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Synthesis of Polyglycidol Hydrogel Films Crosslinked with Carboxyl-terminated Poly(ethylene glycol)

Bong-Soo KIM,[1] Ji-Sun IM,[1] Seung-Tae BAEK,[1] Jang-Oo LEE,[1,†]
Maki SIGETA,[2] and Kohji YOSHINAGA[2]

[1]*Division of Chemical Engineering, Pusan National University, 30 Jangjeon-dong, Geumjeong-gu, Busan 609-735, Republic of Korea*
[2]*Department of Applied Chemistry, Kyushu Institute of Technology, 1-1 Sensui-cho, Tobata-ku, Kitakyushu 804-8550, Japan*

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ABSTRACT: With the attempt to largely increase the water content while keeping mechanical properties, hyperbranched polyglycidol (PGLD) hydrogel films were prepared using the oligomeric crosslinking agent, carboxyl-terminated poly(ethylene glycol) (PEG) of different molecular weights. Both the swelling and mechanical (tensile) properties of PGLD hydrogels crosslinked with PEG were measured and compared with the previous glutaric acid crosslinking system. The resultant PGLD films showed higher gel fraction and greater swelling capacity even at low PEG concentrations compared to those crosslinked with glutaric acid, probably due to the combined effect of the hydrophilicity and long chain effect of the PEG crosslinker. The values of the Young's modulus and tensile strength were also higher for crosslinked films from PEG than from glutaric acid at a given (lower) crosslinker concentration. In addition, both the swelling and tensile properties of the PGLD hydrogels were largely affected by the crosslinker concentration.
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The hyperbranched polyglycidol (PGLD) has attracted considerable interest in recent years because of their many advantages.[1–7] The main advantage of hyperbranched polymers is the ease of their essentially one-step synthesis. More importantly, they have a large number of terminal groups that may have some desirable chemical properties-either enhanced solubility in some solvent or some catalytic property, etc.[8] Especially, the hydrogels from PGLD consisting of glycerine derivatives may have a larger water content, and hence possess potential applications to biodegradability, food additives, or medicines.[2,3,9] Meanwhile the poly(vinyl alcohol) (PVA) has also been widely used in medicine and pharmacy in the form of hydrogels, but it can not give hyperbranched polymer gels due to the difficulty in synthesis.[10,11]

Among the synthesis methods to prepare hyperbranched PGLD, generally both the anionic[2–4] and cationic[5–7] polymerizations lead to well-defined hyperbranched polymers with a large number of branching points and end groups. In a previous study, PGLD hydrogel films with linear and hyperbranched structures were prepared *via* crosslinking reaction with glutaraldehyde and various dicarboxylic acids, and their swelling behavior and mechanical properties (especially, Young's modulus) were investigated as a function of the concentration of the crosslinking agent.[12]

In the present study, another attempt to prepare hydrogel films of hyperbranched PGLD has been made using the oligomeric crosslinking agent, carboxyl-terminated poly(ethylene glycol) (PEG), with the view of largely increasing the water content while maintaining mechanical properties of the films at low crosslinker concentrations. Hence, the equilibrium degree of swelling and mechanical (tensile) properties of hyperbranched PGLD hydrogel films crosslinked with PEG of different molecular weights were measured and compared with the previous glutaric acid crosslinking system.

