7

Recent Progress in the Utilization of Chitin/Chitosan for Chemicals and Materials

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7.1 Structure, Source and Properties of Chitin/Chitosan

Chitin was first identified in 1884, and it is a linear biopolymer synthesized from units of 2-acetamindo-2-deoxy-D-glucose through covalent β-(1–4) linkages [1], as shown in Figure 7.1. It can be considered as a derivative of cellulose (Figure 7.2) with the C(2)-hydroxyl group replaced by an acetamide group. The repeating units of chitin can be up to 1000–3000, and its weight-average molecular weight ranges from 1.03×10^6 to 2.5×10^6 depending on its source and isolation conditions [2].

Chitin is the second most abundant natural polysaccharide next to cellulose. As estimated, the annual production of chitin is around 10^{12}–10^{14} tons in the biosphere on Earth, and it is mainly produced by living organisms in nature [3, 4]. Chitin is a characteristic constituent of the exoskeletons of arthropods such as crustaceans (e.g. lobsters, crabs and shrimps) and insects, the beaks and internal shells of cephalopods (including octopuses and squid), as well as the cell walls of fungi, yeast and algae [5–7]. Moreover, chitin can also be synthesized by the chitinase-catalyzed polymerization of a chitobiose oxazoline derivative

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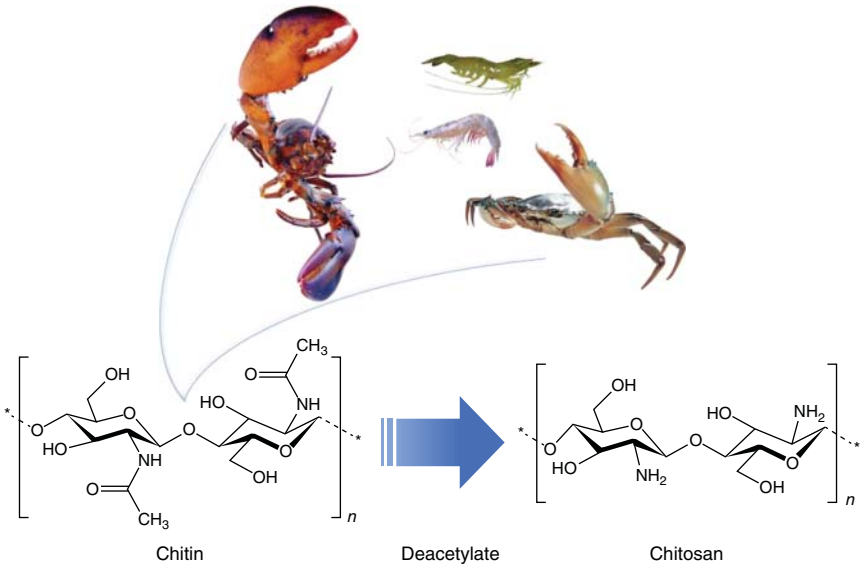


Figure 7.1 *Sources of chitin and the structure of chitin and chitosan.*

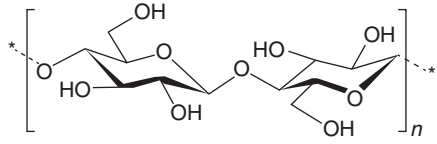


Figure 7.2 *The structure of cellulose.*

(a non-biosynthetic pathway) [8, 9]. In nature, similarly to cellulose, chitin occurs as a highly ordered crystalline structure presenting in three polymorphic forms: α-, β- and γ-chitin [4]. As already known, α-chitin widely exists in a lot of living organisms, is by far the most abundant form and is stable with antiparallel polymer chains, while the polymer chains in the rarer β-chitin (presenting in tubeworms and squid pens) are parallel. With respect to γ-chitin, two of the three chains are parallel and the third one is antiparallel [2]. γ-Chitin is occasionally observed in mollusca and brachiopoda, and it can be thought of as a variant of the α-chitin [10]. These chains are aligned with each other through intra- and intermolecular hydrogen bonds between the carbonyl groups and the amide groups of the nearby chains. In living organisms, chitin chains form crystalline nanofibrillar arrangements, and these fibrils are embedded in a protein matrix with diameters in the range of 2.5–2.8 nm [1]. Compared to α-chitin, N-deacetylation or degradation of β-chitin via chemical or enzymatic approaches [2, 11] is easier, due to its loose packing of molecules.

Chitosan is a very important derivative of chitin, and it can be produced by deacetylation of chitin via chemical or enzymatic methods (Figure 7.1). Chitosan consists of randomly distributed β-(1–4)-linked D-glucosamine (deacetylated unit) and *N*-acetyl-D-glucosamine (acetylated unit) [12]. The molecular fraction of deacetylated unit and acetylated unit is expressed as a degree of deacetylation (DD) and degree of N-acetylation (DA), respectively. DD has influential impact on chitin solubility and solution properties. Chitin is not soluble in water because its DA is typically about 0.90. When DA is lower than 0.50, it becomes soluble in aqueous phase, and it is the so-called chitosan. The typical DA of chitosan is less than 0.35, and 100% of DD is almost never achieved [1, 2].

Chitin is white, hard, inelastic and highly hydrophobic. It is insoluble in water and most organic solvents. The nitrogen content of chitin varies from 5% to 8% depending on the extent of deacetylation, whereas the nitrogen in chitosan is mostly in the form of primary aliphatic amino groups. The percentage of nitrogen in chitin/chitosan is significantly higher than that (1.25%) of synthetically substituted cellulose [1]. However, chitosan is soluble in water and dilute acids (e.g. formic acid, acetic acid). The relatively pure D-glucosamine can also be obtained by hydrolysis of chitin with concentrated acids under drastic conditions. Both chitin and chitosan are biocompatible, biodegradable and non-toxic. As displayed in Figure 7.1, there are reactive amino groups in the molecule of chitosan. Thus, chitosans have good ability to chelate metal ions. On the other hand, compared to cellulose, modification of chitosan by chemical reactions (such as N-acylation and Schiff base reactions) is much easier. Therefore, chitin/chitosan has large applications in the fields of food, biomedicine, water treatment, cosmetics and agriculture [2, 4, 6, 7].

7.2 Isolation and Purification of Chitin/Chitosan

As mentioned earlier, the presence of chitin is widespread amongst living organisms. But the main commercial sources for the production of chitin/chitosan are crustacean wastes, for example, the shells of Antarctic krill (*Euphausia superba*), deep-water shrimp (*Pandalus borealis*), crab (*Scylla serrata*), prawn (*Penaeus indicus*) and lobster (*Panulirus ornatus*), mainly derived from the food processing industry [2, 3]. In these shells, chitin as skeleton is tightly bound in complex with other substances such as minerals, proteins and lipids. Minerals are mainly inorganic carbonate salts imparting the strength to the shells, while proteins render the shells a living tissue [3]. The lipids generally stem from the muscle residues and carotenoids [13]. Therefore, the isolation of chitin requires the removal of proteins, minerals and lipids.

Shown in Figure 7.3 is the typical process of chemical extraction of chitin/chitosan. In general, after washing and grinding of crustacean wastes, a deproteination stage is needed to remove proteins under alkali conditions, and the alkali concentration can range from 0.1 to 2.5 M. Subsequently, the stage

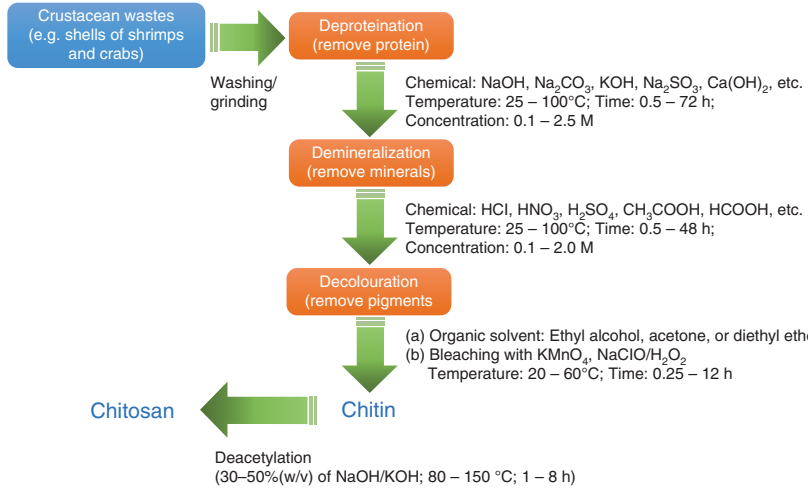


Figure 7.3 *The typical process of chemical extraction of chitin/chitosan.*

of demineralization is conducted in concentrated acid (0.1–2.0 M). Finally, a decolouration stage may be included to remove pigments and lipids. In some cases, the order of the different steps may be reversed depending upon the end use of chitin. An alkaline condition is also needed for the conversion of chitin to chitosan via deacetylation (Figures 7.1 and 7.3). In industrial facilities, NaOH with concentrations from 30% to 50% (w/v) is mainly used as the N-deacetylation agent at temperatures of 120–150 °C for several hours [2, 12].

