable sutures [68]. The polymeric linear chain structure of chitin is expected to give rise to fiber formation and film forming ability similar to those of cellulose [18]. Thus, the presence of the microfibrils of chitin with diameters from 2.5 to 2.8 nm which are usually embedded in a protein matrix indicates that chitin can be spun into fibers [338,339]. The polyamide-type structure should be broken up to enable solubilization of chitin into a solvent [165–167]. This requires either melting or dissolution in appropriate solvents. Melt spinning is ruled out as chitin decomposes prior to melting. There have been many attempts at dissolution of chitin and spinning of chitin and CS into fiber form. Table 2 summarizes the various attempts at dissolution of chitin and spinning of chitin into chitin fibers. The preparation of chitin threads for use in the fabrication of absorbable suture materials, dressings, and biodegradable substrates for the growth of human skin cells fibers has been reported [167,168].

5.2. Blending with other fibers/polymers

The incorporation of chitin fibers in synthetic composites and blends is proposed to give interesting properties [353]. The concept of fibers as composites, where hard and stiff phases are combined with softer polymeric materials especially the deformation mechanism of chitin fibers in comparison to other natural and synthetic polymers has been recently discussed by Young and Eichhorn [354]. In the preparation of blends containing alginate and water-soluble chitin prepared by spinning their mixture solution through a viscose-type spinneret into a coagulating bath containing aqueous $CaCl_2$ and ethanol, the strong interaction from the intermolecular hydrogen bonds and electrostatic forces were used to ensure good miscibility [352]. Best values for the dry tensile strength and breaking elongation were obtained when the water-soluble chitin content was 30 wt%. The wet tensile strength and breaking elongation decreased with the increase of water-soluble chitin content. Additionally, the introduction of water-soluble chitin in the blend fiber can improve the water-retention properties of the blend fiber compared to pure alginate fiber. Chitin fibers when treated with aqueous solution of silver nitrate were found to have good antibacterial activity to *Staphylococcus aureus* [352]. Significant improvement in properties have been reported for blends of chitin/CS fibers with various natural fibers/synthetics to get chitin–cellulose, chitin–silk fibroin, chitin–glycosaminoglycans, chitin–cellulose–silk fibroin, CS–tropocollagen, and chitin–cellulose–silk fibroin, chitin–natural rubber blends [25,355–358]. Chitin fibers incorporated as reinforcement in poly(lactic acid) polymer showed suitable mechanical properties and retention for fixing cancerous bone fractures, but likely had insufficient stiffness for applications such as bone plates for fixing cortical bone fractures [359].

Special properties could be built by appropriate chemical modification to generate a series of chemically modified fibers such as N-acylCSs, N-arylidene- and N-alkylidene-

Table 3
Spinning solvents and properties of chitin [25,30].

Solvent (v/v)	FA–DCA[a] (92/8)		FA–DCA-iPE (83/11/5)		FA–DCA–iPE (83/11/5)	
Coagulation, 1st	EA	iPE	Acetone	Acetone–iPE	EA	EA–iPE
Coagulation, 2nd	EA	50% AcOH:EA (2:5)			Cold water (12–14 °C)	
Stretch ratio	1.32	1.10	1.20	1.35	1.29	1.35
Tenacity (g/d)						
Dry (20 °C)	1.32	0.68	1.26	1.59	1.33	1.02
Wet (20 °C)	0.18	0.23	0.16	0.23	0.27	0.14
Elongation (%)						
Dry (20 °C)	2.7	2.9	3.4	2.7	4.3	2.8
Wet (20 °C)	7.8	10.8	4.6	3.6	8.6	4.6
Knot strength (g/d)	0.45	0.45	0.12	0.08	0.24	0.11
Denier	25.5	3.2	2.0	3.0	2.1	2.0

[a] iPE, isopropyl ether; EA, ethyl acetate; AcOH, acetic acid, RH, room humidity.

CSs, N-acetylCS, chitin–tropocollagen and CS–transition metal complexes [25,354,360–362]. Fig. 11 shows a schematic presentation of a typical wet-spinning production line. Table 3 provides some typical data on the chitin properties and the solvents used. The crystallinity and surface charge density of the deacetylated chitin can be increased on treatment with hydrochloric acid treatment to improve the fiber properties [256]. It should be noted that East and Qin employed heat treatment for preparing regenerated chitin by reaction (N-acetylation) between CS and acetic acid [348]. The best properties for tensile strength (4 g/d) and modulus (100 g/d) for chitin were reported by the mixed ester of chitin or CS acetate/formate polymer. Use of chitin wisker route may be of use preparing high strength fibers [363]. Further improvement in fiber properties could be achieved with the application of spinning fiber from lyotropic liquid crystalline solutions [364].

The property of spontaneous orientation from lyotrpoic liquid crystals was utilized to draw fibers from 2 wt% chitin/LiCl/DMAc that gave best spinnability and best quality of fiber after spinning [365]. Both thermotropic and lyotropic liquid crystalline behaviors have been reported on chitin/CS based polymers [366–378], but there are no attempts at fiber spinning. Fiber spinning from liquid crystalline solutions has significant advantages for increased strength and other properties [369]. Irradiation of chitin-fiber-reinforced poly((-caprolactone) composite showed 45% improvement in tensile strength and tensile modulus with respect to those of the untreated specimens [370]. Polymers such as polyvinylpyrrolidone, methyl cellulose, and sulfite cellulose are reported to be used to modify the properties of chitin fibers added to the spinning solution [371]. Further improvement in fiber properties could be effected through appropriate chemical modifications [3,4,6,9,18,23,76,81,83,84,372,373].

5.3. Biodegradation of chitin fibers

Chitin is considered to be highly biodegradable [374] and easily excreted in urine [375]. Onishi et al. in a study on the biodegradability, body distribution and urinary excretion of 50% deacetylated chitin after the intraperitoneal (i.p.) administration to mice using fluorescein isothiocyanate labeling have shown that there is no problem when chitin accumulates in the body [375]. When attacked by natural fungi, CS films have a built-in source of nitrogen to enhance biodegradation. Surprisingly, information on the *in vivo* biodegradability of CSs with differing chemistries and structures, and which are utilized in multiple applications, is lacking. It is generally believed that lysozyme is mainly responsible for CS degradation in the human body. Lysozyme is present in many tissues and secretions such as tears, saliva, blood and milk, and is released and utilized by phagocytic cells during the inflammatory response to a foreign implant [376–379].

Water-soluble succinyl chitin and CS find applications as long circulating polymer for the treatment of arthritis, etc. [380,381]. The biocompatibility and safety of CS have been revealed through tests involving mutagenicity, acute and subacute toxicity, pyrogens, hemolysis, and sensitization [82]. The US Food and Drug Administration considers CS as a food additive in animal feed when used as a precipitating agent for proteineceous materials [382]. Seo has shown that CS when orally administrated to rabbits, broilers and hens at a dosage of 0.7–0.8 g/kg body weight/day for up to 239 days, no abnormal symptoms were observed [82]. Rabbits digested up to 28–38% chitin and 38–79% CS while broilers and hens digested them completely. Rabbits also did not exhibit any abnormal symptom when CS was intravenously injected. It was also observed that the presence of CS enhanced the absorption of drugs when administrated orally [383–389]. The characteristic property of an ideal surgical suture consists of easy biointegration and tissue adaptation until healing occurs without disturbing the healing process. It should also disappear on completion of healing. The currently available absorbable sutures such as alginate, collagen, catgut and branan ferulate have limitations and not always satisfactory. On the other hand, chitin as a wound healing accelerator has great potentialities from the point of view of absorbable surgical sutures.

6. Chitosan fiber

6.1. Fiber formation

Development of fibers from CS was comparatively easy as it was soluble in dilute acids such as acetic acid. Formation of the fiber was reported as early as 1926 [150]. But CS fibers were found to be expensive due to high production cost [330]. This induced researchers to look into

Table 4
Summary of attempts at fiber formation from CS.

