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An Extensive Review on Chitosan as Versatile Material for Pharmaceutical and Biomedical Application

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Authors' contributions

This work was carried out in collaboration between both authors. Both authors read and approved the final manuscript.

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Review Article

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ABSTRACT

Chitosan is a polysaccharide and is derived from chitin. Chitosan every now and then referred to as a soluble chitin. chitosan is strongly basic polysaccharide. chitosan shows physiochemical and biological properties. This review presents the common source for chitosan manufacturing that is crabs and shrimp. According to researchers it is just a fat inhibitor. some of the application of chitosan in pharmaceutics/drug delivery and in biomedical field are also highlighted. Chitosan act as a diluent, as mucoadhesive excipient, as permeation enhancer, in vaccines delivery, as parenteral delivery, chitosan as food additive, cosmetics industry. chitosan also has a number of medicinal benefits. Chitosan is employed in a variety of applications because it is soluble in acidic aqueous conditions (food, cosmetics, biomedical and pharmaceutical applications). We give a quick overview of the chemical modifications of chitosan, a field in which a number of syntheses have been proposed but not yet realised on a large scale. This review focuses on current articles on these materials' high-value-added applications in medicine and cosmetics.

Keywords: Chitosan; structure; application; biomaterials.

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1. INTRODUCTION

Chitosan is a polysaccharide that is made up of randomly dispersed [1-4] linked D glucosamine and N-Acetyl-D-glucosamine. It is created by processing the shells of shrimp and other crustaceans with the alkali, sodium hydroxide [1]. It is also found in certain microbes and fungi, such as yeast. The word chitosan refers to a group of chitosan polymers with varying molecular weights (50KDa-2000KDa), viscosities (2000MPaS), and degrees of deacetylation (48 percent -98 percent). Chitosan is sometimes referred to as soluble chitin. Chitin is made up of unbranched chains of -(1-4)-2-acetamido-2-acetamido- 2-acetamido- 2-acetamido-2-acetamido- 2-acetamido- 2-acetamido-2-acetamido- 2-acetamido- 2-acetamido-2-acetamido- 2-acetamido- 2-acetamid. The hydroxyl group is replaced with an acetamido residue, making it similar to cellulose. Chitin is essentially insoluble in water, dilute acid, and alcohol, depending on the origin of the substance. Salt is formed when chitosan combines with inorganic and organic acids such glutamic acid, lactic acid, hydrochloric acid, and acetic acid [2]. Fig. 1 depicts the architectures of chitin and chitosan.

2. PROPERTIES

Natural polymers such as fiber, dextrin, pectin, alginic acid, and agar are acidic in nature, but chitosan is a strongly basic polysaccharide. Chitosan characteristics include solubility, viscosity, and the ability of polyelectrolytes to form films.

2.1 Physicochemical Properties

- Chitosan is nitrogenous polysaccharide that is colourless, off white, hard, inelastic, and has molecular weight ranging from 1.03106 to 2.5102 Daltons on average. Chitosan generated through deacetylation, on the other hand is decreased to 1105 to 5105 Daltons.
- Chitin can be easily turned into gels, powders, membranes, fibres, colloidal film and beads.
- It chelates with several transitional metal io ns due to its existence of chitosan, which c an be easily replaced by reactive amino gr oups and hydroxyl groups [3].

2.2 Biological Properties

- Biocompatible: they are compatible with both animal and plant tissue because they lack antigenic characteristic.
- It has hemostatic, hypocholesterolemic, ra dical scavenging, and anticoagulant proper ties.
- It is biodegradable at room temperature,
- It is nontoxic and safe.
- It is associated with mammalian and micro bial cells.
- It has the ability to regenerate connective g um tissue.
- It has hemostatic, hypocholesterolemic, ra dical scavenging, and anticoagulant proper ties [4].

3. THE COMMON SOURCES FOR CHITOSAN PRODUCTION

Shrimp and crabs are the most commonly cited causes in the literature as raw materials for chitosan preparation, there are other family like lobster, cryfishand oyster are also used for chitosan preparation [5-8]. Different creatures have different chitin content (wt percent):

