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Polysaccharides based nanoparticles with suitable applications

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Abstract

Polysaccharides have great interest for many researchers due to its abundant, biodegradable and diverse in size. Polysaccharide-based nanoparticles are also very important because of their safety, stability, biocompatibility, biodegradability and hydrophilicity. A number of polysaccharides including pectin, starch, cellulose, chitosan, and hyaluronic acid have been widely used as polymeric backbones for the formation of nanoparticles. The review focuses on the method of preparation of polysaccharide-based nanoparticles (self-assembled, physical or chemical cross-linked) and their potential application in different fields.

Keywords: nanoparticles; polysaccharides; pectin; starch; cellulose; chitosan; hyaluronic acid; functions

1. Introduction

Carbohydrates are the most abundant and diverse class of organic compounds occurring in nature. Carbohydrates played a key role in the establishment and evolution of life on earth by creating a direct link between the sun and chemical energy. Most carbohydrates in nature are polysaccharides, which form through a series of condensation reactions among monosaccharides. Because of their diversity, carbohydrates are highly information-rich molecules in the body and have many critical biological functions. They serve as a source of cellular energy, the building blocks of nucleic acids, structural components in the cells, and have key roles in cell-cell recognition and adhesion, among other biological processes. A variety of polysaccharides are isolate from different origins including mushroom, algae (alginate and carrageenan), plants (cellulose, pectin, and guar gum), hybrid mushroom, and animals (chitosan, hyaluronan, and chondroitin). Polysaccharides isolated from mushroom have drawn the attention in the area of biochemistry and pharmaceutical science because of their immunostimulatory, anti-tumor, antidiabetic, and antioxidant properties [1, 2, 3].

In last decades polysaccharides have been incorporated into nanoparticles (NPs) and investigated in hydrogels and nanofibers for [4, 5]. Polysaccharide-based nanoparticles are applied to drug, protein/peptide and nucleic acid delivery systems for biomedical purposes [6-10]. In addition to, they can also play an important role in nanoscience because these polysaccharide molecules can easily synthesize metal nanoparticles by reducing their corresponding metal salts and can also function as an excellent template for nucleation and stabilization of nanoparticles. Depending on the chemical structures, they reveal diverse physicochemical properties and carry out a wide range of applications [6, 11, 12]. On the basis of structural characteristics, these nanoparticles are prepared mainly by four mechanisms, namely covalent crosslinking, ionic crosslinking, polyelectrolyte complexation, and self-assembly of hydrophobically modified polysaccharides. Ag-protein (core-shell) nanoparticles using spent mushroom substrate (SMS) [13] was reported. Here, the substrate reduced silver ions to produce silver nanoparticles and the protein secreted by the fungus play the role of protecting agent. Biomolecules are also used in the synthesis of Au nanomaterials [14-18]. It was reported the synthesis of gold nanoparticles using chitosan acts as both reducing and protecting agent [19]. Microorganisms are also used for the synthesis of gold nanoparticles [20-22]. In this review, I focus on the chemical and physical natures of different polysaccharide-based NPs, particularly NPs consisting of pectin, starch, cellulose, chitosan and hyaluronan and their imaging applications.

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2.1 Pectin

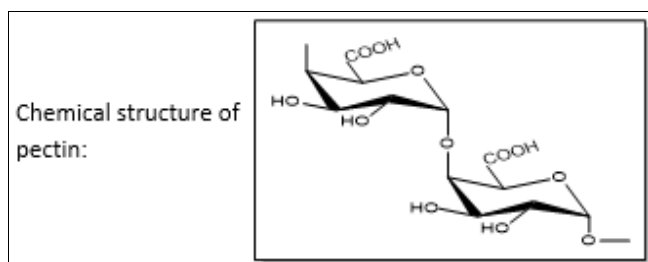


Fig 1: HG, homogalacturonan [poly- α -(1 \rightarrow 4)-D-galacturonic acid]