	Solvent/process	Blend component	Grafting	Properties	Refs.
1.	Inorganic salts	–	–	–	[460,151]
2.	Deacetylated chitin in acetic acid—dry spinning	–	–	Dissolution of the deacetylated chitin in acetic acid	[341]
3.	2% aqueous acetic acid solvent—wet spinning, regenerated	–	–	Improved thermal stability and tensile strength	[392]
4.	Acetic acid—wet spinning, acetylated	–	Improved dry and wet strengths–good thermal stability	CS is reacetylated to chitin	[348]
5.	DMAc–lithium chloride, wet spinning	–	–	–	[20,21]
6.	DMAc–lithium chloride, after treating chitin with p-toluene sulphonic acid and isopropanol	–	–	–	[25]
7.	N-Acylation, treatment with carboxylic anhydrides	–	–	N-Acyl CS,-lower tensile strength. N-Hexanoyl CS, higher tensile strength	[394]
8.	Coagulation bath containg very small amounts of CS	Sodium alginate filaments	–	–	[395]
9.	Viscose spinning route for blending with collagen.	Tropocollagen	–	1.08–1.65 g/d tenacity, 10.9–43.2% elongation, improved blood compatibility	[396]
10.	Treatment with a series of carboxylic anhydrides and aldehydes	Tropocollagen	–	0.86–1.31 g/d tenacity, 8.0–12.1% elongation	[396]
11.	N-acyl and N-propiopnyl CS mixed with sodium cellulose xanthate in 14% NaOH	Cellulose	–	Filament tenacity and elongation values were 0.4–0.7 times as large as cellulose.	[397]
12.	14% aqueous NaOH	Sodium N-acetyl and sodium hyaluronate, sodium heparin, sodium chondroitin 4-sulfate, sodium chondroitin 6-sulfate, or sodium dermatan	–	Mechanicaly weak, sustained release of glycosaminoglycans–biocompatible dressing materials (artificial skin) in the veterinary and clinical fields	[398]
13.	Acetic acid solution, blending with viscose cellulose	Viscose cellulose	Wet strength (tenacity 2.0 gpd) for CS alone.	Improved antimicrobial property, high biocompatibility, anallergicity, high humidity absorption. Trade name: Crabion®	[399]
14.	FA and acetic anhydride, presence of perchloric acid. Solvent: trichloroacetic acid/methylene chloride	–	–	Tenacity 4 g/den, modulus 100 g/den	[351]
15.	Mixures of 5% CS in 2% aqueous acetic acid	–	–		[77]
16.	Fiber drawn from CS acetate/formate polymer	–	–	Tensile strength (4 g/d) and modulus (100 g/d)	[400]
17.	Wet spinning–acetic acid and acetate with pH greater than 3	–		High tensile strength and bioabsorbable	[401]
18.	Self-assembly at an aqueous solution interface	poly(acrylic acid)	–	–	[364]
19.	CS coating onto alginic acid fibers	Composites with alginic acid fibers	–	(% enlongation, 7.3–29.3 and tenacity 1.2–2.7 cN/dtex)	[402,403]
20.	Aqueous solution of sodium thiocyanate			–	[404]
21.	Aqueous acetic acid solution	Phthalate ions, phosphate ions	–	Highest dry mechanical properties	[405]
22.	Wet spinning–Acid solutions,	–	–	Hollow CS fibers for use in ultrafiltration processes	[406]
23.	Powder chitin and CS mixture with viscose pulp, wet spun	Cellulose	–	High moisture keeping property, good dyeability	[393]

blends or composites with other existing yarns. Production of fibers with chemical modification such as grafting has also been reported. Table 4 provides the attempts at production of CS fiber. CS fibers having similar strength to viscose fibers can be obtained by treating chitin with alkali [342]. Shear precipitation is employed by some researchers to the orientation and crystallinity of the fibers [340]. Structural studies on chitin, CS and butyryl chitin have shown that the three types of filaments differed in their crystalline structure, degree of crystallinity and average lateral crystallite sizes [390]. CS fibers with smooth, regular and uniformly striated surface could be obtained by using a highly deacetylated CS (DA = 2.7%) in a pseudo-dry spinning process [391]. Reaceylation have been employed to generate chitin which could be spun into fibers [24,348,392]. CS is dissolved in acetic acid solution and then extruded through the spinneret into a caustic coagulation bath to obtain a regenerated fiber [392]. However, these fibers have poor wet strength (tenacity 2.0 g/d). The acetylation process was affected by the reaction temperature, the treatment time, and the molar ratio of anhydride to amine groups. The fiber properties are affected by spinning conditions, such as spin–stretch ratio, coagulation bath concentration and drying conditions. Fiber can be produced with tenacities up to 0.24 mN/tex. The acetylated CS fibers, or regenerated chitin fibers, showed good thermal stability and improved dry and wet strengths. It was found that, after acetylation, the fibers had an improved cytocompatibilty and cell adhesion on incorporation of surfactants into the coagulation bath [393]. N-Acylation with longer hydrocarbon side chain resulted in a higher spatial organization of the chain to the long axis and showed lower moisture retention [394]. The chemical structure of CS fibers was gradually altered from hydrated form (anti-parallel structure) to dehydrated form (parallel structure) with the treatment of carboxylic anhydrides.

Improved tenacity of up to 4.4 g/d was obtained by incorporation of surfactants into the coagulation bath. These fibers find use in the production of textiles having antimicrobial, antithrombogenic, hemostatic, deodorizing, moisture controlling, and non-allergenic properties. A composite material of chitin/CS and cellulose produced by mixing powder chitin/CS with viscose pulp and then wet spun showed higher moisture keeping property than cellulosic fibers and has dyeability towards direct and reactive dyes [346]. These fibers have the property of keeping skin from drying with out giving no irritation to skin. These clothes are recommended, therefore, babies and old aged people who have weak and sensitive skin [346]. Apart from their use as sutures, there are several applications such as antimicrobial wound dressings [407–410], bandages and textile scaffolds for tissue culture [407], as reinforcement in hydroxyapatite bone cement [411], etc. The antimicrobial property of CS is strongly affected by factors like molecular weight and pH [41]. Synergistic effects were observed by combining random suture filaments and CS in calcium phosphate cement [411]. Li et al. have used CS fibers for reinforcing porous bone scaffolds and the porosity and pore size of the reinforced scaffolds were both satisfactory [412]. Introduction of CS into the dope of viscose rayon was found to enhance the dyeability, absorbency and bacteriostatic

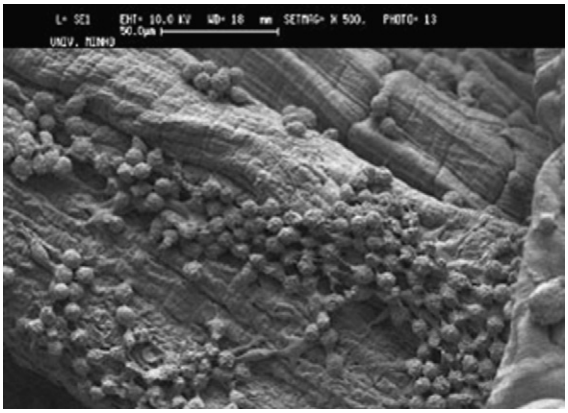

Fig. 12. Osteoblast-like cells proliferating over chotsan based fibers after 7 days of culture (reproduced from Ref. [416] with permission of Wliey–VCH–Verlag).

action of the cellulose fiber. Similar property improvements were observed for alginate fibers also [413–415]. Application studies of CS fibers in 3D fiber mesh scaffolds for tissue engineering showed that both types of structures (fibers and scaffolds) were found to be non-cytotoxic to fibroblasts [416]. Fig. 12 shows the appearance of Osteoblast-like cells proliferating over CS based fibers after 7 days of culture. Qin et al. describes that the antimicrobial properties of CS can significantly improved by introducing silver into CS [417,418]. Shin et al. have shown that CS oligomer imparts antimicrobial finishing to polypropylene non-woven fabric [419]. Properties of CS fibers and properties of CS non-woven fibers are given in Tables 5 and 6 [413]. Urbanczyk studied the fine structural properties such as degree of crystallinity, dimensions of the lattice unit cell and average lateral crystallite sizes as well as morphological features chitin, CS and butyryl chitin filaments and showed that the three types of filaments differed in their crystalline structure, degree of crystallinity and average lateral crystallite sizes [390]. A polypropylene–CS non-woven prepared according to a wet paper method by Niekraszewicz [420] showed stimulation of fibroblast division and accelerates wound healing in animal testing. Fig. 13 shows the surface of the PP/CS non-woven CS fibers. They can be easily processed into non-woven structures and also the fiber surface can be modified by graft copolymerization of vinyl monomers. The crystallinity and surface charge density of the deacetylated chitin have been increased after

Table 5
Some properties of CS fibers.

