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# Applications of chitosan in food, pharmaceuticals, medicine, cosmetics, agriculture, textiles, pulp and paper, biotechnology, and environmental chemistry

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## Abstract

Chitosan is a biopolymer obtained from chitin, one of the most abundant and renewable materials on Earth. Chitin is a primary component of cell walls in fungi, the exoskeletons of arthropods such as crustaceans, e.g., crabs, lobsters and shrimps, and insects, the radulae of molluscs, cephalopod beaks, and the scales of fish and lissamphibians. The discovery of chitin in 1811 is attributed to Henri Braconnot while the history of chitosan dates back to 1859 with the work of Charles Rouget. The name of chitosan was, however, introduced in 1894 by Felix Hoppe-Seyler. Chitosan has attracted major scientific and industrial interests from the late 1970s due to its particular macromolecular structure, biocompatibility, biodegradability and other intrinsic functional properties. Chitosan and derivatives have practical applications in the food industry, agriculture, pharmacy, medicine, cosmetology, textile and paper industries, and in chemistry. In recent years, chitosan has also received much attention in dentistry, ophthalmology, biomedicine and bioimaging, hygiene and personal care, veterinary medicine, packaging industry, agrochemistry, aquaculture, functional textiles and cosmetotextiles, catalysis, chromatography, beverage industry, photography, wastewater treatment and sludge dewatering, and biotechnology. Nutraceuticals and cosmeceuticals are actually growing markets, and therapeutic and biomedical products should be the next markets in the development of chitosan. Chitosan is also the object of numerous fundamental studies. In this review, we highlight a selection of works on chitosan applications published over the past two decades.

**Keywords** Chitosan · Biopolymer · Applications

## Introduction

Main commercial polymers are derived from petroleum-based raw products using processing chemistry that is not always safe or environmental friendly. Over the past three decades, there has been a growing interest in developing natural alternatives to synthetic polymers, namely biopolymers. Biopolymers are polymers derived from living organisms or synthesized from renewable resources. They have expanded significantly due to their biological origin and mostly to their non-toxicity and biodegradable nature. Biopolymers include polysaccharides such as cellulose, starch, chitin/chitosan (Fig. 1), and alginates.

Because of its remarkable macromolecular structure, physical and chemical properties, bioactivities, and versatility, quite different from those of synthetic polymers, the biopolymer chitosan has received much attention in fundamental science, applied research, and industrial biotechnology (Crini 2019; Crini et al. 2009, 2019; Kim 2011, 2014;

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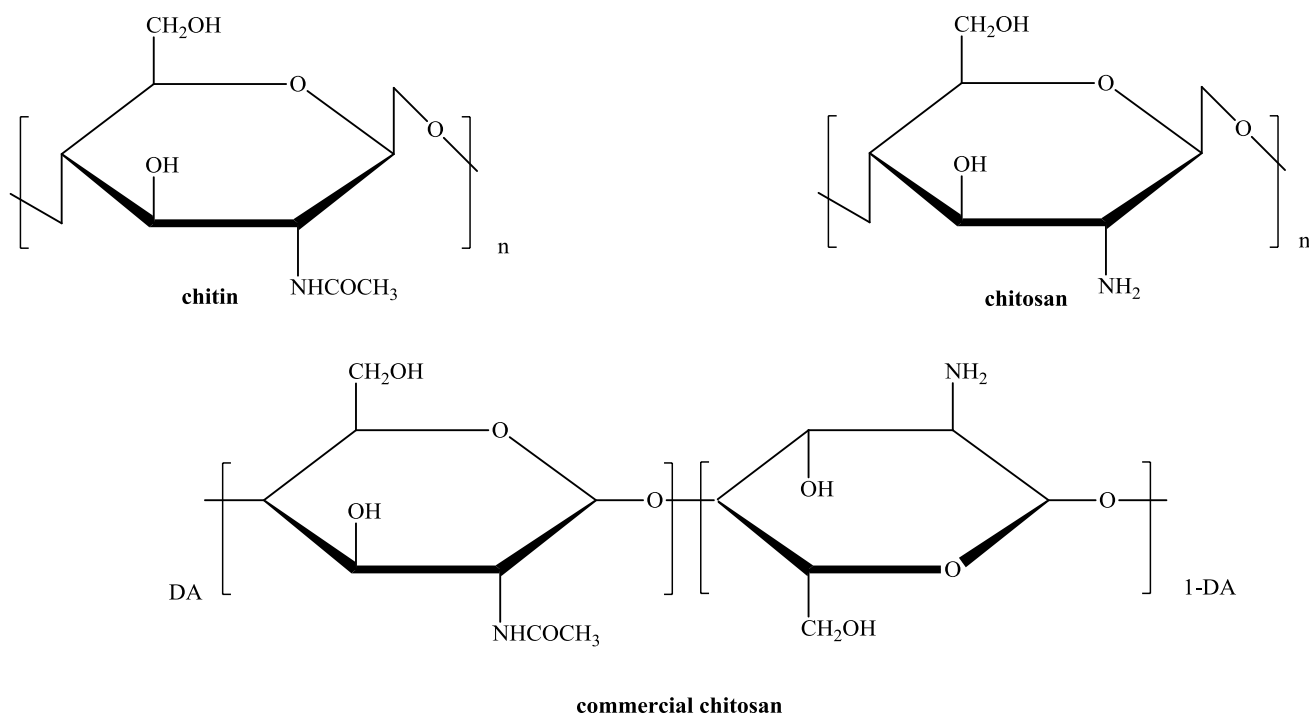
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**Fig. 1** Schematic representation of completely acetylated chitin [poly(*N*-acetyl-β-D-glucosamine)], completely deacetylated chitosan [poly(D-glucosamine)], and commercial chitosan, a copolymer characterized by its average degree of acetylation (DA) per cent

Castro and Paulín 2012; Teng 2012; Sashiwa and Harding 2015; Dima et al. 2017; Philibert et al. 2017). Currently, chitosan and its derivatives have practical applications in the form of solutions, suspensions, particles, e.g., beads, resins, spheres, nanoparticles and sponges, gels/hydrogels, foams, membranes and films, fibers, microscopic threads, and scaffolds in many fields: medicine and biomedicine, pharmacy, cosmetology, hygiene and personal care, food industry and nutrition, agriculture and agrochemistry, textile and paper industries, edible film industry and packaging, biotechnology, chemistry, and catalysis, chromatography, beverage industry and enology, photography, and other emerging fields such as nutraceuticals, functional textiles and cosmetotextiles, cosmeceuticals, nanotechnology, and aquaculture (Sandford 1989; Onsoyen and Skaugrud 1990; No and Meyers 1995; Li et al. 1997; Ravi Kumar 2000; Khor 2001; Struszczyk 2002; Honarkar and Barikani 2009; Crini et al. 2009; Davis 2011; Ferguson and O'Neill 2011; Kardas et al. 2012; Sarmiento and das Neves 2012; Yao et al. 2012; Khor and Wan 2014; Bautista-Baños et al. 2016; Dutta 2016; Hamed et al. 2016; Ahmed and Ikram 2017; Amber Jennings and Bumgardner 2017a, b; Arfin 2017; Badawy and Rabea 2017; Dima et al. 2017; Philibert et al. 2017; Han et al. 2018; Pellá et al. 2018; Sharif et al. 2018; Song et al. 2018; Wei et al. 2018; Zhao et al. 2018). Chitosan as eco-friendly biopolymer is also proposed for environmental purposes and applied in

clarification and water purification, wastewater treatment, remediation, sludge dewatering, and membrane filtration (Crini and Badot 2008; Bhatnagar and Sillanpää 2009; Sudha 2011; Ravichandran and Rajesh 2013; Yong et al. 2015; Barbusinski et al. 2016; Kos 2016; Nechita 2017; Desbrières and Guibal 2018; Pakdel and Peighambaroust 2018; Lichtfouse et al. 2019). Research on chitosan is also very active in electrochemical sensors, bioimaging, biocatalysis, ionic liquids, green solvents, adhesives, and detergents. However, the main markets are the food industry and nutrition, and the pharmaceutical, cosmetic, and medicine industries. The markets for chitin and chitosan are Japan, USA, Korea, China, Canada, Norway, Australia, France, UK, Poland, and Germany (Ferraro et al. 2010; Nwe et al. 2011; Badawy and Rabea 2017; Bonecco et al. 2017). Japan dominated the industry accounting for 35% of the market in 2015. Indeed, since the 1980s, Japan is considerably advanced in the technology, commercialization, and use of these biopolymers (Badawy and Rabea 2017; Bonecco et al. 2017). The market in this country absorbs about 700–800 tons chitosan per year.

In this review, we highlight a selection of works on chitosan applications published over the past two decades. However, the examples presented are not exhaustive due to the very large number of papers published. This article is an abridged version of the chapter published by Morin-Crini et al. (2019) in the series Sustainable Agriculture Reviews.

