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글리콜키토산을 이용한 초다공성 하이드로젤의 제조 및 팽윤거동

광가 · 이정정 · 윤취임 · 육군영 · 허강무†

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Preparation and Swelling Property of Superporous Hydrogels using Glycol Chitosan

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Abstract : Superporous Hydrogels (SPHs) have been extensively investigated for various biomedical applications due to their fast swelling and superabsorbent properties. In this study, glycol chitosan that is one of most abundant natural polymers was used as a cross-linking agent instead of bisacrylamide (BIS), which is a broadly used crosslinking agent for preparation of SPHs. Glycol chitosan was modified to have reactive vinyl groups by chemical conjugation with glycidyl methacrylate (GMA). The vinyl group-containing glycol chitosan (GC-GMA) was characterized by FT-IR and ^{1}H-NMR measurements. SPHs have been prepared in various synthetic conditions to establish the optimum synthetic process for making superporous structure, where the inner pores are interconnected to each other to form a open channel structure. Various SPHs with different GC-GMA contents have been successfully prepared and have been observed to show faster swelling properties than other conventional SPHs. From the study on the swelling behavior of SPHs, the GC-GMA content is considered to be an important factor for controlling their swelling properties.

1. Introduction

Hydrogels are three dimensional networks of hydrophilic polymers that can absorb a significant amount of water but do not dissolve in aqueous media[1]. They have been extensively investigated for biomedical and other applications due to their promising properties such as biocompatible, swelling and flexible properties[2]. Since most dried hydrogels take a long time for swelling ranging from several hours to days due to slow absorption of water by diffusion, one of the challenges has been to make a fast swelling hydrogel that can absorb the water

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and swell to an equilibrium state in a very short time. Over the last years, we have developed various superporous hydrogels with fast swelling and superabsorbent properties[3].

A gas blowing technique has been typically used to generate superporous structures, where the inner pores are interconnected to each other to make open channels in hydrogels, allowing fast water absorption by capillary force[4-6].

Recently, many attempts have been made to use natural polymers in the synthesis of hydrogels due to their advantageous properties in terms of biocompatibility, nontoxicity, and biodegradability[7]. Chitosan, one of the most abundant natural polymers, consists of N-acetyl D-glucosamine and D-glucosamine residues and have been extensively studied for a wide range of biomedical applications including delivery carriers of drugs and genes, tissue engineering scaffold, and wound dressing due to their biocompatibility and good mechanical properties. In this study, glycol chitosan that is a water-soluble chitosan derivative was modified and used as a polymeric cross-linking agent instead of bisacrylamide (BIS), which is a broadly used crosslinking agent for preparation of SPHs. Glycol chitosan was modified to have reactive vinyl groups by chemical conjugation with GMA. GC-GMA was characterized by FT-IR and ^{1}H-NMR measurements. SPHs have been prepared in various synthetic conditions to establish the optimum synthetic process for making superporous structure, where the inner pores are interconnected to each other to form a open channel structure. Various SPHs with different GC-GMA contents have been prepared and their swelling properties were investigated.

2. Experimental

2.1. Materials

Acrylic acid (AA, 99%), acrylamide (AAm, 98%) were purchased from Fluka. *N,N'*-methylenebisacrylamide (BIS, 99%), *N,N,N',N*-tetramethylethylenediamine (TEMED, 99%), ammonium persulfate (APS, 98+%), sodium bicarbonate, glycol chitosan (GC, degree of polymerization≥400) and glycidyl methacrylate (GMA, 97%) were purchased from Sigma-Aldrich. Pluronic® F-127 (PF 127) was obtained from Kumkang Chemical, Co. (Korea). The other chemicals were used as received.

2.2. Synthesis of vinyl group-containing glycol chitosan (GC-GMA)

One gram of glycol chitosan and the predetermined amount of glycidyl methacrylate were dissolved in 100 mL of distilled water and then stirred for 48 h at room temperature. After the reaction, the product was precipitated in acetone, filtered, washed two times in acetone and dried under vacuum for 24 h.