EXPERIMENTAL

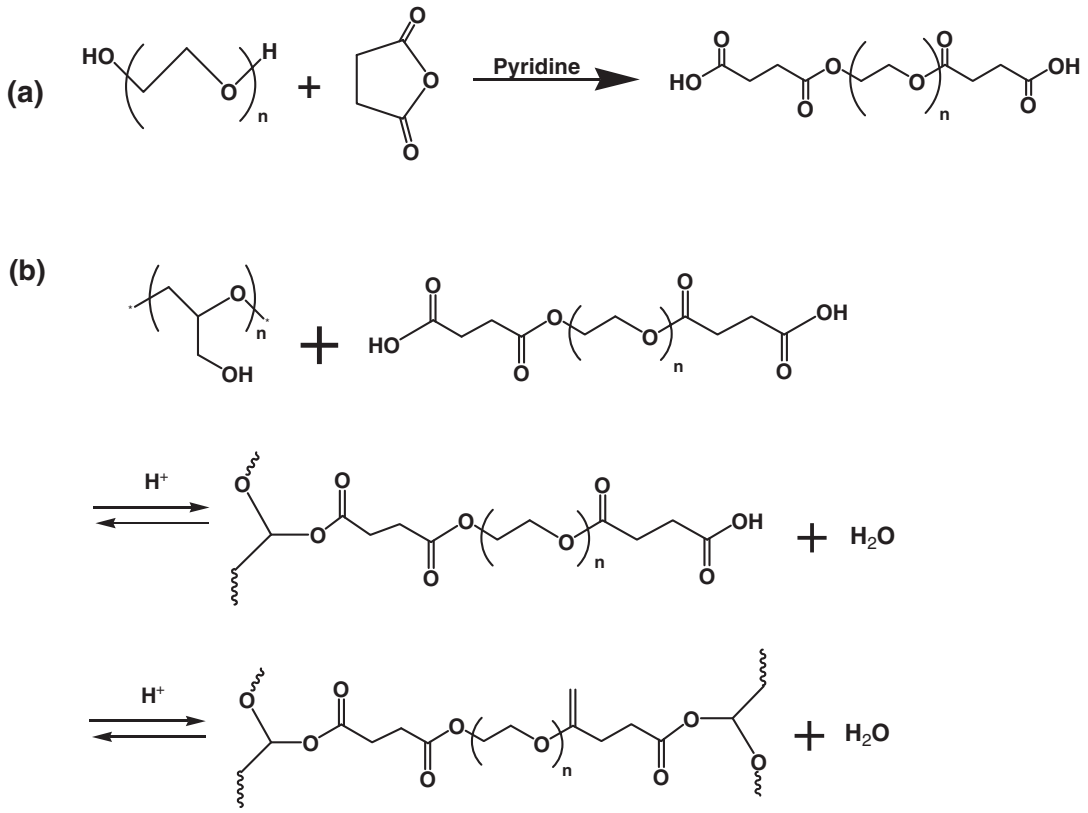
Materials

Glycidol (Wako Pure Chemicals Industries Ltd.) was distilled under reduced pressure prior to use. Diglycerin was supplied from Kashima Chem., Japan. The PEG's with molecular weights of 200, 400, 1000, and 2000 (Wako) were used as the crosslinking agents. Succinic anhydride, sodium, *p*-toluenesulfonic acid, pyridine, and benzene were purchased from Wako Pure Chemicals Industries Ltd.

Synthesis of Hyperbranched PGLD

Hyperbranched PGLD was synthesized by direct anionic ring-opening polymerization of unprotected glycidol according to the following procedure.[12]

[†]To whom correspondence should be addressed (Tel: +82-51-510-2404, Fax: +82-51-513-7720, E-mail: leejo@pusan.ac.kr).



Scheme 1. Mechanisms of (a) synthesis of crosslinking agent and (b) crosslinking of hyperbranched PGLD.

A two-necked flask was charged under nitrogen with sodium and distilled ethanol was cautiously added. The reaction mixture was stirred at ambient temperature until sodium completely reacted. A solution of diglycerin in distilled ethanol was added, and then heated at 120 °C under reduced pressure. After removing ethanol, the initiator was obtained.

A typical polymerization procedure was as follows. In a two-necked flask, the initiator was taken under argon atmosphere and heated up to 120 °C. Glycidol was added at a rate of 1 mL/min with stirring and the polymerization was initiated. After the completion of polymerization, unreacted glycidol was removed after stirring for 30 min at 120 °C under reduced pressure and hyperbranched PGLD was finally obtained as viscous syrup. The dried product was analyzed using the (solid-state) ^{13}C CP/MAS NMR spectroscope.