Property	Specification
(A) Mechanical	
Titre, dtex	1.5–3.0
Tenacity in standard conditions, cN/tex	10–15
Tenacity in wet conditions, cN/tex	3–7
Loop tenacity, cN/tex	3–7
Elongation in standard conditions, %	>10
(B) Structural	
Av. molecular weight, kD	150–300
Polydispersity (Pd)	3.6–6
Crystallinity index, %	35–50

Table 6
Some properties of multi-layer non-woven.

Parameter	Specification
Composition	Fibers PP[a], CS fibers (not more than 15 wt%) in active layer
Specific weight, g/m^2	
Total	80
Active layer	40
Tenacity of supporting layer, N/cm	10
Air permeability 1 m^2 s	1200
Bacteriostatic activity	>0

[a] PP, polypropylene.

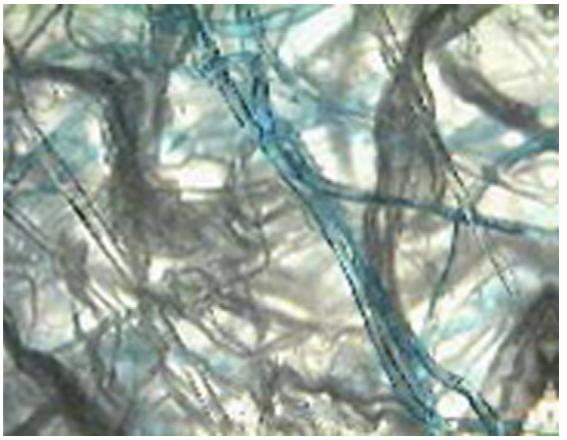

Fig. 13. The surface of the polypropylene/chitosan non-woven, chitosan fibers blue tinted (reproduced from Ref. [420] with permission of Fibers and Textiles in Eastern Europe, Poland).

hydrochloric acid treatment [23]. It has been proved that the DA is significantly lowered when acids other than acetic acid such as formic, propionic and butyric acids are used for derivatisation [256]. The properties of CS–fibroin composite fibers [421] are given in Table 7.

Stęplewski et al. produced alginate–CS fibers by two methods [422]. The first method consists in fiber spinning by feeding CS into a coagulation bath produced alginate–CS fibers with a maximum CS content of about 3.1%. The second method used CS in the finishing process producing alginate–CS fibers with a CS content of up to 9.2 wt%. A maximum tenacity of 22.2 cN/tex and an elongation at break of 19% were obtained for the fiber composite when CS content was as high as 11.6% obtained in the presence of polyvinylpyrrolidione. Fig. 14 shows the SEM photographs of the surface characteristics of the fibers produced by the second method. The properties of blends of CS with various other fibers such as cellulose, silk fibroin, tropocollagen, etc. have been evaluated [23,356,357].

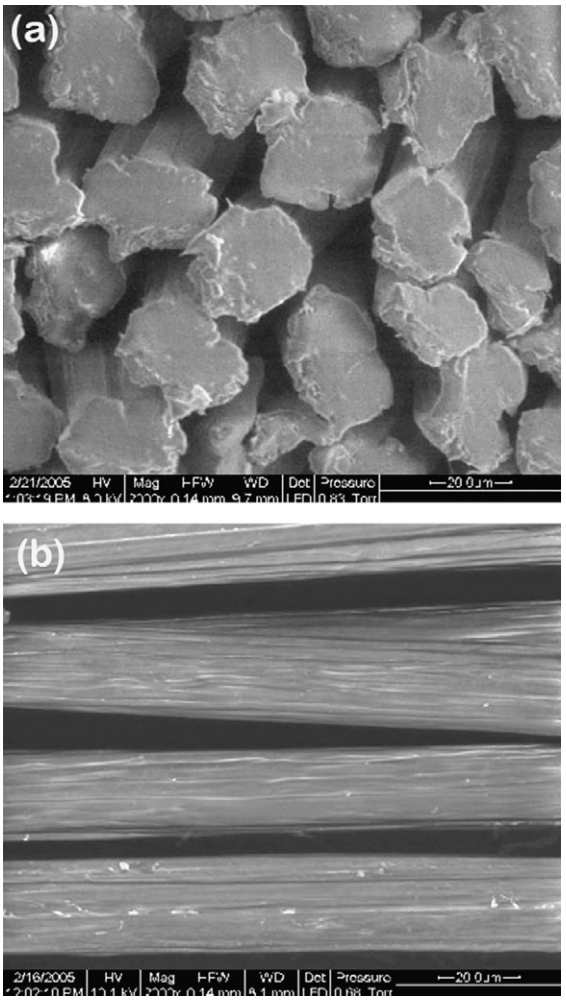

Fig. 14. SEM photos of alginate-CS fibers formed from a spinning solution including 16% of PVP in relation to alginate; (a) cross-sections and (b) surface of the monofilaments (reproduced from Ref. [224] with permission of Fibers and Textiles in Eastern Europe, Poland).

6.2. Biodegradation

When CS is proposed for large-scale use as textile and suture materials, it is important to know its degradation behavior. Several studies have been reported [423–425]. Yang et al. reports that N-acylation can be sued to control the biodegradation of CS fibers [423]. In a study on the use of chitin as a new absorbable suture material, Szosland and others concluded that the chitin fibers fulfill the basic biological requirements set up for the bio-medical devices [235]. Tachibana et al. carried out a comparative study of four absorbable suture materials, namely; chitin, polygly-

Table 7
Properties of CS–fibroin composites [421].

Fiber	Content of fibroin	Tenacity, cN/dtex	Elongation at break, %
CS	0	17.2	9.2
CS–fibroin-1	4	15.9	8.5
CS–fibroin-11	6	15.2	8.1

colic acid (PGA), plain catgut and chromic catgut [426]. The straight pull strength of USP 3-0 size chitin was over 2.6 kg, compared with 3.4 kg of PGA, and 2.0 kg of the catguts [426]. Chitin showed the lowest elongation among the four. The tensile strength retention (TSR) of chitin in muscle was 45% at 14 days and 7% at 25 days, which was similar to that of PGA. The TSR of Chitin was maintained by 35% in gastric juice, 97% in bile and 100% in pancreatic juice after immersion for 30 days. The corresponding values for PGA were 54, 0 and 0%, respectively, whereas both catguts had dissolved within 30 days. The tissue reaction of chitin was similar to that of PGA, whereas the catguts caused more intense tissue reaction [426]. Chitin is considered an appropriate absorbable suture material because it also possesses suitable mechanical properties [28,48]. Masaharu et al. observed good healing which provided evidence for a satisfactory biocompatibility and could not notice any specific tissue reaction [27]. Onishi and Machida examined the biodegradability, body distribution and urinary excretion of randomly 50% deacetylated chitin after the intraperitoneal administration to mice [375]. The *in vitro* biodegradability studies by incubation with lysozyme and murine plasma and urine using fluorescein isothiocyanate labeled CS showed accelerated degradation of CS. Most of labeled CS was excreted into urine after 14 h giving low molecular weight products. Therefore, CS is considered to be highly biodegradable and easily excreted in urine with no problem of accumulation in the body. A study on the influence of physical parameters such as porosity and fiber diameter on the degradation of CS fiber-mesh scaffolds, as a possible way of tailoring the degradation of such scaffolds has shown that the scaffolds with higher porosity degrade faster and that, within the same range of porosity, the fibers with smaller diameter degrades slightly faster. Furthermore, the morphological differences between the scaffolds did not affect the degree of cell adhesion, and the cells were observed throughout the thickness of all four types of scaffolds [427].