The chemical extraction of chitin/chitosan by the strong bases and acids consumes high levels of energy, time and solvents and may increase the cost of wastewater treatment and chitin purification [14]. Hence, biological methods for isolation of chitin/chitosan are also of great interest, because enzymes and microorganisms can be used under mild conditions, and the process is environmentally benign. Kaur and Dhillon [3] have reviewed the recent trends in biological extraction of chitin from marine shell wastes. The utilization of lactic acid bacteria and protease-producing bacteria for demineralization and deproteination is an attractive alternative. These microorganism-mediated fermentation processes can be performed simultaneously or can be improved by utilizing successive two-step fermentations or co-fermentation of microorganism. It was reported that shrimp waste (*Papilio jordani*) was demineralized by a fermentation of a mixed culture of lactic acid bacteria (*Lactobacillus plantarum*, *Lactobacillus acidophilus and Lactobacillus lactis*) within 72 h at 30 °C, and the chitosan produced from the remaining material showed lower protein and ash content compared to the one demineralized with 1 N HCl [15]. These approaches are discussed in more detail in Chapter 6 of this book.

7.3 Derivatives of Chitin/Chitosan

As already known, the solubility of chitin/chitosan is of significant importance for its potential applications, and its solubility is related to its polymorph type and the DA. For example, α-chitin dissolves in concentrated inorganic acids (e.g. H_3PO_4, HCl), while β-chitin is soluble in concentrated formic acid, but the dissolution in formic acid could result in severe reduction of average molecular weight [11]. Chitosan as the most well-known chitin derivative is manufactured by N-deacetylation as mentioned earlier, and its DA is typically lower than 0.35. The solubility of chitosan is highly dependent on the pH value. Chitosan is usually dissolved in aqueous solutions of inorganic acids (e.g. HCl, HNO_3) or organic acids (e.g. formic acid, citric acid), but it is insoluble in aqueous solutions of alkali and in most organic solvents [2].

In order to increase the solubility of chitin/chitosan, chemical modification is usually carried out by reacting with hydroxyl groups or amino groups (Figure 7.4), leading to the generation of chitin/chitosan derivatives with higher solubility, biocompatibility, biodegradability, reactivity and/or bioactivity. For instance, due to the presence of free and protonated amino groups, chitosan could form complexes with negatively charged polysaccharides (e.g. cellulose fibre), dyes, anionic synthetic polymers, lipids, proteins, fat, enzymes or DNA and RNA [16]. Also, the chelating properties of chitosan because of the existing of large number of free amino groups are much more effective in comparison with chitin [17]. The acylation of chitin hydroxyl groups in alkali leads to water-soluble *O*-acylchitin which may differ on the basis of the chain length of the acylation agent used [18]. The O-carboxyalkylation of chitin mainly takes place in substitution of the hydroxyl groups of chitin, and 2-hydroxyethylchitin (glycochitin) can be prepared

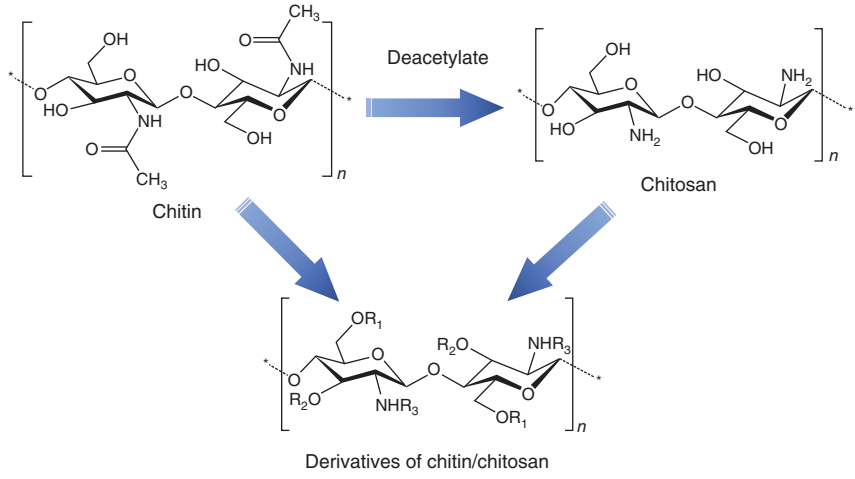


Figure 7.4 *Transitions of chitin, chitosan and their derivatives.*

under heterogeneous conditions with 2-chiloroethanol [2]. Chitin can also lead to sulfation in the presence of pyridine and cyanoethylation. The biodegradable dibutyryl chitin can be used for the manufacture of transparent films, fibres, non-wovens, microspheres, yarns and as a source for electrospinning [19]. The carboxymethylation of chitosan can be obtained in the forms of *N*- and *O*-, *N*-, or *O*-carboxymethylchitosan, and the place and degree of substitution depend on the reaction conditions [1]. Controlled N-acylation with acetic anhydride has been shown to lead to water-soluble, partially N-acetylated chitosan, and other *N*-acyl derivatives (e.g. formyl, acetyl, stearoyl, benzoyl, succinyl) can be produced with the corresponding carboxylic acid anhydrides [1]. Sulfation of chitosan can be conducted using sulfur trioxide and pyridine [20], sulfur trioxide and trimethylamine [21], sulfur trioxide in the presence of sulfur dioxide and chlorosulfonic acid–sulfuric acid [16] or concentrated chlorosulfonic acid [22] and sulfuric acid [23] with varying conditions. Other types of chitosan derivatives such as imines can be produced on the basis of Schiff reactions with aldehydes (e.g. oxygenated starch, phenylacetaldehyde, glutaraldehyde) or ketones (e.g. diphenyl ketone) because of the existence of free amine groups. Then, *N*-alkyl derivatives converted from the resultant Schiff base can be produced by a hydrogenation process using sodium tetrahydroborate or sodium cyanoborohydride, but toxic compounds can be produced in this process [2].

7.4 Utilization of Chitin/Chitosan for Chemicals and Materials

Different chitin/chitosan derivatives have different properties, leading to a wide field of applications, and they can be produced in different forms for utilization, such as powder, flakes, films, membranes, fibres, salts, gel, microcrystalline chitosan (MCCh) and beads or microcapsules, for special applications.

7.4.1 Utilization of Chitin/Chitosan for Chemicals

7.4.1.1 Utilization of Chitin/Chitosan for Organocatalysis

Due to the presence of amine groups and the unique enantiopure polyaminated backbone (chiral amines), chitosan has great potential in asymmetric organocatalysis. In the field of organocatalytic reactions promoted by chitosan (a heterogeneous catalytic material), as shown in Figure 7.5, chitosan can be used either as an insoluble organocatalyst [24] or as a support for organocatalysts [25], which can be easily recycled and reused.

7.4.1.1.1 Chitosan as an Organocatalyst

The primary amino functional groups of chitosan permit the polysaccharide to participate in different kinds of activation related to organocatalysis such as Brønsted base catalysis, aldolization reaction and hydrogen bond catalysis.

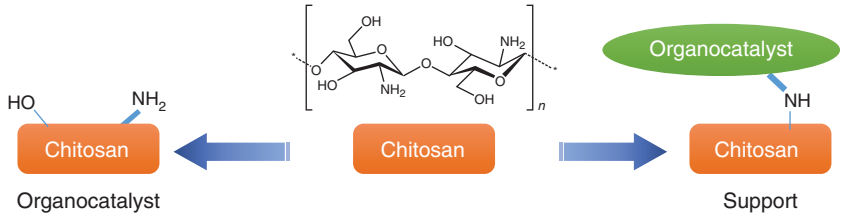
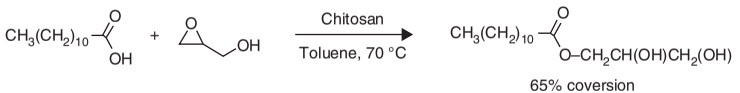
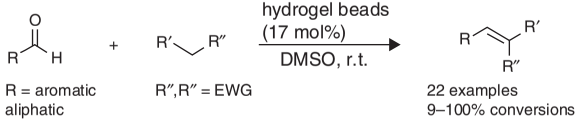
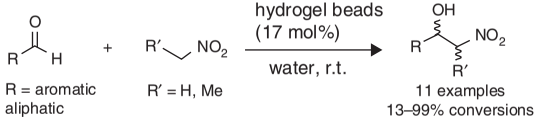