Synthesis of Crosslinking Agent (Carboxyl-Terminated PEG)

We can introduce carboxyl group in the end groups of PEG based on the mechanism sketched in Scheme 1(a). The PEG and benzene were placed in a two-necked flask and azeotropically distilled at 90 °C. Then succinic anhydride, pyridine (as catalyst), and 1,2-dichloroethane was added under nitrogen charge and stirred for 12 h at 75 °C. 1,2-Dichloroethane and benzene were removed by evaporation. The products were analyzed using ^{1}H and ^{13}C NMR spectroscopes.

Crosslinking of Hyperbranched PGLD and Preparation of PGLD Hydrogel Film

The PGLD hydrogel films were prepared by crosslinking with carboxyl-terminated PEG *via* the mechanism as sketched in Scheme 1(b). To an aqueous solution in which crosslinking agent and PGLD were dissolved, *p*-TsOH was added as an acid catalyst. The above solution was cast on polyethylene substrate and covered with Teflon sheet. The solution was then heated at 70 °C until water completely vaporized, resulting in the PGLD hydrogel film. The catalyst remaining in hydrogel films was removed by immersing in water and ethanol.

Measurements

^{1}H and ^{13}C NMR spectra were obtained at 400 MHz on a Bruker DPX-400 using D_2O as solvent. Molecular weight (M_w) of PGLD prepared was estimated by gel permeation chromatography (GPC), based on the calibration with polyethylene glycol standard. The water was used as the mobile phase at a flow rate of 0.5 mL/min. The gel fraction (as a measure of the degree of gelation) of PGLD hydrogel film was determined by extraction with distilled water. The resultant PGLD hydrogel films obtained *via* crosslinking reac-