2.3. Synthesis of SPHs

SPHs were prepared by radical copolymerization of AA and AAM in the presence of GC-GMA. AA (10% w/v), AAm (15% w/v), GC-GMA and PF127 (0.5% w/v) were dissolved in distilled water. Four different amounts of GC-GMA (0.25, 0.5, 1.0, 1.5% w/v) were used to determine their effects on swelling properties. The pH value of the solution was adjusted at a range of 4.0 to 5.0 by adding 8 M NaOH solution. The monomer solution (8 mL) was placed into polypropylene conical tubes (30×115 mm). After APS (0.6% w/v) and TEMED (0.4% w/v) were added, the solution were shaken manually and kept at room temperature for a predetermined time. Sodium bicarbonate (5% w/v) was added to the solution with vigorous stirring. The solution was allowed to stand for more than 30 min to ensure complete reaction. The resultant

SPHs were washed with 70% ethanol and finally dehydrated in ethanol, followed by drying in a convection oven for 24 h.

2.4. Characterization

The chemical composition of GC-GMAs were confirmed by ^{1}H-NMR with D_2O as solvent (JNM-AL400 spectrometer, Jeol Ltd, Akishima, Japan) and FT-IR (MAGNA 560 spectrometer) measurements. Surface and inner pore structures of dried SPHs were observed by SEM (S-2460N, Hitachi, Tokyo, Japan). The contact angles of SPHs were measured by a drop shape analyzer (DSA 100, KrÜss, Germany) by Sessile drop method. Because SPHs are not directly available for the measurement because of the porous structure, the non-porous hydrogel samples with the same chemical compositions were synthesized in a film type without foaming process for comparison. For swelling measurements, SPH samples were cut into disks (2 mm in thickness) and then dried under vacuum for 24 h. The samples were immersed in distilled water and weighed at predetermined time intervals after removal of excessive surface water by lightly tapping the samples with a filter paper. The weight swelling ratio (S) of the SPHs was calculated from the equation, S=(Ws/Wd)/Wd. Here, Ws and Wd are the weights of swollen and dried SPHs.

3. Results and Discussion

3.1. Synthesis of vinyl group-containing glycol chitosan (GC-GMA)

Vinyl group-containing glycol chitosans were successfully synthesized by the reaction of glycol chitosan with glycidyl methacrylate. The presence of methacrylate groups in GC-GMA was confirmed by ^{1}H-NMR spectrum (Fig. 1). As shown in Figure 1, the peaks of double bonds of the methacrylate group appeared at 5.75 and 6.2 ppm. The other protons of the glycidyl methacrylate (-COO-CH_2-, >CH-O-, -CH_2-NH- groups) were located in the 4.2, 3.7, and 3.4 ppm. The signals from the methacryloyl group are observed at 1.9 ppm (methyl protons)[8,9]. The number of viny groups in GC-GMA could be controlled by varying the relative amount of GMA in feed and the GC-GMA with 8~9 vinyl groups per 100 glucose units was used as a polymeric crosslinker for preparation of SPHs. The synthetic result was further confirmed by FT-IR measurements as shown in Fig. 2. All the FT-IR spectra of glycol chitosan, GC-GMA, and SPHs showed the peaks at 3400 cm^{-1} and 2900 cm^{-1} due to O-H stretching and C-H stretching, respectively. The spectrum of glycol chitosan shows amide-I band at 1660 cm^{-1}, amide-II band at 1599 cm^{-1} and C-O stretching band at 1064 cm^{-1}. GC-GMA showed the peak at 1669 cm^{-1} assigned to the vibration of C=C groups of GMA which disappeared after polymerization. SPHs showed both characteristic peaks from amide and carboxyl groups at 1560 cm^{-1} and 1708 cm^{-1} resulting from AA and AAm monomers.

