



Chitosan Based Scaffolds and Their Applications in Wound Healing

Shakeel Ahmed¹, Saiqa Ikram^{*,1}

Bio/Polymers Research Laboratory, Department of Chemistry, Jamia Millia Islamia (A Central University), New Delhi-110025, India

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ABSTRACT

Over the last decade, much interest has been developed in biopolymer based materials due to their biocompatible, biodegradable, non-toxic and non-allergenic nature. Chitosan is a unique biopolymer that exhibits outstanding properties, besides biocompatibility and biodegradability. Most of these peculiar properties arise from the presence of primary amines along the chitosan backbone. Many works have been done to obtain chitosan based scaffolds, including surface modifications, the fabrication of chitosan based blends, chitosan based composite scaffolds, and drug-loaded scaffolds. This study provides an overview of the key features of inherent properties of chitosan, their modification, and its use in biomedical engineering particularly toward anti-inflammatory and wound healing.

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* Corresponding author.

E-mail addresses: shakeelchem11@gmail.com (S. Ahmed), sikram@jmi.ac.in (S. Ikram).

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¹ Tel.: +91-11-26981717X3255.

Introduction

In all biomedical applications today, polymers are playing an important role. Many notable advances in technology have followed exploitation of the properties offered by new polymeric materials like blends and composites (Kittur et al., 2002; Muzzarelli and Muzzarelli, 2005; Qin et al., 2012; Chee, 1990; Sun et al., 1992). Biopolymers include the polysaccharides such as cellulose, starch, the carbohydrate polymers produced by bacteria and fungi and animal protein based biopolymers such as chitin, chitosan, wool, silk, gelatin and collagen; biopolymers, especially the carbohydrate origin, have been found to have a very promising industrial application in various forms (Singh, 2011). Most commercial polysaccharides (e.g., cellulose, dextran, pectin, alginic acid, agar-agar, agarose, starch, carrageenan, and heparin) are either neutral or acidic, but chitosan is a basic polysaccharide. In neutral or basic pH, chitosan contains free amino groups and is insoluble in water, while in acidic pH, chitosan is soluble in water due to protonation of amino groups. The solubility depends on the distribution of free amino and *N*-acetyl groups (Wu and Bough, 1978; Costa-Pinto et al., 2011). Chitosan is a linear polyelectrolyte at acidic pH. It has high charge density, one charge per glucosamine. The pH and ionic strength have an important impact on the intrinsic viscosity of polyelectrolytes. Chitosan in aqueous acid solution has been surface reacted with polyanion aqueous solutions (heparin, sodium alginate, carboxymethyl chitin, polyacrylic acid) to give polyelectrolyte complexes (Rinaudo and Domard, 1989; Dutkiewicz and Tuora, 1992).

Chitosan

Chitosan is a copolymer which consists of β -(1 \rightarrow 4)-linked 2-acetamido-2-deoxy-D-glucopyranose and 2-amino-2-deoxy-D-glucopyranose units. This is generally obtained by alkaline deacetylation of chitin, which is the main component of the exoskeleton of crustaceans, such as shrimps. Chitin is a naturally abundant mucopolysaccharide and is second to cellulose in terms of the amount produced annually by biosynthesis. Chitin is a common constituent of the exoskeleton in animals, particularly in crustaceans, mollusks and insects. The structure of chitosan (deacetylated chitin) is very similar to cellulose (Fig. 1); however less attention has been paid to chitin than cellulose, primarily due to its inertness. Hence, it remains an essentially unutilized resource. Deacetylation of chitin yields chitosan, which is a relatively reactive compound and is produced in numerous forms, such as powder, paste, film and fibre. Chitosan is soluble in dilute aqueous acetic, lactic, malic, formic and succinic acids (Skotak et al., 2011; Shakeel et al., 2014; Shakeel and Saiqa, 2015a; Mudasir et al., 2015a). Chitosan is polycationic at pH < 6 and it readily interacts with negatively charged molecules, such as proteins, anionic polysaccharides (e.g., alginate and carrageenan), fatty acids, bile acids and phospholipids. Nonetheless, chitosan may also selectively chelate metal ions such as iron, copper, cadmium and magnesium (Mudasir et al., 2015b). Much attention has been paid to chitosan based biomedical materials, because of its unique properties such as biodegradability, non-toxicity, anti-bacterial effect and biocompatibility. Chitosan is a benefit to wound healing because it stimulates haemostasis and accelerates tissue regeneration. For a material to be used for biomedical research, a natural product is preferred because these materials are more biocompatible than synthetic materials. Chitosan is metabolized by certain human enzymes, such as lysozyme, thus, it is biodegradable. Chitosan is an attractive material for a tissue engineering scaffold because it has structural similarities to glycosaminoglycans and is hydrophilic. Chitosan's monomeric unit, *N*-acetylglucosamine, occurs in hyaluronic acid, an extracellular macromolecule that is important in wound repair (Muzzarelli, 1996; Keong and Halim, 2009).

Modifications of Chitosan

An effective approach for developing a clinically applicable chitosan is to modify the surface of the material to provide excellent biofunctionality and bulk properties. Surface modification techniques to blend various compound derivatives include coating, oxidation by low-temperature plasma and surfactant addition in order to blend with various derivatives. Furthermore, chitosan can be fabricated into a stable, porous bioscaffold via surface modification and lyophilization. However, blending with various additives may affect its biocompatibility. Therefore, evaluation of the biocompatibility of various biomedical-grade chitosan derivatives is necessary to engineer material that is of high quality and biocompatible for human wound management. They offer the advantage of being easily processed into gels, membranes, nanofibres, nanofibrils, beads, microparticles, nanoparticles, scaffolds and sponge-like forms (Fig. 2). Due to these properties and its biocompatibility, it has versatile applications in tissue engineering, wound healing, as excipients for drug delivery and gene delivery (Anithaa et al., 2014).

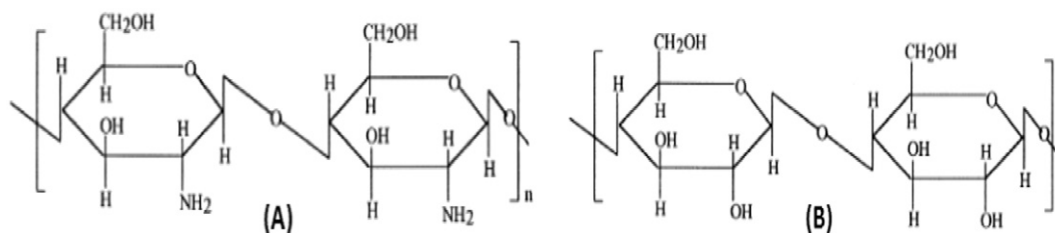


Fig. 1. Structure of (A) Chitosan and (B) Cellulose.

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