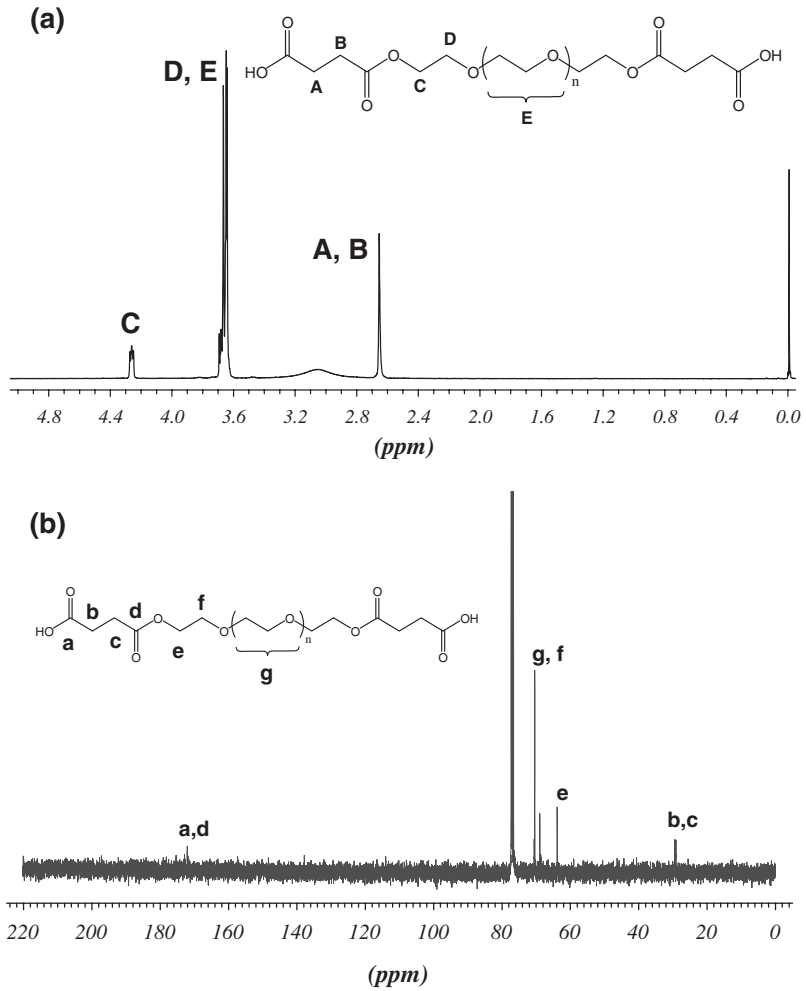


Figure 1. ^{1}H NMR (a) and ^{13}C NMR (b) spectra of carboxyl-terminated PEG as a crosslinking agent.

tion were weighed after drying. They were then immersed in distilled water and extracted. After subsequent drying, extracted samples were weighed. The gel fraction was calculated using the following relationship:

$$\text{Gel fraction } (\%) = \frac{W}{W_0} \times 100,$$

where W_0 and W were the weights of dried sample before extraction and after extraction.[13,14] The water content of the PGLD hydrogel films after swelling was investigated as follows. The samples were immersed in distilled water. The sufficiently swollen films were weighed. After drying, the samples were re-weighed. The equilibrium degree of swelling was calculated according to the following equation:

$$\text{Equilibrium degree of swelling} = \frac{(W_s - W_d)}{W_d} \times 100,$$

where W_s and W_d denote the weights of dried and swollen PGLD hydrogel films, respectively. Mechanical (tensile) properties of the hydrogel films were measured using thermal mechanical analyzer (TMA) at an extension rate of 50 mm/min. Strip-shaped specimens with dimensions of 20 × 3.5 mm and thickness of around 1.2 mm were used for the tensile test at 30 °C. The (initial) Young's modulus, ultimate tensile strength, and elongation of break were measured in a static mode.

RESULTS AND DISCUSSION

The direct anionic ring-opening polymerization of unprotected glycidol yields highly branched polymers, confirmed by ^{13}C NMR spectroscope in our previous work.[12] The resultant PGLD was transparent and light yellow syrup. The number average molecular weight (M_n) of hyperbranched PGLD as determined by GPC was 6,800 and polydispersity (expressed as M_w/M_n) was 2.2. As stated before, we prepared hydrogel films of hyperbranched PGLD using carboxyl-terminated PEG as crosslinking agent instead of dicarboxylic acids.[12] Carboxyl-terminated PEG with the degree of end functionality over 95 mol % (as confirmed by ^{1}H NMR) was synthesized by reaction PEG with succinic anhydride in the presence of pyridine catalyst.