## Food industry

Table 1 describes applications of chitosan and its oligosaccharides in food industry. Chitosan has been approved by the US Food and Drug Administration as a generally recognized as safe food additive, dietary fiber (hypocholesterolemic effect), and functional ingredients for the consumer. Chitosan is also approved as a food additive in Japan and in Korea since the 1990s (Vidanarachchi et al. 2011; Gutiérrez 2017). Due to its bioactive nature and cationic character, chitosan is used as nutritional ingredient (food additives, functional food), antimicrobial and antioxidant agent (food protection), for antimicrobial coatings for fruits and vegetables, in anticholesterolemic dietary products, and as nutraceuticals (Shahidi et al. 1999; Agulló et al. 2003; Synowiecki and Al-Khateeb 2003; Vidanarachchi et al. 2011; Kardas et al. 2012; Je and Kim 2012, 2013; van den Broek et al. 2015; Gutiérrez 2017; Han et al. 2018).

Friedman and Juneja (2010) pointed out the outstanding antimicrobial activities of chitosan in solution, powders, and edible films and coating against microorganisms. The better results were obtained with low molecular weight

chitosan. Actually, research is directed to new chitosan derivatives and oligomers that can be applied as antimicrobial agent against food microorganisms. These derivatives seem promising, in particular for nutraceutical applications. Kardas et al. (2012) demonstrated that chitosan and its derivatives offer a wide range of unique applications in the food industry including preservation of foods from microbial deterioration, shelf-life extension, formation of biodegradable films, and food packaging. The products used as a packaging or coating material can be formed into fibers, films, gels, beads, or nanoparticles. Van den Broek et al. (2015), reviewing the development of chitosan films and blends as packaging material, also reported a similar conclusion. Due to its antimicrobial and film-forming activities, chitosan has been considered as an appropriate alternative as source of food preservative or coating material for replacing the non-biodegradable and non-renewable polymers, and also reducing the extensive application of harmful pesticides in food protection. Indeed, its films have a selective permeability to gasses (Friedman and Juneja 2010; Fernandez-Saiz et al. 2010; Kardas et al. 2012; Elsabee and Abdou 2013; Muñoz-Bonilla et al. 2014; van den Broek et al. 2015). In addition, the chitosan films have shown superior results and good mechanical

**Table 1** Applications of chitosan and its oligosaccharides in the food industry

Topic	Forms	Applications
Food technology	Solution	Additives: fining agent, texture controlling agent, natural flavor extender, emulsifying agent, gelling agent, color stabilizer, dye-binding properties, thickener and stabilizer for sauces, flavor extender
Nutrition	Film	
Functional foods	Blend	Improve nutritional quality
Food additives	Coating	Bioactivities: antibacterial, antifungal, antioxidants
Food mimetic	Bead	Preservation of foods from microbial deterioration: protective for fruits
Food protection		Filmogenic properties; microbial films (bactericidal, fungicidal); food wrapping
Food preservation		Edible films: controlled release of antioxidants, flavors or nutrients; antimicrobial substances
Seafood quality preservation		controlled release; reduction of oxygen partial pressure; moisture transfer control; temperature control; controlled rate of respiration
Industrial bio-products		
Nutraceutical ingredients		Diet foods and dietary fibers: not digestible by humans; glucose dialysis; water holding capacity
Dietary food additives		Hypolipidemic and hypocholesterolemic activities: reduction of lipid absorption, bind fats/lipids, reduce cholesterol
Dietary fiber		
Prebiotic ingredient		Astringency: able to precipitate saliva proteins
Flavors/Aromas		Non-digestible feed ingredients: prebiotics
Essential oils		Production of single cell protein
Feed additives		Enhancement of the calcium absorption
Immobilization of enzymes		Encapsulation of nutraceuticals
Edible film industry		Fractionation of agar
Packaging		Biotechnology: immobilization matrix
Coating material		Bioconversion for the production of value-added food products
Food processing wastes		Recovery of waste material from food-processing discards
Removal of substances		Infant feed ingredient Animal feed additive Undesired substances removal: dyes, suspended solids Water purification

Goosen (1997), Muzzarelli and de Vincenzi (1997), Shahidi et al. (1999), Domard and Domard (2001), Struszczyk (2002), Agulló et al. (2003), Peniche et al. (2003), Roller and Valley (2003), Bégin et al. (2004), Cagri et al. (2004), Shahidi (2004), Krajewska (2005), Borderias et al. (2005), No et al. (2007), Fernandez-Saiz et al. (2010), Rodrigues et al. (2012), Je and Kim (2012, 2013), Alishahi (2012), Coma (2012), Elsabee and Abdou (2013), Muñoz-Bonilla et al. (2014), van den Broek et al. (2015), Zivanovic et al. (2015), Gallo et al. (2016), Hamed et al. (2016), Gutiérrez (2017), Han et al. (2018), Perinelli et al. (2018), Wang et al. (2018), de Farias et al. (2019) and Hu and Ganzle (2019)

properties and they have the advantage of being able to incorporate functional substances such as vitamins and as carriers releasing of antimicrobial agents. However, chitosan films in packaging application are highly permeable to water vapor, and due to their hydrophilic character, they also tend to exhibit resistance to fat diffusion and selective gas permeability. A discussion on the different strategies to overcome these drawbacks can be found in the reviews by Kardas et al. (2012), Elsabee and Abdou (2013), van den Broek et al. (2015), and Wang et al. (2018). Blends, composites, and multilayer systems containing chitosan have been proposed as films in food packaging fields and seem promising.

The field of food industry and nutrition is the most important user of chitosan (Gutiérrez 2017; Philibert et al. 2017), and the main markets are localized in Asia (Japan, Korea, China), North America, and Europe. In the USA, the market in food and beverages is estimated to be 2288 metric tons in 2018. The demand for chitosan is growing rapidly, in particular for potential applications in nutraceutical ingredients and feed stocks. Nutraceuticals as an industry emerged in the early 1990s in Asia, in particular in Japan. The nutraceutical industry includes functional foods, dietary supplements, and herbal/natural products. Actually, the US market represents the largest nutraceutical market in the world and the Europe (Germany, France, Netherlands, Sweden) the second. China is expected to be the world's largest consumer of nutraceuticals by 2030. Many products available (ChitoClear<sup>®</sup>, Chitoseen<sup>™</sup>-F, MicroChitosan NutriCology<sup>®</sup>, etc.) are marketed as fat reducers and cholesterol-lowering agents and also as antioxidant agents. For instance, ChitoClear<sup>®</sup> is noted as a natural, safe, and effective weight loss supplement when used in conjunction with a healthy lifestyle (PRIMEX,

Iceland). It seems to have a potential in weight management and obesity treatment. However, there is a debate surrounding the effectiveness of chitosan at blocking fat absorption. The nutraceutical properties of chitosan include its antibacterial, anti-inflammatory, antioxidant, anti-carcinogenic, and antiulcer bioactivities, along with its application as a dietary fiber. Chitosan has non-digestibility in the upper gastrointestinal tract, high viscosity, and high water binding properties (Muzzarelli and de Vincenzi 1997; Roller and Valley 2003; Badawy and Rabea 2017). As a dietary fiber, it has ability to lower cholesterol by blocking the absorption of dietary fat and cholesterol. Chitosan and its derivatives have been shown to facilitate weight and body fat loss in the human body, thus decreasing systolic and diastolic blood pressure (Philibert et al. 2017). Additionally, it significantly increases the excretion of highly atherogenic saturated fatty acids compared with other fibers. As a valuable prebiotic, chitosan can also promote colonic conditions. Gutiérrez (2017) reported that chitosan and its derivatives also exert strong antioxidant activity and their effects are similar to those of phenolic antioxidants. Chitosan products also offer benefits as components of animal feeds, and this is also a growing market. They permit food processors to recycle protein from biowastes into animal feed. They have beneficial nutritional properties, and they can control the release of feed additives in animals.

## Beverage industry

Table 2 summarizes the potential uses of chitosan in beverage industry. In wine production, it can be used for clarification, de-acidification, stabilization, elimination of ochratoxin A, enzymes, and other undesired substances, e.g., metals

**Table 2** Applications of chitosan and its derivatives and oligosaccharides in the beverage industry

Topic	Form	Applications
Beverages	Solution	Filtration and clarification of fruit juices and beverages (wines, beer, tea)
Functional beverages	Particle	Natural flocculant: turbidity removal, removal of suspended solids and colloids (polyphenols, proteins, polysaccharides, minerals)
Enology	Bead	Acidity-adjusting agent: de-acidification of fruit juices and beverages
Beer industry		Stabilization of beverages (white wines)
Packaging		Preservative in fruit juices, wines and milk
		Color stabilizer
		Prevention of oxidation of the wine color
		Antimicrobial agent: preservation of drinks from microbial deterioration (bacteria, yeasts, molds)
		Natural flavor extender
		Bioactive compounds encapsulation: protection to oxidation, to improve the bioavailability of probiotics, making of undesirable taste
		Preservatives and active packaging
		Complexing agents in wine industry: metal removal
		Removal of dead yeast, excess tannin, particulates
		Water purification

Shahidi et al. (1999), Struszczyk (2002), Chatterjee et al. (2004), Bornet and Teissedre (2005, 2011), Rungsardthong et al. (2006), Domingues et al. (2012), Gassara et al. (2015), Tastan and Baysal (2015) and Rocha et al. (2017)

and pesticides (Bornet and Teissedre 2011). Chitosan is also used as eco-friendly coagulant for passion fruit clarification (Domingues et al. 2012) and natural flocculant for beer clarification (Gassara et al. 2015). Rocha et al. (2017) presented an overview of the recent chitosan-based matrices used for clarification, preservation, encapsulation, and active and intelligent packaging of different beverage types, such as alcoholic, dairy-based drinks, and non-alcoholic, including fruit juices, nectars, concentrated fruit juices, tea, coffee, and tisanes. Only the clarification using chitosan of fungal origin (Oneobrett<sup>®</sup>, Bactiless<sup>™</sup>) seems to be well implemented in the market.