Pectins are a group of complex heterogeneous polysaccharides, consisting of HG (homogalacturonan), RG-I (rhamnogalacturonan I) and RG-II (rhamnogalacturonan II) types [23]. The HG composed of linear chains of poly- α -(1 \rightarrow 4)-D-galacturonic acid residues. RG-I consists of alternating sequences of Rha and GalA, with side chains at Rha moieties. RG-II composed of alternating sequences of Rha and GalA, with side chains at both the Rha and GalA moieties. Pectins have been used in the food industry as gelling and thickening agents, the production of fruit, dairy, and pharmaceuticals [24]. Pectins exhibit prebiotic activity, and reduce the glucose and blood cholesterol level [25]. Nanoparticles from thiolated pectin have been prepared by the ionotropic gelation method using magnesium chloride as ionic crosslinker for encapsulating different bioactive compounds including pharmaceutical drugs [26]. Pectin nanoparticles for the encapsulation of highly hydrophobic compounds have been prepared from nanoemulsion templates formed by high-pressure homogenization of pectin–chloroform mixtures [27].

2.2 Starch: Starch is a polymer of α -(1 \rightarrow 4)-linked D-glucose units. Starch is composed of two polysaccharides: α -amylase (contained 10-20% starch) [Fig. 2] and β -amylase or amylopectin (contained 80-90% starch) [Fig. 3]. α -amylase is unbranched with molecular weight 10,000 to 1,000,000 whereas amylopectin occurred in branching form with molecular weight 50,000 to 10,000,000. The novel nanoelements: nanocrystals and nanoparticles are made from starch due to the presence of its crystalline structures [28]. Several methods are available for the preparation of starch nanoparticles (SN). Starch nanocrystals are also called as starch crystallites or microcrystalline starch, obtained by acid hydrolysis of the amorphous domains of the granules.

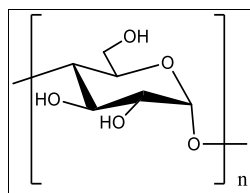


Fig 2: α -Amylose, the linear component of starch

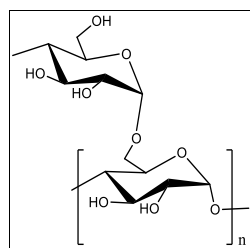


Fig 3: Branching point in amylopectin, α -(1 \rightarrow 4), α -(1 \rightarrow 6) glucose polymer

Platelet nanocrystals obtained from waxy maize starch (with only 1% amylose content) using 2.2 N hydrochloric acid and length of the crystal was 20–40 nm [29]. It is reported that the lengths of starch nanocrystals depends on sources: 40–70 nm for potato and 30–150 nm for pea [28]. Starch nanocrystals have been prepared through a complex formation between amylose and a variety of hydrophobic compounds such as *n*-butanol [30]. The crystalline complexes are commonly referred as V-amylose, based on their X-ray diffraction pattern. These starch nanocrystals have great potential as nanocarriers for small bioactive compounds, since they have a helical cavity which can host different hydrophobic compounds.

2.3 Cellulose

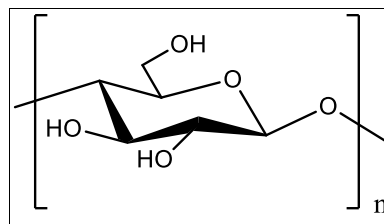


Fig 4: Cellulose, linear condensation of glucose units linked by β -(1 \rightarrow 4) glycosidic bonds

Nanocrystalline cellulose particles have many applications in food technology, biotechnology and medicine. Cellulose nanoparticles are prepared by treatment of cellulose fibers with acidic solutions (HCl, H₂SO₄ or a mixture of both) at different temperatures [31]. Cellulose nanoparticles are rod-like with sizes of 150–200 \times 10–20 nm depending on conditions of sulphuric acid [32]. Carboxymethyl cellulose nanoparticles are prepared by the use of calcium chloride and look like spherical with diameters between 150 and 200 nm to encapsulate bioactive compounds [33].