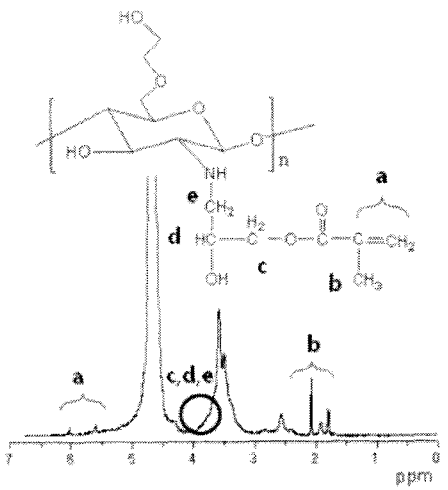

Fig. 1. ^{1}H-NMR spectrum of GC-GMA.

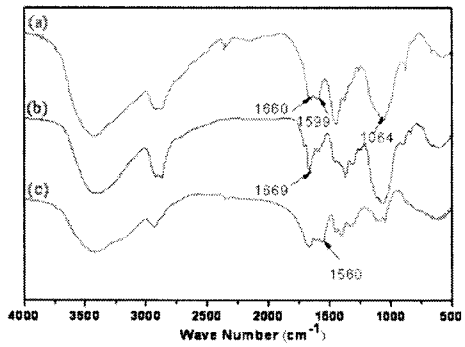

Fig. 2. FT-IR spectra of glycol (a) chitosan, (b) GC-GMA, and (c) SPH.

3.2. Synthesis of superporous hydrogels (SPHs).

For making homogeneous superporous hydrogels, the timing of foam formation and polymerization process is one of critical factors. If the foaming started too early or the polymerization proceeded too early, poorly porous or heterogenous hydrogels were observed. Therefore, it is significant to find the optimum timing for the addition of the foaming agent and the onset of crosslinking reaction to make a homogeneous superporous hydrogels. From the previous studies, APS/TEMED initiator system initiated the polymerization reaction within 1~ 2 min around neutral pH condition, but showed a delayed initiation under an acidic environment[3,4]. Here, the pH of monomer solutions containing AA, AAm, GC-GMA, and APS/TEMED was adjusted to the pH=4.5 for preventing the initiation reaction. Since the addition of sodium bicarbonate leads to an increase in the environmental pH and thus may act as a trigger system for polymerization, the time for addition of sodium bicarbonate was controlled from 30 to 120 sec. Once the sodium bicarbonate was added, the polymerization reaction proceeded rapidly and the reacting mixture became viscous over time. At the same time, bicarbonate interacted with the acid component of the system to produce CO_2 gases required for the blowing process. The two processes need to be conducted in such a way to enable harmonized foaming and gelation. This harmonization is a basic element for successful preparation of homogeneous SPHs.

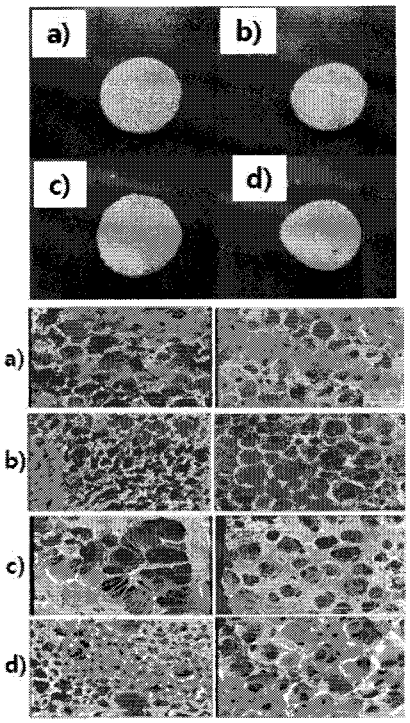

Fig. 3. Photographs (top) and SEM images (bottom) of SPHs prepared for different foaming time: a) 30 sec, b) 60 sec, c) 90 sec, and d) 120 sec. (scale bar=1 mm)

The morphological studies of SPHs were performed by SEM and the photographs and SEM images (left-inner, right-surface) of SPHs synthesized at different foaming time (30, 60, 90, and 120 sec) are presented in Fig. 3. The figure shows that the SPHs from the foaming time of 30 and 60 sec have good pore structures where the pores of even size (200~300 um) were interconnected to create

open channels. They swelled to the equilibrium state within 2 min (Seq=280) and their swelling ratios were relatively higher that those from 90 and 120 sec. The other SPHs were observed to be poorly and heterogeneously porous and show delayed swelling behavior with relatively lower swelling ratios. Because the polymerization proceeded earlier to forming process, pores were not formed or formed poorly. As a result, the optimum foaming time was found at a range of 30 to 60 sec.