6.3. Blending with other fibers

The biological properties, toxicity, skin physiology, etc. of CS have been reported by several authors [132,211,424,428–434]. Modification with gelatin showed that the modified CS fibers have an improved mechanical property and biocompatibility [430]. The lysozyme biodegradation test on collagen/CS scaffolds demonstrated that the presence of CS, especially the high-molecular weight species, could significantly prolong the biodegradation. *In vitro* culture of L929 mouse connective tissue fibroblast evidenced that low-molecular weight CS was more effective to promote and accelerate cell proliferation, particularly for scaffolds containing 30 wt% CS. The results elucidated that the blends of collagen with low-molecular weight CS have a high potential to be applied as new materials for skin–tissue engineering [431]. Nanofibrous composite of poly(lactide-co-glycolide) (PLGA) and CS/poly(vinyl alcohol) (PVA) membranes prepared by simultaneously electrospinning PLGA and CS/PVA from two different syringes showed that the introduction of CS/PVA component changed the hydrophilic/hydrophobic balance

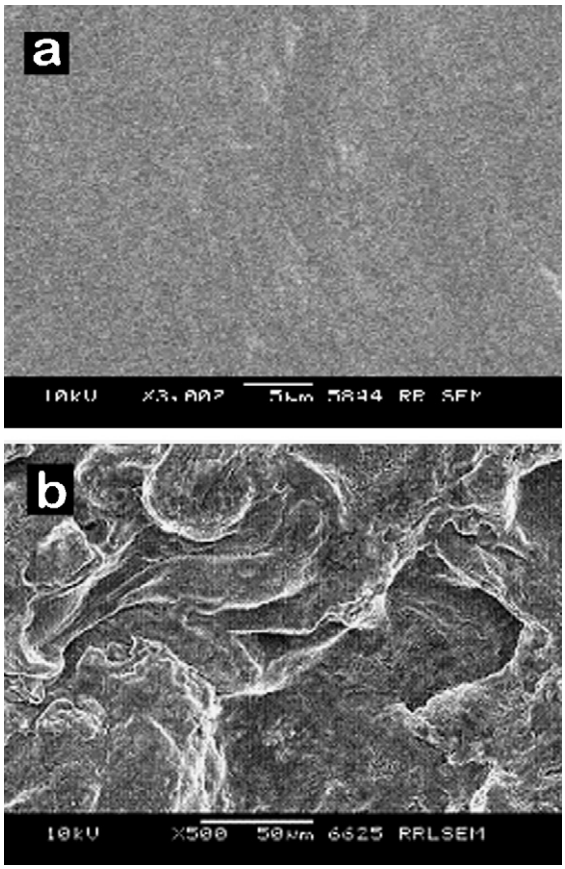

Fig. 15. SEM micrographs of hydrolytically degraded samples taken after 80 days of immersion in deionized water (a) chitosan/oligo L-lactide graft copolymer before degradation and (b) chitosan/oligo L-lactide graft graft copolymer after degradation (reproduced from [435] with permission of Elsevier Science).

and, thus, influenced degradation behavior and mechanical properties of the composite membranes during degradation [433]. The cells could not only favorably attach and grow well on the composite membranes, but were also able to migrate and infiltrate the membranes. Therefore, the results suggest that the composite membranes can positively mimic the structure of natural extracellular matrices and have the potential for application as three-dimensional tissue-engineering scaffolds for human embryo skin fibroblasts (hESFs) culture [433]. Studies by Gisha and Pillai showed that the rate of degradation of CS–polylactide graft copolymers can be controlled by adjusting the amount of lactide content in the CL graft copolymers, with biodegradation decreasing with increase in LLA content which may find wide applications in wound dressing and in controlled drug delivery systems [435]. Fig. 15 shows that hydrolytic degradation takes place preferentially on the amorphous portion of graft copolymer and the resulted short chains are dissolved out into water by creating pores on the surface.

6.4. Structural modification

Researchers are focusing on the modification of structure of chitin polysaccharides with a view to enhance the

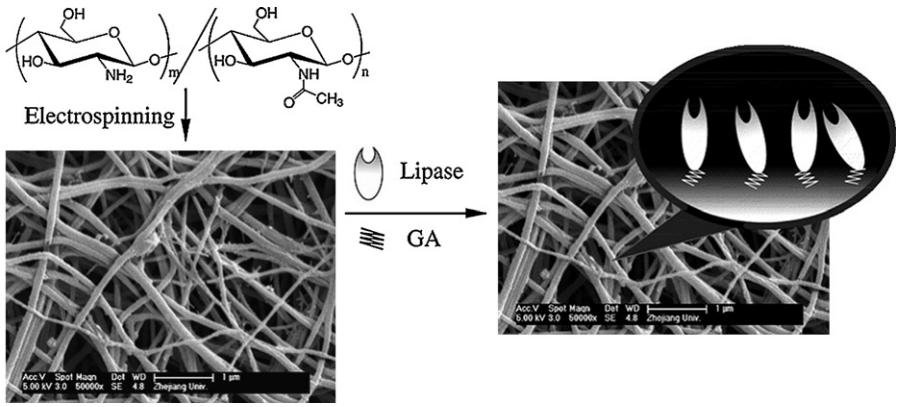

Fig. 16. Schematic representation for lipase immobilization on the chitosan nanofibrous electrospun membrane (reproduced from Ref. [444] with permission of Elsevier Science, Amsterdam).

mechanical and chemical properties. Agnihotri et al. has shown that chemical modification of CS has improved the stability of the polymer [436]. Chitin with enhanced tensile strength (4 g/d) and modulus (100 g/d) was produced from chitin or CS acetate/formate polymer [349,350]. Fibers spun from lyotropic liquid crystalline solution possess highly oriented chains both in amorphous as well as crystalline regions and thus offer higher breaking strength and modulus [363]. Knaul et al. showed that the properties of chitin produced by microwave-medicated reaction are at par with those derived from conventional chemically modified ones [437,438]. A blend of CS with konjac glucomannan (KGM) fibers showed good antibacterial activity to *Staphylococcus aureus*. The structure analysis by FTIR, SEM and XRD indicated that there were strong interaction and good miscibility between the CS and KGM molecule which resulted from strong intermolecular hydrogen bonds [439]. Coating cellulose with CS, it was shown that novel bioactive cellulosic-CS fibers could be developed [440]. The post-chemical modification of CS fiber gives rise to a series of chemically modified fibers: N-acylCSs, N-arylidene- and N-alkylidene-CSs, N-acetylCS (chitin)-tropocollagen, and CS–transition metal complexes with significant property changes [24].

7. Chitosan fibers and blends by electrospinning technique

Electrospinning is emerging as a promising and highly versatile method to process solutions or melts, mainly of polymers, into continuous fibers with diameters ranging from a few micrometers to a few nanometers [372,441]. Application of this method has provided CS nanofibers and CS fiber blends with nanofibers with improved properties [442]. Parameters such as type of solvent (fluorinated solvents such as trifluoracetic acid, fluoroalcohols, etc. are also being used for electrospinning [442]), pH, concentration of CS viscosity, charge density, applied voltage, solution flow rate, distance from nozzle tip to collector surface and time play a role in the characteristics of the obtained nanofibrous structures [443]. It was shown that for longer production time, the nanofibers split and form short side arms on the main fiber possibly due to distortion of the electrical field during fiber deposition [443].

The electrospinning process was employed by Xu and coworkers [444] to prepare stabilized CS nanofibrous membrane as support for enzyme immobilization. Fig. 16 shows the schematic representation of lipase immobilization on CS nanofibers. CS can provide an optimal microenviron-

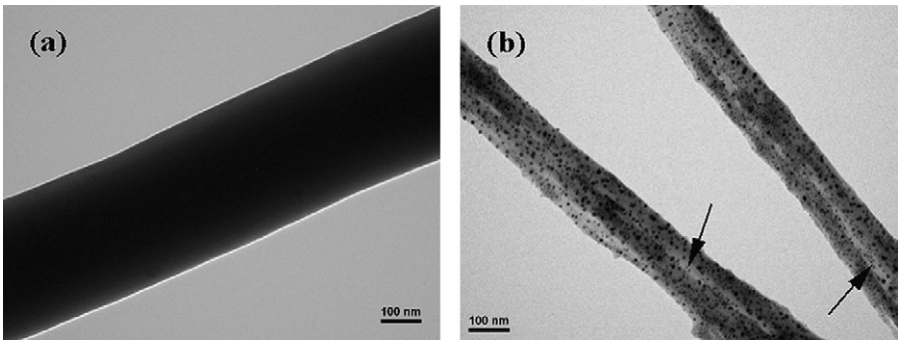

Fig. 17. TEM photographs of (a) original chitosan/PVA nanofiber without any treatment and (b) the nanofiber after 4 h treatment in 0.5 M NaOH (reproduced from Ref [444] with permission of Elsevier Science, Amsterdam).