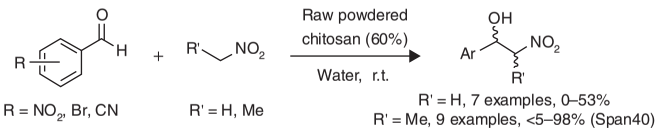
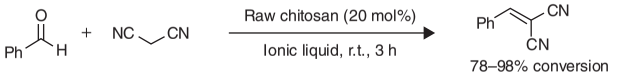
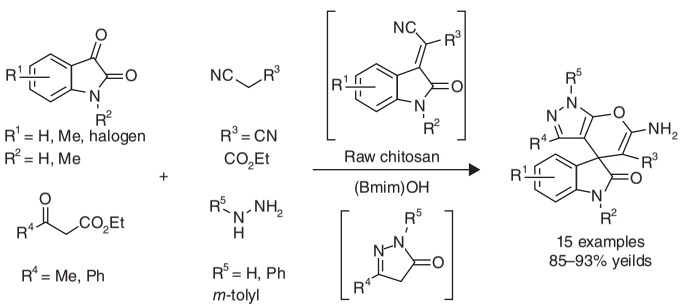
Figure 7.5 *Chitosan as an organocatalyst or a support in organocatalysis.*

Chitosan has a basic character overall due to the presence of primary amines at the C-2 position of the glucosamine unit, and its average pK_a in water is about 6.5, but it is not easy to accurately determine this because this property is associated with the chitosan's origin, the total number of free amino groups and its crystalline structure and so on [25, 26]. The selected reactions of Brønsted base catalysis promoted by chitosan are listed in Table 7.1. Quignard and coworkers [27] studied utilization of chitosan as a basic catalyst for the synthesis of a monoglyceride through epoxide ring opening by a fatty acid. The chitosan used was a commercial product with a DA of 10% and a molar mass of 500,000 g/mol. They found that the lyophilized chitosan beads did not catalyze the reaction, while the aerogel beads promoted the generation of the monoglyceride with 65% conversion. Hydrogel beads of chitosan could be used as basic organocatalyst for the Knoevenagel reaction [28]. As summarized in Table 7.1, with malonate-type nucleophiles and various aromatic or aliphatic aldehydes in DMSO at room temperature, the chitosan hydrogel beads were found to be efficacious catalysts and provided almost perfect selectivity to the dehydrated products over the aldol products. In addition, the hydrogel beads could be recycled and reused three times without loss of their catalytic activity.

On the other hand, raw chitosan (or commercial chitosan) can also be used as the organocatalyst for Brønsted base catalysis. It was found that when Henry reactions between nitromethane or nitroethane and aromatic aldehydes were conducted in water, chitosan hydrogel and powdered commercial chitosan showed similar catalytic activities [29]. However, the recycling of the chitosan hydrogel beads was ineffective in this study. Cui *et al*. used chitosan powder as a catalyst for Henry reactions between aromatic aldehydes and nitromethane or nitroethane [30]. Results showed that water was the optimal medium for this reaction. In the presence of surfactants, micelles could form in the water. This led to improvements of yield and diastereoisomeric ratio. In this work, the chitosan catalyst could be reused up to seven times, although there was a 10% loss of yield in the second run. The chitosan-catalyzed Knoevenagel reaction could also be conducted in ionic liquid media as green solvents. Phan *et al*. evaluated the effects of three different ionic liquids in the Knoevenagel condensation between malonitrile and benzaldehyde [31]. The ionic liquids used were 1-butyl-3-methylimidazolinium hexafluorophosphate ([BMIM][PF_6]) and its hexyl ([HMIM][PF_6]) and octyl ([OMIM][PF_6])

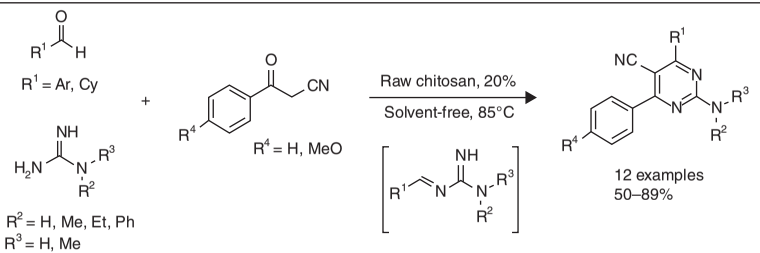
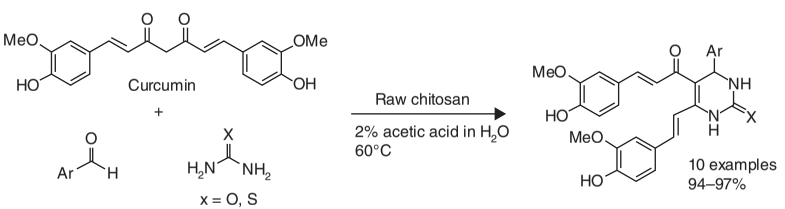
Table 7.1 *Selected reactions of Brønsted base catalysis promoted by chitosan.*

Reaction	Equation	Form	Reuse times	References
Monoglyceride synthesis		Aerogel beads	Two times	[27]
Knoevenagel condensations		Hydrogel beads 8.3–25% DA	Three times	[28]
Henry reactions		Hydrogel beads/powered commercial chitosan	Ineffective recycling	[29]

Henry reactions		Chitosan powder	Seven times	[30]
Knoevenagel condensations		Commercial chitosan 13% DA	Five times	[31]
Synthesis of spiro-oxindoles		Commercial chitosan	Six times	[32]

(*Continued*)

Table 7.1 *(Continued)*

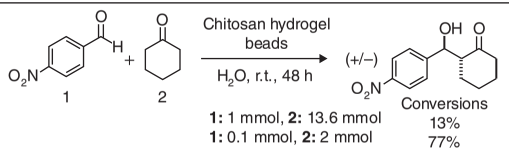
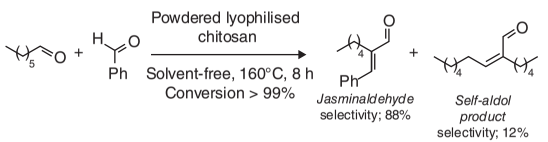
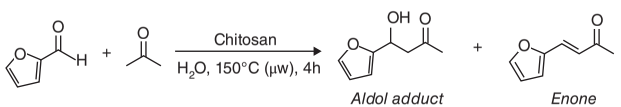
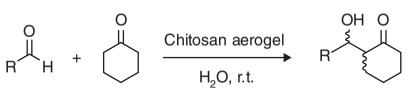
Reaction	Equation	Form	Reuse times	References
Synthesis of aminopyrimidines		Commercial chitosan	Five times	[33]
Biginelli condensation		Raw chitosan 15–25% DA	Five times	[34]

equivalents. Unmodified commercial chitosan with DA of 13% (tested by IR spectroscopy) was used as the catalyst. Results showed that the shorter the carbon chain, the faster the reaction. When [OMIM][PF_6] was used, the conversion was below 80%, while complete reaction could be achieved by the use of [BMIM][PF_6] under the same reaction conditions. Moreover, both chitosan and the ionic liquids could be recycled and reused for at least five times together or independently without significant loss of conversion. In addition, raw chitosan could also be used as a basic organocatalyst for the synthesis of spiro-oxindole derivatives [32], Biginelli-type synthesis of aminopyrimidines [33], Biginelli condensation reaction between a dienone-activated methylene compound (curcumin), urea and benzaldehyde [34], as well as the syntheses of heterocycles [35].

Chitosan has a chiral poly(primary amine) backbone with a multifunctional feature because of the presence of hydroxyl groups as hydrogen bond donors [25]. Therefore, chitosan has strong potential as a solid aminocatalyst involved in aldolization reactions.