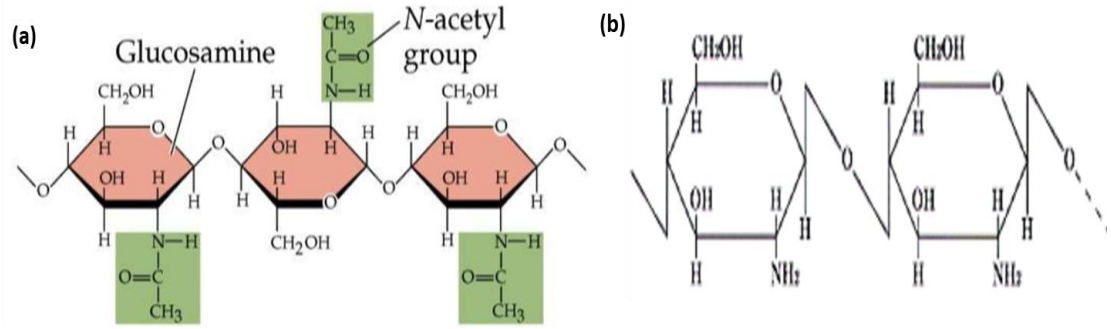

Fig. 1. Chemical structure of (a) chitin, (b) chitosan

crustacean shell waste on average contains 30 percent - 50 percent by weight of calcium carbonate and 20 percent - 30 percent by weight of chitin, whereas in some genera of lobsters, such as Nephrops sp. and Homarus sp., the shell contains 60 percent - 75 percent by weight of chitin content, which is the highest among all chitin containing species [9,10].

Current research on the synthesis of chitin or chitosan from crustacean by-products containing 20% (wt%) or higher chitin has yielded encouraging findings as industrial feedstocks for chitosan manufacture. For example, Procambarus clarkii (crayfish) by-products (which included the entire animal body, thorax, and claws) were originate to comprise almost 20% - 23% (by weight) of chitin, which now permits its usage as an economically worthwhile cause for chitin manufacture on an industrial scale due to its complete convenience and little cost [10-12]. Current literature has also suggested the commercial and eco-friendly benefits of such crustacean causes for chitosan preparation, because 40 percent - 50 percent by weight of the total mass of the crustacean for social eating ends up as left-over, and the majority of such leftover is discarded into the sea and becomes important toxins in sea zones [9,13]. As a result, crustacean leftovers such as lobster cephalothorax can be recognised as a viable source for chitosan production on a large scale.

4. HISTORY

Chitosan (pronounced Kite-O-San) has long been thought to be a "fat magnet." According to researchers, it is just a obese inhibitor that seems to perform wonders for people looking for a safe approach to decrease body fat. About 20 ages later, there was a gentleman who authored an article on creatures in which he noted that alike material was existing in the structure of creatures as well as the structure of plants. He subsequently dubbed this incredible chemical "chitin." The term chitin is taken from Greek and means "tunic" or "envelope." Lassaigne proved the existence of nitrogen in chitin in 1843, expanding on the notion [3]. Rouget addressed the deacetylation method of chitosan, and numerous studies have emphasised the want to understand and examine the material, from improved manufacturing, purifying techniques, to changes of the fundamental structure and its uses. Chitosan is a possible cause of bioactive material, but it has numerous restrictions for use in biological systems, including poor solubility under physiological conditions. To overcome these limitations, scientists focused on the Derivatisation of chitosan through chemical alterations. These changes result in enhanced solubility in liquid as well as biological diluents [14].

Chitosan, primarily for increasing the plant resistance, are created on how this amine containing polymer impact on the bio-chemical and molecular biology of the plant cell. Chitosan is typically used as a natural seed treatment and shrub development enhancers and as eco welcoming bio pesticides substances that increases the inhere capability of plant to protect themselves against further infections [15].

5. PROCESSING OF CHITOSAN

Chitin may be extracted chemically from crustacean shells. It entails the following processing steps (Fig. 2):

a) Dfemineralization entails acid treatment (HCl) to remove inorganic particles, primarily calcium carbonate [16].
b) Deproteinization: this requires extracting protein matter in an alkaline medium (NaOH).
c) Decoloration: bleaching the product with organic substances to accomplish a colourless product [17].

6. APPLICATION OF CHITOSAN IN PHARMACEUTICS/DRUG DELIVERY

Chitosan has a number of medicinal benefits (Fig. 3).

- Polymers, micelles, liposomes, and nanoparticles have recently gained considerable interest as medicinal carriers [18-20].
- These systems have several benefits, the most notable of which is improved medication effectiveness and safety.
- Depending on the type of the carrier, these schemes can contain both hydrophobic and hydrophilic dynamic chemicals.
- They can also provide greater therapeutic stability against chemical and enzymatic degradation, prolonged drug impact in the target tissue, higher bioavailability, and drug targeting by including particular ligands [21].