## Pharmacy

For chitosan, pharmaceutical applications started to appear in the late 1980s (Nagai et al. 1984; Felt et al. 1998; Ravi Kumar 2000). In this field, chitosan and its derivatives have been mainly explored as excipients in drug formulations and drug delivery systems (Badwan et al. 2015). The new approach consisted of replacing potentially toxic compounds by natural products, which rapidly proved to be promising. The pharmaceutical industry rapidly understood the advantages of using chitosan. Although hundreds of papers and patents related to chitosan-based pharmacy have been published since the late 1980s, this sector continues to interest both the scientific community and the industry, mainly in terms of bioactivities. The most important features and advantages of chitosan can be found in the review by Bernkop-Schnürch and Dünnhaupt (2012). Its derivatization also contributed to expansion of application and decrease toxicity.

The main properties used in the pharmaceutical field are: controlled drug release, e.g., anti-inflammatory naproxen, mucoadhesive properties, in situ gelling properties,

transfection enhancing properties (deoxyribonucleic acid- and small interfering ribonucleic acid ribonucleic acid-based drugs form stable complexes with chitosan), and permeation enhancing properties (Bernkop-Schnürch and Dünnhaupt 2012). Chitosan also exhibits efflux pump inhibitory properties like other polysaccharides. Chitosan and its derivatives may be used as solutions, gels, tablets, capsules, fibers, films, and sponges (Ali and Ahmed 2018). Consequently, they may be used in oral, ocular, nasal, vaginal, buccal, parenteral, intravesical, and transdermal administration, and as implants for drug delivery in both implantable and injectable forms. Table 3 reports different methods for the preparation of chitosan-based drug delivery systems (Felt et al. 1998; Ravi Kumar 2000; Peniche et al. 2003; Ravi Kumar et al. 2004; Dash et al. 2011; Ali and Ahmed 2018). Akbar and Shakeel (2018) recently discussed the various forms of chitosan materials as drug delivery devices and attempted to report the vast literature available on chitosan-based systems in drug delivery applications. Hamed et al. (2018) also summarized the potential applications of chitosan-based hydrogels for pharmaceutical and biomedical uses, particularly with regard to drug delivery in wound dressings.

Drug delivery applications include not only controlled drug release systems, e.g., site-specific antibiotics delivery in the stomach and controlled release of proteins, but also vaccine and gene delivery (Singh et al. 2018). Chitosan is used as safe excipients in oral dosage form over the past two decades (Felt et al. 1998; Ravi Kumar 2000; Ravi Kumar et al. 2004). Chitosan tablet can exhibit a sustained drug release compared to commercial products. Bernkop-Schnürch and Dünnhaupt (2012) reported that tablets are the likely most favorable dosage form since they provide an accurate dosage, are easy to manufacture and handle, and are favored by patients. The buccal route is an alternative choice to deliver drugs. Chitosan is interesting to be

**Table 3** Chitosan-based drug delivery systems prepared by different methods

Form	Applications	Drug(s)
Microspheres	Water-in-oil emulsion cross-linking Coacervation/precipitation Spray-drying Ionic gelation Sieving method	Diclofenac, aspirin, 5-fluorouracil
Beads	Coacervation/precipitation	Bovine serum albumin, salbutamol
Nanoparticles	Emulsion-droplet coalescence Coacervation/precipitation Ionic gelation Reverse micellar method	Insulin, cyclosporin A
Gels/Hydrogels	Cross-linking reactions	Caffeine, lidocaine
Tablets	Matrix coating	Diclofenac, salicylic acid
Capsules/Microcapsules	Capsule shell	Insulin
Films	Wet casting from salt solutions	Testosterone, trypsin
Sponges/Foams	Freeze drying Reactions in supercritical fluids	Triamcinolone acetoneide

used for buccal delivery due to its mucoadhesive bioactivity and absorption enhancement property. Strong permeation enhancing properties are also mentioned.

Injectable preparations containing chitosan have received considerable attention in recent years. The properties of chitosan also resulted in the development of vaccine delivery (Bernkop-Schnürch and Dünnhaupt 2012). The transmucosal administration of drugs has been described in detail by Illum and Davis (2004). The transmucosal absorption promoter effect of chitosan is important for nasal and oral delivery of polar drugs to administrate peptides and proteins, and for vaccine delivery. Films and fibers prepared using chitosan and chitin were developed for tissue engineering and wound care dressing, as oral mucoadhesive and water-resisting adhesive by virtue of their release characteristics and adhesion (Kato et al. 2003; Illum and Davis 2004). The chitosan-based fiber production was discussed in detail by Pillai et al. (2009).

Promising developments were under way not only in biomedicine but also in emerging domains such as nutraceuticals and cosmeceuticals. Indeed, pharmaceutical formulations containing chitosan and derivatives are proposed for slimming application, body weight management and as cosmetics to enhance skincare efficacy for example. The use of nanocomposites in drug delivery also seems promising as recently reported by Ali and Ahmed (2018). Other applications of chitosan and its derivatives are described in Table 4.

## Medicine

The medical and biomedical potential applications of chitosan include pharmaceutical formulation and drug delivery (antibiotics, anti-inflammatory substances, vaccines, proteins, peptides, growth of factors), antimicrobial applications, gene delivery, gene therapy, wounds healing and burns, regenerative medicine, tissue engineering (bone, ligament, cartilage, tendon, liver, neural and skin regeneration), cancer applications (treatment, therapy, diagnostic strategy), dermatology, ophthalmology, dentistry, biosensors, and many other applications such as bioimaging (magnetic resonance imaging), support for immobilized enzymes, and veterinary medicine (Table 5).

For medical applications, chitosan and its derivatives as chitoooligosaccharides can be easily processed into different forms such as solutions, gels/hydrogels, sponges, microparticles/nanoparticles, membranes and films (pure films or blends, adhesives), and fibers/nanofibers (Allan et al. 1984; Hon 1996; Dumitriu 2001; Yilmaz 2004; Jayakumar et al. 2010, 2011b; Riva et al. 2011; Elieh-Ali-Komi and Hamblin 2016; Amber Jennings and Bumgardner 2017a, b; Rijal et al. 2017; Ali and Ahmed 2018; Hamedi et al. 2018; Liaquat and Eltem 2018). The use of chitosan-based materials in 2D scaffolds such as films and fibers and 3D scaffolds such as gels and sponges is discussed in the reviews by Croisier and Jérôme (2013), Anitha et al. (2014), Ahmed and Ikram (2016), and LogithKumar et al. (2016), with a special focus on tissue engineering and wound healing applications. Their

**Table 4** Applications of chitosan and its derivatives including oligosaccharides in pharmacy

Topic	Form	Applications
Excipients	Solution	Excipients
Drug delivery	Powder	Encapsulation of sensitive drugs: to increase and to modulate drug release rate
Drug release	Microsphere	Controlled drug delivery carriers
Vaccines	Bead	Controlled release of proteins and peptides
Biopharmaceutics	Tablet	Gene delivery (nucleic acid)
Nutraceuticals	Capsule, microcapsule	Dermatological products: to treat acne
Body weight management	Nanoparticle	Hydrating agent
Cosmeceuticals	Nanocomposite	Hemostatic and anticoagulant
Dermatology	Sponge	Bacteriostatic agent
Ophthalmology		Mucoadhesion
Oral drug delivery		Biological adhesive: water-resisting adhesive
Imaging agents		In situ gelation
		Transfection
		Permeation enhancement
		Healing: wound healing, self-healing
		Efflux pump inhibitory properties
		Products for radiopharmaceutical domains
		Nutraceutical ingredients

Goosen (1997), Illum (1998), Dodane and Vilivalam (1998), Felt et al. (1998), Ravi Kumar (2000), Hejazi and Amiji (2001), Agnihotri et al. (2004), Canh et al. (2004), Ravi Kumar et al. (2004), Prabakaran and Mano (2005), Varshosaz (2007), Dash et al. (2009), Kang et al. (2009), Hamman (2010), Riva et al. (2011), Bernkop-Schnürch and Dünnhaupt (2012), Xiao et al. (2012), Zhao (2012), Yong and Wong (2013), Badwan et al. (2015), Mateescu et al. (2015), Majekodunmi (2016), Lucio and Martínez-Ohárriz (2017), Parhi (2017), Ahsan et al. (2018), Akbar and Shakeel (2018), Ali and Ahmed (2018), Krishnaswami et al. (2018), Naskar et al. (2018), Tripathi and Singh (2018) and Rajoka et al. (2019)

