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Characteristics of xanthan gum-based biodegradable superporous hydrogel

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ABSTRACT

A novel biopolymer-based superporous hydrogel (SPH) was synthesized through chemical crosslinking by graft copolymerization of 2-hydroxyethyl methacrylate (HEMA) and acrylic acid (AA) on to xanthan gum (XG) via redox initiator system of ammonium persulfate (APS) and *N*, *N*, *N′*, *N′*-tetramethylethylenediamine (TMED), in the presence of *N*, *N′*-methylenebisacrylamide (MBA) crosslinking agent, sodium bicarbonate foaming agent, a triblock copolymer of polyoxyethylene/polyoxypropylene/polyoxyethylene as a foam stabilizer. Characterization of SPH was done by FT-IR, TGA, SEM, HPC and GCMS. The effects of pH and salinity on the swelling aptitude of the SPH were investigated along with its degradability in *Streptococcus bovis* medium.

1. Introduction

Superporous hydrogels (SPHs) are lightly crosslinked hydrophilic polymers that can absorb, swell and retain aqueous solutions upto hundreds of times their own weight within minutes, to the equilibrium swollen state regardless of their size in the dried state [1]. The unique property of size independent fast swelling kinetics of SPHs is accounted for by their interconnected open cellular structure. The macroporous structure allows extremely fast absorption of water into the center of the dried matrix by capillary action and permeation of soluble substances is enhanced by the diffusion through the phases formed by the water filling the pores. The porosity plays the multiple role of enhancing the total water sorption capability and the rate of response by reducing the transport resistance. Therefore, creation of porosity in hydrogels has been considered as an important process in many ways. The phase-separation technique, the water-soluble porogens and the foaming technique are three different methods for preparing porous hydrogel structures. Due to their superporous structures, the equilibrium swelling usually is more than 100 and reaches its equilibrium within minutes. Based on these fast swelling and superabsorbent properties, SPHs have potential for various pharmaceutical and biomedical applications.

Biomaterials have an enormous impact on human health care. They are widely used in biomedical applications, including drug delivery devices and tissue-engineering matrices [2–4]. Because of their biocompatibility, biodegradability and non-toxicity, polysaccharides and protein-based hydrogels have created extensive interest as biomaterials. Xanthan gum (XG) is an extracellular polysaccharide secreted by the microorganism *Xanthomonas campestris*. It is complex polysaccharide consisted of a primary chain of β-D-(1, 4)-glucose backbone, which has a branching trisaccharide side chain composed of β-D-(1, 2)-mannose, attached to β-D-(1, 4)-glucuronic acid, which terminates in a final β-d-mannose. XG has been widely used in oral and topical formulations as a suspending and stabilizing agent, and a release sustaining agent in hydrophilic matrix tablets and pellets [5]. It has become one of the most successful hydrocolloids largely due to its high functionality, particularly in difficult environments such as acid, high salt and high shear stress. The anionic character of XG is due to the presence of both glucuronic acid and pyruvic acid groups in the side chain [6]. XG, therefore, offers a potential utility as a drug carrier because of its inertness and biocompatibility [7]. XG is classified E 415 in the European List of Permitted Food Additives. According to JECFA (Joint WHO/FAO Expert Committee on Food Additives) it has the status of ADI-non-specified (Acceptable Daily Intake), i.e., no quantitative limitation is stated, and, as such XG is recognized as a nontoxic additive for human consumption. According to the U.S. FDA/CFSAN, ethanol precipitate of XG enjoys the GRAS (Generally Recognized as Safe, GRAS Notice No. GRN 000211) status.

2-Hydroxyethyl methacrylate (HEMA) is a commercially important monomer that has been widely used in the manufacture of soft contact lenses and intraocular lenses. HEMA is a favorable biomaterial because of its excellent biocompatibility, good blood compatibility and physicochemical properties (EWC of 40%) similar to those of living tissues [8,9]. It also exhibits good chemical and

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hydrolytic stability and good tolerance for entrapped cells. Other biomedical applications for poly (HEMA) based materials include an embedding substrate for the examination of cells using light microscopy, and inert matrices for the slow release of drugs [10,11]. Poly (acrylic acid) is a typical pH responsive polyelectrolyte polymer able to form ions when subjected to an aqueous environment causing considerable volume swelling due to hydrogen bridge or covalent bond formation. It has been widely used in the area of site-specific delivery to specific regions of the gastro-intestinal tract. However high water solubility has limited their use as a drug carrier to a certain extent; because of dissolution before the drug can be delivered. In order to overcome the above drawback, acrylic acid (AA) is polymerized with either hydrophilic or hydrophobic monomers in the presence of organic crosslinkers to form copolymers of tunable physicochemical properties.

Several reports were available on the synthesis of porous hydrogels made from HEMA and AA monomers [12–14], but no substantial work has been reported related to grafting of HEMA and AA onto XG. The present article is based on the synthesis and characterization of a novel biodegradable superporous hydrogel through chemical crosslinking by graft copolymerization of HEMA and AA onto XG.

