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Review

Chitosan-based nanomaterials: A state-of-the-art review

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A B S T R A C T

This manuscript briefly reviews the extensive research as well as new developments on chitosan based nanomaterials for various applications. Chitosan is a biocompatible and biodegradable polymer having immense structural possibilities for chemical and mechanical modification to generate novel properties and functions in different fields especially in the biomedical field. Over the last era, research in functional biomaterials such as chitosan has led to the development of new drug delivery system and superior regenerative medicine, currently one of the most quickly growing fields in the area of health science. Chitosan is known as a biomaterial due to its biocompatibility, biodegradability, and non-toxic properties. These properties clearly point out that chitosan has greater potential for future development in different fields of science namely drug delivery, gene delivery, cell imaging, sensors and also in the treatment as well as diagnosis of some diseases like cancer. Chitosan based nanomaterials have superior physical and chemical properties such as high surface area, porosity, tensile strength, conductivity, photo-luminescent as well as increased mechanical properties as comparison to pure chitosan. This review highlights the recent research on different aspect of chitosan based nanomaterials, including their preparation and application.

Contents

1. Introduction

In the current review article, the state-of art-research activities related to chitosan and chitosan based nanomaterials are described. This review deals with the historical and structural background of chitosan, unique properties of chitosan followed by methods of their modifications, different kinds of chitosan based nanomaterials, and their potential applications in the field of water treatment, drug delivery and biosensors in last decade.

Several nanoparticles precedents from biodegradable polymers have been proposed for mucosal drug delivery [1–3]. Among them nanoparticles based on the polysaccharide chitosan have

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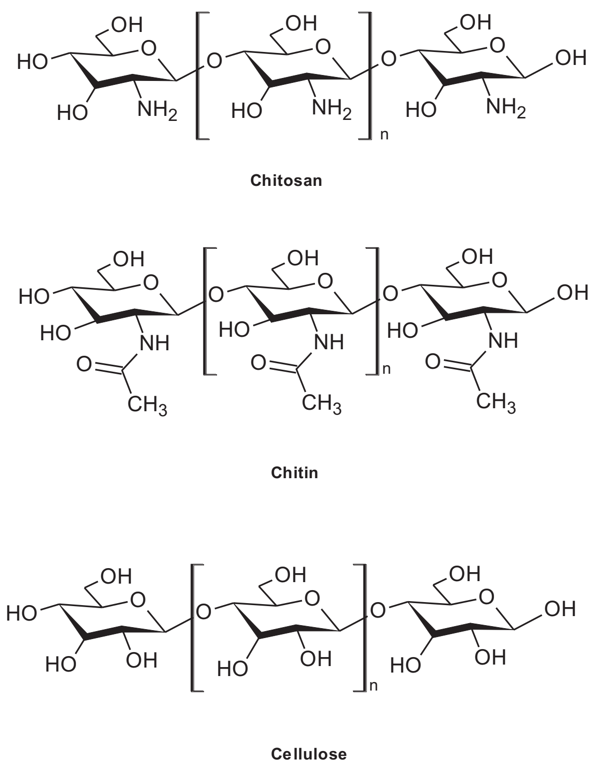

Fig. 1. Structure of chitosan, chitin, and cellulose.

received attention from the 19th century, when Rouget [4] discussed the deacetylated forms of the parent chitin natural polymer in 1859. During the past 20 years, a considerable amount of work has been reported on chitosan and its potential use in various bio-applications. Chitosan is a bio-compatible, bio-degradable, bio-renewable, and non-toxic polymer with mucoadhesion like properties along with the ability to transiently open the tight junction of the intestinal barrier [5,6]. Chitosan is a natural product and most important derivative of chitin. It is the second most bountiful natural polysaccharide after cellulose in the universe. Chitosan is derived from naturally occurring sources, including the exoskeletons of insects, arthropods such as crustacean shells, shellfish like shrimp, prawns, crabs, and beaks of cephalopods as well as cell walls of fungi [7].

