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BIOPOLYMER AS A PROMINENT MEMBER OF MEDICAL IMAGING

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ABSTRACT

Chitosan nanoparticles are being extensively used in various biomedical applications due to their small size to volume ratio. Modern breakthroughs in the fields of medical science have widened the horizons of nanotechnology for applications and medical imaging one of them. Chotosan nanoparticles are an obvious choice due to their amenability of synthesis and functionalization, less toxicity and ease of detection. This review is an join up of recent advances in the field of medical science with chitosan nanoparticles. Present article is confined about medical imaging application of chitosan, which is gaining rapid attention.

Key words: Chitosan, Medical imaging, Biomedical applications

INTRODUCTION

The interplay between nanoscience and nanomedicine continues to be the hallmark of current scientific research worldwide, promising to change every aspect of human life via creating revolutionary materials of biological origin for use in the diagnosis and treatment of devastating human diseases. Two of the key factors in determining the successful performance of such multidisciplinary technology are the properties of the surface chemistry and surface morphology; where the bio–inspired material and the biological system meet and interact. Hence, the synthesis of novel biocompatible polymeric-based nanomaterials and nanostructures that are hundreds (or less) of nanometers in diameter provides, through supramolecular surface chemistry, an ability to absorb or bind drugs, receptors, cell adhesive peptides and/or ligands, given their favourable size, rendering them ideal vehicles for drug, protein and/or growth factor delivery[1].

Over the last decade, functional biomaterials research has developed new drug delivery systems and improved scaffolds for regenerative medicine that is currently one of the most rapidly growing fields in the life sciences. 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. This is a highly interdisciplinary field that encompasses polymer synthesis and modification, cell culturing, gene therapy, stem cell research, therapeutic cloning and tissue engineering. In this regard, chitosan, as a biopolymer derived macromolecular compound, has a major involvement. Chitosan is a polyelectrolyte with reactive functional groups, gel-forming capability, high adsorption capacity and biodegradability. In addition, it is innately biocompatible and non-toxic to living tissues as well as having antibacterial, antifungal and

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antitumor activity. These features highlight the suitability and extensive applications that chitosan has in medicine. Micro/nanoparticles and hydrogels are widely used in the design of chitosan-based therapeuticsystems. The chemical structure and relevant biological properties of chitosan for regenerative medicine have been summarized as well as the methods for the preparation of controlled drug release devices and their applications.

The history of chitosan dates back to the 19th century, when Rouget discussed the deacetylated forms of the parent chitin natural polymer in 1859. During the past 20 years, a substantial amount of work has been reported on chitosan and its potential use in various bioapplications. Chitosan is derived from naturally occurring sources, which is the exoskeleton of insects, crustaceans and fungi that has been shown to be biocompatible and biodegradable. Chitosan polymers are semi-synthetically derived aminopolysaccharides that have unique structures, multidimensional properties, highly sophisticated functionality and a wide range of applications in biomedical and other industrial areas. They have become interesting not only because they are made from an abundant renewable resource but because they are very compatible and effective biomaterials that are used in many applications. Chitosan is a linear copolymer of β-(1–4) linked 2-acetamido-2-deoxy-β-D-glucopyranose and 2-amino-2-deoxy-β-D-glycopyranose. It is obtained by deacetylation of its parent polymer chitin, a polysaccharide widely distributed in nature (e.g. crustaceans, insects and certain fungi). Due to chitin's poor solubility in aqueous solution and organic solvents, it does not find practical applications whereas chitosan as an artificial variant of chitin is more suitable for useful bioapplications. The positive facets of excellent biocompatibility and admirable biodegradability with ecological safety and low toxicity with versatile biological activities such as antimicrobial activity and low immunogenicity have provided ample opportunities for further development[2].

Physical features of chitosan

Chitosan molecule is a copolymer composed of Nacetyl- D-glucosamine and d-glucosamine units available in different grades depending upon the degree of acetylated moieties. It is a polycationic polymer that has one amino group and two hydroxyl groups in the repeating glucosidic residue. The carbohydrate backbone is very similar to cellulose, which consists of β-1,4-linked d-glucosamine with a variable degree of N-acetylation, except that the acetylamino group replaces the hydroxyl group on the C2 position. Thus, chitosan is a copolymer consisting of N-acetyl-2-amino-2-deoxy-d-glucopyranose and 2-amino-2-deoxy-d-glucopyranose, where the two types of repeating units are linked by (1 → 4)-β-glycosidic bonds. After refinement, chitosan has a rigid crystalline structure through inter- and intra-molecular hydrogen bonding[3].