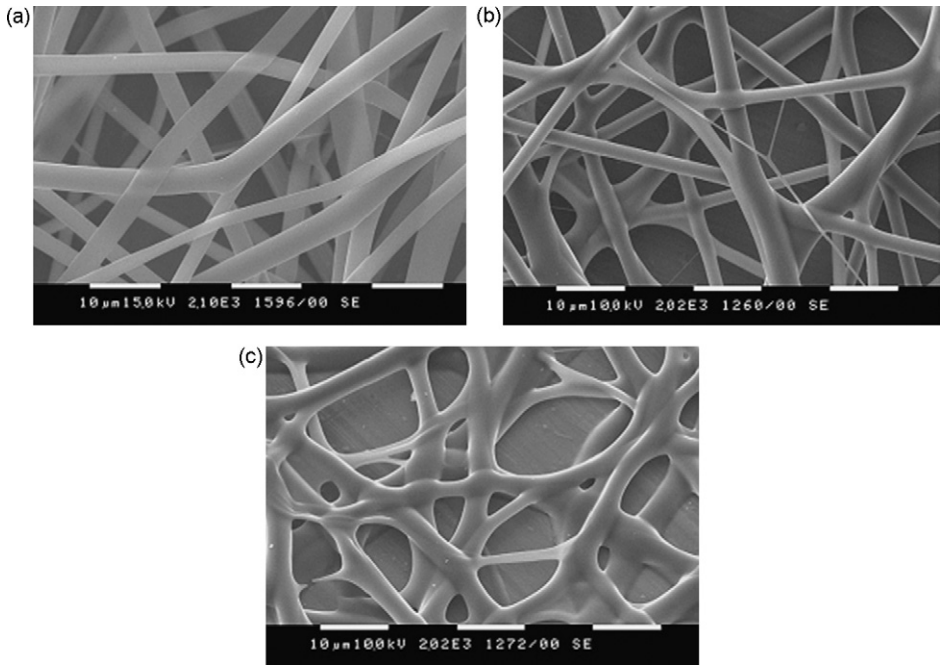

Fig. 18. Effect of the water vapor and water on the morphology of the photo-crosslinked quaternized chitosan/PVP fibers. Non-treated photo-crosslinked mat (a), after contact with water vapor for 6 h (b), and after contact with water for 6 h (c). Weight ratio QCS:PVP = 2:3, total polymer concentration 20 wt% (H_2O:DMSO = 92:8 w/w), AFS 2.2 kV/cm (reproduced from Ref. [448] with permission of Elsevier science, Amsterdam).

ment for the immobilized enzyme to maintain relatively high biological activity and stability. CS nanofibrous membrane was directly fabricated from a mixed solution of CS with poly(vinyl alcohol) (PVA) and then treated in a NaOH solution to remove PVA and stabilize the morphologies of CS nanofibrous membrane in aqueous media. Treatment with 0.5 M NaOH could remove most of the PVA in the nanofibers as can be seen from Fig. 16.

It can be seen that the nanofiber after the removal of PVA was covered by elongated surface grooves and pores along the fiber direction (Fig. 17b), while the original CS/PVA nanofiber showed a regular fibrous structure and smooth surface (Fig. 17a). The study involving the enzyme loading, activity and kinetic parameters, optimum pH and temperature, reusability and storage stability of the immobilized lipase, etc. demonstrated that CS nanofibrous membrane with stable morphology could be prepared by this process for enzyme immobilization.

In another development, introduction of a dry-jet-stretching step could improve the mechanical properties of the CS fibers substantially (Young's modulus of 82 g/d and tenacity of 2 g/d) [445]. Ignatova and coworkers proposes that the CS nanofibrous obtained by electrospun mats are promising for wound-healing applications as they could demonstrate the antibacterial activity of the photo-crosslinked electrospun mats against *Staphylococcus aureus* and *Escherichia coli*. The fibers were prepared by electrospinning of quaternized CS solutions mixed with poly(vinyl alcohol) [446]. Their group also prepared successfully nanofibers of the polyampholyte (N-carboxyethylCS) by electrospinning adding a non-ionogenic water-soluble polymer poly(acrylamide) to the spinning solution [447]. The electrospun mats dissolved when put in contact with water or water vapor. To render the nanofibers insoluble, experiments on their cross-linking were performed by heat treatment. They could achieve the preparation of continuous defect-free fibers from quaternized CS (QCS) derivative by electrospinning of mixed aqueous solutions of QCS with poly(vinyl pyrrolidone) (PVP) [448]. Fig. 18 shows the effect of water vapor on the nanofibers [448]. On blending with poly(ethylene oxide), CS nanofibers could be produced with diameters in the range 40–290 nm by electrospinning of CS/poly(ethylene oxide) (PEO) blend aqueous solutions. The diameters of the nanofibers were in the range 40–290 nm [449].

Ultrafine fibers could be generated by controlling the addition of PEO in 2:1 or 1:1 mass ratios of CS to PEO from 4–6 wt% CS/PEO solutions [450]. It was also shown that addition of PEO brings about additive effects in enhancing the formation of a fibrous structure [451]. A scanning electronic microscopic study showed that electrospun CS fiber mats were indeed aligned and there was a slight cross-linking between the parent fibers. The electrospun mats have significantly higher elastic modulus (2.25 MPa) than the cast films (1.19 MPa). Viability of cells on electrospun CS mats indicated the potential to be processed into three-dimensional scaffolds for cartilage tissue repair [452].

In an interesting study based on cell stain assay and SEM imaging, CS nanofibers produced by electrospinning were shown to exhibit cellular biocompatibility [453]. It was found that the nanofibrous structure promoted the attachment of human osteoblasts and chondrocytes and maintained characteristic cell morphology and viability throughout the period of study [453]. Bead formation was

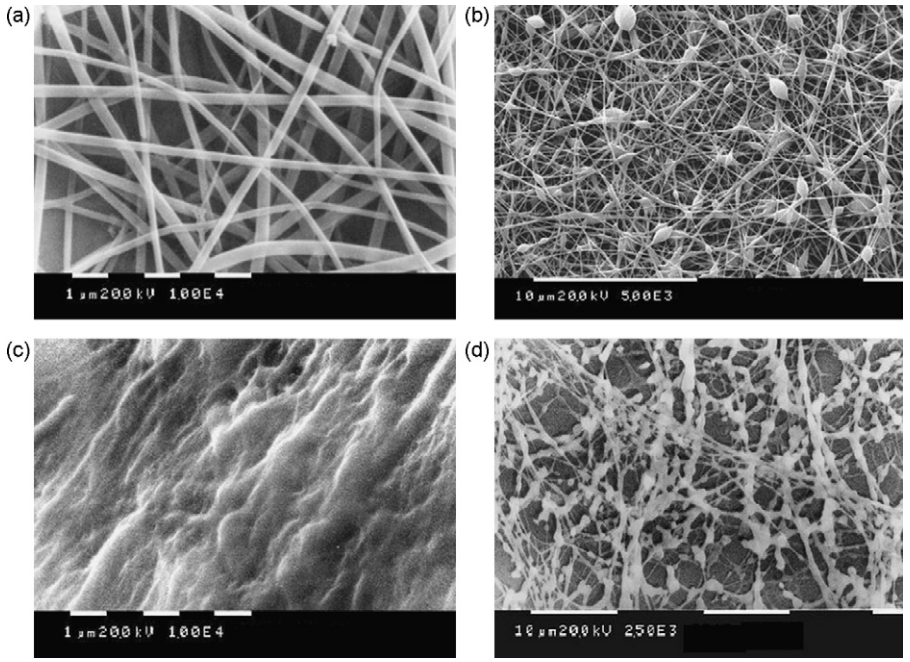

Fig. 19. SEM micrographs of nanofibers containing N-carboxyethylchitosan and PVA at weight ratio CECS/PVA = 1:8 (a and c) and 1:3 (b and d) after heating at 100 °C for 10 h (a and b) and after subsequent contact with water for 1 week (c and d); AFS 1.6 kV/cm (reproduced from Ref. [457] with permission of Elsevier Science).