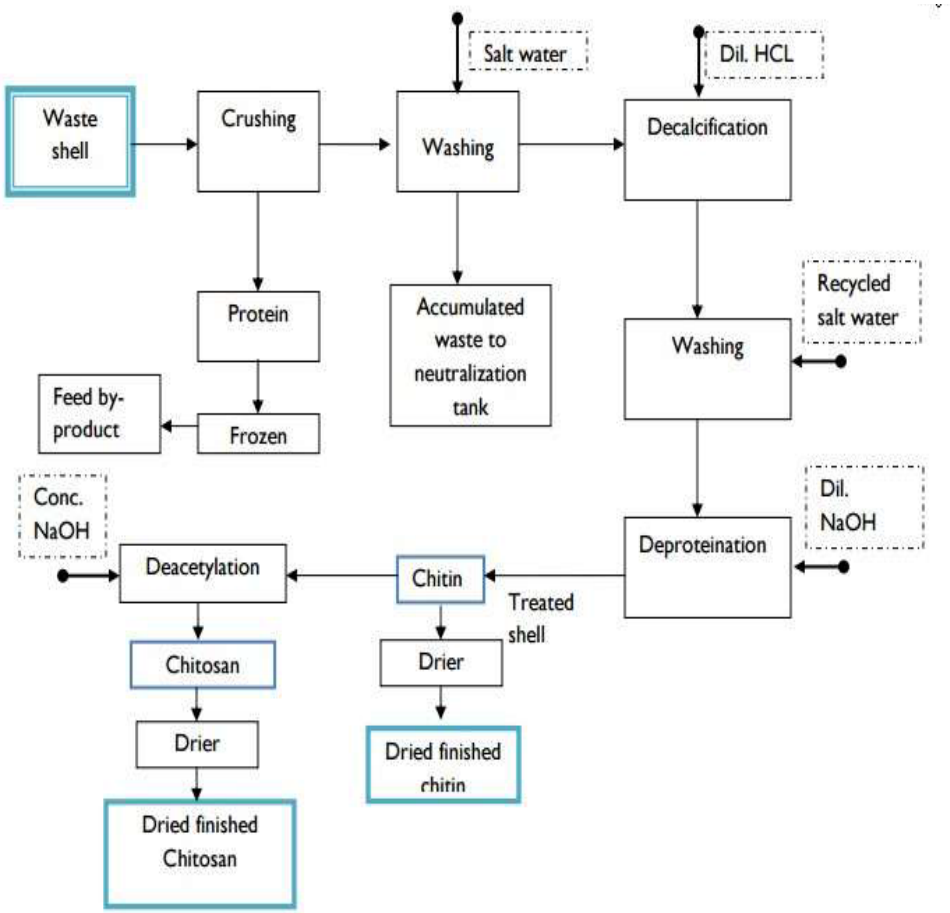

Fig. 2. Manufacturing process of chitosan

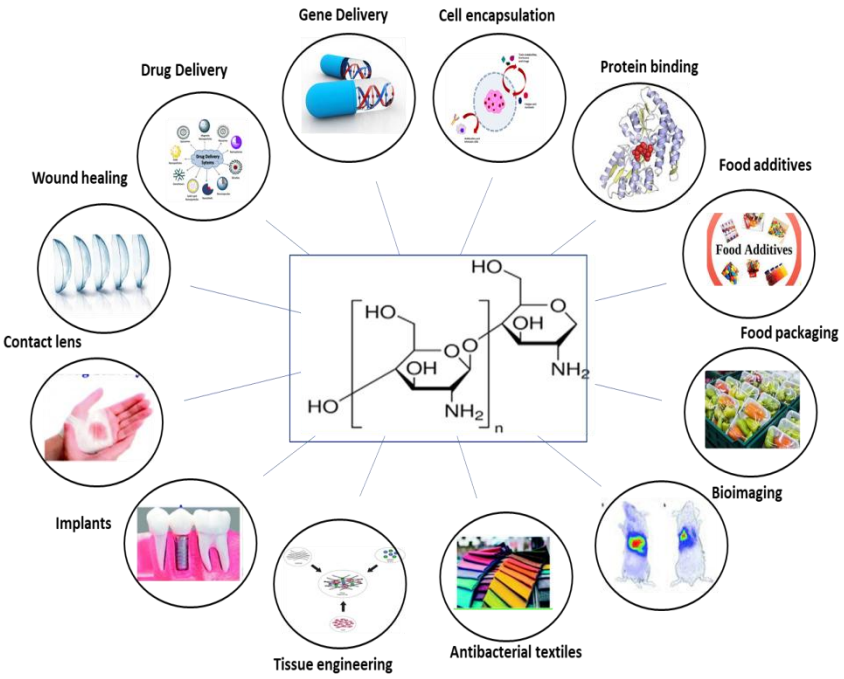

Fig. 3. A schematic indicating pharmaceutical applications of chitosan in various areas