**Table 5** Applications of chitosan and its oligosaccharides in medicine and biomedicine

Topic	Forms	Applications
Drug delivery	Solution	Drug delivery: delivery of antibiotics, peptides, proteins, vaccines
Biomedicine	Gel/hydrogel	Growth factor delivery
Biomedical engineering	Powder	Biological response modifier
Biofabrication	Microsphere	Gene delivery, targeted delivery, deoxyribonucleic acids therapy, gene therapeutics, small interfering ribonucleic acid delivery
Tissue engineering	Microcapsule	
Regenerative medicine	Bead	Antifungal, antimicrobial, anti-infectious
Wound dressing	Nanoparticle	Hemostatic effects; enhances blood coagulation
Growth factor	Film	Anticoagulant hydrogel containing heparin
Biomedical adhesives	Fiber, nanofiber	Blood cholesterol control
Medical materials	Nonwoven bioactive fiber	Adjuvant properties
Medical devices	Sponge	Bioadhesive
Implants	2D- and 3D-scaffolds	Artificial skin; skin burn
Orthopedics	Shaped object	Promotes tissue growth; tissue repair and regeneration
Therapeutic domains	Adhesive	Cartilage tissue engineering
Microbiology		Scaffolds for cell culture; stimulates cell proliferation
Immunization		Material supporting nerve repair
Immunology		Wound healing properties
Gene therapy		Scaffolds for bone regeneration: bone substitutes and cements; rebuilding of bone
Cell biology		
Cell therapy		Biocompatible and biodegradable materials for use as implants, blood substitutes, blood vessels, or wound dressing material
Cell adhesion and proliferation		
Cell–biomaterials interactions		Anti-tumor agent, tumor inhibition
Protein adsorption onto biomaterials		Treatment of leukemia, diabetes
Cancer diagnosis		Sutures, surgical threads, bandages, sponges
Cancer therapy		Dental implants
Carriers of anticancer drugs		Contact lenses
Ophthalmology		Magnetic resonance imaging
Biosensing		
Bioimaging		
Bioprinting		
3D printing		

Francis Suh and Matthew (2000), Khor and Lim (2003), Elder et al. (2004), Berger et al. (2004a, b), Illum and Davis (2004), Sashiwa and Aiba (2004), Barbosa et al. (2005), Yi et al. (2005), Shi et al. (2006), Jayakumar et al. (2007), Lee (2007), Alves and Mano (2008), Kang et al. (2009), Muzzarelli (2009, 2011), Venkatesan and Kim (2010), Khor (2011), Sahoo and Nayak (2011), Dash et al. (2011), Dutta et al. (2011), Jayakumar et al. (2011a), Lakshmanan et al. (2011), Liu et al. (2011), Luna-Bárceñas et al. (2011), Sarmiento and das Neves (2012), Wang et al. (2012), Croisier and Jérôme (2013), Kim and Pangestuti (2013), Anitha et al. (2014), Jana et al. (2014), Junginer and Sadeghi (2014), Muñoz-Bonilla et al. (2014), Vera Balan and Verestiuc (2014), Azuma et al. (2015), Pokhrel et al. (2015), Dutta (2016), Ahmed and Ikram (2016), Elieh-Ali-Komi and Hamblin (2016), Choi et al. (2016), LogithKumar et al. (2016), Ahmad et al. (2017b), Amber Jennings and Bumgardner (2017b), Balagangadharan et al. (2017), Bano et al. (2017), Ellis and Korbitt (2017), Harris et al. (2017), Layek and Singh (2017), Vunain et al. (2017), Aljohani et al. (2018), Ahsan et al. (2018), Ahmed et al. (2018), Ahsan et al. (2018), Ali and Ahmed (2018), Anraku et al. (2018), Baranwal et al. (2018), De Mori et al. (2018), Dimassi et al. (2018), Ding et al. (2018), Hamed et al. (2018), Hu et al. (2018), Li et al. (2018), Komi et al. (2018), Krishnaswami et al. (2018), Liaqat and Eltem (2018), Mohandas et al. (2018), Nezakati et al. (2018), Oryan et al. (2018), Pellá et al. (2018), Qasim et al. (2018), Shariatnia and Jalali (2018), Singh et al. (2018), Tripathi and Singh (2018), Xing et al. (2018), Vasconcelos and Pomin (2018), Xu et al. (2018), Zhao et al. (2018), Avcu et al. (2019), Barbosa et al. (2019), Chuan et al. (2019), Kalantari et al. (2019), Kravanja et al. (2019), Rajoka et al. (2019), Shanmuganathan et al. (2019) and Sharnshina et al. (2019)

bacteriostatic and fungistatic properties are particularly useful for wound treatment. This application combines two of the most interesting properties of chitosan: antimicrobial activity and biocompatibility. Chitosan and its oligosaccharides have also a stimulatory effect on cells.

Materials in the forms of nonwovens, nanofibers, composites, films, and sponges can accelerate wound healing and dermal regeneration. These products have been on the market since the early 1990s, mainly in North America and Asia, and more recently in Europe (Germany, France). Actually, the main biomedical commercial applications of chitosan are in wound healing. Various forms of wound dressing

chitosan-based materials are commercially available in the market: HemCon<sup>®</sup> Bandage, ChitoGauze<sup>®</sup> PRO, ChitoFlex<sup>®</sup> PRO, ChitoSam<sup>™</sup>, Syvek-Patch<sup>®</sup>, Chitopack C<sup>®</sup> and Chitopack S<sup>®</sup>, Chitodine<sup>®</sup>, ChitosanSkin<sup>®</sup>, TraumaStat<sup>®</sup>, TraumaDEX<sup>®</sup>, Celox<sup>™</sup>, etc. For example, HemCon<sup>®</sup> Bandage is an engineered chitosan acetate preparation designed as a high-performance hemostatic dressing (HemCon Medical Technologies, Inc., USA).

Other biomedical products are in the market. Reaxon<sup>®</sup> (Medovent, Germany) is a chitosan-based nerve conduit which is resistant to collapse and helps to avoid the undesired drawbacks of autografts. This hydrogel is bioactive



(supports nerve regeneration equivalent to the autograft), biocompatible (prevents irritation and inflammation), anti-adhesive (inhibits scar tissue and neuroma formation), and antibacterial (prevents infection). Its particular structure also facilitates the transport of nutrients and oxygen. ChitoSeat™ is a family of chitosan-based hemostatic sealants that are suitable for surgical hemorrhage of hard and soft tissue (LUNA, USA).

In tissue engineering, the aim is to restore or replace damaged body parts or lost organs by transplanting supportive scaffolds with appropriate cells that in combination with biomolecules generate new tissue (Dash et al. 2011; Saravanan et al. 2013; Ahmed et al. 2018). Dash et al. (2011) reported that chitosan is an ideal dressing in wound healing applications due to the fact that not only it protects the wound from bacterial infection but also it promotes healing and it produces less scarring. In addition to the reparative nature of the material, it can also deliver a therapeutic payload to the local wound, for example fibroblast growth factor 2, which stimulates angiogenesis by activating capillary endothelial cells and fibroblasts. The potential use of chitosan in this topic is, however, limited due to its poor solubility in water, faster in vivo depolymerization/degradation, hemo-incompatibility, and also weak antimicrobial property. To overcome these problems, chitosan derivatives have been proposed as novel scaffold materials for tissue engineering. A discussion on the use of many derivatives in bone tissue engineering as emerging products can be found in the reviews by LogithKumar et al. (2016) and Ahmed et al. (2018).

For bone regeneration, several injectable materials were used. Chitosan-calcium phosphate composites appear to have a promising clinical application. Chemically modified hyaluronic acid–chitin and chitosan–hyaluronic acid material were reported to be osteoinductive and exhibited rapid degradation and neovascularization in vivo. Chitosan scaffolds are potentially a useful alternative to synthetic cell scaffolds, also for cartilage tissue engineering. Anitha et al. (2014) reviewed the use of chitosan-based membranes and scaffolds not only for tissue engineering and wound healing but also as anticancer drug delivery, osteogenic drug delivery, and growth factor delivery. The key features of these biomaterials are their biodegradability, cytocompatibility, multi-functionality, and specific mechanical properties. *n*-Lauryl-carboxymethylcellulose has been proposed as carrier for hydrophobic cancer drugs. This amphiphilic substance is safe in terms of membrane toxicity. Materials for cancer chemotherapy are important but still under development (Saneja et al. 2016). Chitosan-based biomaterials were proposed against diabetes and related complications (Kim and Karadeniz 2013; Kim and Pangestuti 2013; Karadeniz and Kim 2014a, b) and also as new adhesives (Mati-Baouche et al. 2014).

Chitosan is a biocompatible substance with no antigenic properties, and thus, it is perfectly compatible with living tissues. Its hemostatic and antithrombogenic bioactivities make it suitable in all fields of medicine: for controlled drug release, drugs encapsulation, enzymes and cells immobilization, and also as gene carriers. Chitosan is biodegradable and enzymes break it down into oligo-products which are then processed by metabolism. Many chitosan derivatives are also biocompatible and non-toxic with living tissues. Other advantages of chitosan-based materials often cited are related to their hydrophilic property, biodegradability, antibacterial activity, bioadhesivity, mucoadhesivity, and complexing property.

Like alginate polysaccharide, chitosan has the characteristic of forming gels in addition to possessing viscosity-related properties, complete biodegradability, and even anti-tumor influence. Chitosan forms films that are permeable to air. It facilitates cellular regeneration while protecting tissues from microbial attacks. Chitosan has also a stimulating effect on the regeneration of tissues. It is used in making an artificial skin for skin grafts on high-degree burns and in surgical applications (suture threads). Chitosan can trap lipids at their insolubilisation pH in the digestive tract. It considerably reduces the level of cholesterol in the blood. Chitosan possesses bioadhesive properties which make it of interest in adhesive sustained release formulation required. Mucoadhesivity permits to enhance the adsorption of drugs especially at neutral pH (Dash et al. 2011; Liu et al. 2011; Dutta 2016; Amber Jennings and Bumgardner 2017a, b; Vunain et al. 2017).