found to occur during electrospinning and could be controlled by controlling the molecular weight of CS and the solvent used for spinning [454,455]. Blended fibers of hexanoyl CS/polylactide blend fibers were prepared without the presence of beads by electrospinning from solutions in chloroform with the H-CS solution content of less than or equal to 50% (w/w) [455]. In another, bicomponent system consisting of poly(vinyl alcohol) (PVA, M_w = 124–186 kDa) and 82.5% deacetylated CS (M_v = 1600 kDa) in 2% (v/v) aqueous acetic acid, fewer beaded structures and more efficient fiber formation were observed on electrospinning with increasing PVA contents. The improved uniform distribution of CS and PVA in the bicomponent fibers was attributed to better mixing mostly due to the reduced molecular weight and to the increased deacetylation of the CS [456]. On replacing CS by N-carboxyethylchitosan (CECS), it was observed that the electrospinning of CECS-containing nanofibers was enabled by the ability of PVA to form an elastically deformable entanglement network based on hydrogen bonds. The average diameters of the bicomponent fibers were in the range 100–420 nm [457].

Nanofibers of ionogenic polymers are thus of great interest because of the peculiarities of the polyelectrolytes, and also because of the possibility of nanofiber modification on a subsequent step. Incorporation of polyacrylamide into N-CECS allowed the preparation of fibers with average diameters 50 nm; the difficulties in cross-linking the fibers focused the search to the preparation of nanofibrous CECS-based materials using PVA as the second component [457]. PVA is known to be a non-toxic, non-ionogenic and water-soluble polymer. Therefore, the nanofibrous materials prepared by electrospinning of CECS/PVA aqueous solutions, dissolved when put in contact with water as can be seen from Fig. 19. Cross-linking by heating was adopted to stabilize the system, but after heating at 100 °C the fiber structure collapsed for the high PVA system whereas the CECS/PVA mat at low PVA content was promising. It is proposed that the CECS/PVA nanofibrous mats can find application as tissue engineering scaffolds [457].

FTIR, XRD, and DSC studies demonstrated that there were strong intermolecular hydrogen bonds between the molecules of CS and PVA in the PVA/CS blend nanofibrous membranes [458]. SEM images showed that the morphology and diameter of the nanofibers were mainly affected by concentration of the blend solution, weight ratio of the blend, respectively [458]. It appears that electrospinning may emerge as a versatile method to manufacture CS fibers.

8. Structure–property correlation

8.1. Comparative evaluation of the merits of various processes

It is appropriate at this stage to discuss the comparative merits of various methods that have been developed for fiber formation and spinning of chitin and CS polymers. One of the major hurdles was the necessity to use strong acids and polar solvents to induce chitin solubility [6,18,112–114]. Chlorohydrocarbons used in some processes [159–165] are well known as environmentally unacceptable solvents and HFP and HFAS [169–171] are toxic. CH [157,158] is a sedative and hypnotic drug. FA can act as a sensitizer. At very high levels, carbon disulfide [171–175] may be life-threatening because it affects the nervous system. Apart from the environmental concerns of using strong acids and polar solvents, there is the problem of serious degradation

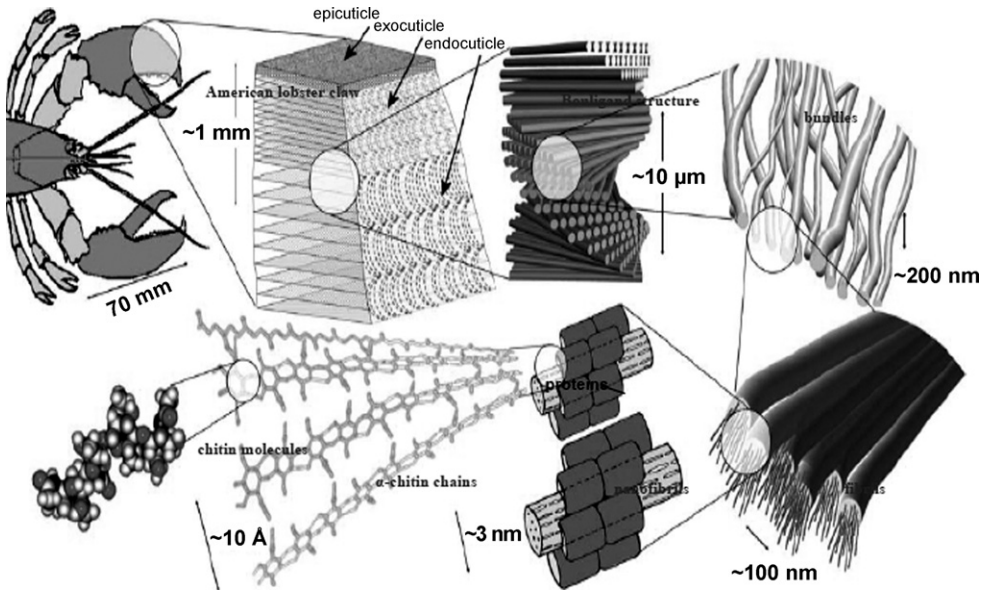

Fig. 20. The Hierarchical structure of cuticles showing the ordered structure of chitin (reproduced from Ref. [463] with permission of Elsevier Science Ltd.).

of chitin by cold concentrated acids reducing the strength of the fibers substantially [18,459].

The problem of removal of the solvents some of which are high boiling is also to be looked into. Certain after-treatments were required in some cases to remove them. This is especially applicable in the case of trichloroacetic acid and chloral that exhibit a strong affinity for chitin [166]. When Lithium thiocyanate [152] was used, solvent removal was not successful even at 200 °C [50]. Some of the processes gave low wet tenacities probably due to low crystallinity and poor consolidation of the fiber. Although dry tenacities of above 3 g/d could be achieved with some of the halogenated solvent systems and the amide–lithium system, the wet tenacities were still low.

The solvent system that has been highly used by many researchers for fiber drawing and fiber studies consists of LiCl–DMAc or LiCl–NMP [68,158,183]. It is to be noted here that the stability of chitin precipitated from this solvent system is yet to be investigated. Moreover, it has been observed that LiCl cannot be completely removed. So, applications of chitin obtained from this process in biomedical area require careful consideration.

Of the several techniques adopted to induce better solubility for chitin, the formate–acetate technique [348,349] appears to be more practical and cost effective and provides fibers of comparatively better properties for biomedical applications than those of other processes. The solubility of chitin-based polymers has been enhanced by introducing organic substituents such as acetate and formate which facilitate dissolution in organic solvent systems, e.g. trichloroacetic acid/methylene chloride by disrupting the crystalline, strongly hydrogen-bonded structure of native chitin, which itself constitutes a significant barrier to dissolution. The loss of molecular weight as evidenced by a decrease in solution viscosity with time is greatly reduced with the mixed substituent derivatives. Mixed substituent derivatives such as acetate/formate are especially attractive in aiding the dissolution and spinning processes in that their fiber-forming ability and viscosity are very well suited for spinning at concentrations exceeding 10 wt% and would therefore be attractive for commercial scale manufacture. The chitin acetate/formate and CS acetate/formate derivatives can be extruded from optically anisotropic solutions through an air gap and into a coagulating bath to form high strength fibers.

The preparation of chitin fiber through the butyryl chitin process [213,218] could have served better, but for the reagent butyric anhydride whose smell could be intolerable. This problem is, however, compensated when the fiber spinning is made quite simple by using a common solvent such as ethyl alcohol that serve as solvent for the polymer and as a component of the coagulation bath [220].