2.4 Chitosan

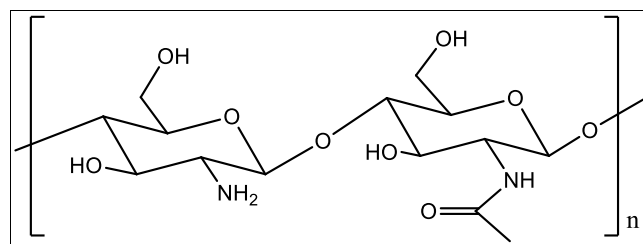


Fig 5: Chitosan (CS), a polymer of glucosamine and N-acetylglucosamine linked by(1 \rightarrow 4)-glycosidic bonds

Chitosan play important properties such as biodegradability, non-toxicity and a good antimicrobial activity [34]. It exhibits many applications such as antioxidant, hypocholesterolemic agent, preservative and thickener [35]. Chitosan nanoparticles are good attractive carriers for bioactive compounds. Several methods are available for preparation of chitosan nanoparticles: ionotropic gelation, microemulsion, emulsification solvent diffusion and polyelectrolyte complexation [36]. The polycations, polyanions, and polyampholyte biodegradable chitosan nanoparticles were obtained by the condensation reaction between carboxylic groups of natural acids and the pendent amino groups of chitosan. Hydrophilic chitosan-polyethylene oxide nanoparticles with a diameter of 200–1000 nm were used as protein carriers [37] and chitosan–carbon nanotubes composites were used in regenerative medicine and tissue engineering [38].

It is reported ^[39] that nanoparticles (NPs), consisting of chondroitin sulfate (CS) and fucoidan (FC) with chitosan are used for therapeutic purposes. The anticoagulant activity was measured by FC NPs and compared with FC solution at the same concentration. FC NPs exhibited better anticoagulant activity and increased coagulation up to two-fold even at a lower concentration than free polysaccharide solution. FC NPs showed cytotoxic and permeability activities using Caco-2 cell monolayer and exhibiting no toxic effect in this cell line. Chitosan-based nanoparticles exhibit antimicrobial activity against several pathogenic bacteria ^[34]. Tripolyphosphate (TPP)-chitosan nanoparticles have been used to deliver drugs and macromolecules ^[40]. Due to the cationic nature of chitosan, it is of great interest in tissue engineering. Chitosan has been used largely in gene delivery in both plasmid DNA ^[41] and siRNA ^[42] due to its cationic property.

2.5 Hyaluronic acid

Hyaluronic acid (HA) or hyaluronan is a natural polysaccharide composed of alternating disaccharide units of (1→4)-β-D-glucuronic acid and (1 → 3)-β-N-acetyl-D-glucosamine. It is biodegradable, biocompatible, non-toxic, and has non-immunogenic properties ^[43]. HA and its derivatives have been used for various biomedical applications such as arthritis treatment ^[44], scaffolds for wound healing applications ^[45], ocular surgery, and tissue augmentation.

HA based nanoparticles deliver anticancer drugs into the CD44-overexpressing tumor cells through the receptor-mediated endocytosis, and after enzymatic degradation sustained the nanoparticle's substance ^[46]. Amphiphilic hyaluronic acid conjugate nano particles were synthesized by chemical conjugation of hydrophobic 5β-cholanic acid to the backbone of HA and used for drug delivery system for cancer therapy ^[47]. This amphiphilic HA conjugate could be capable of being self-assembled to form a stable nanoparticle structure in an aqueous environment. It is reported that Amphiphilic HA-5β-cholanic acid conjugates (HACA) have been used in head and neck ^[48], breast ^[49], and colon ^[50] cancer animal models. HACA-NPs labeled with Cy5.5 are used for tumor-targeted optical/photoacoustic (PA) image-guided photothermal therapy (PTT) ^[51].

3. Conclusion

Polysaccharides are used as carrier materials in the preparation of numerous nanoparticles for both diagnostic and drug delivery purpose for their attractive physicochemical and biological features. Polysaccharide-based nanoparticles have outstanding properties such as biodegradability, hydrophilicity, non-toxicity, and low cost. Various processes have been developed for the preparation of nanoparticles with different shapes and sizes which depend on chemical reactions or physical treatments. The Food and Drug Administration (FDA) approval of nanoparticles in humans seems more probable for clinical applications due to its biological origin. I expect that many researchers will use polysaccharides for the fabrication of nanoparticles and nanotechnology, leading to a more delicate therapy in the near future.

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