The selected aldolization reactions promoted by chitosan are listed in Table 7.2. The aldol addition between aromatic aldehydes and acetone was studied by Reddy *et al*. [28]. The reaction was conducted in DMSO at room temperature, catalyzed by chitosan hydrogel beads, and the used chitosan had a DDA between 75% and 85%. Although several factors could potentially affect the reaction results, they found that only a decrease in reaction scale allowed a significant change in the outcome, improving the conversion of starting aldehyde from 13% (1 mmol scale) to 77% (0.1 mmol scale) (Table 7.2) [29]. They also found that the reactions did not take place with air-dried chitosan beads or commercial raw chitosan, indicating that the form of chitosan played an important role in the reaction. The synthesis of jasminaldehyde (a perfume chemical) was investigated in the presence of powdered lyophilized chitosan with a surface area of 1.04 m^2/g and an average pore size of 128 Å [36]. It was reported that the highest degree of conversion (99%) and the best selectivity of 88% could be achieved at 160 °C for 8 h under solvent-free conditions, and the loading of chitosan was 13 mg/mol of heptanal. The chitosan could be reused in six consecutive cycles without loss of activity and selectivity. Aldol addition was also studied by adding acetone to furfuraldehyde, leading to the aldol adduct and its dehydrated product as valuable chemicals. For instance, the effect of chitosan shaping on aldol addition with furfuraldehyde was investigated, and results showed that using commercial raw chitosan only yielded a conversion in the range of 40–60%, while the level of conversion could reach 84% and >95% by using cryogel chitosan beads and aerogel beads, respectively [37]. This was mainly due to the elaboration of a porous structure of chitosan catalyst. In the case of aerogel, its surface area was 250–280 m^2/g with a mesoporous pore size of 4 nm. Regarding the asymmetric aldol additions catalyzed by aerogel chitosan beads, Quignard and coworkers reported a significant enantiomeric excess induced by the chiral backbone of chitosan [38]. They found several remarkable features accompanying these

Table 7.2 *The selected aldolization reactions promoted by chitosan.*

Reaction	Equation	Form	Reuse times	References
Aldol addition		Hydrogel beads	–	[28]
Synthesis of jasminaldehyde		Powdered lyophilized chitosan	Six times	[36]
Aldol addition		Raw chitosan cryogel aerogel	Ten times	[37]
Asymmetric aldol addition		Aerogel chitosan beads	Four times	[38]

reactions: (i) the major diastereomers were obtained with moderate-to-good enantioselectivities (25–85% ee), although with a moderate diastereoselectivity quasi-exclusively in favour of the anti-isomers. This showed the potential of the chitosan backbone to transfer its chirality in an organocatalytic process. (ii) In the reaction between *p*-nitrobenzaldehyde and cyclohexanone, chitosan hydrogel beads performed well, giving a 75% yield along with 80% ee. This result was in contrast with that of the work of Reddy, discussed earlier, who did not observe chiral induction by hydrogel microspheres under similar conditions. (iii) Using glucosamine (i.e. chitosan monomeric unit) as a catalyst, the yield, diastereoselectivity and enantioselectivity dropped drastically, indicating the potential of the polymeric structure of chitosan to act as a multiple-interaction nanoreactor. (iv) The proposed asymmetric induction model involved multiple contributions of the chitosan structure with the formation of *E*-enamines followed by hydrogen-bond-oriented approach of the aldehyde, leading to anti-aldol reaction after nucleophilic attack of the enamines. In the case of α-hydroxy ketone, an intramolecular hydrogen bond favoured the formation of the *Z*-enamine, explaining the reverse diastereoselectivity of the hydroxy-aldol adduct. (v) Water played a crucial role in the reactions, as the reactions did not proceed in organic solvent when aerogel chitosan was used in the absence of water. (vi) The use of additives (e.g. fatty acids, PEG, SDS) could improve the catalytic activity of chitosan [25, 39].

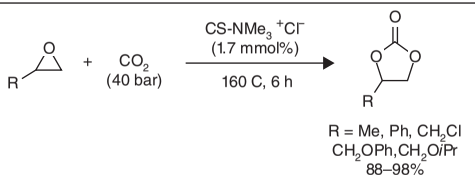
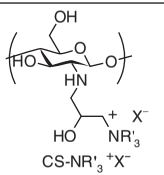
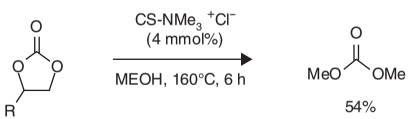
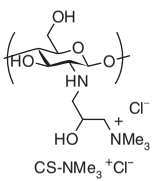
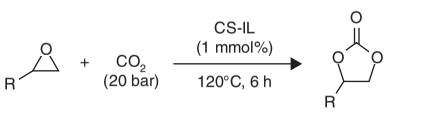
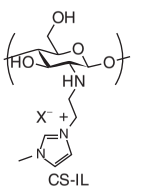
In addition, the Strecker reaction, a typical method for the preparation of α-amino acids [40], could also be catalyzed by chitosan, which has a high concentration of primary amines and hydroxyl groups. The chitosan-catalyzed Strecker reaction was considered as a bifunctional heterogeneous poly-H-bond donor in this multicomponent reaction between an amine, a carbonyl group and a cyanide [41]. The chitosan used was a commercial product with a molecular weight of 600–800 kDa, and its catalytic performance was attributed to hydrogen bond activation of aldehyde and imine by the hydroxy and amine groups of the chitosan, during the nucleophilic attack of the amine substrate and cyanide, respectively.

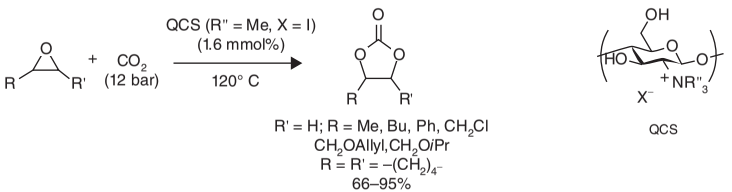
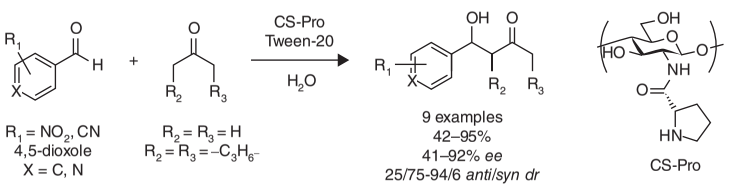
7.4.1.1.2 Chitosan as a Support for Organocatalysis

Due to its unique structure, chitosan can also be used as a support for organocatalysis, in order to reach the optimal degree of functionalization/substitution of catalyst and a high catalytic efficiency by increasing the accessibility/diffusion ability of catalyst. The related reactions could be classified as Lewis base catalysis, Brønsted base catalysis, Brønsted acid catalysis and phase-transfer catalysis, and they are briefly introduced in this section.

CO_2 cycloadditions are typical Lewis base catalysis reactions, which are commonly catalyzed by ammonium salts. To improve catalyst recovery and recycling, various chitosan-supported ammonium salts have been studied (Table 7.3). Zhao *et al*. prepared 2-hydroxyisopropyl-tethered trialkylammonium halides on chitosan with DA of 9%, and the catalytic activity of the prepared

Table 7.3 *The selected Lewis base catalysis promoted by chitosan-supported catalyst.*

Reaction	Equation	Supported catalyst	Reuse times	References
CO_2 cycloaddition catalyzed by chitosan-supported ammonium salts			Five times	[42]
Dimethyl carbonate synthesis			Five times	[43]
CO_2 cycloaddition catalyzed by chitosan-supported ionic liquids			Five times	[44]

CO_2 cycloadditions catalyzed by quaternized chitosan			Four times	[45]
Aldol reaction catalyzed by chitosan-supported proline			Three times	[46]

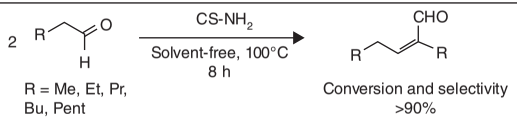
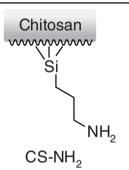
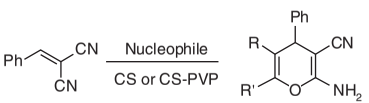
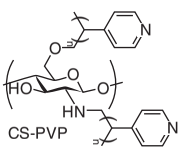
chitosan-supported ammonium salts was evaluated [42]. They found that chitosan alone was inactive for this reaction, and no product could be obtained without a catalyst. Results also showed that the grafted ammonium halide salts were at least as efficient as their homogeneous equivalents. In the case of Me_4NCl, only 1% yield of carbonate could be achieved, while the yield could be strikingly increased to 73% with CS-$N^+Me_3Cl^-$. The reaction yields depended on the leaving abilities and nucleophilicities of halide anions with an order of catalytic activity: I^- (100%) > Br^- (95%) > Cl^- (73%), while the cation part of catalyst seemed to have less influence [25]. The obtained cyclic carbonates could be transformed to dimethyl carbonates via transesterification with methanol in the same catalytic system (Table 7.3) [43]. In addition, CO_2 cycloaddition reactions could also be promoted by the use of the chitosan (10% DA) functionalized by ionic liquids as a recyclable catalyst [44] and the quaternized chitosan [45].

