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Synthesis and Characterization of Injectable Photocrosslinking Poly (ethylene glycol) Diacrylate based Hydrogels

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Summary

The poly (ethylene glycol) diacrylate (PEGDA)-based hydrogels were prepared by UV radiation under nitrogen, using PEGDA and 2-hydroxyethyl methacrylate (HEMA) as precursors. The PEGDA and HEMA precursors were respectively added into distilled water at a predetermined feed ratio. 2-Hydroxy-1-[4-(hydroxyethoxy)-phenyl]-2-methyl-1-propanone (Irgacure2959) was used as a photoinitiator. The PEGDA-based hydrogels were characterized by FT-IR spectra, interior morphology, equilibrium swelling ratio, and Dynamic contact angle (DCA). The results showed: (1) -C=C- bonds of PEGDA and HEMA disappeared after photocrosslinking, which indicated hydrogel formation by consuming -C=C- bonds; (2) swelling ratio of the hydrogels were greatly influenced by the additive precursor ratios and microporous net; (3) with HEMA content increasing in PEGDA-based hydrogels, equilibrium water content (EWC) increased and the contact angle decreased, which resulted from the strong H-bonding interactions of HEMA between the polymer and water.

Introduction

Hydrogels, crosslinked hydrophilic polymers, have many advantages that make them prime candidates for cartilage tissue engineering applications: relative biocompatibility, tissue-like water contents and tissue-like elasticity [1~3], which can encapsulate cells when they crosslink [4]. In addition, hydrogels, three-dimensional networks of hydrophilic polymers that are able to be swell large amounts of water, can be made to resemble the physical characteristics of soft tissue [5]. Cell-carrier materials for cartilage tissue engineering have obtained great attentions, for cartilage, unlike other tissues, has a poor ability for self-repair. Photopolymeriaztion is very useful technique on crosslinking a liquid, macromer solution to form a hydrogel with temporal and spatial control over

polymerization, so photopolymerized hydrogels can be used as cartilage tissue engineering materials in situ in a minimally invasive manner such as by injection [6].
Polyehtylene glycol (PEG) with amphiphilic characteristic and good biocompatibility have been used as drug delivery, surgical barriers, cell encapsulation for transplantation, and cartilage tissue engineering scaffolds[7-9]. Furthermore, PEG can be readily excreted from the body via kidney and liver, and forms nontoxic metabolites, which makes it more suitable for tissue engineering applications. PEG-based products have been approved by FDA for human intravenous, oral and dermal applications [10]. It is reported that cartilage-like tissue are prepared by PEG-based photopolymerizing hydrogels after encapsulation of bovine chondrcytes both in vitro and in vivo [11]. Poly (2-hydroxyethyl methacrylate) is one of important hydrophilic macromolecules, which are not enzymatically degraded directly with acidic or alkaline solutions [12].
Properties and applications of hydrogels are greatly influenced by the surface characteristics, especially by the orientation of hydrophobic and hydrophilic properties [13, 14]. However, few studies have directly addressed how the hydrophobic and hydrophilic properties influenced the biological and wettability properties of hydrogels. In this study, PEGDA-based hydrogels were prepared and their characteristics and properties were investigated.

Materials and methods

Materials

Poly (ethylene glycol) diacrylate (PEGDA, Mn=600) was obtained from Sartomer company. 2-hydroxyethly methacrylate (HEMA) was purchased from Acros Organic Company. 2-hydroxy-1-[4-(hydroxyethoxy) phenyl]-2-methyl-1-propanone (a water soluble UV initiator commercially available as Irgacure2959) was bought from Ciba Specialty Chemicals, Switzerland.

Preparation of the PEGDA-based hydrogels

All of the Chemical reagents used for photopolymerizable hydrogels were added into distilled water at a predetermined feed ratio and stirred well. The aqueous solutions were made up of total of 20% monomers of PEGDA and HEMA, and 0.5wt % (relative to the amount of monomer) of photoinitiator Irgacure2959 dissolved in N-vinyl pyrrolidinone (NVP). Then the solutions were placed into Teflon module and polymerized by UV light (λ_{max}=365nm, intensity 800μV/cm^2) under nitrogen for 10 minutes at room temperature. After polymerization, the hydrogels were washed in distilled water for 48h to remove the unreacted precursor and residual chemicals. The distilled water was replaced periodically. Finally, the hydrogels were soaked into distilled water until swelling equilibrium and then removed and dried in a vacuum oven at 36°C for 2 days before the following characterizations.