Genetic materials such as deoxyribonucleic acids and ribonucleic acid are used in gene therapy as pharmaceutical agents to treat various diseases (Lee 2007; Dash et al. 2011; Kedjarune-Leggat and Leggat 2011; Choi et al. 2016; Badawy and Rabea 2017). However, the use of genetic materials is limited due to rapid degradation by nuclease, large size, poor cellular uptake, high anionic charge density, and also non-specificity. To overcome these problems, non-viral vectors as cationic chitosans were proposed as promising delivery biomaterials in gene therapy (Kedjarune-Leggat and Leggat 2011). Chitosan is a prominent system-based gene delivery vector due to its facility to form complexes, biodegradability, and biocompatibility, although its transfection efficiency and cell specificity are low. Its role in gene delivery is supported by its ability to protonate in acidic media forming a complex with deoxyribonucleic acids through electrostatic interactions (Choi et al. 2016). The chitosan–deoxyribonucleic acids complexes are easy to prepare and are more effective compared to the commonly used systems. Chitosan–deoxyribonucleic acids complexes were reported to transfect into various cell types: human embryonic kidney cells, cervical cancer cells, primary chondrocytes, and fibroblast cells. As recently reviewed by Badawy

and Rabea (2017), the transfection efficiency of chitosan depends on the degree of acetylation, molecular weight, pH of the transfecting media, cell type, and the charge ratio of the luciferase plasmid to chitosan. Limitations in the use of chitosan for non-viral gene therapy were previously reported by Kedjarune-Leggat and Leggat (2011). Most of the results on gene therapy using chitosan were obtained from experiments in vitro, and further research is needed in vivo. In addition, studies still need to understand the effects of the characteristics of the carriers on cellular entry and intracellular trafficking processes (Choi et al. 2016).

Sulfated chitosan has the ability to interfere with blood clotting process. This is a subject of extensive medical applications. Compared to heparin, this derivative has been shown to possess high anticoagulant potency. Unlike heparin, sulfated chitosan does not show anti-platelet activity, which causes excessive bleeding in patients (Badawy and Rabea 2017). Another example of extensive medical studies concerns the production of chitosan-based vaginal tablets used as drug delivery systems due to their adequate release properties and good adhesive properties (El-Kamel et al. 2002; Raafat and Sahl 2009; Bernkop-Schnürch and Dünnhaupt 2012). However, as claimed by Raafat and Sahl (2009), the antimicrobial properties of chitosan might have a negative impact on the vaginal microflora. Its vaginal use for treatment of chronic diseases has therefore to be seen with caution. Another application related to chitosan is based on the fact that its modified particles provide an excellent template for bioimaging. Chitosan-based nanoparticles containing imaging agents were studied for radiopharmaceutical applications and magnetic resonance imaging (Ravi Kumar et al. 2004; Dash et al. 2011).

The medical and biomedical potential applications of chitosan also include ophthalmology, dentistry, and veterinary medicine. In ophthalmology, due to their non-toxic character and permeation enhancing properties, chitosan-based

formulations are used as drug delivery systems including coated colloidal systems, hydrogels, and nanoparticles (Bernkop-Schnürch and Dünnhaupt 2012; Elieh-Ali-Komi and Hamblin 2016; Krishnaswami et al. 2018). Chitosan possesses all the characteristics required for making an ideal contact lens: optical clarity, mechanical stability, optical correction, gas (oxygen) permeability, wettability, and immunological compatibility (Elieh-Ali-Komi and Hamblin 2016; Badawy and Rabea 2017). The antimicrobial activity, film-forming ability, and wound healing properties also make chitosan suitable for the development of ocular bandage lenses for traumatic injuries (Elieh-Ali-Komi and Hamblin 2016).

## Dentistry

The relevant properties of chitosan cited for dentistry are: bioactivity, anti-inflammatory, wound healing, hemostatic activities, and bone repair (Queiroz et al. 2015; Kmiec et al. 2017; Navarro-Suarez et al. 2018; Zheng et al. 2018). Chitosan is used in the form of solution (acetic or methanesulfonic acid used as solvents), microspheres, hydrogel, and toothpastes, and its association with additives such as amorphous calcium phosphate, amelogenin, and quinic acid improved the ability of these chitosan preparations in preventing dental caries and enamel erosion. Its applications in dentistry are described in Table 6. Chitosan in gel/hydrogel form applies to the treatment of chronic periodontitis and canker sores. Due to its inherent versatility, efficiency, and ability to act as a protective barrier to the penetration of acids into enamel and its mineral loss, chitosan can play an important role in preventive dentistry. In addition, when associated with remineralizing agents, chitosan preparations are able to repair early caries lesions (Queiroz et al. 2015). Toothpastes, mouthwashes, and chewing gums based on chitosan and herbs fullness functions antimicrobial effect on oral biofilm and reduction in the number of *Streptococcus*

**Table 6** Applications of chitosan and its oligosaccharides in dentistry

Topic	Form	Applications
Dental surgery	Solution	Agent to prevent diseases: dental caries, periodontitis, erosive lesion, dental plaque inhibitor
Dental therapy	Hydrogel	Ingredient in dentifrices
Dental materials	Toothpastes	Oral care, dental care: toothpaste, chewing gum
Implants	Bioadhesive	Chitosan-containing chewing gum having antibacterial effects or to increase salivary secretion
Drug delivery systems	Powder	Delivery of fluoride
Oral hygiene	Granule	Dental adhesives
Antibacterial effect	Nanoparticle	Nanobiomaterials
Restorative dentistry	Sponge	Agent to promote wound healing in bone tissue
Dental composites	Composites	Scaffolds and carriers for molecular therapy
Wound healing		Cell protective activity
Nanodentistry		

Sapelli et al. (1986), Khor and Lim (2003), Stamford Arnaud et al. (2010), Hayashi (2011), Keegan et al. (2012), Hayashi et al. (2013), Farea et al. (2014), Queiroz et al. (2015), Kmiec et al. (2017), Wieckiewicz et al. (2017), Elkassas and Arafa (2017), Ahsan et al. (2018), Navarro-Suarez et al. (2018) and Zheng et al. (2018)

*mutans* in the oral cavity (Kmiec et al. 2017). They freshen the breath and prevent the formulation of plaque and tooth decay. Salts of chitosan added to tooth paste mask the unpleasant taste of silicon oxide and bind powders, so that they maintain their granular shapes. Chitosan complex and fluoride microparticles increase fluoride absorption and protection cavities. Endodontic cements based on chitosan reduce inflammation and support bone regeneration. Navarro-Suarez et al. (2018) recently discussed the use of nanotechnology in dentistry and the latest innovations in nanobiomaterials products. Zheng et al. (2018) also reviewed the application of biomaterials in dentistry, with a focus on new techniques using a combination of scaffolds, cells, and biologically active molecules to assemble functional constructs that restore, maintain, or improve damaged tissues for dental purposes.

### Veterinary medicine

Senel and McClure (2004) previously reviewed the applications of chitosan in veterinary medicine including wound healing, bone regeneration, and analgesic and antimicrobial effects. They also discussed the potential application of chitosan to drug and vaccine delivery in veterinary species and as nutritional ingredient. Given the restrictions imposed by financial and animal restraint considerations, especially in fanning applications, the veterinary drug delivery areas most likely to benefit from chitosan are the delivery of chemotherapeutics such as antibiotics, antiparasitics, anesthetics, painkillers, and growth promotants to mucosal epithelium for absorption for local or systemic activity, and the delivery of immunomodulatory agents to the mucosal associated lymphoid tissue for induction or modulation of local immune responses. Other applications in veterinary medicine are shown in Table 7. The use of nanoparticles for drug delivery, diagnostics, and vaccine formulation has described by Underwood and van Eps (2012). Nanomedicine

using innovative nanosystems seems to be a promising domain. Products have already reached the market. For instance, chitosan-based nutritional supplements (Epakitin™, Nutri + Gen®) are commercially available for use as essential nutrients supplement or in chronic kidney disease in dogs and cats. The Epakitin formulation containing both chitosan and calcium carbonate is a safe and highly palatable kidney-protective phosphate binder. Many body cares are also available (ChitoCure®, ChitoClear®): shampoo, ear cleaner, conditioner, sprays for companion animals, etc.

### Cosmetics

It is possible to produce chitosans as well as chitosan derivatives with varying chain lengths and differentiated properties for applications in cosmetics, hygiene, and personal care. The molecular weight of most chitosan products is so high that they cannot penetrate the skin and this is an important advantage that makes it suitable for skin care. These materials include chitosan hydrochloride, chitosan acetate, chitosan lactate, carboxymethyl chitosan, quaternized derivatives, oligosaccharides, and also chitin sulfate and carboxymethyl chitin. They can be dissolved in aqueous solutions or used in solid form. In cosmetics, the specific properties employed are: cationic (chitosan and hair carry opposite electrical charges), bacteriostatic, fungistatic, antistatic, film-forming, moisture-retaining (chitosan retains moisture in low humidity and maintains hair's style in high humidity), and controlled release of bioactive agents. Chitosan is also of great interest in cosmetic formulations because it is compatible with other ingredients such as starch, glucose, saccharose, polyols, oils, fats, waxes, acids, nonionic emulsifiers and nonionic water-soluble gums. However, chitosan is incompatible with ionic gums, sulfonated surface-active agents, alkalis, and sulfuric acids. Chitosan and its derivatives can be combined with other hydrating agents, solar filters, and other bioactive products used in the formulations.