2. Materials and methods

2.1. Materials

Xanthan gum (XG) was purchased from Sigma, USA. Ammonium persulfate (APS), *N*, *N*, *N′N′*-tetramethylethylenediamine (TMED), *N*, *N′*methylenebisacrylamide (MBA), and sodium bicarbonate ($NaHCO_3$) were purchased from Fluka (Buchs, Switzerland). Lutrol F®127 was obtained from BASF (Ludwigshafen, Germany). Acrylic acid and 2-hydroxyethyl methacrylate (Merck, Darmstadt, Germany) were vacuum distilled at 63 °C/12 mm Hg and 50 °C/50 mm Hg, respectively, prior to use in order to remove the inhibitor. In HEMA vacuum distillation, hydroquinone was added to prevent polymerization. All other chemicals were also of analytical grade. Milli-Q grade deionized water was used for preparing the solutions.

2.2. Synthesis

2.2.1. Synthesis of homopolymers, pHEMA, pAA and copolymer poly [HEMA-co-AA]

The above homopolymers and copolymers were synthesized as per the earlier reports [15] with little modification as described below without adding XG.

2.2.2. Synthesis of graft copolymer, XG-g-poly [HEMA-co-AA]

A pre-weighed amount of XG (1.0 g) was added to 30 ml deionized water in a 500 ml reactor equipped with a mechanical stirrer (RZR 2021, a three-blade propeller type, Heidolph, Schwabach, Germany) and stirred (250 rpm) for 10 min. The reactor was placed in a thermostated water bath to control the reaction temperature at 80 °C. After dissolving XG and homogenizing the mixture, the monomers HEMA, AA and the crosslinker, MBA, Lutrol F®127 (foam stabilizer) were simultaneously added and the reaction mixture was stirred for 15 min. Then the initiator APS (oxidant) and TMED (reductant), $NaHCO_3$ (forming agent) was added (Table 1). The solution was stirred at 400–500 rpm while maintaining the temperature and inert atmosphere. The temperature was maintained at 80 °C and the reaction mixture was stirred continuously for 4 h. The low molecular weight substances remaining in the samples after polymerization were extracted with boiling ethanol for 24 h. The product was collected by centrifugation and dried in the oven under vacuum at 60 °C for 24 h. The dried graft polymer was added to 300 ml deionized water. It was allowed to swell during agitation in a water bath at the constant temperature of 60 °C for 24 h. Then it was extracted with ethanol in a soxhlet for 6 h followed by water at 100 °C for 72 h. The precipitate was filtered and dried under vacuum at 60 °C.

Table 1
Composition of the feed mixture.

Polymer code	MBA (g)	APS (g)	TMED (ml)	HEMA (ml)	AA (ml)	ES (g/g)
H_1	0.1	0.1	0.1	2.5	2.5	83.5
H_2	0.2	0.1	0.1	2.5	2.5	72.1
H_3	0.3	0.1	0.1	2.5	2.5	56.5
H_4	0.1	0.2	0.1	2.5	2.5	91.6
H_5	0.1	0.3	0.1	2.5	2.5	78.2
H_6	0.1	0.2	0.2	2.5	2.5	108.0
H_7	0.1	0.2	0.3	2.5	2.5	84.0
H_8	0.1	0.2	0.2	5.0	2.5	77.9
H_9	0.1	0.2	0.2	7.5	2.5	67.1
H_{10}	**0.1**	**0.2**	**0.2**	**2.5**	**5.0**	**120.6**
H_{11}	0.1	0.2	0.2	2.5	7.5	109.3

Reaction conditions: xanthan gum: 1 g, Lutrol F®127: 100 mg, $NaHCO_3$:0.5 g, H_2O:30 ml, temperature: 80 °C.
Bold values signify that the polymer code H10 was found to be best among various feed mixtures in connection to its equilibrium swelling capacity (ES). The same sample was used for all comparatative studies.

2.3. FT-IR spectra

FTIR spectra of individual and crosslinked polymers were recorded in the range 400–4000 cm^{-1} on a Perkin Elmer Paragon 500 FTIR spectrophotometer using KBr pellets.

2.4. Thermogravimetric analysis

The thermo gravimetric analysis data were recorded with a shimadzu DTG-50 thermal analyzer. The samples were heated from room temperature to 600 °C at a heating rate of 10 °C per min.

2.5. Scanning electron microscopy

The SEM of gold-coated samples were obtained using JSM - 6390LV scanning electron microscope (Jeol Ltd, Japan) at a magnification of ×5 to 300,000 (Resolution-HV 3.0 nm).

2.6. Determination of residual AA by high performance liquid chromatography (HPLC)

Residual AA was detected and quantified by HPLC (Prominence, Shimadzu Corporation, Japan). The chromatographic system consisted of a computer-controlled pump (model LC 20AT), autosampler (model SIL-10AF) equipped with a 200 μl sample loop, photodiode array (PDA) detector (model SPD-M20A). Shimadzu LC Solution software was used for the system and data management. The separation was performed in isocratic mode at a flow rate of 1.5 ml/min and a temperature of 40 °C on an analytical column Luna 5 μ C18, 250 × 4.6 mm (Phenomenex, USA). The mobile phase was aqueous 0.01% orthophosphoric acid [16] and the injection volume was 25 μl.

2.7. Determination of residual HEMA by gas chromatography (GCMS)

Residual HEMA analysis was performed by using GCMS (Agilent 6890N GC coupled with 5975 inert MSD). The GC was equipped with an autosampler (Agilent 7683 B). For chromatographic separation, a capillary column with following specifications was used: HP-5MS with length 30 m, id. of 0.25 mm and a film thickness of 0.25 μm (J&W Scientific). The carrier gas was helium with a constant flow of 0.7 ml/min. Injection was splitless and purge flow of helium gas