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Silk fibroin/poly(vinyl alcohol) photocrosslinked hydrogels for delivery of macromolecular drugs

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ABSTRACT

Hydrogels are three-dimensional polymer networks widely used in biomedical applications as drug delivery and tissue engineered scaffolds to effectively repair or replace damaged tissue. In this paper we demonstrate a newly synthesized cytocompatible and drug releasing photo-crosslinked hydrogel based on poly(vinyl alcohol) methacrylate and silk fibroin which possesses tailorable structural and biological properties. The initial silk fibroin content was 0%, 10%, 20%, 30%, 40% and 50% with respect to the weight of poly(vinyl alcohol) methacrylate. The prepared hydrogels were characterized with respect to morphology, crystallinity, stability, swelling, mass loss and cytotoxicity. FITC–dextrans of different molecular weights were chosen as model drugs molecules for release studies from the hydrogels. The hydrogels containing different silk fibroin percentages showed differences in pore size and distribution. X-ray diffraction analysis revealed that amorphous silk fibroin in poly(vinyl alcohol) methacrylate is crystallized to β-sheet secondary structure upon gelation. The sol fraction increased with increasing fibroin concentration in the co-polymer gel (from 18% to 45%), although the hydrogel extracts were non-cytotoxic. Similarly, the addition of silk fibroin increased water uptake by the gels (from 7% to 21%). FITC–dextran release from the hydrogels was dependent on the silk fibroin content and the molecular weight of encapsulated molecules. The study outlines a newer type of photo-crosslinked interpenetrating polymer network hydrogel that possess immense potential in drug delivery applications.

1. Introduction

Hydrogels are insoluble three-dimensional (3-D) networks of crosslinked hydrophilic homopolymers, co-polymers or macromers with a high degree of water uptake in aqueous environments [1]. Hydrogels are widely used in biomedical applications, such as drug delivery vehicles [2], encapsulation materials for immunoisolation-based cell therapeutics, wound dressings and tissue engineered scaffolds [3]. Polymers can be prepared and combined in the form of blends, co-polymers, and interpenetrating polymer networks (IPN). IPN are unique combinations of crosslinked polymers in which at least one component is synthesized and/or crosslinked in the presence of the other [4]. IPN are often created to deliver key attributes of one of the components while maintaining the critical properties of the other polymer. When two polymers form a co-polymer network but only one of them is crosslinked and the other is simply mixed into the network a semi-IPN is formed [5]. IPN formation has been shown by numerous researchers to improve the performance of crosslinked hydrogels. Semi-IPN are usually synthesised by polymerizing a monomer or prepolymer around existing polymer chains. Alternatively they can be developed by diffusing polymer chains within a preformed polymer network [6].

The chains comprising semi-IPN network hydrogels may be based on natural, synthetic or hybrid combinations of these materials. Hydrogel formation can be achieved when polymer chains interact either physically or chemically into networks [1]. The physical structure and characteristics of hydrogels depend upon the starting monomers and macromers, synthesis and fabrication methods, degradation, etc. Synthetically derived hydrogels have the advantage of controlling the specific gel properties and are tailorable through the use of specific molecular weight, block structure and cross-linking densities [7–9]. Furthermore, hydrogels synthesized from natural macromers generally induce fewer immunogenic reactions as they are produced from basic molecules already used by the body. Biological molecules are incorporated into synthetic hydrogel networks to improve cell attachment and, hence, encapsulation [10,11].

Poly(vinyl alcohol) (PVA) is particularly advantageous, as it offers the possibility of attaching cell signalling molecules or drugs via the numerous hydroxyl groups present on the backbone [12]. PVA can be modified into multifunctional, multivinyl macromers through the plethora of pendant hydroxyl groups, which can be

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