The viscosity of calcium chloride–methanol process [200] which is considered to be environmentally friendly is so high that practical limits of spinning might restrict its large scale application. Another process [155] that has recently emerged uses NaOH–urea solution to dissolve chitin, but it requires a low temperature of −20 °C as the appropriate temperature for its operation as chitin aqueous solution is sensitive to temperature and will transform it to a gel when temperature increases. Possibly, a gel stretch technique that additionally provides orientation to the other fibers could be evolved [460].

In the case of CS, electrospinning appear to be emerging as a promising and highly versatile method to process solutions or melts, mainly of polymers, into continuous fibers with diameters ranging from a few micrometers to a few nanometers [442–458]. Although initial results on using the xanthate process [171–175] were not encouraging for chitin fiber development, recent findings involving the acetyl derivative of CS have given rise to CS fibers that are white and having good mechanical properties [461].

Ionic liquids represent a unique class of solvents that offer unprecedented versatility and tunability. Recent work

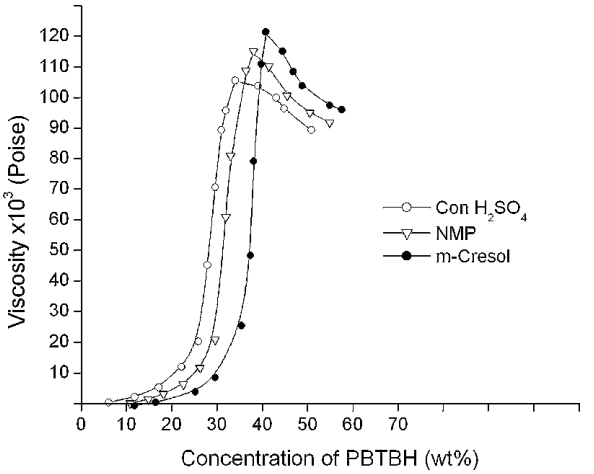

Fig. 21. Viscosity behavior of lyotropic polymers under shear as a function of concentration (reproduced from 474 by permission of Elsevier).

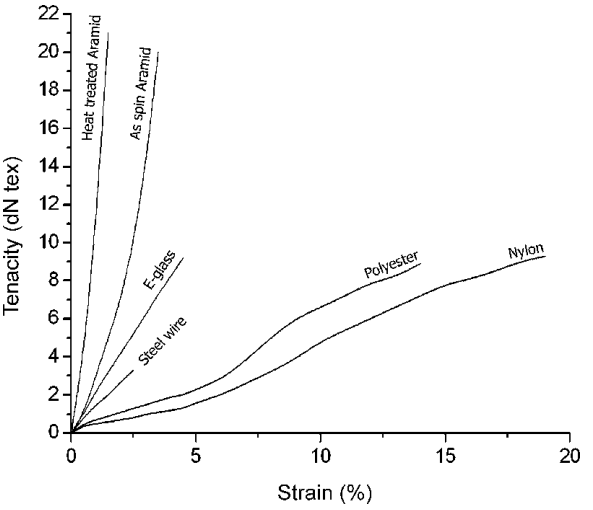

Fig. 22. Stress–strain behavior of Kevlar fiber in comparison with other fibers (reproduced from [471] by permission of Wiley-VCH-Verlag GmbH & Co. KGaA).

has shown the potential of ionic liquids as solvents for the dissolution and processing of biopolymers. Although it is costly, it would be worthwhile to try ionic liquid for fiber formation of chitin and CS [111,462].

8.2. Strategies to increase chitin fibers strength

The preceding discussion possibly indicates that there exists several inadequacies in terms of both technology and cost of production as far as the present status of the production of chitin fiber is concerned and therefore, it appears that there exists a lacuna for newer methods to be evolved. The following is a discussion for evolving a strategy for the development of high strength fibers from chitin. As discussed earlier, chitin occurs in nature as ordered crystalline microfibrils forming structural components in the exoskeleton of arthropods or in the cell walls of fungi and yeast. It is also produced by a number of other living organisms in the lower plant and animal kingdoms, serving in many functions where reinforcement and strength are required [43,212]. Fig. 20 shows the hierarchical structure of chitin microfibrils in the cuticle of a lobster [463]. The exocuticle (outer layer) is characterized by a very fine woven structure of the fibrous chitin–protein matrix ('twisted plywood' structure) and by a high stiffness (8.5–9.5 GPa). The observation of a parallel array of microfibrils brings the hope that there is possibility of improving the mechanical properties of chitin fibers [464]. The polyamide-type structure with polysaccharide backbone is expected to generate, as in the cases of cellulose and aramide, organized fluid phases with a pronounced anisotropy in shape that self-assembles to give spontaneous orientation and so impressive properties for the fibers can be generated in solution. The viscosity of lyotropic liquid crystalline polymers has been shown to increase steeply with concentration to a sharp maximum (critical concentration) and then falls [465] (Fig. 21). This behavior, as against the monotonically increasing viscosity of conventional polymers, is typical of polymers having liquid crystalline phases. The phenomenon of the peculiar effect of the concentration and molecular weight on viscosity was originally described by Flory [466] and later Hermans [467] for polypeptides and also later described by Paplov et al. [468] for polybenzamide. The viscosity of lyotropic liquid crystalline solutions goes through a maximum and this point can be associated with the phase transition [465–469]. The drastic drop in inherent viscosity and the appearance of the anisotropic phase can be made use of for generating the organized phases by making use of appropriate concentration and spinning technique for better strength. This method has been utilized in the development polyaramide fibers by Dupont [470–472]. While chitin has a polymer backbone similar to that of cellulose, it has amide pendant groups that give rise to extensive hydrogen bonding. So, the strength of chitin can be equivalent to or slightly above that of cellulose. The strength could be further improved by inducing the orientations typical of liquid crystalline behavior. The crustacean exoskeleton is an example of a structurally and mechanically graded biological nanocomposite material [463].

Fig. 22 gives a comparison of the strength properties of a few fibers in comparison with polyaramide (poly(p-phenyleneterephthalamide)) commonly known as Kevlar. Apart from contributions from the extensive hydrogen bonding as shown in Fig. 23, the hierarchical arrangement of the fiber (Fig. 24) resulting from the organized flow due to the mesophase structures, have pronounced influence on the fiber properties [470–472]. Because these polymers are very rigid and rod like, in solution they can aggregate to form ordered domains in parallel arrays [473]. This is contrasted to more conventional, flexible polymers, which in solution can bend and entangle, forming random coils [474].

There were some earlier attempts towards fiber formation through the liquid crystalline phase [363,364,475]. But, the approach of using the liquid crystalline phases above the critical viscosity under shear conditions might generate better properties. The structural hierarchy of arrangement

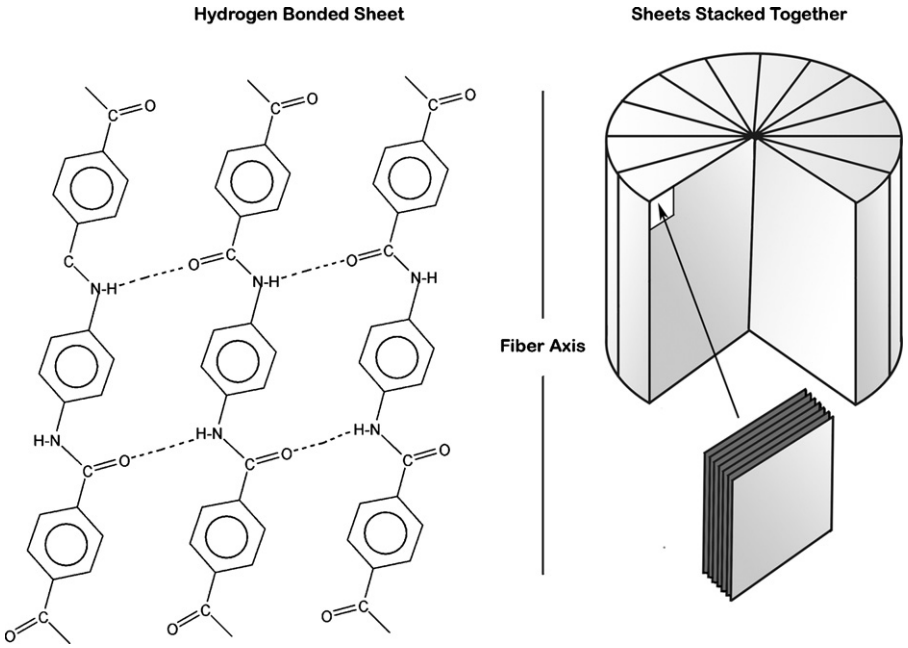

Fig. 23. The hydrogen bonding and the perfect sheet like stacking in polyaramide structure (reproduced from [471] by permission of Wiley-VCH-Verlag GmbH & Co. KGaA).

