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Chitosan—A versatile semi-synthetic polymer in biomedical applications

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ABSTRACT

This review outlines the new developments on chitosan-based bioapplications. 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 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.

Abbreviations: AL, alginate; ASGPR, asialoglycoprotein receptor; RGD, arginine–glycine–aspartic acid; BAL, bioartificial liver; BMP, bone morphogenetic protein; CP, calcium phosphate; CPC, calcium phosphate cement; CSF, colony-stimulating factor; DD, degree of deacetylation; DCs, dendritic cells; DTPA, diethyl triamine penta acetic acid; EDC, 1-ethyl-3-[3-imethylaminopropyl]carbodiimide hydrochloride; EGFP, enhanced green fluorescent protein; ECM, extra cellular matrix; FGF-2, fibroblast growth factor-2; FRET, fluorescence resonance energy transfer; FHF, fulminant hepatic failure; Gd, gadolinium; GC, galactosylated chitosan; GDNF, glial cell line-derived nerve growth factor; GP, glycerophosphate; GAGs, glycosamine glycans; GM-CSF, granulocyte-macrophage colony-stimulating factor; GTR, guided tissue regeneration; hGH, human growth hormone; hUCMSCs, human umbilical cord mesenchymal stem cells; HA, hydroxyapetite; HEC, hydroxyethyl cellulose; IBL, implantable bioartificial liver; ^{131}I-NC, ^{131}I-norcholesterol; IL, interleukin; IPN, interpenetrating network; ILs, ionic liquids; LCST, lower critical solution temperature; MRI, magnetic resonance imaging; MSCs, mesenchymal stem cells; NHS, N-hydroxysuccinimide; NCT, neutron-capture therapy; pDNA, plasmid DNA; PAA, poly(acrylic acid); PEC, polyelectrolyte complex; PEO, polyethylene oxide; PEI, poly(ethylenimine); PVP, poly(vinyl pyrrolidine); PNIPAM, poly(N-isopropylacrylamide); PVA, poly vinyl alcohol; RES, reticuloendothelial system; RII, retrograde intrabiliary infusion; RTILs, room temperature ionic liquids; RWM, round window membrane; SCs, Schwann cells; TPP, sodium tripolyphosphate; SPIOs, super paramagnetic iron oxide; SBF, synthetic body fluids; TCP, tricalcium phosphate; TGF-β1, transforming growth factor β1; TEM, transmission electron microscopy; TAA, triamcinolone acetonide; UV, ultra-violet; WSC–LA, water-soluble chitosan–linoleic acid; XRD, X-ray diffraction.

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Contents

1. Introduction

The history of chitosan dates back to the 19th century, when Rouget [1] 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 [2]. 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 [3–5]. 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 [6–8]. 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 (Fig. 1). It is obtained by deacetylation of its parent polymer chitin, a polysaccharide widely distributed in nature (e.g. crustaceans, insects and certain fungi) [9,10]. 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 [11]. 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 [12–17].