Hydrogels Characterization

Fourier Transform Infrared (FT-IR) Spectroscopy
Fourier transform infrared spectroscopy was used to confirm the structure of PEGDA and HEMA macromer precursors and semi-IPN PEGDA-based hydrogels by a Shimadzu's FTS400 spectrometer.

Morphologies of PEGDA- based hydrogels

The hydrogels specimens were immersed into distilled water for 48h at room temperature to reach their swelling equilibrium. Then swollen hydrogels were firstly frozen in refrigerator at –20°C, and subsequently freeze-dried in a Christ Alpha 2-4 Freeze Drier under vacuum at –60°C for 48 hours until the samples became completely dry prior to morphological observation. Scanning electron microscopy (SEM, a Philips 30XLFEG.) was used to observe morphology and microstructure of samples at 10Kv. Samples were sputter coated with gold before SEM observation.

Swelling behaviors

The swelling properties of the PEGDA-based hydrogels were determined through gravimetrical method. Dry hydrogel specimens of known weight (W_d) were immersed into distilled water to swell water at room temperature. The swollen hydrogels were removed from water at predetermined intervals, and its weight (W_s) of the hydrogel after wiping of excess water on the surface with a filter paper was weighed. The processes were repeated until the weight of the swollen hydrogels didn't increase. Equilibrium water content (EWC) was calculated according to Eq. (1)

$$EWC(\%) = \frac{W_s - W_d}{W_s} \times 100 \qquad (1)$$

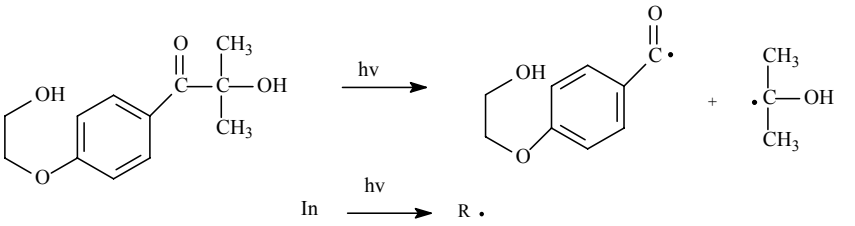
Contact angle measurements

Contact angles (water-in-air), $\theta_{w/a,}$ of PEGDA-based hydrogel membranes were identified using the sessile drop method at 25°C±0.5. Dynamic contact angle (DCA) measurements were quantified using a dynamic contact angle analyzer (A video based contact angle measuring system (OCA15) from Future Digital Scientific with SCA20 software). Every contact angle of the hydrogels was determined at four different spots on the sample.

Results and Discussion

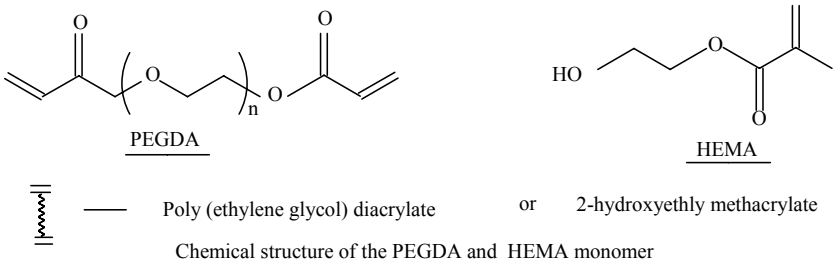
Radical photopolymerization of PEGDA-based hydrogels

PEG-DA and HEMA monomers, which were relatively hydrophilic and had -C=C- bonds at their chain ends, were easily photocrosslinked by themselves or by other macromer precursors containing -C=C- bonds, so the two kinds of monomers can form a solid network through photopolymerization. PEGDA-based hydrogels were synthesized of different weight ratio of the two macromer precursors, with a small amount of the Irgacure2959 as pohtoinitiator, by a long-wavelength UV lamp (365nm). The photopolymerization process was showed in Scheme 1. Firstly, photoinitiator molecules absorbed UV light and dissociated into radicals. Secondly, the initiation is when radical so formed with the monomer generating active center, which propagated through carbon-carbon double bonds present on the macromers to form growing, kinetic chains. Then a radical propagates through a pendant vinyl group, a crosslinked network will form. Finally, the 3-D network formed hydrogels via a radical chain polymerization.