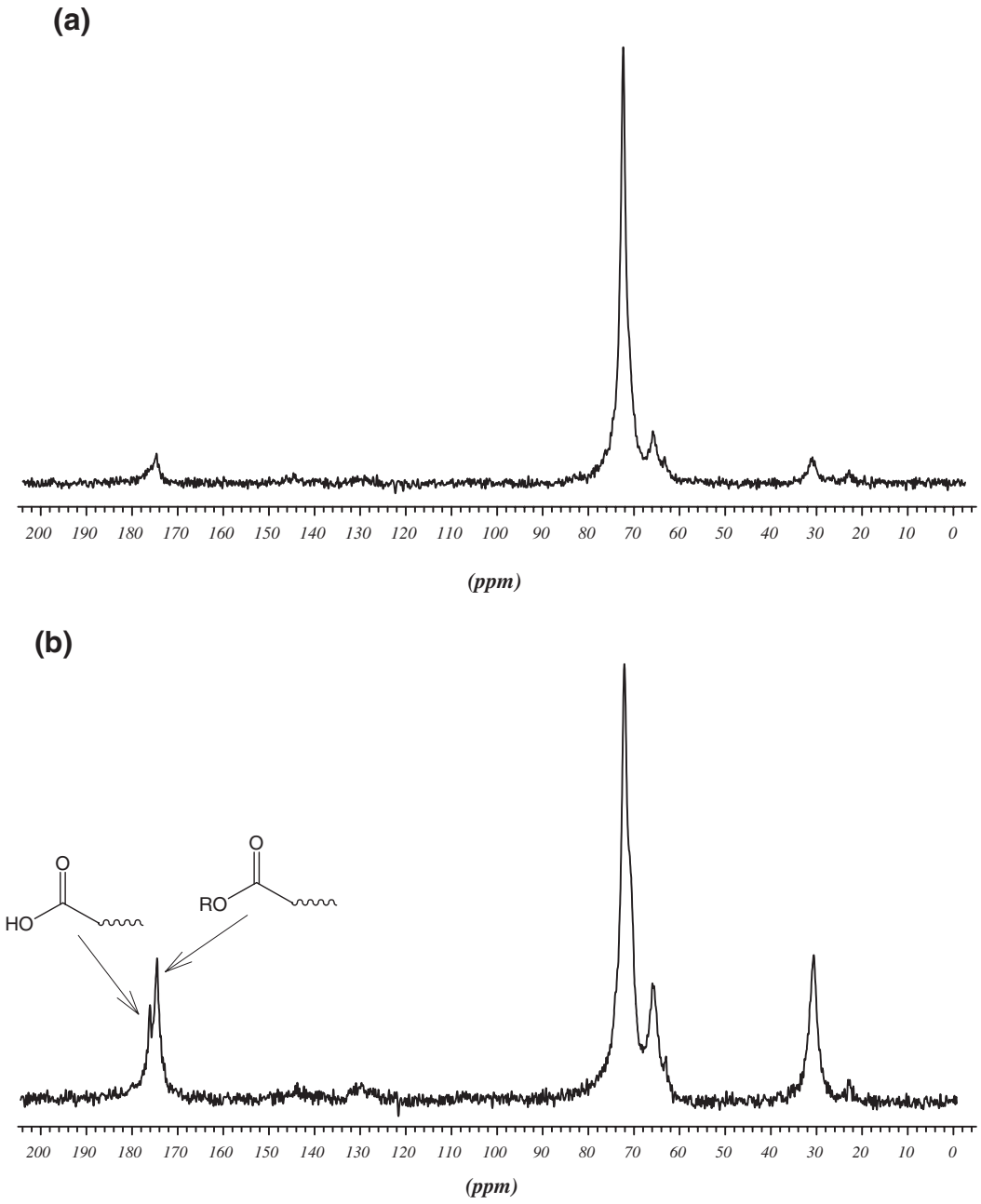


Figure 2. Solid-state ^{13}C NMR spectra of the PGLD hydrogel films crosslinked at two different PEG concentrations: (a) mole ratio [–COOH]/[–OH] = 0.25 and (b) mole ratio [–COOH]/[–OH] = 1.50.

The structure of the carboxyl-terminated PEG obtained has been confirmed from the ^{1}H and ^{13}C NMR spectra (Figure 1).

The crosslinking reaction took place through the reaction between the hydroxyl groups of hyperbranched PGLD and the carboxylic groups of carboxyl-terminated PEG, leading to formation of ester. When PEGs with (nominal) molecular weights of 200 and 400 (PEG 200 and PEG 400) were used as the crosslinking agent, the solid films of the PGLD hydrogels obtained were transparent and light yellow, and did not show any phase separation. When employing PEGs with MWs of 1000 and 2000, however, hydrogel films showed phase separation. Also, the phase separation was observed for PEG 400 with the concentration larger than 150 mol %, probably due to the low compatibility between PEG and PGLD arising from the amphiphilic character of PEG molecule. The samples which showed no phase separation were therefore chosen for the swelling behavior and mechanical properties studies.