7. APPLICATION OF CHITOSAN IN BIOMEDICAL FIELD

As diluents: Chitosan and 2-hydroxyethyl starch are miscible mixes due to interactions between their reactive hydroxyl and amino groups, and we may create a variety of controlled release formulations using these combinations. The combination of matrix tablet diffusion and disintegration is to blame [22,23].

Adnan A. Badwan and his colleagues Chitin and chitosan, as well as their derivatives, can be employed as excipients in pharmaceutical applications involving DC dispensing. Its value as a standalone and coprocessed excipient in pharmaceutical formulations is enhanced by the range of physicochemical properties of semi-crystalline nature, DDA, and MW. In addition, their wide surface area, porous structure, and plastic distorting nature promote particle attachment and tablet ability in the DC mode, with minimal lubrication vulnerability. Chitin and chitosan can be employed as a single multifunctional excipient when co-processed with other excipients [24].

As mucoadhesive excipient: Bioadehesion is a regulated drug delivery technology focused particularly at the gastrointestinal tract. When chitosan is compared to other polymers, the cationic polymer outperforms natural polymers in terms of bioadhesion10. Chitosan has a mucoadhesive property due to the presence of OH and the amine group. The drug's residence time is extended due to the presence of mucoadhesion. As a result, gastrointestinal absorption and bioavailability are improved [11,24,25].

Chitosan is a cationic polymer that is used in the delivery of medications as a regulated drug delivery system. As a result of its interactions with anionic polymers, polyion complexes occur. In therapeutic applications, poly ion complexes and their fundamental properties have been used [26].

As permeation enhancer: Chitosan's cationic nature allows it to open cell membrane tight junctions. This property has sparked a lot of interest in using chitosan as a permeation enhancer for hydrophilic medications with low oral bioavailability, including peptides. To test the permeation enhancing effect of different chitosan formulations, Yu-jie Zhang et colleagues used the permeation coefficient of fluorescein isothiocyanate recombinant hirudin-2 over the activated rabbit nasal epithelium in vitro. Chitosan, with or without specific enhancers, was found to successfully restore nasal absorption of recombinant hirudin while avoiding significant mucosal ciliotoxicity. For nasal administration of recombinant hirudin, a chitosan manufacturing approach would be effective [27].

In vaccines delivery: The use of chitosan as a latent transfer mechanism for intravenously given disabled virus vaccines has been examined. According to studies, nanoparticles of low molecular weight chitosan have the potential to be a unique long-term nasal vaccine delivery vehicle [15]. Chitosan microparticles have the ability to interact with large amounts of ovalbumin (model vaccination for diphtheria toxoid). Chitosan microparticles do not disintegrate in an acidic environment, protecting the antigen from deprivation by trapping it inside their permeable structure. The chitosan microparticles transfer the associated ovalbumin into the peyer's patch. Because antigen uptake by Peyer's coverings is a critical step in oral injection, these porous chitosan microparticles are an excellent injection transfer device [28-30].

As parenteral delivery: Because extremely cleansed chitosan fractions were found to be neither toxic nor hemolytic, they have the ability to complex DNA and nuclease deprivation, and low molecular weight chitosan can be administered intravenously without accumulating in the liver, low molecular mass chitosan has the potential to be used in a synthetic gene therapy system [31].

Chitosan in fuel cell: Electrochemical devices that convert mechanical energy to electrical energy are known as fuel cells. Fuel cells have received a lot of interest due to its potential as a viable alternative to traditional power sources. Chitosan, a biopolymer that is both effective and environmentally acceptable, has recently been extensively investigated as a novel material for use in fuel cells. This biopolymer can be utilised in a variety of fuel cells, including alkaline polymer electrolyte fuel cells, direct methanol fuel cells, and bio fuel cells, as a membrane electrolyte and an electrode [32].

Chitosan as a food additive: Chitosan is a promising raw material for edible films or coatings because of its capacity to form films and act as a barrier. Chitosan's antibacterial and antifungal qualities, as well as its antifilm forming

ability, make it ideal for usage as a biodegradable antimicrobial packaging material that can help destructible foods last longer. Several studies have shown that chitosan can be utilised to increase the quality and shelf life of a variety of diets by acting as a film forming or preservative. The US FDA has approved chitosan as a food additive [33].