In order to promote an enamine-type mode of action, L-proline was supported on chitosan for asymmetric direct aldol reactions between aromatic aldehydes and acetone or cyclohexanone, and it was also found that the reaction could be further promoted by the supplement of surfactant (such as Tween-20 with the best efficiency) [46].

Table 7.4 shows several Brønsted base catalysis reactions promoted by chitosan-supported catalyst. Chitosan-supported primary amines were prepared by the treatment of a suspension of commercial raw chitosan with aminopropyltrimethoxysilane in toluene at reflux for 24 h, and the prepared catalyst was used to promote self-aldolizations of linear aliphatic aldehydes under solvent-free conditions [47]. The chitosan-supported primary amines were found to be an efficient catalytic material for the selective formation of dehydrated self-aldol products, probably because of the more accessible remote amine groups. But the catalytic activity was slightly lower with longer chain aldehydes with lower acidity of α-carbonyl protons, which was due to an increasing positive inductive effect in longer aliphatic carbon chains [25]. Chitosan could also be used as a support for pyridine motifs to promote Michael-type additions for heterocycle syntheses, and it was found that chitosan-supported pyridine was more efficient compared to raw chitosan, with a yield improvement between 15% and 35% [48]. Cui *et al*. immobilized cinchona alkaloids quinine and cinchonine on chitosan [49]. The catalytic activity of the prepared materials was measured in the Michael reactions between *N*-benzylmaleimide and β-dicarbonyl compounds (Table 7.4). Chitosan alone was almost inactive. They also studied the positive effect of a chitosan-supported L-proline catalyst on asymmetric Henry reactions between nitromethane and arylaldehydes [30].

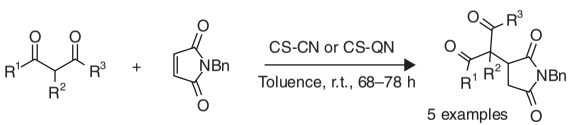
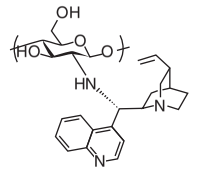
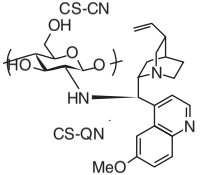
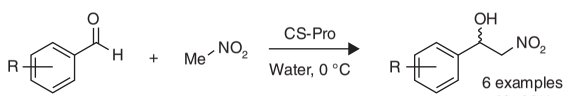
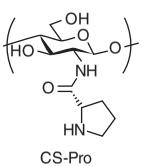
In addition, Reddy *et al*. prepared chitosan-supported sulfonic acid by the treatment of a raw chitosan suspension with chlorosulfonic acid in pyridine [50]. The obtained sulfonic acid was found to be an efficient heterogeneous acidic catalyst for Friedländer annulation reactions (Brønsted acid catalysis) with good yields in less than 1 h (Figure 7.6), and the catalyst could be reused in at least three

Table 7.4 *Selected Brønsted base catalysis promoted by chitosan-supported catalyst.*

Reaction	Equation	Supported catalyst	References
Self-aldolization			[47]
Michael additions to benzylidenemalononitrile			[48]

(*Continued*)

Table 7.4 *(Continued)*

Reaction	Equation	Supported catalyst	References
Michael additions catalyzed by chitosan-supported cinchona alkaloids		 	[49]
Henry reactions			[30]

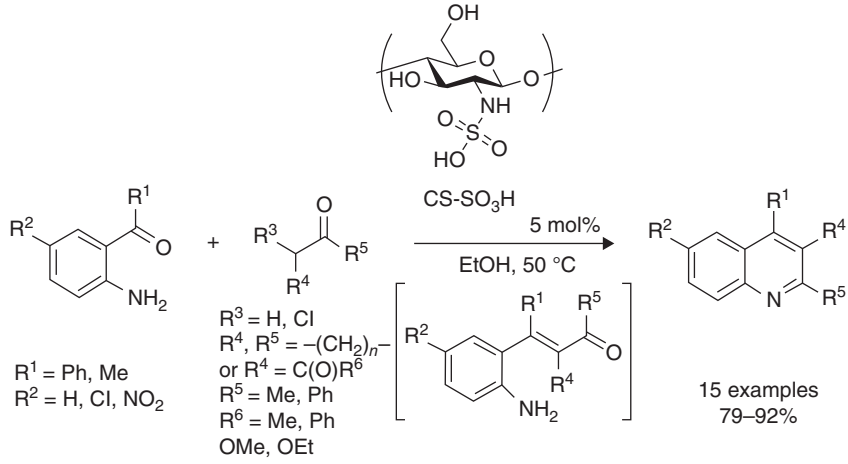


Figure 7.6 *Friedländer annulation catalyzed by a chitosan-supported sulfonic acid.*

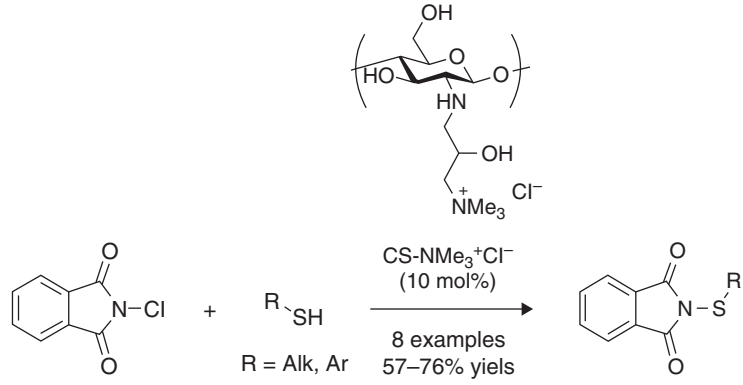


Figure 7.7 *Synthesis of* N*-thiophthalamides catalyzed by chitosan-supported ammonium salts.*

times with yields maintained above 80%. It was also reported that quaternized ammonium chloride salts could be immobilized on chitosan, and the obtained material could be used as phase-transfer catalyst to promote the synthesis of *N*-thiophthalimides from various thiols and *N*-chlorophthalimide in MeCN at 80 °C, providing yields in the range of 57–76% (Figure 7.7) [25].

7.4.1.2 Production of Chemicals from Chitin/Chitosan

Chitin/chitosan can also be potentially directly used as feedstock to produce useful chemicals. For example, chitin/chitosan can be hydrolyzed to mono-, di- and oligosaccharides. As reported, colloidal chitin could be hydrolyzed to yield a dimer

of *N*-actyl-glucosamine $(NAG)_2$ and chitobiose, using *Vibrio furnissii chitinase* (*chi* E, 89 kDa) in DMSO-LiCl buffered with NH_4HCO_3 at pH 7.9 [51]. NAG could also be produced from crude chitin powders by chitinase hydrolysis with nearly 100% conversion of the substrate crude chitin powders [52]. Concentrated HCl could be used to produce NAG at 45 °C for 3 h (40.5 g from 300 g chitin), but enzymatic production of NAG is greener and more attractive mainly due to its high yield and mild reaction conditions. It has be known that NAG and glucosamine (GlcN) salts, as well as chitin/chitosan oligomers, have biological, antitumorigenic, antibacterial and antifungal properties [53].

Furthermore, by the use of the N-containing renewable feedstock (i.e. chitin/chitosan, NAG, etc.), small organic molecules can be produced via pyrolytic methods or chemical methods [53, 54]. For instance, pyrolysis of NAG under vacuum generated a tar, from which 3-acetamido-5-acetylfuran, acetamidoacetaldehyde and 3-acetamidofuran could be isolated with the yields of 2%, 3% and 5%, respectively [53]. Through chemical methods, levulinic acid [55], 5-hydroxymethylfurfural (5-HMF) [56], 5-(chloromethyl)furfural [57] and 3-acetamido-5-acetylfuran (3A5AF) [58] with yields in the range of 7.5–11% could be produced from chitin/chitosan. In addition, Yan's group converted NAG into polyols over transition metal catalysts and H_2 in water, and the best yields of *N*-acetylmonoethanolamine (NMEA), C4 polyols and C6 polyols (N-containing) were 8.7%, 6.1% and 71.9%, respectively, with Ru/C as the catalysts [59]. Most recently, they also transformed chitin and raw shrimp shells into acetic acid (HAc, with yields of 38.1% and 47.9%, respectively) by a catalytic method by the use of metal oxide and O_2 in basic water, and heterocyclic compound pyrrole was also generated as the major N-containing product in the reaction system [60]. These studies opens new avenues to transform shellfishery waste into platform chemicals. The potential of using chitin/chitosan as a starting material for chemicals is a very fast growing area in the context of biorefinery [53, 54].