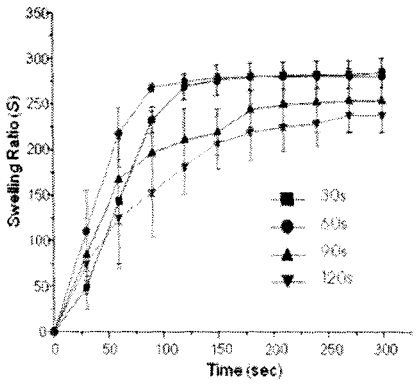

Fig. 4. Swelling properties of SPHs prepared for different foaming time.

3.3. Swelling properties of SPHs.

Fig. 5 shows dynamic swelling behavior of SPHs with different contents of GC-GMA. The result clearly indicates that as the amount of GC-GMA increased, the equilibrium swelling ratio of SPHs decreased. It is reasonable that the increase in the GC-GMA content led to an increase in the degree of crosslinking in the polymer networks that restricted the chain relaxation process, thus causing a decrease in equilibrium swelling ratio. SPHs synthesized with GC-GMA content of 0.5, 1.0, and 1.5% (w/v) swelled very fast and could reach their equlibrium swelling within two minutes. SPHs synthesized with GC-GMA content of 0.25% (w/v) shows a larger equilibrium swelling ratio, but a slower swelling rate.

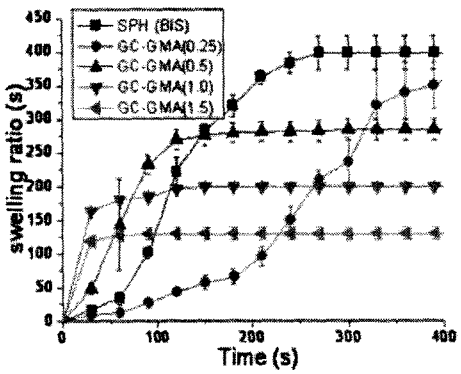

Fig. 5. Dynamic swelling behavior of SPHs from different contents of GC-GMA (0.25, 0.5, 1.0, and 1.5% w/v)

On the other hand, the time for equilibrium swelling is inversely dependent on the GC-GMA content. The equibrium time was achieved in the order of SPHs with a higher content of GC-GMA. Since the capillary force that is a main mechanism for fast water absorption in SPHs is directly affected by the surface hydrophilicity, the surface hydrophilicity was identified by the contact angle measurements. The corresponding non-porous hydrogel films with the same chemical compositions were synthesized and their contact angles were compared to each other. The contact angle of the conventional SPH crosslinked with BIS (0.25% w/v) was 90.55°. The contact angles of hydrogels crosslinked with GC-GMA content of 0.25, 0.5, and 1.0 % (w/v) are 87.8°, 74.61° and 33.4°, respectively. The hydrogel with a higher content of GC-GMA showed a higher hydrophilicity, demonstrating a fast swelling to squilibrium even though it had a lower equilibrium swelling ratio due to higher crosslinking density. It may be why the SPHs from GC-GMA had a shorter equilibrium time than the SPH from BIS and the SPH with the smallest GC-GMA content exhibited the slowest swelling behavior as shown in Fig. 5.

4. Conclusions

Superporous hydrogels with fast swelling and superabsorbent properties were prepared using a gas blowing method synchronized with radical polymerization using vinyl group-containing glycol chitosan (GC-GMA) as a cross-linking agent. The homogeneous pore structure could be obtained from the optimum foaming time. The amount of GC-GMA was also an important factor to control the swelling properties of SPHs. The SPHs exhibited a faster swelling and comparable superabsorbent properties, compared to BIS-based conventional SPHs due to high surface hydrophilicity. Their functional properties and the use of biocompatible and mechanically resilient glycol chitosan would extend the potential applications of SPHs in various fields, including biomedical and other industrial applications.

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