**Table 7** Applications of chitosan and its oligosaccharides in veterinary medicine

Topic	Forms	Applications
Delivery systems	Solution	Time release drugs for animals
Vaccine delivery	Powder	Mucosal formulations
Adjuvant	Microsphere	Mucosal delivery of antigens
Biological properties	Microcapsule	Improve the immune response
Mucosal immunization	Nanoparticle	Hemostatic
Wound healing	Gel, hydrogel	Wound healing activity
Tissue regeneration	Sponge	Regenerative medicine: tissue engineering
Nutritional supplement	Film	Vaccines
Nanomedicine	Filament	Surgical threads
		Food for dogs
		Reduce urea levels
		Body-care products: shampoo, sprays

Şenel and McClure (2004), Şenel (2011), Underwood and van Eps (2012), Drewnowska et al. (2013), Gerdts et al. (2013) and Tonda-Turo et al. (2016)

**Table 8** Applications of chitosan and its oligosaccharides in cosmetics

Topic	Form	Applications
Toiletry	Solution	Functional additives
Hygiene	Powder	Moisturizers: maintain skin moisture, tone skin
Personal care	Film	Thickening agent
Skin care		Hydrating and film-forming agent
Oral care		Role in surfactant stability; stabilize emulsion
Dental care		Antistatic effect
Hair care		Bacteriostatic
Cosmeceuticals		Encapsulating agent
Fragrances		Delivery systems
Essential oils		Products: shampoos, creams, skin creams, creams for acne treatment, lotions, bath lotions, nail polish, fixturs, make-up powder, lacquers, nail lacquers, nail enamel, varnishes, hair sprays, hair colorants, wave agents Cleaning products: cleansing milk, face peel, facial toner, soap, bath agent Hair care: elastic film on hair, increase its softness and mechanical strength, improve suppleness of hair, remove oils and sebum from hairs; reduce static electricity in hair, retain moisture and maintain hair's style Oral care, dental care: toothpaste, chewing gum

Goosen (1997), Struszczyk (2002), Rinaudo (2006), Crini et al. (2009), Muñoz et al. (2012), Lima et al. (2012), Senevirathne et al. (2012), Chalongsuk and Sribundit (2013), Jimtaisong and Saewan (2014), Costa and Santos (2017) and Rahangdale and Kumar (2018)

They facilitate their effects. Some derivatives of chitosan can form foam and create emulsifying actions.

Some of the chitosan applications (Table 8) are: hair care, e.g., shampoos, coloring products, hairspray, and setting lotion, creams and lotions (face, hand, and body products), color cosmetics (make-up, nail polish, eye shadow, and lipstick), deodorizing products, micro-encapsulation of active agents, and dental care, e.g., toothpaste, tooth gel, and mouth wash. Chitin is also interesting in cosmetology because it is well tolerated by the skin. It is an effective hydrating agent and a film-forming tensor having two advantages often cited: It supplies water and it avoids dehydration. Chitosan and chitin also present chelating properties toward metals that are responsible for very many contact allergies. Carboxymethyl chitosans products are mainly used in cosmetics as antioxidant agent, moisture absorption–retention agent, antimicrobial agent, delivery system, and emulsion stabilization. Jimtaisong and Saewan (2014) comprehensively discussed the utilization of carboxymethyl chitosans as multifunctional ingredients in the formulation of cosmetics. They also included in their review information on cytotoxicity of these products to ensure their safety.

Numerous chitosan-based products for cosmetic use are commercially available: Curasan™, Hydamer™, Zenvivo™, Ritachitosan®, Chitosan MM222, etc. Cosmetic industry is a strongly growing market. The cosmeceutical market has also been growing particularly rapidly of late. Cosmeceuticals (Chitoseen™-K) are cosmetics with pharmaceutical/medicinal benefits. These products seem to provide not only a health benefit but also cosmetic qualities. They contain essential oils and active ingredients such as vitamins, enzymes, antioxidants, and phytochemicals. They can be applied as creams, lotions, and ointments (Lima et al. 2012; Muñoz et al. 2012; Senevirathne et al. 2012). For the past

decade, they have continued to revolutionize the world of hair, lip, tooth, and skin care by offering safe and natural ingredients for consumer's personal use.

## Agriculture

Applications of chitosan in agriculture are summarized in Table 9. Chitosan products are used in plant protection from the 1990s against plant pathogenic bacteria that induce decay and harmful effects of agricultural crops during the growing season and postharvest phase (Yin and Du 2011). They behave as bactericidal (killing the bacteria) and/or bacteriostatic (hindering the growth of bacteria). However, the exact mechanism is still not fully understood. A discussion on models proposed for antibacterial actions of chitosan can be found in the review by Muñoz-Bonilla et al. (2014). The most accepted mechanism involves the polycationic character of chitosan which permits to interact with negatively charged species (bacterium cell membrane). The chelating properties of chitosan also make it an excellent antifungal agent (Rabea et al. 2003; Muñoz-Bonilla et al. 2014; Badawy and Rabea 2016; Divya and Jisha 2018). The presence of chitosan activates many defense responses in plants. Usually, it is employed in plant disease control as a powerful elicitor.

Chitosan products were proposed as devices for controlling the release of agrochemicals (fertilizers, pesticides). They are used as biocides either alone or blended with other products against plant diseases (control of plant bacteria and fungi), pests and insects, plant growth promotion, seed coating, and postharvest (Divya and Jisha 2018; Grande-Tovar et al. 2018; Sharif et al. 2018). Chitosan has also inhibitory effect on viruses and viroid of plants. It has a great potential as biopesticide. It can function as a seed-soaking agent, a

**Table 9** Applications of chitosan and its oligosaccharides in agriculture

Topic	Form	Applications
Plant protection	Solution	Protection of plants
Antimicrobial agent	Spray	Coating material: seeds, fruits, vegetables
Antioxidant	Coating	Stimulation of plant growth and plant production
Horticulture	Powder	Increase of crop yields
Agrochemistry	Gel	Reduce the growth of phytopathogenic fungi
Soil enrichment	Powder	Effects on gene expression
Postharvest	Nanoparticle	Pest control
Edible films		Soil treatment (nutrients)
		Modify plant–microbial interactions
		Elicitor to stimulate the accumulation of secondary metabolites and to induce plant defenses
		Frost protection
		Controlled agrochemical release
		Fertilizers and biocontrol agent (time release of products)
		Biofertilizer, fertilizer protectant
		Spray for pesticide removal (fruits)
		Pesticide formulations; biopesticides; biofungicides

Goosen (1997), El Hadrami et al. (2010), Yin and Du (2011), Sharp (2013), Muñoz-Bonilla et al. (2014), Katiyar et al. (2014), Xing et al. (2015), Badawy and Rabea (2016, 2017), Bautista-Baños et al. (2016), Hadwiger (2017), Ippólito et al. (2017), Orzali et al. (2017), Divya and Jisha (2018), Grande-Tovar et al. (2018), Sharif et al. (2018) and Malerba and Cerana (2019)

root-applying agent, and a spray agent. These activities play an important role on plant disease control and stress resistance. Blending of chitosan with other products, such as gum, starch, and alginate, is a convenient method to improve its properties for slow release of pesticides. The use of chitosan products can elicit defense to more than 60 diseases on several plants. Their potent effect on plant disease control is from their antimicrobial and plant innate immunity elicited activity. The inhibition activity was observed on different stages of fungal growth such as mycelia, sporulation, spore viability and germination, and production of fungal virulence factors.

Chitosan products can be used in various ways: coating seed (soybean, cotton, cucumber, wheat, rice), soil enrichment (for potato, soybean lettuce, spinach), foliar spraying (for peanut, soybean, cabbage, rice, maize, cotton), supplement in hydroponic (rice, wheat, peanut), and supplement in plant tissue culture medium (*Chrysanthemum*, *Limonium*, carrot). As seed-coating agent, they protect plants, e.g., cotton, tomato, wheat, and have a positive effect on germination rate, seedling growth parameters, and the yield of different cultivars, e.g., soybean sprouts, ornamental plants, maize, wheat, lentil, rice, and peanut. Their bioactivities as antifungal activity, enhancement crop yield, induction of defensive system of plants, and plant growth promotion play key roles in their application for agriculture.

The two main problems of chitosan in agriculture applications are commercial chitosan standardization and solubility. Indeed, chitosan bioactivities are dependent on several parameters including degree of acetylation, molecular weight, concentration of chitosan, pH of the solution, its viscosity, and the target of microorganism. The antimicrobial

activity of non-modified chitosan against various microorganisms such as bacteria, yeasts, fungi, and viruses has received much attention in the past two decades. The literature data showed that this bioactivity property depends on various factors such as molecular weight, which is probably the main factor affecting the efficacy, although the literature is sometimes contradictory. Generally, the antibacterial activity increases as the molecular weight decreases. However, it is difficult to find a clear correlation between the molecular weight and this bioactivity (Badawy and Rabea 2017). In spite of its unique biological aspects, the water-insoluble property is another major limiting factor for its wide application in agriculture. Recently, to overcome these problems, chitosan derivatives and oligomers produced by enzymatic and chemical modifications have been proposed. It is expected that these modified biopolymers would be promising candidates in agriculture. Research is also in progress on the mechanisms of chitosan-induced defense and on the signal perception of chitosan. Nanotechnology using innovative chitosan nanoparticles seems to be a promising domain. The methods of preparation of chitosan nanoparticles and their potential applications as antimicrobial agent, plant growth-promoting agent, and plant protector have been discussed in the recent review by Divya and Jisha (2018).