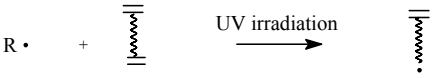


In = 2-hydroxy-1-[4-(hydroxyethoxy)phenyl]-2-methyl-1-propanone

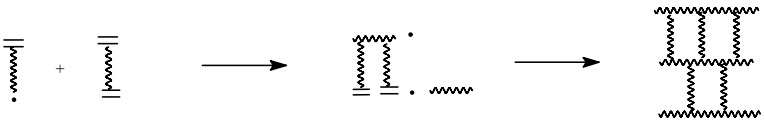
Step 1. The dissociation of the photoinitiator by UV exposure



Chemical structure of the PEGDA and HEMA monomer



Step 2. Redical initiation, when so formed reacts with the monomer generating active center



Step 3. Network Formation

Scheme 1. The photopolymerization process of PEGDA-based hydrogels

FT-IR spectra of Macromer precursors and PEGDA-based hydrogels

The FT-IR spectra of the PEGDA-based network hydrogels and the macromer precursors were showed in Fig.1. Compared with the spectrum of PEGDA/HEMA copolymer (b) and PEGDA polymer (c), the spectrum of PEGDA and HEMA monomer (a) had the typical double bond absorption bands at about 1640 cm^{-1}. Furthermore, the double band at 1640 cm^{-1} completely or mostly disappeared from spectra a to c, which contributed to the consumption of -C=C- bonds during photo-crosslinking reaction. The results indicated that the -C=C- double bonds were successfully incorporated into the PEGDA/HEMA copolymer and PEGDA polymer and finally PEGDA-based hydrogels formed through consumption of these -C=C- bonds. A visible weak peak of -C=C- bonds were observed in Fig.1b because PEGDA/HEMA copolymer had the lower HEMA content (20wt %) and its spectrum was mostly dominated by the PEGDA component (80wt %). The peak at 1106cm^{-1} was assigned to the C-O asymmetric stretching vibration of group (-C-O-C-). The characteristic broad band at 3400cm^{-1} was corresponding to the O-H stretching

vibration of the hydroxyl group of HEMA. The sharp band at 1721cm^{-1} corresponds to the C=O stretching of the acetate group of HEMA.

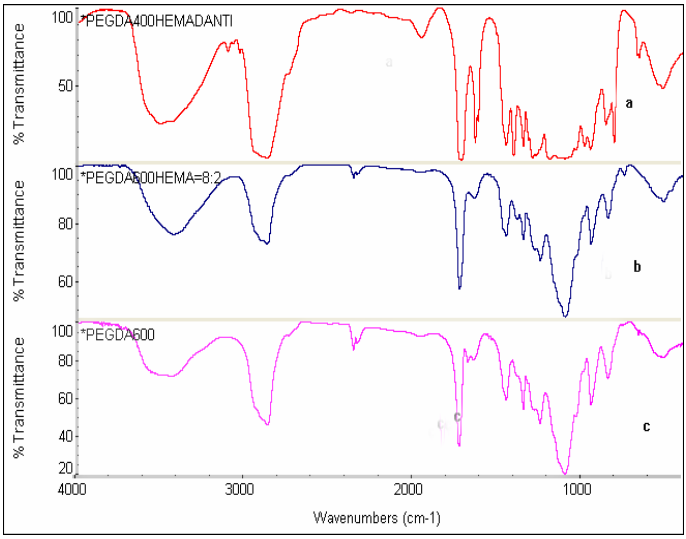
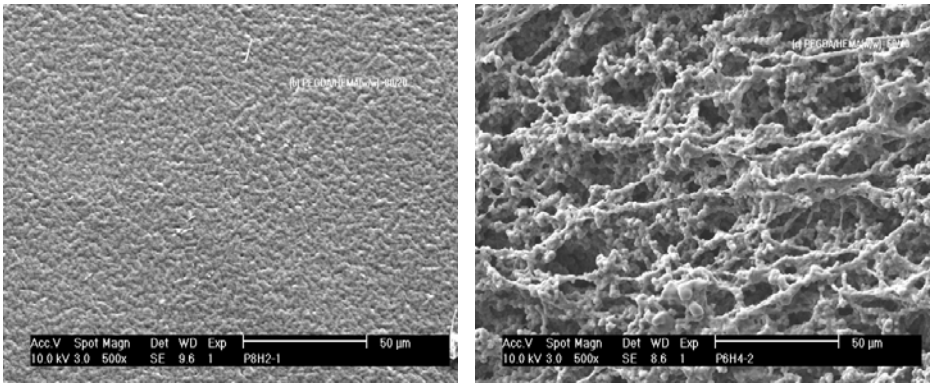