of chitin polymer [463], Fig. 20 might not be exactly parallel to that of polyaramide. Chitin has a polysaccharide back bone whereas Kevlar has polyamide back bone structure. The amide groups are pendant to the polysaccharide backbone. So, contribution of hydrogen bonding through the amide groups to the strength may not be as expected [476]. However, the spontaneous orientation achieved during spinning from a lyotropic solution will be considerable and hence it is possible to prepare chitin fibers with improved strength by making use of the mesophase properties of chitin. High strength cellulosic fibers have been prepared using the liquid crystalline phase behavior [477].

9. Novel applications

Porous CS fibers have been shown to be useful as reinforcement in CS based nerve conduits fabricated from CS yarns and a CS solution by combining an industrial braiding method with a mold casting/lyophilization technique [478]. The compressive load of the reinforced conduits was significantly higher than that of a non-reinforced control conduit at equal levels of strain. The tensile strength of the reinforced conduits was also increased from 0.41 ± 0.17 to 3.69 ± 0.64 MPa. An *in vitro* cytotoxicity test showed the conduits were not cytotoxic to Neuro-2a cells. Preliminary *in vivo* implantation testing indicated that the conduits were compatible with the surrounding tissue [478,479]. Another significant development is in the area of cartilage engineering. A novel approach involving a replica molding technique for the production of fibers with controlled dimensions in the micron regime from CS as fibrous CS scaffolds was demonstrated recently [480]. A three-dimensional scaffold fabricated from the CS-based hyaluronic acid hybrid polymer fibers whose porous structure could be controlled was also recently developed [481]. These scaffolds showed high mechanical properties compared with liquid and gel materials. The data derived from this study suggest great promise for the future of a novel fabricated material with relatively large pore size as a scaffold for cartilage regeneration. In another interesting development, CS and cellulose acetate (CA) blend hollow fibers with high CS contents were prepared through the use of a non-acidic organic dope solvent. The CS/CA blend dope solution for spinning the blend hollow fibers was prepared by the addition of CA into nanoparticles of CS (about 50–150 nm) prepared using a surfactant, sodium dodecyl sulfate (SDS) and dispersed in NMP. FTIR analysis indicated that SDS interacted with CS. The blend hollow fibers were highly porous and gave a tensile stress at break greater than 1–2 MPa [482]. Yet another interesting work reports that the surface of poly(ethylene terephthalate) (PET) textiles was modified by electrospinning a blend of PET/CS nanofibrous mats. The method introduced antibacterial activity and biocompatibility to the surface of PET textiles [483]. In combination with alginate fibers, CS could be fabricated into a fibrous scaffold for annulus fibrous cell culture using a wet-spinning and lyophilization technique. The work also demonstrated the feasibility of using this scaffold for application for intervertebral disc tissue engineering [484]. Chitin fibers are also finding applications in wool knitted fabrics [485]. Novel methods have been recently devised for the preparation of chitin threads for the fabrication of absorbable suture materials, dressings, and biodegradable substrates for the growth of human skin cells (keratinocytes and fibroblasts) [168]. Chitin fibers have been extracted recently using ultrasonic techniques to obtain fibers with uniform diameters in the range of 25–120 nm and possessing the optimized hierarchical supramolecular structures

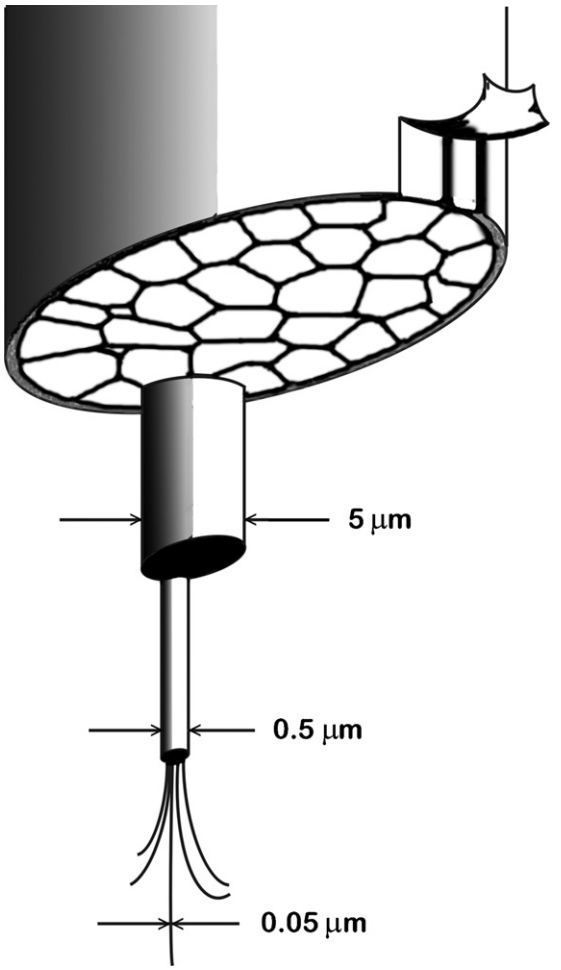

Fig. 24. Cross-section of aramide fiber showing hierarchy of arrangement (reproduced from [471] by permission of Wiley-VCH-Verlag GmbH & Co. KGaA).

[486]. This methodology might be valuable to provide a convenient, versatile, and environmentally benign fabrication method for producing bionanofibers at an industrial scale.

A recent article reports the finding of the occurrence of silica–chitin fiber composite in skeletons of marine sponges. This is the first report of a silica–chitin's composite biomaterial found in nature. From this perspective, the view that silica–chitin scaffolds may be key templates for skeleton formation [487]. This structural information could be useful in developing scaffolds for tissue engineering and other applications. In an vitro study on the degradation and biocompatibility of poly(L-lactic acid)/CS (PLLA/CS) fiber composites, excellent adhesion between osteoblast and PLLA/CS fabrics was observed, indicating good biocompatibility of the fabrics with osteoblast and its possible use as supporting materials for chest walls and bones [488]. Chitin fiber is also employed to fabricate novel biomimetic nanostructured bicomponent scaffolds consisting of chitin and silk fibroin (SF) nanofibers by an electrospinning process. Cytocompatibility and cell behavior studies on this system indicated that the hybrid matrix with 25% chitin and 75% SF could be a potential candidate for tissue engineering scaffolds [489].

10. Conclusion

Chitin and CS are biopolymers having immense structural possibilities for chemical and mechanical modifications to generate novel properties, functions and applications especially in the biomedical area. Despite its huge availability, the utilization of chitin has been restricted by its intractability and insolubility. Several attempts have been reported on solving these problems, which have been reviewed. However, there are several drawbacks that need to be addressed. The corrosive and degradative nature of solvents has always been a problem. Additionally, the environmental acceptability of these solvents has to be assessed. The high viscosities of chitin solution in certain solvents create difficulties in processing and need to be tackled. With all problems, fibers with excellent properties equal to or better than cellulose have emerged. The best properties for tensile strength (4 g/d) and modulus (100 g/d) for chitin were reported by the mixed ester of chitin or CS acetate/formate polymer. The data available in the case of cellulose fibers and similar fibers could be of potential reference for further development. Chemical modification is another possibly route through which improvement in fiber properties could be achieved. The application of electro-spinning method for the production chitin nanofibers which can possibly improve fiber properties remarkably needs also to be stressed here. Further improvement in fiber properties could be achieved with the application of spinning fiber from lyotropic liquid crystalline solutions.

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