7.4.2 Utilization of Chitin/Chitosan for Materials

7.4.2.1 Utilization of Chitin/Chitosan as Adsorbent for Wastewater Treatment

Wastewater treatment by removing heavy metals, colour, odour and organic matter is of crucial importance from the point of view of environmental protection and health concerns. Chitosan is a known green adsorbent particularly for the removal of heavy metals and dyes due to the presence of amino and hydroxyl groups, which can serve as the active sites [61].

Compared to chitin, chitosan has superior adsorption ability for heavy metals because of its higher content of amino groups [62]. If chitosan is completely deacetylated, its amino group concentration is 6.21 mmol/g. It has been known that the adsorption of transition metals on chitosan is mainly affected via coordination with unprotonated amino groups [63], and the coordination of divalent heavy metals (e.g. Cu^{2+}, Zn^{2+}) with the amino groups of chitosan can be achieved

by a molar ratio of 1:1 [64], 1:2 [65] or 1:4 [66] (Figure 7.8). However, it is also possible that multiple kinds of metal coordination exist on chitosan chains, including intermolecular chelation with four different forms and intramolecular chelation with three different configurations [67]. As already known, the type of coordination plays a crucial role in adsorption performance (such as kinetics and capacity), and the theoretical maximum adsorption capacity of divalent metals is 6.2, 3.1 and 1.6 mmol/g when the divalent metal and amino group are bound by the molar ratio of 1:1, 1:2 and 1:4, respectively [62].

However, chitosan is very sensitive to pH, because it can dissolve or form a gel depending on the pH value [68]. Therefore, to improve its performance, chitosan can be treated by cross-linking, substitution or preparation of chitosan composites. Cross-linking can be achieved by using cross-linking reagents such as formaldehyde, glyoxal, epichlorohydrin, glutaraldehyde, isocyanates and ethylene glycon diglycidyl ether [69]. Substitution of chitosan leads to the generation of chitosan derivatives containing nitrogen, phosphorus and sulfur as heteroatoms [70]. Different types of organic/inorganic substances can be used to form composite with chitosan, such as ethylenediaminetetraacetic acid (EDTA)/diethylenetriaminepentaacetic acid (DTPA) [71], polyvinyl alcohol [72], polyvinyl chloride [73], cellulose fibres [74], activated clay [75], bentonite [76], montmorillonite [77], kaolinite [78], oil palm ash [79], perlite [80], magnetic particles [81] and graphene [82].

Table 7.5 lists the adsorption capacities and experimental conditions of selected chitosan-based sorbents for various heavy metal removal from aqueous solutions. In general, cross-linking or substitution of chitosan could lead to a decrease in

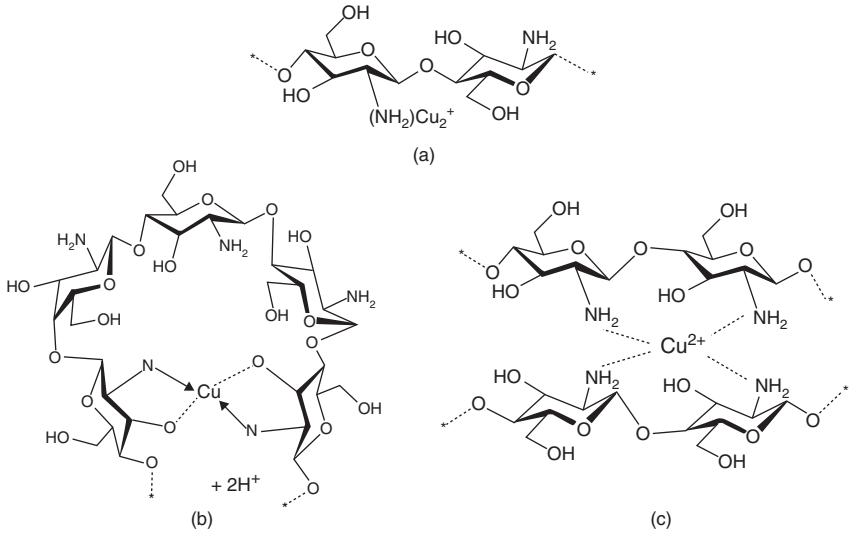


Figure 7.8 *Coordination of Cu^{2+} with the amino groups of chitosan by a molar ratio of (a) 1:1, (b) 1:2 and (c) 1:4.*

Table 7.5 *Adsorption capacities and experimental conditions of selected chitosan-based sorbents for various heavy metal removal from aqueous solutions.*

Sorbent	Metal ions	Adsorption capacity (mg/g)	pH	Temperature (°C)	Isotherm	References
Pristine chitosan	Cu^{2+}	198.91	6.5	30	Langmuir	[62]
Thiolated chitosan beads	Cu^{2+}	50.30	5.6	25	–	[83]
Chitosan/cotton fibers (via Schiff base bond)	Cu^{2+}	24.78	6.5	25	Langmuir, Freundlich	[84]
Chitosan/cellulose	Cu^{2+}	26.50	–	25	Langmuir	[74]
Chitosan/perlite	Cu^{2+}	104.00	4.5	25	Langmuir	[85]
Chitosan/clinoptilolite	Cu^{2+}	719.39	5.0	25	Langmuir	[86]
Pristine chitosan	Cd^{2+}	382.16	6.5	30	Langmuir	[62]
Thiolated chitosan beads	Cd^{2+}	54.30	5.6	25	–	[83]
Chitosan encapsulated magnetic Fe_3O_4 nanoparticles	Cd^{2+}	200.00	–	–	Langmuir	[81]
Chitosan/PVA	Cd^{2+}	142.90	6.0	50	Langmuir	[72]
Pristine chitosan	Zn^{2+}	289.11	6.5	30	Langmuir	[62]
Chitosan/cellulose	Zn^{2+}	19.81	–	25	Langmuir	[74]
Chitosan/PVA	Zn^{2+}	8.77	5.0	30	Langmuir	[87]
Pristine chitosan	Ni^{2+}	66.32	6.5	30	Langmuir	[62]
Chitosan/cotton fibres (via Schiff base bond)	Ni^{2+}	7.63	6.5	25	Langmuir, Freundlich	[84]
Chitosan/magnetite	Ni^{2+}	52.55	6.0	–	Langmuir	[88]
Chitosan/cellulose	Ni^{2+}	13.21	–	25	Langmuir	[74]
Chitosan/ceramic alumina	Ni^{2+}	78.10	4.0	25	Langmuir, Freundlich, Redlich –Peterson	[89]
Chitosan/clinoptilolite	Ni^{2+}	247.03	5.0	25	Langmuir	[86]
Pristine chitosan	Pb^{2+}	238.28	6.5	30	Langmuir	[62]
Chitosan/cotton fibres (via Schiff base bond)	Pb^{2+}	101.53	6.5	25	Freundlich	[84]
Chitosan/cellulose	Pb^{2+}	26.31	–	25	Langmuir	[74]
Chitosan/graphene oxide composite	Pb^{2+}	461.30	6.0	45	Langmuir	[90]
Pristine chitosan	Cr^{6+}	156.00	3.0	25	Langmuir	[91]
Magnetic chitosan	Cr^{6+}	69.40	4.0	–	Langmuir	[92]
Chitosan/cellulose	Cr^{6+}	13.05	–	25	Langmuir	[74]
Chitosan/graphene oxide composite	Cr^{6+}	310.4	3.0	45	Langmuir	[90]
Chitosan/cotton fibres (via Schiff base bond)	Hg^{2+}	104.31	5.0	35	Langmuir, Freundlich	[93]
Chitosan/cotton fibres (via C—N single bond)	Hg^{2+}	96.28	5.0	25	Langmuir, Freundlich	[93]
Chitosan (raw) membrane	Hg^{2+}	415.00	6.0	25	Langmuir	[94]
Chitosan (glutaraldehyde-cross-linked) membrane	Hg^{2+}	888.00	6.0	25	Langmuir	[94]
Chitosan (raw) sphere	Hg^{2+}	375.00	6.0	25	Langmuir	[94]
Chitosan (glutaraldehyde-cross-linked) membrane	Hg^{2+}	647.9	6.0	25	Langmuir	[94]

adsorption ability, and the decrease strongly depended on the type and degree of cross-linking, because some amino groups in chitosan chain are involved in cross-linking. But the reduction of adsorption capability can be compensated with the required properties of chitosan such as the stability in acidic environment ($pH < 2$) and mechanical properties [68].

