UV 경화형 키토산/지방족 폴리에스터 Hydrogel IPN 제조 및 약물투과

조성민, 김소연, 이영무, 성용길*, 조종수**
한양대학교 공과대학 공업화학과, *동국대학교 이과대학 화학과,
**서울대학교 농업생명과학대학 천연섬유학과

Synthesis, Properties and Permeation of Solutes through Hydrogels based on Poly(ethylene glycol)-co-Poly(lactones) diacrylate Macromers and Chitosan

S. M. Cho, S. Y. Kim, Y. M. Lee, Y. K. Sung* and C. S. Cho**
School of Chemical Engineering, College of Engineering, Hanyang University
*Department of Chemistry, Dongguk University, **Department of Natural Fiber Science,
College of Agriculture and Life Science, Seoul National University

ABSTRACT

Triblock copolymers from poly(ethylene glycol) (PEG) and D,L-lactide or ε-carprolactone were synthesized to prepare semi-interpenetrating polymer network (semi-IPN) with chitosan by U.V. irradiation method. Then, solute permeation through these semi-IPNs hydrogels were investigated. The structures of semi-IPNs were confirmed by FT-IR spectroscopy and wide angle X-ray diffractometer (WAXD). Equilibrium water content (EWC) of these hydrogels was in the range of 67-75%. The crystallinity, thermal properties and mechanical properties of semi-IPNs hydrogels were studied. All the hydrogels revealed a remarkable decrease in crystallinity as compared with PEG macromer itself. The tensile strengths of semi-IPNs hydrogels in dry state were rather high, but those of hydrogels in wet state decreased drastically. The permeabilities of solutes of hydrogels followed the swelling behaviors and were regulated by solute size.

INTRODUCTION

The class of biodegradable polymers is the most successful, important and commercially used biomaterial in orthopedic surgery, drug control/release devices, coating materials for suture, vascular grafts and surgical meshes to facilitate wound healing after dental extraction. As to the particular area of tailored ether-ester block copolymers based on various lactones and poly(ethylene glycol) (PEG), many studies have been reported concerning their synthesis and characterization. Such types of triblock copolymers have been synthesized in bulk by a ring opening polymerization mechanism without any added catalysts in order not to leave any toxic residues like organometallic catalysts in the final product. These polymers are hydroxy terminated and can be used to prepare acrylates as end groups that undergo very rapid photopolymerization.

Chitin, chitosan and their derivatives have become useful polysaccharides in biomedical area because of its biocompatible, biodegradable and non-toxic properties. In our previous articles, we reported on the preparation of semi-IPNs hydrogels based on chitin and poly(ethylene glycol) macromer (PEGM) or PEG-co-poly(lactones) diacrylate macromers. The incoporation of chitin improved the mechanical properties of the swollen networks and preserved their biocompatibility. However, chitin has a problem on solubility because there are only a few strong acidic solvents to prepare solution such as formic acid which may irritate human tissues. However, chitosan, the deacetylated product of chitin, is dissolved in water by adding a small amount of acetic acid, so that the hydrogel can be prepared under milder conditions. Therefore, it might be expected that chitosan would be a strong candidate for hydrogel preparation in biomedical application. Moreover they are degraded by lysozyme. Aliphatic polyether can also be degraded by hydrolysis in the human body. Therefore, semi-

IPNs hydrogel composed of chitosan and polyether for a drug carrier has been investigated and developed. The semi-IPN is superior to chitosan hydrogel in reversible responsibility of swelling and deswelling in acid and alkali, respectively, and in flexibility of the semi-IPNs hydrogel.

In this study, we deal with the synthesis, characterization, and swelling behavior of semi-IPNs hydrogels. The solute permeation through swollen hydrogels was investigated as well.

EXPERIMENTAL METHODS

Synthesis of semi-IPNs

0.45g chitosan was dissolved in 28.6ml of 0.33N acetic acid and mixed with PEG-co-poly(lactones)diacrylate macromers with different compositions. Then, (4-cenzoylbenzyl) trimethylammonium chloride (0.05M of PEGCM (or PEGLM) was added with agitation. The mixture was poured into petri dishes and exposed to a 450W ultraviolet (UV) lamp (Ace Glass Co.) placed above the mould at a height of 20cm for 30min with nitrogen gas blowing until gelation occurred. The samples were then dried completely under vacuum for 2 days.

Characterization

The changes in chemical structure of block copolymers, PEGCM or PEGLM, and semi-IPNs were investigated by FT-IR (Nicolet Model Magna IR 550 spectrometer). X-ray diffraction patterns were performed on a Rigaku Denki RAD-C X-ray diffractometer. To measure the equilibrium water content (EWC), preweighed dry samples were immersed in distilled water. After excessive surface water was removed with filter paper, the weight of swollen samples was measured. The procedure was repeated until there was no further weight increase. EWC was determined according to the following equation,

$$EWC(\%) = [(W_S - W_d)/W_S] \times 100 \quad (1)$$

where W_S and W_d represent the weight of swollen and dry samples, respectively. Differential scanning calorimetry (DSC, Perkin-Elmer DSC-7 instrument) were employed to investigate the crystallinty, melting endotherm of dry hydrogels and water state in the swollen hydrogels with different water content. Mechanical properties of semi-IPNs hydrogels were measured on a universal testing machine (UTM, Hounsfield 10KM) with a crosshead speed of 2mmmin^{-1} under 50kg load cell.

Partition of solutes and permeation studies

Solute permeation experiments were performed using three representative solutes with different molecular weights and hydrodynamic sizes. We used the theophylline (UV absorbance λ_{max}= 274nm), vitamin B_{12} (UV absorbance λ_{max}= 361nm) and bovine serum albumin (UV absorbance λ_{max}= 280nm) as nonionic solutes.

CONCLUSIONS

Semi-IPNs hydrogels composed of PEGCM (or PEGLM) and chitosan were prepared by U.V. irradiation method and the solute permeation through these hydrogel membranes were investigatied. FTIR specrtroscopy and WAXD patterns confirmed the structure of semi-IPNs . All hydrogels exhibited a high EWC in the range 67%-75%. The hydrogels show higher EWC with less degree of crosslinking and more chitosan content. Mechanical strength of semi-IPNs hydrogels depended upon the crosslinking degree of network and chitosan content. The permeation of solutes increased according to higher swelling in semi-IPNs hydrogel. Smaller solutes and higher swelling of IPN hydrogel produced a higher diffusion coefficient. Changing the molecular composition in semi-IPNs could selectively control the permeated amount of solute.

REFERENCES

1. Y. M. Lee and S. S. Kim and S.H. Kim, *J. Mater. Sci., Materials in Medicine*, **8**, 537 (1997)
2. S. S. Kim, Y. M. Lee and C. S. Cho, *J. Polym. Sci., Polym. Chem.*, **33**, 2285 (1995)
3. Y. M. Lee and S. S. Kim, *Polymer*, **38**, 2415 (1997)
4. H. S. Shin, S.Y. Kim, Y. M. Lee, K. H. Lee, S. J. Kim and C. E. Rogers, *J. Appl. Polym. Sci.*, **69**, 479 (1998)
5. F. G. Pearson, R. H. Marchessault and C. Y. Liang, *J. Polym. Sci.*, **43**, 101 (1960)