POLYSACCHARIDE-BASED HYDROGELS FOR BIOMEDICAL PURPOSES BY RADIATION-INDUCED SYNTHESIS

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Introduction

Dextran is a non-toxic, bacterial polysaccharide mainly composed of linear α-1-6,linked D-glucopyranose residuals with a low content of α-1-2, α-1-3 and α-1-4-linked side chains [1]. Its biocompatibility and biodegradability are well documented, thus dextran has been extensively explored in the field of biomaterials [2]. Dextran has been clinically used for more than five decades as a plasma volume expander, it is able to decrease vascular thrombosis, reduce inflammatory response and promote vascularization, hence it is a perfect candidate for soft tissue regeneration. This biopolymer and nowadays its applications extend to new biomedical applications including hydrogel-like scaffolds for tissue engineering [2,3].

Chemical structure of dextran enables a wide range of chemical modification. Incorporation of crosslinkable moieties (e.g. methacrylic groups, -MA) into dextran structure results in derivatives capable for crosslinking initiated by UV or ionizing radiation [4,5].

The radiation technique is a very efficient and clean tool for modifying polymers. Unquestionable advantages of using radiation include possibility of processing materials in any physical state, at a convenient temperature (usually room temperature), typically with no need of application of additional chemicals, i.e. potentially toxic initiators or catalysts [6]. Moreover, if sufficient dose is applied (typically 25 kGy) the sterilization can be accomplished simultaneously with the processing. In our recent study we have demonstrated possibility of radiation synthesis of hydrogels based on biocompatible dextran methacrylate (Dex-MA) [6].

The current work was aimed to synthesize dextran-based hydrogels with addition of another biocompatible polysaccharide – sodium hyaluronic acid (NaHA), and to develop conditions suitable for formation of macroscopic polymeric network with use of radiation technique.

Materials and Methods

Dextran (from *Leuconostoc ssp.*, Mr = 70,000) was purchased from Sigma-Aldrich (Canada), dimethyl sulfoxide (DMSO, 99.5%) and chloric acid (HCl, 36-38%) were obtained from Chempur (Poland). Glycidyl methacrylate (GMA 97%, stabilized by 0.005% hydrochinone monomethylether) was purchased from Sigma Aldrich, 4-(*N,N*-dimethylamino)pyridine (DMAP) were obtained from Sigma Aldrich (USA). Dextran derivatives have been synthesized using procedure of van Dijk-Wolthuis by coupling glycidyl methacrylate with this polysaccharide, yielding Dex-MA of various degrees of methacrylate substitution (DS) [7]. Synthesized Dex-MAs were characterized using FTIR and NMR spectroscopy. Dextran-based hydrogels were manufactured through polymerization/crosslinking of methacrylic groups of Dex-MA in aqueous solutions with radiation initiation. 3 and 5% aqueous solutions of Dex-MAs were prepared with addition of sodium hyaluronic acid (NuSci Pure Hyaluronic Acid HA Sodium Hyaluronate Powder, 91,6%) of two different molecular weights – 75 and 1029 kDa at concentrations of 0, 0.5 and 1%. Solutions of polysaccharides were deoxygenated and subsequently irradiated by electron beam (1 – 25 kGy). Following the irradiation, the samples of permanent chemical hydrogels underwent sol-gel analysis to determine basic parameters, i.e.: equilibrium degree of swelling in deionized water (EDS) and gel fraction (GF).

Results and Discussion

The main goal was to study the influence of NaHA additive on radiation-initiated synthesis of dextran-based hydrogels. Crosslinking of pure Dex-MA in aqueous solutions was found to be an efficient process yielding gels with high insoluble fraction content (up to 100 %). The swelling encompasses the wide range of 20 – 120 g of water absorbed per g of crosslinked polymer dependently on DS of used Dex-MA, and processing conditions. Addition of NaHA increase significantly swelling ability of the hydrogels, even up to 520 g of absorbed water. In general, hydrogels with NaHA are characterized by higher EDS, while retaining high content of insoluble fraction. Based on collected data it can be concluded that the utility characteristic of these polysaccharide-based hydrogels can be tailored by appropriate selection of parameters of polymer and the solution, such as molecular weight, DS, concentration, and irradiation conditions.

Conclusions

In this work, a series of Dex-MA was synthesized by the reaction of dextran with GMA. Irradiation of aqueous solution of Dex-MA with addition of sodium hyaluronic acid in absence of low-molecular-weight additives (crosslinkers) resulted in formation of macroscopic hydrogels even at doses as low as 100 Gy. Thus, obtaining hydrogel based on Dex-MA using ionizing radiation, i.e. crosslinking through unsaturated C=C bonds of -MA substituents, seems to be interesting alternative in comparison to other methods (chemical and UV-crosslinking). Moreover, it is possible to immobilize other biopolymers within crosslinked Dex-MA network. End-characteristics of these hydrogels can be tailored by manipulation of processing conditions. This, combined with well-known biological activity and functionality of dextran, and wide application of hyaluronic acid in the field of biomaterials implies possibility of biomedical applications of presented dextran-based hydrogel, especially in the field of soft tissue regenerative medicine.

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