## Aquaculture

A prerequisite for the greater use of chitin in industry is cheap manufacturing processes and/or the development of profitable processes to recover chitin and by-products such as proteins and pigments. It is well known that the recovery of chitinous products from wastes is an additional

source of revenue. Crustacean shells contain considerable quantities of carotenoids which so far have not been synthesized, and which are marketed as a fish food additive in aquaculture, mainly for salmon. The use of chitosan and its derivatives in the aquaculture was described by Alishahi and Aider (2012). It can be used as functional food, nutritional supplements (synbiotics), carrier abilities for bioactive compounds, drug release, encapsulation of pathogens, or nucleic acids, and for pollutant removal from water and wastewaters (Table 10). There is also a constant need for the development of efficient vaccines and delivery systems to prevent and control the emerging and re-emerging infectious diseases in aquaculture. There are innumerable infectious diseases for which the development of efficient vaccines has been difficult to achieve. The failure is mainly due to the inability to design vaccines evoking appropriate immune responses. The use of chitosan-based nanoparticles has provided a tremendous opportunity to design vaccine delivery systems that are efficient in targeted delivery, providing stability to antigens, and act as efficient adjuvants. Many of the nanoparticles are able to enter the antigen-presenting cells by different pathways and induce appropriate immune responses to the antigen. Vinay et al. (2018) recently reviewed the use of chitosan for the delivery of fish vaccines and compared

the potential of these delivery systems for the development of new vaccines against different fish pathogens.

## Textile industry

Applications of chitosan and its derivatives in textile industry are described in Table 11. Among the possible approaches initiated by the textile industry, the use of chitosan presents an innovative possible avenue for large-scale development of bioactive textiles (Giri Dev et al. 2005; Enescu 2008; Sahan and Demir 2014; Gutiérrez 2017; Roy et al. 2017). Indeed, more research and practical use results indicate that chitosan might act as active compounds in textiles, e.g., as antimicrobial finishing of textiles, and cosmetotextiles. The characteristics of chitosan used in textile industry include cost-effectiveness, non-toxic, biocompatible, biodegradable, antimicrobial activity, antistatic activity, chelating property, deodorizing property, film-forming ability, chemical reactivity, dyeing improvement ability, thickening property, and also wound healing activity. Although the antimicrobial activity of chitosan is well documented in the literature, its mode of action is yet not fully understood (Islam et al. 2013). There are many possibilities for the development of new textile and cosmetic products containing

**Table 10** Applications of chitosan in aquaculture

Topic	Form	Applications
Quality water	Powder	Removal of organic compounds and inorganic nutrients; removal of bacteria, of ammonia
Nutrition	Microsphere	Functional food; to enhance gelling properties
Functional foods	Bead	Micro-carrier abilities for bioactive compounds: proteins, pigments
Nutritional supplements		Probiotics to improve feed conversion, growth rates, weight gain, immune system and disease resistance of fish
Probiotics/prebiotics		Micro-encapsulation of drugs and drug delivery; oral delivery (vaccination)
Controlled release of compounds		Immuno-stimulant against bacterial diseases
Treatment of seafood effluents		Antimicrobial, antioxidant and antioxidative stress

Chung et al. (2005), Chung (2006), Borgogna et al. (2011), Cerezuela et al. (2011), Alishahi and Aider (2012), Harikrishnan et al. (2012), Niu et al. (2013), Zaki et al. (2015), Lian et al. (2016), Bernardi et al. (2018) and Vinay et al. (2018)

**Table 11** Applications of chitosan and its derivatives in the textile industry

Topic	Forms	Applications
Textiles	Microcapsule	Dye binder for textiles
Functional textiles	Gel	Impregnated textile materials
Cosmetotextiles	Gelatinous dispersion	Binding agent for nonwoven
Medical textiles	Coating	Surface modification of textiles
	Fiber	Textiles with antibacterial properties
		Textile printing and antimicrobial finishing
		Textile preservative and deodorant agent
		Non-allergenic fibers
		Sanitary fibrous products
		Surgical threads

Giri Dev et al. (2005), Enescu (2008), Ummu Habeeba et al. (2007), Crini et al. (2009), Francesko et al. (2010), Islam et al. (2013), Şahan and Demir (2014), Hamed et al. (2016), Voncina et al. (2016), Gutiérrez (2017) and Roy et al. (2017)

chitosan-based nanoparticles with advanced properties (UV blocking, water repellence, self-cleaning). Their applications seem promising.

### Pulp and paper industry

Applications of chitosan in pulp and paper industry are described in Table 12. The first use of chitosan in the papermaking industry was reported in 1936 (Struszczyk 2002). The main use was to improve wet strength of paper. Chitosan as functional material is also able to interact with cellulose pulp during the formation of paper and to be film-forming to offer cohesive resistance to rupture (Song et al. 2018). This biopolymer is also non-toxic, biodegradable, and eco-friendly in order to facilitate compliance with environmental regulations. Chitosan as chelating and complexing agent is also used in the decontamination of pulp and paper wastewaters for removal of lignin, color, and undesired contaminants, and for the decrease in total organic carbon and chemical oxygen demand. Samyn et al. (2018) recently reviewed the use of nanoparticles and nanostructured materials in papermaking.

### Biotechnology

Some applications of chitosan in biotechnology are described in Table 13. Numerous enzymes (lysozyme, urease, *Escherichia coli* cells, amylases) were immobilized with chitosan. They are entrapped and absorbed in the macromolecule chains. In biochemistry, chitosan is used as a support for enzymes, mainly by cross-linking reactions. Chitosan and its derivatives have also shown biotechnology applications as biosensors and biodevices. Depolymerization and de-*N*-acetylation of chitin by chitinases and deacetylases generate a series of derivatives such as chitooligosaccharides which find numerous applications in biotechnology as recently reviewed by Grifoll-Romero et al. (2018).

### Chemistry

Table 14 describes some applications of chitosan in chemistry. Chitosan is the object of numerous studies concerning applications in chromatography, green chemistry, catalysis, membrane technology, and electrochemistry. It has been proposed in thin-layer chromatography for the separation of nucleic acids and in green chemistry for the generation of green solvents. It is believed that chitosan will play a

**Table 12** Applications of chitosan and its derivatives in the pulp and paper industry

Topic	Form	Applications
Papermaking industry	Coating	Wet strength agent; strengthening additive
Pulp and paper	Powder	Retention and drainage agents
Water treatment	Nanoparticle	Paper sizing and finishing
Papermaking-related industries		Surface coating application: coated papers with antibacterial and antimicrobial properties
		Confer strength to paper against moisture
		Biodegradable packaging for food wrapping
		Wrapping and toilet paper
		Chromatography paper
		Card board
		Carbonless copy paper
		Modification of cellulose fibers
		Photochromic paper
		Papermaking wastewater treatment

Struszczyk (2002), Crini et al. (2009), Cheba (2011), Samyn et al. (2018) and Song et al. (2018)

**Table 13** Applications of chitosan and its derivatives in biotechnology

Topic	Form	Applications
Enzymology	Powder	Enzyme and cell immobilization
Enzyme technology	Bead	Cell recovery
Separation	Microsphere	Cell-stimulating materials
Bioseparation	Nanoparticle	Protein separation
Biomembranes	Sponge	Matrix for affinity and gel permeation chromatography
Electrodes	Membrane	Electronic devices, biosensor construction
Biosensors		Metabolic analysis of biological fluids

Zikakis (1984), Struszczyk (2002), Krajewska (2005), Wang (2012), Suginta et al. (2013), Philibert et al. (2017) and Grifoll-Romero et al. (2018)

**Table 14** Applications of chitosan and its derivatives in chemistry

Topic	Form	Applications
Analytical chemistry	Solution	Analytical reagent
Chromatography	Ionic liquids	Reverse osmosis
Dialysis	Powder	Permeability control
Reverse osmosis	Film	Solvent separation
Ultrafiltration	Coating	Organic/organic separation
Gas permeation	Fiber	Alcohol/water selective pervaporation
Pervaporation	Membrane	Transport direction of target molecules
Evapomeation technique	Composite	Membranes for lithium batteries
Carrier transport membranes	Blend	Biosensors, electrochemical devices
Green chemistry	Sensors	CO <sub>2</sub> recovery
Green solvents		Alternative solvents in catalytic organic reactions
Catalysis/Biocatalysis		Adhesive role between metallic surfaces
Adhesives		Corrosion protection of aluminum
Corrosion protection		Ionic liquids
Polymer science		Deep eutectic solvents
Click chemistry		
Electrochemistry		

