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Biopolymer-based functional composites for medical applications

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ABSTRACT

Over the last decade, numerous biopolymers have received more attention in medical applications involving novel biomaterials because of their biocompatibility, biodegradability, and ease of processing. To date, many biopolymer-based functional composites have been developed to increase the value of raw biopolymers obtained from natural sources or microbial systems. This review article covers general information on various biopolymers, important methods for biopolymer-based composites preparation including their advantages and disadvantages, and surface topography for tissue engineering. In addition, this article provides comprehensive knowledge and highlights recent research on functional biopolymer composites used in various medical applications, such as tissue engineering comprising skin, bone, cartilage, vascular graft, and other organs, implantable medical devices including stent and barrier membrane, and some delivery systems of bioactive agents. Furthermore, the article presents a brief overview on several challenges and future scope in this field.

Contents

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1. Introduction

An ideal biomaterial for regenerative medicine should be non-toxic, biocompatible and promoting cellular interactions to tissue development, with adequate mechanical and physical properties. Naturally derived biopolymers are similar to biological macromolecules that are recognized by and metabolized in the biological environment. In addition, these biopolymers do not induce chronic inflammatory or immunological reactions and toxicity, which are often associated with synthetic polymers, because of their similarity to the extracellular matrix (ECM). The degradation rates of biopolymers within biological systems can be manipulated by modifying their processing conditions [1–4]. Regenerative medicine has the potential to regenerate damaged tissues and organs in the human body; this involves growing tissues and organs in the laboratory and implanting them in a patient's body to promote healing (Fig. 1) [5–7]. Current strategies of regenerative medicine focus on the restoration of pathologically altered tissue architectures by using supportive scaffolds containing bioactive molecules. Scaffolds have been used for the engineering of tissues such as the skin, bone, cartilage, vascular tissues, and organs, and as vehicles for controlled and targeted release of drugs, growth factors, genes, and cells [8–11]. In this review article, the first section presents general information on various biopolymers, the second section reviews important methods for fabricating biopolymer-based composites, and surface topography for tissue engineering scaffold. The final section focuses on the medical applications of biopolymer-based composites.

2. Biopolymers

Naturally derived biopolymers are suitable for medical applications because of their biocompatibility, biodegradability, non-toxicity, and ability to adsorb bioactive molecules. However, some disadvantages hamper the development of natural polymers for medical use. These biopolymers are exposed to the external environment during production. Therefore, microbial and heavy metal contamination may occur. This can be prevented during handling and by using preservatives. In addition, batch-to-batch variation and slow processing hinder the mass production of biopolymers for medical use. The manufacturing of synthetic polymers is a controlled procedure involving fixed quantities of ingredients; however, the productibility and production rate of biopolymers depend on the environment and many physical and other factors. In this review, we have divided biopolymers into three classes according to their chemical structure and source: (i) polysaccharides, (ii) proteins, and (iii) microbial polymers [3,12].

(i) Polysaccharides are composed of monosaccharides linked by glycosidic linkages (Fig. 2a–e). Polysaccharides perform different physiological functions and may have various applications in the fields of tissue engineering and regenerative medicine (Table 1) [7,13].
(ii) Proteins are large biological molecules composed of one or more long chains of amino acid residues. Proteins display quintessential motility, stabilization, elasticity, scaffolding, as well as protection of cells, tissues, and organisms. Thus, they are extensively used in drug delivery and tissue engineering scaffolds [14–16].
(iii) Microorganisms naturally produce various biopolymers such as polysaccharides, polyesters, and polyamides (Table 2, Fig. 2f–j). Genetic manipulation of microorganisms allows the biotechnological production of biopolymers with tailored properties that make them suitable for high-value medical applications such as tissue engineering and drug delivery [17]. Several bacterial polymers have already been commercially produced through medium to largescale fermentation [18,19].

2.1. Polysaccharides

2.1.1. Hyaluronic acid

Hyaluronic acid (HA) is a major component of the ECM of the skin, cartilage, and vitreous humor. Almost 50% HA in the human body is present in the skin, especially in the intracellular space, where its concentration reaches up to 2.5 g/l. HA can affect cell proliferation, differentiation, and tissue repair [20,21]. HA was first described in the vitreous humor of bovine eyes and was subsequently synthesized *in vitro*. Since then, it has been used in various medical applications [22,23]. The first HA-based biomedical product was developed in the 1970s and was approved by the FDA for use in corneal transplantation. HA is a non-sulfated, linear natural polysaccharide composed of d-glucuronic acid and d-*N*-acetylglucosamine linked together by alternating β-1,4 and β-1,3 glycosidic bonds. It has high molecular mass and interest-