The Figure 2 shows the solid-state ^{13}C NMR spectra giving the information on the chemical structures of PGLD hydrogel films crosslinked at two different mole ratios of crosslinker (carboxyl-terminated PEG) to PGLD: (a) [–COOH]/[–OH] = 0.25 and (b)

Table I. The gel fraction and equilibrium degree of swelling of PGLD hydrogel films

No.	Crosslinking agent	Mole ratio [–COOH]/[–OH]	Gel fraction (%)	Equilibrium degree of swelling (%)
1	PEG 200	0.075	90	543
2		0.15	96	300
3		0.25	94	180
4		0.45	98	111
5		0.75	98	71
6		1.50	95	45
7	PEG 400	0.075	91	545
8		0.15	97	319
9		0.25	91	200
10		0.45	99	139
11		0.75	99	136

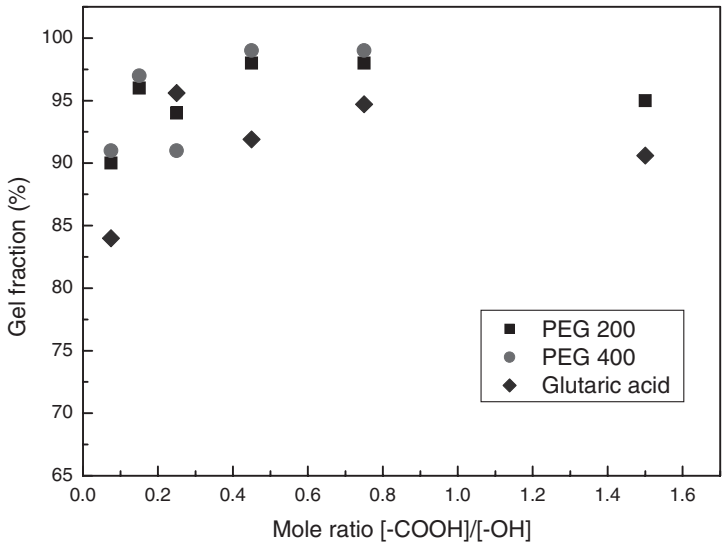


Figure 3. Effect of concentration of crosslinking agent on the gel fraction of PGLD hydrogel films crosslinked with PEG 200, PEG 400, and glutaric acid.

[–COOH]/[–OH] = 1.50. In this figure, the characteristic chemical shifts of carbon in hyperbranched PGLD appeared between 60 and 80 ppm, confirmed in our previous work.[12] It can also be seen from Figure 2 that the ester carbon of crosslinking site (–COO–) appeared at 174 ppm and the aldehyde carbon of uncrosslinked end groups of crosslinking agent appeared at 176 ppm with the corresponding intensities stronger in (b) than in (a), as expected. The methylene carbons of carboxyl-terminated PEG give peaks at 30 and 66 ppm, respectively.

Both gel fraction and equilibrium degree of swelling for PGLD hydrogels prepared at different crosslinker concentrations were measured to estimate the extent of crosslinking and the water content, respectively. Table I lists the values of the gel fraction and swelling behavior of PGLD hydrogel films crosslinked with carboxyl-terminated PEG of two chain lengths, *i.e.*, PEG 200 and PEG 400. In Figure 3, the values of gel fraction for PGLD hydrogels crosslinked with PEG 200 and PEG 400 are displayed as a function of the crosslinker concentration (expressed as the mole ratio [–COOH]/[–OH]) in comparison with the glutaric acid system. From Figure 3, we can see that the gel fraction increases initially with the increasing crosslinker concentration, and later becomes saturated at higher concentrations for all three crosslinker systems. Interestingly enough, PGLD hydrogel films crosslinked with carboxyl-terminated PEGs show a remarkably higher gel fraction even at low crosslinker concentrations compared to the glutaric acid crosslinking system, the tendency being more pronounced in the PEG 400 system. The reason for this could be qualitatively understood by considering the following fact. Carboxyl-terminated PEG can be extensively bridged between polymer chains (intermolecular crosslinking) as well as intramolecular crosslinking due to their long chain length leading to achieve the enhanced gel fraction whereas the crosslinking ability of glutaric acid with short chain length