Goosen (1997), Guibal (2005), Krajewska (2005), Crini et al. (2009), Cheba, (2011), Dash et al. (2011), Suginta et al. (2013), Mati-Baouche et al. (2014), Carneiro et al. (2015), Salehi et al. (2016), Thakur and Voicu (2016), Osman and Arof (2017), Argüelles-Monal et al. (2018), Galiano et al. (2018), Marpu and Benton (2018), Xie and Yuan (2018), Zdanowicz et al. (2018), Jiang and Wu (2019) and Molnar (2019)

very important role in these new developments. The utilization of chitosan as a catalyst support is also of particular interest. This application combines several up-to-date techniques (freeze drying, utilization of supercritical CO<sub>2</sub>) to increase the surface exchange capabilities and/or utilization of ionic liquids. Chitosan contributes to the implementation of green chemistry principles. The state-of-the-art review of the design of electrochemical biosensor applications based on chitosan and chitin was presented by Suginta et al. (2013) and comprehensively discussed. Membranes are produced by casting chitosan solutions either alone or with suitable ingredients (reagents, polymers) to give desired properties for target applications. Preparation and application of chitosan-based adsorptive membranes for separation and for water purification were reviewed by Salehi et al. (2016) and Thakur and Voicu (2016), respectively. Chitosan has been proposed for the separation of organic liquid mixtures using evapomeation membranes. This membrane separation technique makes use of the advantage of pervaporation and simultaneously removes a fault of pervaporation. The main applications of chitosan membranes are their use in biomedicine and biotechnology. Albumin-blended chitosan membranes have been used in hemodialysis, artificial skin, and also drug targeting. Further developments are expected in the near future in these domains (Galiano et al. 2018).

## Environmental chemistry

A growing number of papers have been published since the 1980s concerning chitosan for applications in environmental chemistry (Table 15). This natural polymer possesses

several intrinsic characteristics that make it an effective material for environmental purposes. Its use is justified by four important advantages: (1) its relatively low cost compared with commercial activated carbon or organic resins, (2) its outstanding pollutant-binding capacities and excellent selectivity, (3) its versatility, and (4) its possible biodegradability after use. Indeed, one of the major applications of chitosan is based on its great ability to tightly bind a whole range of pollutants. In addition, chitosan and its derivatives can be used in soluble or insoluble forms including gels, beads, sponges, films and membranes, and fibers through coagulation-, filtration-, flocculation-, or adsorption-oriented processes.

In a previous review, Crini and Badot (2008) comprehensively discussed the development of chitosan-based materials (grafted and cross-linked derivatives) used as useful adsorbent polymeric matrices for dye removal. Their review highlighted results that have been obtained in their decolorizing application as biosorbents. The effects of various parameters such as chitosan's characteristics, the activation conditions, the process variables, the chemistry of the dye, and the experimental conditions used in batch systems on biosorption were presented and discussed. The authors also reviewed the various adsorption mechanisms involved. They concluded that the biosorbents were efficient in pollutant removal with the additional advantage of being cheap, non-toxic and biocompatible. More recently, Kyzas et al. (2017), Desbrières and Guibal (2018) and Pakdel and Peighambar-doust (2018) also indicated that biosorption onto chitosan is a promising alternative to replace conventional adsorbents used for decolorization purposes, and metal and organic removal.



**Table 15** Main applications of chitosan and its derivatives in environmental chemistry

Topic	Form	Applications
Water treatment	Solution	Coagulant/flocculant: clarification of drinking water, pools and spas, wastewaters
Wastewater treatment	Gel/hydrogel	Adsorbent/biosorbent: recovery of precious metals; metal chelation; dye removal; removal of
Coagulation	Powder	pesticides, phenol derivatives, PCB and radioisotopes
Flocculation	Microsphere	Interactions with proteins and amino acids
Adsorption	Bead	Reduce odors
Biosorption	Nanoparticle	Antifouling agent
Solid-phase extraction	Fiber	Polymer-assisted ultrafiltration
Filtration	Hollow fiber	Sludge treatment and dehydration agent
Membrane filtration	Membrane	Drilling muds
Remediation	Sponge	
Biological de-nitrification		

Hirano (1997), Varma et al. (2004), Crini (2005, 2006, 2015), Krajewska (2005), Tang et al. (2007), Gérente et al. (2007), Alves and Mano (2008), Crini and Badot (2008), Li et al. (2008), Bhatnagar and Sillanpää (2009), Elwakeel (2010), Sudha (2011), Rhazi et al. (2012), Ravichandran and Rajesh (2013), Vakili et al. (2014), Liu and Bai (2014), Boamah et al. (2015), Yong et al. (2015), Azarova et al. (2016), Barbusinski et al. (2016), Kos (2016), Ahmad et al. (2017a), Crini et al. (2017), Sudha et al. (2017), Nechita (2017), Alaba et al. (2018), de Andrade et al. (2018), Desbrières and Guibal (2018), El Halah et al. (2018), Pakdel and Peighambaroust (2018), Van Tran et al. (2018), Wei et al. (2018), Barbosa et al. (2019), Escudero et al. (2019), Saha et al. (2019), Sarode et al. (2019) and Vidal and Moares (2019)

Chitosan-based versatile materials are also widely proposed in clarification and water purification, and water and wastewater treatment as coagulating and flocculating agents (Crini et al. 2009). As eco-friendly materials, they can be a potential substitute for metallic salts and synthetic polyelectrolytes in the treatment of water for the removal of both particulate and dissolved substances. However, despite a large number of studies on the use of chitosan for pollutant recovery in the literature, processes are basically at the stage of laboratory-scale study in spite of unquestionable progress. Indeed, these research fields for chitosan have failed to find practical applications on the industrial scale. The actual

applications in industry remain rather rare, e.g., Pennofloc™ for water clarification, ChitoVan™ for biofiltration, as concurrent flocculating and adsorbing agents are cheaper. Even if chitosan shows better performances in terms of pollutant elimination, the conventional products are sufficient to fulfill current regulatory frameworks.

## Miscellaneous

Table 16 describes applications of chitosan in miscellaneous domains. Due to its optical characteristics, film-forming ability, and reactions with silver complexes, chitosan and

**Table 16** Applications of chitosan in miscellaneous domains

Field	Main form	Applications
Photography	Solution	Photographic paper
Detergents	Powder	Film-forming ability
Surfactants	Coating	Fixing agent for color photography
Paints	Nanoparticles	Color film
Adhesives	Nanoclusters	Nanoimprinting lithography
Wood industry		Antifouling paints
Cement industry		Thermosensitive materials
Leather		Improvement of wood quality
Plastics		Wood adhesive
Bioplastics		Protection of wood (fungicide)
Cigarette industry		Lithium batteries
Semiconductors		Specific targeting
Luminescent nanoparticles		Cellular imaging
Photonics		Bioimaging and cancer research
Imaging applications		Bioconjugation to biomolecules
Quantum dots		Sensors and biosensing
Carbon dots		Temperature sensing
		Detection

Struszczyk (2002), Crini et al. (2009), Elsabee et al. (2009), Heuser et al. (2009), Pelletier et al. (2009), Desbrières et al. (2010), Banerjee et al. (2011), Cheba (2011), Heuser and Cárdenas (2014), Mati-Baouche et al. (2014), Al-Naamani et al. (2017), Argüelles-Monal et al. (2017), Galiano et al. (2018), Marpu and Benton (2018) and Jiang and Wu (2019)

derivatives found applications in photography. In color photography, chitosan has been proposed as a fixing agent for acid dyes in gelatin and also acts as an aid to improve diffusion (Dutta et al. 2004). Ecological concerns about antifouling paints containing nongreen tin and copper compounds have highlighted the need for environmentally friendly alternatives (Pelletier et al. 2009; Banerjee et al. 2011). Novel chitosan-based technologies may prevent fouling by means of unfavorable surface chemical and physical properties or by concentrating antifouling compounds around surfaces. A prototype of antifouling paints was proposed as a possible replacement for traditional antifouling paints by Heuser and co-workers (Heuser et al. 2009; Heuser and Cárdenas 2014). In cement industry, chitosan has been proposed as water proofing and water repellent (Cheba 2011). Chitosan has been also explored in the production of plastics (Galiano et al. 2018) or in the stabilization of photonic materials (Marpu and Benton 2018).

## Conclusion

In this review, the objective was to present an overview of the state of the art in chitosan applications, based on a large number of relevant references published over the past two decades. Of course, this is an ambitious project and the examples presented in this article are not exhaustive but clearly demonstrate the interest of chitosan in many areas. The main markets for chitosan are the food, pharmaceutical, and cosmetic industries. The chitosan market is expected to grow rapidly due to increased consumption not only in cosmetics but also in water treatment, beverage industry, and nutrition. Indeed, nutraceuticals and cosmeceuticals are growing markets. There is also an increased demand for chitosan in emerging countries. Therapeutic and biomedical products are also expected to have a positive impact on the market. It is important to note that, although many papers and patents have been reported over the past two decades, chitosan applications in the biomedical field are still limited, mainly due to the extreme difficulty of accessing sufficient purity and reliability of the biopolymer at its source. In addition, the development of new materials is quite limited, mainly due to their cost, which remains higher than that of petroleum-based polymers with similar properties. Finally, in vivo studies are currently limited. Further industrial developments are expected in the near future in the following areas: anticancer drugs, gene delivery, catalysis, sensor applications, wrapping materials and packaging, cosmetotextiles, and bioimaging.

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