The polymeric forms of chitosan are semi-synthetically derived amino-polysaccharides that have unique structures, multidimensional properties, highly sophisticated functionality and a wide range of applications in biomedical and other industrial areas [8,9]. Chitosans are interesting, not only because they are made from an abundant renewable resource but they are also very compatible and effective biomaterials that are used in many applications [10–12]. Chitosan is more suitable for the bio-applications than chitin because of its better solubility in water and organic solvents [13]. As a co-polymer, chitosan is made up of linear β-(1 → 4) glycosidic linkages which are similar in structure to cellulose. In chitosan, 2-acetamido-D-glucose and 2-amino-D-glucose units are combined with glycosidic linkages, as shown in Fig. 1. Chitosan is produced by removing an acetate moiety from chitin through hydration (i.e. amide hydrolysis under alkaline conditions (concentrated NaOH)) or through enzymatic hydrolysis in the presence of chitin deacetylase (Fig. 2) [14,15].

The primary $-NH_2$ groups in chitosans are very useful in pharmaceutical applications in comparison to other natural polymers. Under acidic conditions, chitosan can be dissolved in water after the amino protonation to confer positive charges, gelations, and membrane forming properties [16]. The glycosidic bond of chitosan is hemiacetal, and thus is not stable in an acidic media and can be hydrolyzed under an acidic environment, resulting in decreased viscosity and molecular weight. The physical and chemical properties of chitosan depend mainly on its molecular weight and degree of deacetylation. The chitosan system has been thoroughly explored by scientists with respect to its origin, composition, structure, and physico-chemical properties. The functional characterization of chitosan and its derivatives is nowadays one of the most productive research areas. Due to these unique characteristics, chitosan and its derivatives have found fruitful applications in various fields such as water treatment [17,18], food industry [19–21], cosmetics [22,23], agriculture [24], and biomedicine [25,26].

2. Physical and chemical properties of chitosan

The majority of naturally occurring polysaccharides such as pectin, dextrin, agar, agarose, carragenas, and cellulose are acidic in nature, while chitosan is a highly basic polysaccharide. Chitosan exhibit special properties such as viscosity, solubility in various media, mucoadhesivity, polyoxysalt formation, polyelectrolyte behavior, ability to form films, metal chelations, optical, and structural characteristics. It also has the potential to bind antagonistically with microbial and mammalian cells. Chitosan is considered a good candidate for tissue engineering, due to its regenerative effect on connective gum tissue [27]. It plays an important role in the formation of osteoblast which accounts for bone formation. It also shows fungi-static, spermicidal, haemostatic, and antitumor as well as anti-cholesteremic activities [28,29]. The hetero-polymer form of the chitosan compresses of glucosamine and acetyl-glucosamine units. These units are available in different grades depending upon the degree of acetylated moieties. The relative proportion of chitosan determines the degree of acetylation, that controls many properties of the polymer such as solubility and as well as acid–base behavior [30,31]. The backbone of the carbohydrate is less similar to cellulose, and consists of β-(1 → 4) linked D-glucosamine with a variable degree of N-acetylation. In chitosan, the –OH group on the second carbon atom of the cellulose is replaced by the acetyl $-NH_2$ group. Therefore, chitosan is a type of copolymer which consist of two repeating units i.e. N-acetyl-2-amino-2-D-glucopyranose and 2-amino-2-deoxy-D-glucopyranose. These two repeating units are linked by β-(1 → 4)-glycosidic bond. Because of this type of arrangement, chitosan shows a rigid crystalline structure through inter- and intra-molecular hydrogen bonding [32,33]. Chitosan is a polycationic polymer that has one $-NH_2$ group and two –OH groups on each and every glucosidic residue [34]. Owing to the presence of these two reactive groups, chitosan exhibits marvelous chemical as well as biological properties. The active primary amino group in chitosan is reactive and provides a specific platform for side group attachment under mild reaction conditions. This makes chitosan an ideal candidate for bio-fabrication [35]. The side group on chitosan provides flexibility to materials with specific functionality, and is also responsible for altering its biological as well as physical properties [36]. Chitosan has a capability to bind with various metal ions i.e. chelating. The intrinsic pK_a value of chitosan strictly depends upon the degree of deacetylation, ionic strength, and the charge neutralization of $-NH_2$ groups. Practically, for fully neutralized amine functions with a degree of acetylation of not more than 50%, the pK_a value always lies between 6.3 and 6.7 [31,37]. Protonation of the amine group accelerates dissolution in acidic solutions (Fig. 3).

Protonation of the amine group leads to the sorption phenomenon of metal cations in acidic media because proton and metal cations compete for interaction with the amine group. When chitosan is used as a catalyst support on colloids, its chain stiffness,