On the other hand, the introduction of new functional groups (e.g. hydroxyl, carboxyl and amino groups) or another adsorbent (e.g. polyacrylamide) into chitosan can enhance the interaction with metal ions, thus improving the adsorption. For instance, it was reported that the adsorption capacity of Cd^{2+} increased 4.2 times in comparison with raw chitosan, after cross-linking with glutaraldehyde and then with CS_2 in NaOH solution [62]. The effective coordination site for Cd^{2+} was the $–OCS_2^-$ group rather than an amino group. Certainly, the adsorption ability of a material is also highly associated with many factors, such as the nature of chitosan used, the dosage of adsorbent, solution pH value, temperature, contact time, the initial concentration of metal ions and the type or nature of counter ion (e.g. SO_4^{2-}, NO_3^-) [62, 93, 94]. Therefore, chitosan-based adsorbent should be made to have both high adsorption capability to metal ions and good durability in various environments. For example, Liu *et al*. prepared magnetic hybrid hydrogels with a novel polymeric coating consisting of chitosan and cellulose in the solvent of ionic liquid (Figure 7.9) [95]. In this hybrid material, cellulose could provide strong mechanical strength and improve the chemical stabilities of the hydrogel beads under acidic conditions. Chitosan could serve as an effective coating to stabilize Fe_3O_4, preventing particle agglomeration, and provide free amine groups to remove heavy metals. Furthermore, Fe_3O_4 made this material easy to be separated and recovered in magnetic field. Results showed that the prepared magnetic hybrid hydrogels had high adsorption capacities for different heavy metal ions (Cu^{2+}, Fe^{2+} and Pb^{2+}), and they could be efficiently recycled and reused.

In addition, chitin/chitosan-based adsorbents are also effective in removing dyes to address the colour issue of water. The adsorption capacities of selected chitin/chitosan-based adsorbents for the removal of various dyes from wastewater are summarized in Table 7.6.

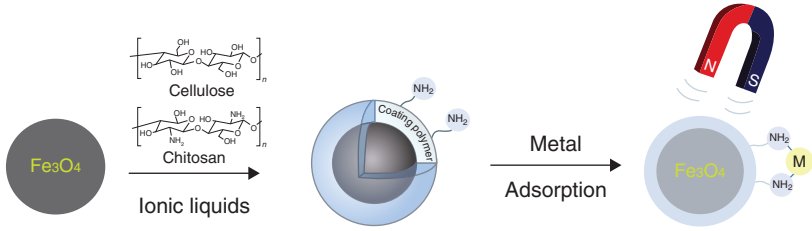


Figure 7.9 *The scheme of the preparation of magnetic chitosan–cellulose hydrogels and adsorption of heavy metals.*

Table 7.6 *The adsorption capacities of selected chitin/chitosan-based adsorbents for the removal of dyes.*

Adsorbent	Dyes	Adsorption capacity (mg/g)	pH	Temperature (°C)	Isotherm	References
Chitosan	Congo red	81.23	7.0	30	Langmuir	[77]
Chitosan/montmorillonite nanocomposites	Congo red	54.52	7.0	30	Langmuir	[77]
Chitosan/polyurethane	Acid violet 48	30.00	7.0	30	Langmuir	[96]
Chitosan/bentonite	Tartrazine	294.1	2.5	47	Langmuir	[97]
Chitosan/bentonite	Malachite green	435.0	6.0	37	Langmuir	[76]
Chitosan/oil palm	Reactive blue 19	909.1	6.0	50	Redlich–Peterson	[79]
Chitosan/CTAB beads	Congo red	385.90	5.0	30	Langmuir	[98]
Chitosan/CNT beads	Congo red	450.40	5.0	30	Langmuir	[99]
Chitin beads	Congo red	112.36	6.0	25	Langmuir	[100]
Chitosan–tripolyphosphate beads	Congo red	166.67	6.0	25	Langmuir	[100]

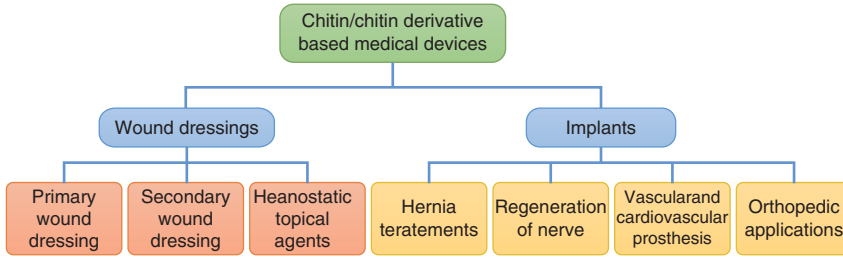


Figure 7.10 *The most important utilization of chitin/chitin derivatives for the design of medical devices.*

7.4.2.2 Utilization of Chitin/Chitosan for Biomedical Application

Due to their appealing biological properties such as non-toxicity, biodegradability, antibacterial activity, biocompatibility, low immunogenicity and wound-healing capacity, chitin/chitosan and its derivatives have great potential application in the medical field [2]. They can be used as wound dressing materials, drug delivery systems, tissue engineering scaffolds, antimicrobial agents, biosensors and so on [101]. The most important medical applications of chitin and its derivatives as biomaterials are presented in Figure 7.10.

Healing prevents organisms from deregulation of homeostasis and restores integrity of the injured tissue. An ideal dressing should maintain a moist environment at the wound interface, act as a barrier to microorganisms, allow gaseous exchange and remove excess exudates [102]. Therefore, the adhesive nature of

chitin and chitosan, together with their permeability to oxygen and their antifungal and bactericidal property, is of crucial importance for the treatment of wounds and burns. Types of wound dressings using chitin/chitin derivatives with different forms are shown in Figure 7.11. Primary wound dressing should assure a suitable environment for wound healing and is connected with the synergistic mode of the physical properties (e.g. formation of absorbing exudate gels, moisture control) and bioactivity of chitin and its derivatives. Secondary wound dressings containing chitin and its derivatives mainly have two important properties: (i) antibacterial guarding and (ii) the possibility to form semipermeable or absorbing exudate usable forms of biopolymers [2]. The hemostatic properties of chitosan and its oligomers have been commercially applied in several topical hemostatic dressings which differ in their usable form. The mode of hemostatic action of chitosan is highly dependent upon its physical and chemical nature and structure. It has been reported that the hemostatic properties of chitosan differ in molecular weight and DD to local activation of platelets and turnover of the intrinsic blood coagulation cascade [103, 104].

Jayakumar *et al*. reviewed the recent progress of chitin- and chitosan-based wound dressing [102]. As already known, the fibrous materials based on chitin and its derivatives have the properties of high durability, liquid absorption, low toxicity, good biocompatibility and antibacterial activity [105]. These properties could promote wound healing. Chitosan/collagen membrane could be used to hasten wound healing and induce cell migration and proliferation because of its antibacterial activity and better healing effect [106].

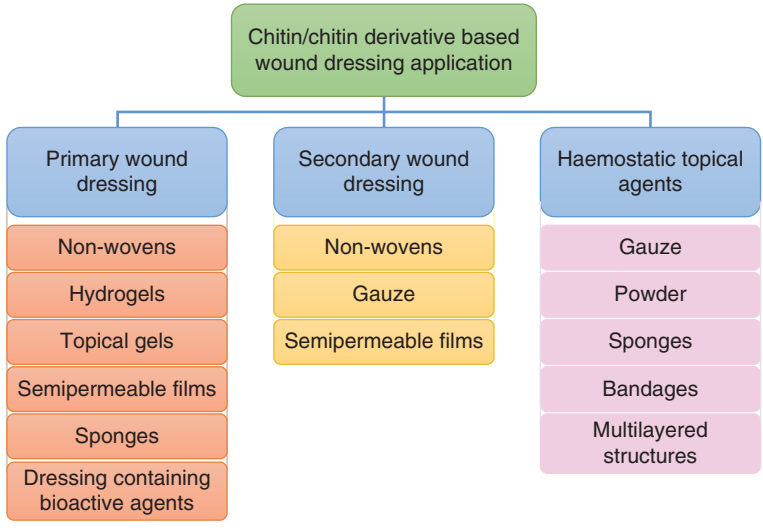


Figure 7.11 *Types of wound dressings using chitin/chitin derivatives with different forms.*

Polypropylene–NIPAAm–collagen–chitosan membrane could be used as a temperature-sensitive material that could act as an automatic release of the dressing material, once the wound is healed [107]. Chitin- and chitosan-based hydrogels may be considered as an occlusive dressing for wound management due to their ability to accelerate wound contraction and healing [108]. Moreover, the moisture permeability of the hydrogels may prevent the accumulation of fluid in heavily exudating wounds, and the gelling properties of chitosan promote the formation of a physical barrier against massive bleeding [109].

