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Polysaccharide-Based Hydrogels as Biomaterials in Drug Delivery

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The recent trends of using polysaccharides and hydrogels of these polymers are widely explored in biomedical areas in view of their excellent biocompatibility/biodegradability and tissue adhesion properties. Developing hydrogels from such polymers as smart delivery devices depends on its intrinsic property that they are capable of swelling and shrinking at the predetermined rates depending on external stimuli and this has greatly revolutionized these materials in drug delivery or drug targeting areas. Other advantages are that they will maintain therapeutic plasma concentrations in the surrounding tissues or in circulation for a longer time as well as regulate the release of cargo through a highly regulated feedback mechanism. This has prompted active research efforts on utilizing these biomaterials in biomedicine and bioengineering.

Naturally occurring polysaccharides have unique features required in drug delivery area as they can form conjugates or complexes with proteins and peptides as well as other biopolymers due to their versatile functionalities. Apart from these, polysaccharides offer considerable advantages in terms of resemblance to biological macromolecules (both from chemical and physical viewpoints) and these are recognized by the cell surface receptors, affecting adhesion, spreading and proliferation [1-3]. In view of their similarity to extracellular matrix, they tend to avoid stimulation of chronic inflammation or immunological reactions and toxicity, which is often observed with other synthetic polymers.

Polysaccharides in combination with other polymers (synthetic or natural) offer the desired chemical and biological advantages over the conventional type polymers [4]. These biopolymers in the form of hydrogels serve as the most useful biomaterials in tissue engineering, organ replacement, implants, blood substitutes, wound dressings, bone replacement composite materials, scaffolds, semipermeable membranes, etc. Some of the prime candidates from polysaccharide family are chitosan (CS), sodium alginate (NaAlg), carrageenan, agarose, dextran sulfate, and hyaluronic acid. Of all the biopolymers used in drug delivery area, chitosan and sodium alginate seem to have received the widest attention [5-8].

Chitosan is a copolymer of β-(1→4)-linked 2-acetamido-2-deoxy-D-glucopyranose and 2-amino-2-deoxy-D-glucopyranose, obtained by alkaline deacetylation of chitin, which is the main component of exoskeleton of crustaceans like shrimps and crabs. Its molecular weight and degree of deacetylation greatly influences its characteristics when used as a drug delivery polymer. CS has many interesting properties like ease of modification, cationic charge at the physiological pH, biocompatibility, bioadhesivity and biodegradability. It is metabolized by certain human enzymes, especially by lysozyme, chitotriodidase, di-N-acetylchitobiase and N-acetyl-β-D-glucosamineidase [9]. Thus, it finds use as scaffolds for hepataocyte attachments and enzyme immobilization as films for fabrication of amperometric glucose biosensor, material for supporting nerve repair, wound dressing, as implants and blood substitutes.

Chitosan is widely used in tissue engineering and drug delivery. Various techniques like ionic gelation, chemical crosslinking and in situ gelation are used to produce hydrogels of CS and injectable in situ hydrogels are widely reported for delivery of cells and various bioactive agents [5]. The cationic amine group of CS would induce stability to hydrogels under mild physiological conditions (when injected into the human body) either by ionic gelation or by thermoreversible gelling [6]. This ability of CS was used to develop thermal and pH responsive in situ hydrogels using inorganic phosphate salts as acid neutralizer and gelling agent.

Sodium alginate is an anionic water soluble polysaccharide that is one of the most abundantly available biosynthesized materials, derived primarily from brown seaweed and bacteria, which contains blocks of (1–4)-linked β-D-mannuronic acid (M) and α-L-guluronic acid (G) monomers that are composed of three different forms of polymer segments viz., (a) consecutive G residues, (b) consecutive M residues and (c) alternating MG residues [9]. Numerous reports on producing hydrogels of NaAlg by chemical crosslinking using glutaraldehyde and genipin [6] have been reported, illustrating the versatility of this polymer.

Sodium alginate is widely used in biomedical field as a supporting matrix for tissue repair and regeneration due to its non-antigenicity and chelating ability [10]. In drug delivery area, NaAlg is used for targeting drugs at lower intestine since they exhibit pH-responsivity due to the presence of functional carboxyl groups and its high swelling is observed at increasing pH values due to the polymer chain expansion. Modification of synthetically derived NaAlg hydrogels has expanded its utility in therapeutic applications, especially in extending the release time of drugs having short plasma time [11].

NaAlg-based biomaterials are used in tissue engineering as wound dressing sponges and electrospun mats that are the promising substrates for wound healing due to advantages like hemostatic capability and gel-forming ability upon absorption of wound exudates. Similar to CS, NaAlg has many critical elements desirable for developing wound dressing material. For instance, NaAlg dressings (like Kaltostat®) enhance wound healing through selective stimulation of monocytes to produce cytokines such as interleukin-6 and tumor necrosis factor-α [12]. Many blends of NaAlg have been produced by mixing with other polymers for improving its drug delivery properties [13,14].

The future research depends on challenging tasks that includes development of novel biomaterials in biomedicine and biopharmaceutical disciplines.

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