Cosmetic industry: New quaternary chitosan derivatives are used in the formulation of cosmetic compositions for hair or skin treatment. Chitosan byproducts bind well to hair keratin and provide hair strengthening and conditioning characteristics. In oxidation hair-coloring formulas, hair setting lotions, gel form, and skin creams, chitosan is employed [34].

Colon specific drug delivery: Enteric coating resources are used for colon definitive medication transference since chitosan is eliminated in the colon. Anti-inflammatory medicines, such as sodium diclofenac, are smuggled into the chitosan microspheres' main compartment. These microspheres are subsequently protected by an enteric coating, which is then employed to transmit drugs. Sodium diclofenac begins to be released in the intestines after a period of roughly 12 hours [34].

8. CHITOSAN IN NANO DRUG FORMULATION AND CONTROLLED DRUG RELEASE

Chitosan micro-/nanoparticles have shown considerable promise in oral, parenteral, topical, and nasal applications, among the innovative drug delivery systems explored. 48–50 The drug is either restricted and surrounded by a polymeric membrane, or uniformly diffused in the polymer matrix, in these systems [35]. The size and surface properties of the produced particles have a significant impact on their ability to cross biological cell membranes. These particles could be utilised to deliver a regulated and, in some cases, site-specific dose of the pharmaceutically active drug. Because of the extended drug interaction with the mucosal layer and the high surface-to-volume ratio of nanoparticles that may further boost this impact, the mucoadhesive property of chitosan renders the produced particles capable of improving both drug absorption and bioavailability. Mucoadhesion, in which chitosan adheres to specific mucosal surfaces in the body such as the buccal, nasal, and vaginal cavities, can also be used to accomplish drug release at a specific place and for an extended period of time [36,37].

Because of their mucoadhesive qualities and particle size reduction by micronization, chitosan microparticles have a wide range of applications in the administration of a variety of substances. By improving medication water solubility, systemic absorption, bioavailability, and stability, chitosan nanoparticles have maximised the benefits of chitosan as a polymeric drug carrier [38]. Curcumin is a common example of these medications, and it has been observed that making curcumin-loaded chitosan nanoparticles improves drug solubility and stability in the GI tract. Because of improved tumour targeting, the capacity to load diverse hydrophobic anticancer medicines, and the ability to adjust the anticancer drug-release rate, chitosan nanotherapeutics have recently gained a lot of attention in the field of oncology. Drug coated with the chitosan polymer, also used for the PEGylation process, thus increases the long circulation properties of drug molecules and release also enhances [39].

Because of their great ability to improve mucosa absorption and stability, chitosan NPs have been employed as a DNA vaccine carrier. The development of oral DNA vaccines has been impeded by DNA breakdown in the gut. Chitosan and its derivatives, notably in the form of micro- and nanoparticulates, have a lot of potential as adjuvants and delivery vehicles. This review looked into and assessed several chitosan changes that could help carry vaccines more efficiently into APCs [40], resulting in stronger immune responses. Furthermore, numerous features of chitosan have been significantly improved following functional alteration, including increased stability, membrane permeability, mucoadhesivity, and controlled release behaviour, indicating that they are viable vaccine carrier systems. To accomplish targeted vaccine administration, certain ligands, such as mannose, have been coupled with chitosan derivatives for particular interactions with desired cell types. Despite these benefits, chitosan still faces a number of problems, including inconsistent dispersion and limited physical stability, which must be addressed carefully in future applications [41,42]. Despite this, the potential of chitosan and its derivatives in the field of vaccine delivery should motivate researchers to continue their studies.

9. CONCLUSION

Chitosan is a natural polymer that has the properties of a hard, inelastic polysaccharide. It's a biodegradable, non-toxic, and safe linear polymer. The major core material utilised in the creation of chitosan is chitin, which is produced from shrimp and other crustacean shells. Chitosan is used in the pharmaceutical business for a variety of purposes, including tablet diluents, mucoadhesive excipients, permeation enhancers, and wound healing. Chitosan is a material that has lately been used in vaccine administration. Chitosan is used as a fuel agent and an anti-dot in metal detection, in addition to the pharmaceutical business. This examination provides comprehensive information on the physical properties and applications of chitosan.

CONSENT

It's not applicable.

ETHICAL APPROVAL

It's not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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