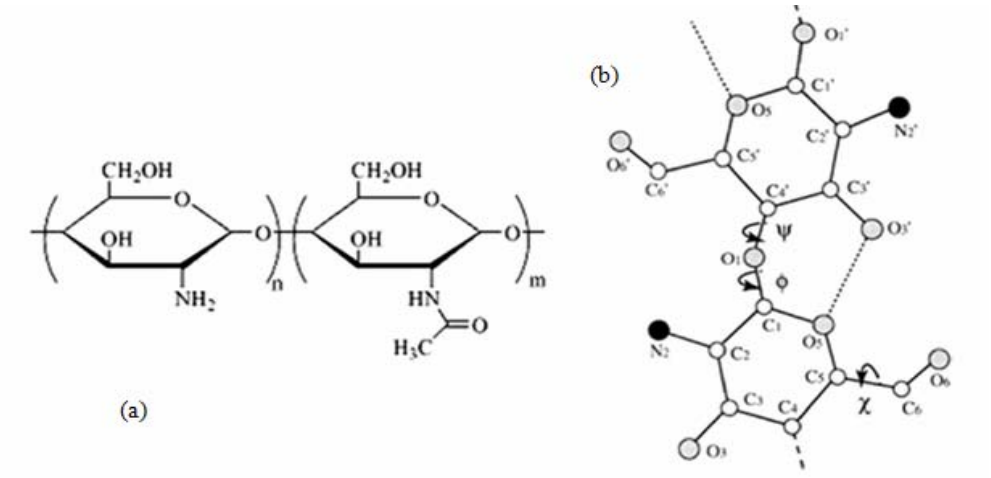

Fig. 1: (a) Chitosan structure; (b) Chemical structure of chitosan. (adopted from 3)

Source of chitosan, relationship between structural parameters and properties

The source of chitosan is a naturally occuring polymer, the chitin that is the second most abundant polysaccharide in nature, cellulose being the most abundant. Chitin is found in the exoskeleton of crustacea, insects, and some fungi. The main commercial sources of chitin are the shell waste of shrimps, lobsters, krills and crabs. In the world several millions tons of chitin are harvested annually and

hence this biopolymer represents a cheap and readily available source[4-6]. Chitosan is obtained by the thermochemical deacetylation of chitin in the presence of alkali and naturally it occurs only in certain fungi (Mucoraceae)[4]. Several alkaline methods have been proposed, most of them involving the hydrolysis of the acetated position using sodium or potassium hydroxide solutions as well as a mixture of anhydrous hydrazine and hydrazine sulfate[7]. The degree of deacetylation dependent relationship between structural parameters and properties are shown in table 1[2].

Table 1: Relationship between properties and structural parameters

Physical properties	Structural characteristics
Solubility	↑ DD
Crystallinity	↓ DD
Biodegradability	↓ DD, ↓ Molecular weight
Viscosity	↑ DD
Biocompatibility	↑ DD Biological
Mucoadhesion	↑ DD, ↑ Molecular weight
Analgesic	↑ DD
Antimicrobial	↑ DD, Molecular weight
Permeation enhancing effect	↑ DD
Antioxidant	↑ DD, ↓ Molecular weight
Hemostatic	↑ DD

↑ – Directly propotional to property; ↓ – inversely propotional to property; DD-degree of deacetylation

