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Chitosan-Based Hydrogels in Biomedicine

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Chitosan is a naturally occurring biopolymer abundantly available that is obtained from chitin, a principal component of crustacean exo-skeleton. The hydrogels derived from chitosan have been the most widely used biomaterials in Nano medicine such as drug delivery and tissue engineering [1-5]. Recent studies have witnessed a tremendous growth in producing various types of chitosan-based hydrogels in the form of micro and nanoparticles that are required in specific biomedical applications [6-16]. This research short note highlights some of the latest state-of-the-art technology in producing these materials having relevance to biomedicine.

Hydrogels, being three dimensional network structures, are capable of imbibing a large quantity of water or biological fluid and these respond to various external stimuli like pH, temperature, ionic strength, and magnetic field strength that make them interesting smart materials. They swell in water-rich environment and resemble closely to biological tissues, but remain undissolved due to the presence of chemical and/or physical cross-links originated from ionic interactions, H-bonding, polar interactions and van der Walls forces.

Chitosan has a created greater importance in biomedical area than any other biopolymer in pharmaceutical industries due to its biocompatibility, biodegradability and non-toxicity, useful properties in wound healing, drug delivery and tissue engineering. This is because of the advantages in its structural modifications, which generates several favorable characteristics such as its functions and applications within the biomedical field. These properties have created much interest in agriculture, industry and medicine.

A key problem in biology and medicine has been to search for novel materials to solve the problem of human diseases. Due to recent advances in molecular biology and genetic engineering, various types of therapeutics developed require effective time release delivery devices that are biologically acceptable. For these, chitosan stands as one of the few biomaterials that have been developed as hydrogels for site specific delivery as well as in tissue engineering.

Upon administration of a drug through a delivery device, drug has to transport across several membrane barriers before reaching the target site. In many instances, reaching the target site is far lower than the effective level, resulting in patient compliance and side effects. There is thus an urgent need to develop formulations based on such biomaterials for site specific and time controlled delivery. Thus, chitosan stands truly one of the most ideal materials for these applications.

Some other useful applications of chitosan have been cited in the published literature and these include: therapeutically active proteins, peptides, small interfering RNA (siRNA), DNA, vaccines, other bioactive molecules like antihypertensive, anti-tubercular, and a variety of other drugs [6-16]. Hydrogels of chitosan have been produced through a variety of protocols consisting of homo and copolymerization techniques in addition to semi-interpenetrating and interpenetrating polymer networks including blends with other biopolymers like sodium alginate, poly(vinyl alcohol), poly(N-isopropyl acrylamide), poly(2-hydroxyethyl methacrylate), etc. The abundant amino and hydroxyl functional groups on CS bestow specific functionalities that are beneficial to improve its aqueous solubility, antimicrobial, muco-adhesivity, enzymatic degradability, tight junction opening ability and pH sensitivity. The amino group also gives additional scope to form polyelectrolyte complexes (PECs).

Some recent findings suggest their use in drug delivery, vascular prostheses, tissue engineering, diagnostics, contact lenses and coatings for stents and catheters, as surgical sutures, bandages, orthopedic materials as well as in dentistry [17,18]. Due to its hemostatic and wound healing properties, chitosan is widely used in the treatment of wounds, ulcers and burns as well as a scaffold in tissue engineering [19].

PECs of chitosan are a kind of ionic interactions involving other anionic polymers, which are large molecules involving a broader molecular weight range [20]. Ionic interactions in PECs are stronger than van der Waals forces and H-bonded interactions, but the preparation methods of PECs do not involve organic precursors, catalysts or covalent cross-linkers, making these bio-acceptable. The stability of PECs is greatly affected by solvent, ionic strength, charge density, pH and temperature.

The cationic nature of chitosan is especially suitable for delivering drugs through GIT to the intestine that depends upon pH of the medium. Efforts to overcome passage through GIT have addressed the use of suitable anionic polymers for masking the net positive charge of CS and to avoid the cargo release in the stomach, particularly, while releasing a peptide (insulin).

The excellent mechanical properties, fast in-situ gelation, good biocompatibility and ability to encapsulate live cells at the physiological conditions make these hydrogels ideal for tissue engineering, especially cartilage regeneration. Homogenous, *in situ* thermo gelling, highly tough, non-toxic injectable hydrogels from chitosan and hyaluronic acid co-cross-linked with β-glycerophosphate and genipin are being produced. Many tissue analogues including cartilage, bone, liver, and nerve have been prepared using this engineering technology. Chitosan was extensively used in bone tissue engineering as it is known to promote cell growth and mineral rich matrix deposition by osteoblasts cells in culture [21].

A series of injectable *in situ* forming chitosan-based hydrogels have been prepared by chemical cross-linking using genipin through ionic bonds between chitosan and sodium salts at room temperature. Their cell viability assays exhibited low toxicity and localized in situ gel formation as detected after subcutaneous injections in rat. Cur cumin with low bioavailability was chosen as a drug model and *in vitro* release showed initial burst release. These hydrogels have the potential

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for delivering cur cumin, an antibiotic drug, widely explored in recent years for many purposes.

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