To improve the wound-healing properties, chitin- and chitosan-based membranes have been developed with different types of polymers such as polyethylene glycol diacrylate, alginate, hyaluronic acid, γ-poly(glutamic acid), poly(vinyl alcohol) and 2-hydroxyethyl methacrylate. Due to their composite nature, these membranes were found to have the desired properties for wound-healing applications. As reported, the Ag/ZnO-incorporated chitosan membranes are less cytotoxic compared to the traditionally used materials and may be very potential wound dressings with antibacterial capability to prevent an injured skin from infections [110]. Based on the improved antibacterial activity, cell attachment ability and oxygen permeability, it is concluded that chitin and chitosan scaffolds/sponges could be a promising candidate for wound dressing [102]. Some commercial wound dressings utilizing chitin or its derivatives are listed in Table 7.7.

Implantable applications of chitin and its derivatives include hernia treatment, vascular prosthesis, nerve regeneration and orthopaedic applications (Figure 7.10). Other applications of chitin and its derivatives in drug delivery, tissue engineering and targeted regenerative medicine have been most recently reviewed by Ding *et al*. [101] and Anitha *et al*. [112]

7.4.2.3 Utilization of Chitin/Chitosan for Other Applications

7.4.2.3.1 Food and Animal Feed

The use of chitosan in the food industry is well known as it is not toxic for warm-blooded animals [6]. Microcrystalline chitin (MCC) shows good emulsifying properties, and it is a superior thickening and gelling agent for stabilizing foods [2]. MCC is also used as a dietary fibre in baked foods. Using MCC solved some of the problems introduced by other sources of fibre with regard to flavour, colour and shelf life of food products. It could be of special importance for producing protein-enriched bread, even without such ingredients as emulsifiers and shortenings. MCC can also be used as a non-absorbable carrier for highly concentrated food ingredients such as nutrients and food dyes. As an additive, MCC can enhance the flavour and taste of foods. Nutritional studies in the United States showed that chicks fed on a diet containing dried whey and chitin utilized whey more efficiently and gained more weight than those fed similarly but with a chitin-free diet. Results also showed that small amounts of chitin added to

Table 7.7 *Commercial wound dressings utilizing chitin or its derivatives.*

Trade name	Company name	Function (shape)	References
Beschitin®	Unitika, Japan	Accelerates granulation phase; no scar formation (in the form of nonwoven)	[103]
ChitiPack® S	Eisai Co., Japan	Accelerates wound healing; no scar formation (sponge-like product)	[103]
ChitiPack® P	Eisai Co., Japan	For large skin defects especially with difficulty to suture (fabric)	[103]
ChitiPack® C	Eisai Co., Japan	Regeneration and reconstruction of body tissue, subcutaneous tissue and skin (fibrous)	[103]
Chitodine®	IMS	Disinfection and cleaning of wounded skin and as a primary wound dressing (powder)	[103]
Vulnsorb®	Tesla	Dermis regeneration (sponge)	[103]
HemCon® bandage	HemCon Medical Technologies	Stops massive blood bleeding; reduces secondary infection; seals and stabilizes the wound	[103]
Syvatek® patch	Marine Polymer Technologies	Reduces fibrin clot formation time; causes aggregation of red blood cells (fibre form)	[109]
ChitoSeal®	Abbott Vascular Devices	Controls moderate-to-severe bleeding	[109]
TraumaStat®	Ore-Medix	Controls moderate-to-severe bleeding	[2]
ExcelArrest®	Hemostasis LLC Co.	Limits and controls moderate-to-severe bleeding (foam)	[2]
Tromboguard®	TRICOMED SA	Local hemostasis; antibacterial; accelerates wound healing	[104]
Tegasorb®	3M	Accelerates wound healing	[111]
Tegaderm®	3M	Accelerates wound healing	[111]

the diets of chicks and calves enabled the animals to digest milk lactose via increased growth of specific intestinal bacteria. These bacteria impede the growth of Rother types of organisms and generate the enzyme required for lactose digestion [2].

Chitinous polymers offer a wide range of unique applications including preservation of foods from microbial deterioration [113], bioconversion processing for the production of value-added food products [114], recovery of waste material from food processing discards [115], formation of biodegradable films [116] and clarification and deacidification of fruit juices [117]. Chitosan has cholesterol-lowering effects [2], and low-molecular-weight (50–190 kDa)

chitosan can be used to mitigate the formation of acrylamide [118]. Chitosan as a dietary food additive or as a dietary supplement does not need federal drug agency (FDA) approval, and chitin/chitosan and their derivatives have a range of potential uses as food additives and aids to beverage processing and packaging agents. Foods containing chitosan, or chitosan complexes with fatty acids, could be designed to reduce cholesterol levels, obesity and the incidence of colon cancer [2]. Films made from chitosan are biodegradable with low permeability to oxygen. Chitosan also has potential as a coating to preserve fruits. *N*-Carboxymethyl chitosan reacts with monochloroacetic acid to form a strong film that is selectively permeable to oxygen and carbon dioxide. Apples coated with the material and left in cold storage retain their freshness for more than 6 months and retain their titratable acids for about 250 days. The film can be removed by washing with water before consumption of the fruits. In addition, chemical food preservatives can be replaced with chitin-based formulations which are safer. They also can protect food products against microbial invasion due to their antimicrobial activity [119].

7.4.2.3.2 Agriculture

Because both chitin and chitosan have antiviral, antibacterial and antifungal properties, they can be utilized to control disease or reduce their spread, to chelate nutrient and minerals or to enhance plant innate defence [2, 6]. Chitosan has been shown to inhibit the systemic propagation of viruses and viroids throughout the plant and to enhance the host's hypersensitive response to infection [120]. Chitosan used to control plant pathogens has been extensively explored with more or less success depending on the pathosystem, concentration, the used derivatives, viscosity, degree of deacylation and the applied formulation (i.e. soil amendment, foliar application, chitosan alone or in association with other treatments) [121]. Chitosan can be applied as seed coating agent to increase seed resistance to certain diseases and improve their quality and/or their ability to germinate [122]. Chitosan can also be applied as foliar treatment agent to increase stomatal conductance and transpiration rate, reduce water use and control the growth, spread and development of many diseases [123]. In addition, chitosan can be used for soil amendment [124].

7.4.2.3.3 Cosmetics

Chitosan is the only natural cationic gum that becomes viscous upon being neutralized with acid, and it is compatible with many biologically active components incorporated in cosmetic products [2]. Chitin and its derivatives can be used in three areas of cosmetics: skin care, hair care and oral care [125]. Chitosan and its derivatives have two advantages that make them suitable for skin care: their positive electrical charge and the fact that the molecular weights of most chitosan

products are so high that they cannot penetrate the skin. Chitosan (positive) and hair (negative) are complementary. Chitosan shows an antistatic activity, which enables hair protection from waving and bleaching agents. It helps to retain moisture in low humidity and to maintain hair's style in high humidity. In many cases, cosmetic companies use the same derivatives and formulations for hair care that they apply in products for skin care. Also, both chitin and chitosan can be used in toothpaste, mouthwashes and chewing gum; they freshen the breath and prevent the formation of plaque and tooth decay.

Besides the applications mentioned earlier, chitin/chitosan as a special material can be utilized for enzyme immobilization [126], adhesives [127, 128], electrochemical biosensor [129], which are also reviewed in the literature.

7.5 Closing Remark and Perspectives

Chitin and chitosan are renewable and abundant polysaccharides in nature. They have unique structure and many remarkable properties, such as biodegradability, biocompatibility, non-toxicity, antibacterial activity and low immunogenicity. Therefore, chitin/chitosan has very wide potential applications in the fields of organocatalysis (either as organocatalyst or as support), production of platform chemicals, wastewater treatment (as adsorbent for the removal of heavy metals, dyes, etc.), biomedical devices (e.g. wound-healing dressings, implant, drug delivery), food industry, agriculture, cosmetic, adhesives, enzyme immobilization and biosensors. However, there are also some challenges during manufacture and application. For example, it is difficult to fabricate reproducible products from various sources of raw material and different collection periods; there is no standardization for chitinous raw materials and end-product quality assay regarding their specific applications (e.g. medical devices); there are no validated processes of biopolymer manufacture; a reliable quality assessment system for chitinous derivatives production is unavailable; its production cost is still too high for non-specialized applications. Therefore, a prerequisite for the reproducible processing of chitinous raw products is understanding and control of the important parameters of sources and final products. It needs standardized measurement methods for biological, physical and chemical characterization. Particularly, the future application of chitin and its wide scope of derivatives in medical fields significantly depend on the proper description of the base requirements in a range of chemical and physical characterizations and chemical purity determination as well as biological conformity assessments. We believe that, with a better understanding and control of raw material properties, manufacturing processes and end-product requirements, the reduction of production costs, the establishment of standard characterization methods, as well as the development of shell biorefinery, new chitin/chitosan-based products with stable quality will be developed, and the chitin/chitosan market will keep growing in the future.

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