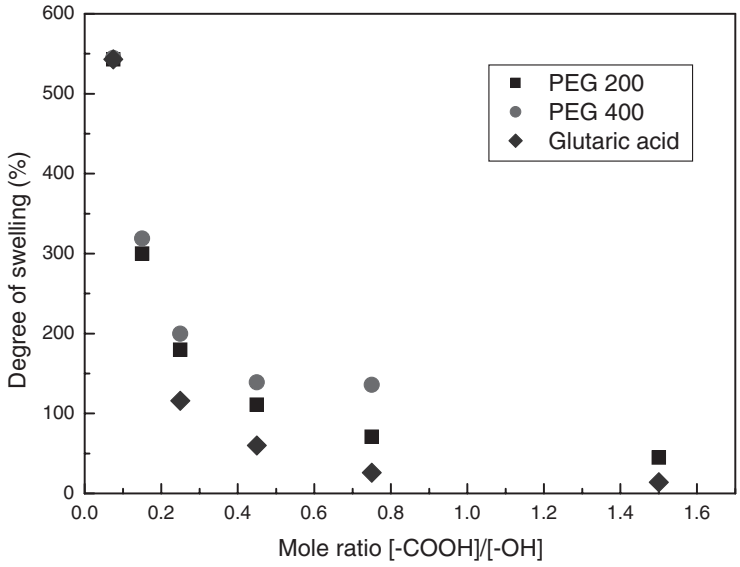


Figure 4. Effect of concentration of crosslinking agent on the degree of swelling of PGLD hydrogel films crosslinked with PEG 200, PEG 400, and glutaric acid.

Table II. The mechanical properties of PGLD hydrogel films

No.	Crosslinking agent	Mole ratio [–COOH]/[–OH]	Young's modulus (MPa)	Tensile strength (MPa)	Elongation at break (%)
1	PEG 200	0.075	0.85	0.096	95
2		0.15	1.00	0.159	16
3		0.25	1.32	0.220	36
4		0.45	3.54	0.215	36
5		0.75	2.07	0.139	6.5
6		1.50	1.92	0.199	22
7	PEG 400	0.075	2.46	0.212	37
8		0.15	2.54	0.149	11
9		0.25	1.30	0.126	40
10		0.45	3.43	0.169	7.2
11		0.75	1.89	0.143	17

is restricted within intramolecular crosslinking at low concentrations.

Swelling behavior of hydrogel films was investigated by the measurement of mass changes of the samples at static conditions. Figure 4 shows the values of the equilibrium degree of swelling for PGLD hydrogel films crosslinked with PEG 200 and PEG 400 measured at different crosslinker concentrations in comparison with the glutaric acid system. As expected, the degree of swelling of chemically crosslinked hydrogel films has been significantly decreased with the crosslinker concentration, irrespective of the kind of the crosslinking agent. That is, the crosslinking density generally increases with the increasing crosslinker concentration, thereby causing the difficulty of water molecules to diffuse into the polymer network. Moreover, hydrogel films prepared by crosslinking with carboxyl-terminated PEG exhibited greater swelling behavior at a given (lower) crosslinker concentration than those by glutaric acid, the tendency also being more pronounced in PEG 400. This could also be explained as follows. The PEG will provide more sufficient space for the solvent penetration into the polymer network due to the longer chain length between crosslinks, contrary to the glutaric acid. In addition, the increase of hydrophilicity between PEG chain and water molecules may contribute to the increase of degree of swelling for hydrogel films.