Fig.1 FI-IR spectra of (a) PEGDA and HEMA monomers, (b) PEGDA/HMEA copolymer, (c) PEGDA polymer



(a) PEGDA/HEMA=80/20 wt% (b) PEGDA/HEMA=60/40 wt%

Fig.2 SEM micrographs of PEGDA-based hydrogels

Interior Morphology of the PEGDA-based hydrogels

The interior morphologies of the freeze-dried and swollen PEGDA-based hydrogels samples were shown in Fig.2. These SEM images showed well-defined, though irregular, three-dimensional porous network structures. As the HEMA monomer feed ratio decreased, the crossliking density of the PEGDA-based hydrogel became higher and led to a tighter network structure reflected in a lower selling ratio. For example, as the HEMA monomer increased beyond 40wt%, the PEGDA-based hydrogel network

became more open, the pore size became bigger, the PEGDA-based hydrogel (PEGDA/ HEMA=60/40 wt%) showed the different-diameter pores from 5μm to 40 μm.

Swelling behavior of the hydrogels

The PEGDA-based hydrogels were immersed into distilled water for 72h at room temperature in order to attain an equilibrium state. Fig.3 showed the influences of concentration of PEGDA monomer on equilibrium swelling content in hydrogels at room temperature. The data displayed that the equilibrium swelling content in hydrogels decreased when the concentration of PEGDA monomer increased from 10% to 50%. Fig.4 showed the results of the swelling ratios of the PEGDA-based hydrogels at different content of HEMA. The results indicated that their equilibrium water content was influenced by the content of HEMA. As the HEMA content in the hydrogel increased, the equilibrium swelling content in the hydrogel increased. The PEGDA-based hydrogels with higher HEMA content had higher swelling ratio because the HEMA can provide more hydroxyl group and strong H-bonding interactions between the hydrogels and water. It was well established that strong H-bonding with water of the hydroxyl groups of HMEA also enhanced the hydrophilicity of the system [15]. The experimental results of swelling ratio of PEGDA-based hydrogels with different HEMA content were in good agreement with the microstructures of the hydrogels (Fig.2), which suggested the swelling ratio of those PEGDA-based hydrogels also depended on the characteristic of their network structure.

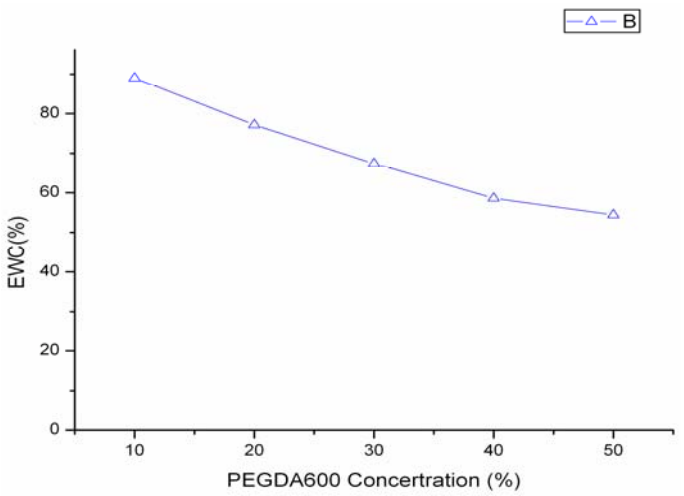


Fig.3 Influence of concentration of monomers on EWC of PEGDA-based hydrogels

Hydrophilicity

Hydrophilicity and wettability of the hydrogel membranes were investigated by using the sessile drop method at 25°C. Table 1 showed the testing results of contact angles and the equilibrium water contents of the hydrogels with various monomer ratios. The data demonstrated that the hydrophilicity of the hydrogels increased and the contact