Chitosan in bioimaging applications

Chitosan appears to be an exemplary polymer in biological applications owing to its biocompatible properties. In this context, its use in bioimaging applications is also gaining rapid attention. The incorporation of imaging agents is enabling its use for bioimaging, for example, the incorporation of imaging agents such as Fe_3O_4 for Magnetic Resonance Imaging (MRI) into the self-assembled nanoparticles could enhance hepatocytetargeted imaging[8] and the particle could serve as MR molecular imaging agent. Several inorganic materials including metals are being incorporated into the chitosan composite preparations and their combined characteristics are proving beneficial for biomedical applications[3]. Chitosan polyion complex composites can be prepared by interactions of chitosan with natural and synthetic polyanion molecules[9]. PAA (Carbopol), an anionic synthetic polymer having mucoadhesive properties, is extensively used with chitosan to form polymer composites, which have longer circulation times in vivo, resulting in higher bioavailability of incorporated therapeutic agents. These composite systems are being widely

investigated by incorporating contrast agents for imaging purposes. Preparing fluorescent chitosan quantum dot composites enables the combination of targeted drug and gene delivery with optical imaging. Lee et al. have developed novel self-assembling nanoparticles composed of amphipathic water-soluble chitosan–linoleic acid (WSC–LA) conjugates for encapsulation of super paramagnetic iron oxide (SPIOs) as a contrast agent to target hepatocytes. The WSC–LA conjugates self-assembled into core–shell structures in aqueous solution. Since its incorporation in nanoparticles, its potential for in vivo molecular imaging applications has increased tremendously (Fig. 2).

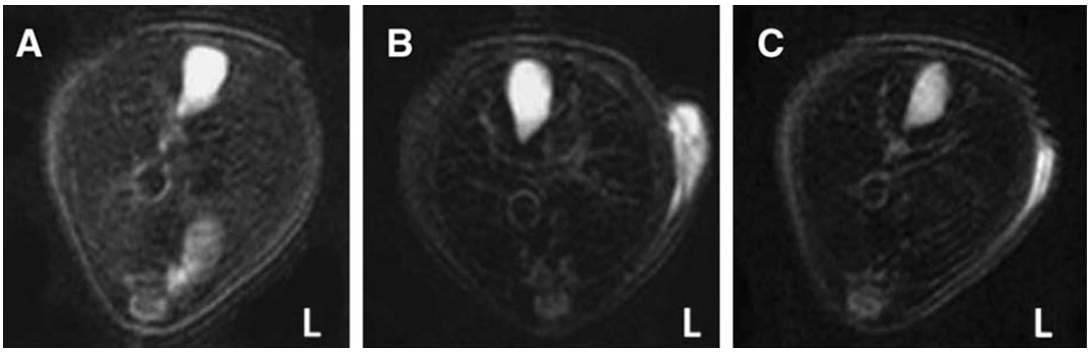

Fig. 2: **MR images of the central region of mouse liver before (A) and after (B–C) injection of SPION-loaded WSC–LA nanoparticles. Images were obtained at (B) 30 min and (C) 1 h after injection of the nanoparticles. L = left (adopted from[8])**

Bioimaging with chitosan-quantum dots

A facile approach to prepare CdSe/ZnS quantum dot-encapsulated chitosan hybrid nanospheres (CS-QD) is developed by utilizing ethanol-aided counterion complexation in aqueous solution reported by Lin *et al*. The obtained CS-QD hybrid nanospheres have not only the loading space provided by the chitosan spherical matrix for loading multiply QDs but also unique fluorescent properties provided by the encapsulated QDs. Moreover, these hybrid nanospheres possess good biocompatibility and optical stability in physiological environment. It is demonstrated that CS-QD hybrid nanospheres can be internalized by tumor cells and hence act as labeling agent in cell imaging by optical microscopy. In addition, CS-QD hybrid nanospheres can be used for imaging of tumor in tumor-bearing mice via intratumoral administration and can accumulate at tumor site via the blood circulation based on intravenous injection. Thus, on the one hand, chitosan nanospheres provide the protection in both colloidal and optical stability arising from QDs and offer biocompatibility. On the other hand, the encapsulated QDs light up polymer nanospheres and display the fate of polymer nanospheres in cells and bodies[10].

CONCLUSION

The degree of biocompatibility of chitosan is very high which make it prominent member of medical imaging. The physical properties of chitosan like solubility, viscosity, biocompatibility, mucoadhesion, analgesic, antimicrobial, permeation enhancing effect, antioxidant, hemostatic are directly proportional to degree of deacetylation (DD) and crystallinity is inversely proportional to degree of deacetylation(DD). Bioimaging with Chitosan-Quantum Dots is also precise approach of medical imaging.

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