The mechanical (tensile) properties (Young's modulus, tensile strength, and elongation at break) of PGLD hydrogel films prepared at different crosslinker concentrations for the PEG 200 and PEG 400 systems are listed in Table II. From this table, we can see that both Young's modulus and tensile strength of PGLD hydrogel films tend to initially increase whereas the elongation at break decreases initially with the in-

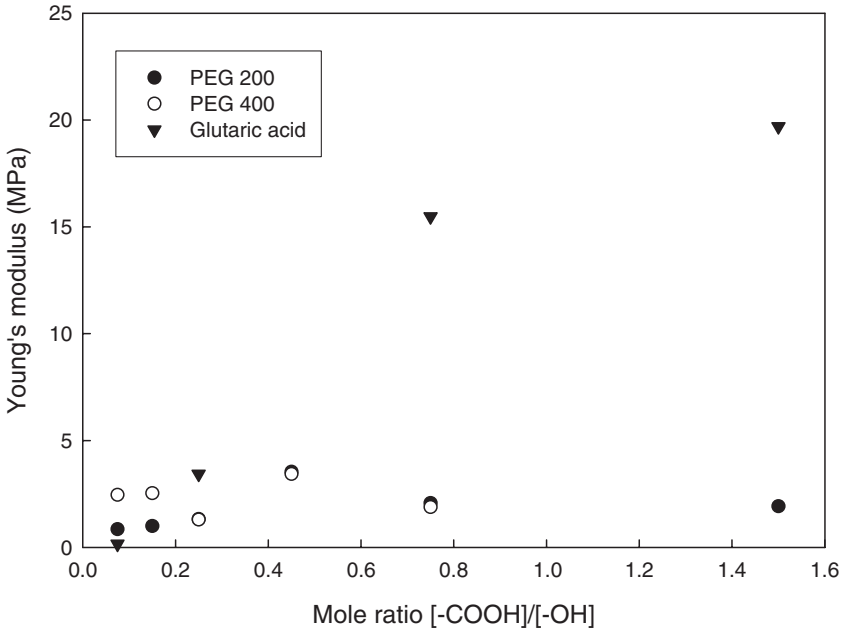


Figure 5. The Young's modulus of PGLD hydrogel films as a function of concentration of crosslinking agent for PEG 200, PEG 400, and glutaric acid crosslinking systems.

creasing crosslinker concentration for both systems. The values of the mechanical properties observed may indicate that a significant stiffening of the PGLD hydrogel films was obtained even at low concentrations of carboxyl-terminated PEG probably due to the enhanced chemical crosslinking, as inferred from the gel fraction result.

Figure 5 shows the effect of concentration of crosslinking agent on the (initial) Young's modulus of PGLD hydrogel films for PEG 200, PEG 400, and glutaric acid crosslinking agent systems. Examination of Figure 5 reveals that PGLD hydrogel films crosslinked with carboxyl-terminated PEG posess higher tensile strength and Young's modulus than those crosslinked with glutaric acid at low crosslinker concentrations. This is probably because the carboxyl-terminated PEG as a crosslinking agent will provide the hydrogel film with the increased elasticity resulting from a higher gel fraction compared to the glutaric acid. On the other hand, as the concentration of crosslinking agent increased, the PGLD hydrogel films crosslinked with carboxyl-terminated PEG exhibited much lower Young's modulus, which may be attributable to the increase of molecular weight between crosslinks due to the long chain effect of PEG involved.

CONCLUSIONS

The hyperbranched PGLD was chemically crosslinked with the oligomeric crosslinker, carboxyl-terminated PEG in an aqueous solution state. The resultant PGLD hydrogel films exhibited higher gel fraction and greater swelling behavior even at low concentrations of carboxyl-terminated PEG when compared to those crosslinked with glutaric acid. This may be due to the combined effect of the hydrophilic character and the long chain effect of PEG, which gives rise to extensive intermolecular (as well as intramolecular) crosslinking and thus provides a sufficient space for the solvent penetration into polymer network. The tensile strength and Young's modulus of PGLD hydrogels increased (initially) with the crosslinker concentration for all the crosslinker systems probably because of the chain stiffening effect. In addition, the crosslinked PGLD films from PEG exhibited the enhanced mechanical properties compared to those from glutaric acid at a given (lower) crosslinker concentration.

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