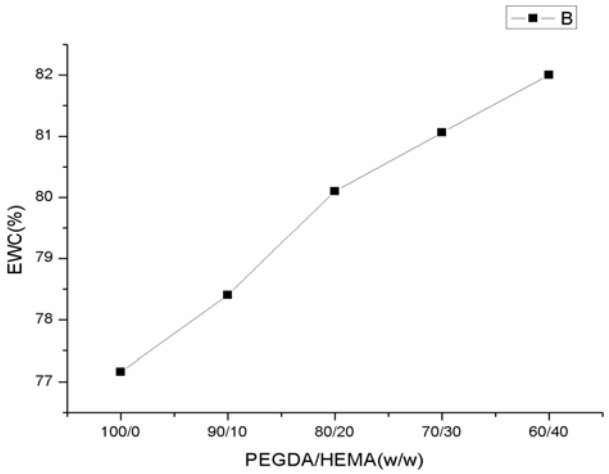


Fig.4 Influences of the feed ratio of PEGDA/HEMA monomer on EWC of the PEGDA-based hydrogels

Table.1. Effect of composition on contact angles and equilibrium water content of PEGDA-based hydrogels

Samples PEGDA/HEMA(w/w)	Contact angle (θ,degree)	Equilibrium water content (%)
100/0	52.0	77.2
90/10	46.3	78.3
80/20	43.5	80.1
70/30	39.4	81.4
60/40	33.0	82.0

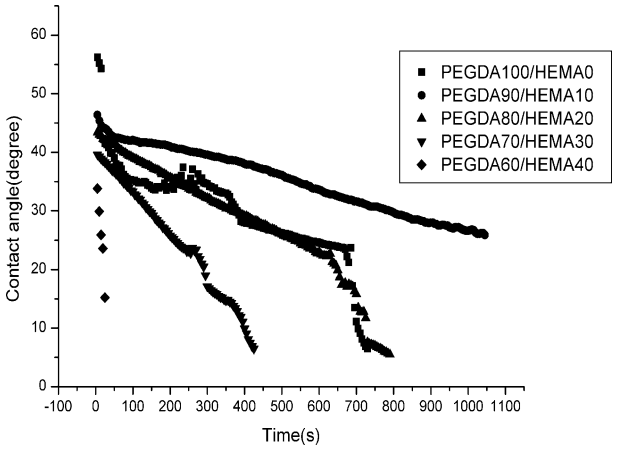


Fig.5 The dynamic contact angles curves of PEGDA-based hydrogels

angle decreased when the HEMA content in the hydrogel increased. As showed in Fig.5, the PEGDA-based hydrogels exhibited a wide range of contact angles. The hyrogel composed of PEGDA had the largest contact angles, and the PEGDA-based hydrogels with 40% HMEA had the smallest contact angle. So the contact angles were greatly affected by the content of HMEA within the hydrogel matrix. On the other hand, the $\theta_{w/a}$ values of the PEGDA-based hydrogels decreased rapidly with the time extending (Fig. 5). In terms of equilibrium water content, the greatest uptake was exhibited by HEMA hydrogel whereas PEGDA hydrogel displayed minimal uptake.

Conclusion

The highly cross-linked PEGDA-based hydrogels with different contents of HEMA were prepared by photo-polymerization of aqueous precursor solution. The surface hydrophilic characteristic and equilibrium water content of the PEGDA-based hydrogels were greatly influenced by HEMA content of the hydrogels. PEGDA-based hydrogels with higher contents of HEMA showed more surface hydrophilic characteristic and lower contact angles. PEGDA-based hydrogels with higher HEMA content had higher swelling ratio and equilibrium water content. So the PEGDA-based hydrogels showed a great potential as a cartilage scaffold for tissue engineering application.

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