Preparation of biodegradable porous hydrogels cross-linked with polyphosphates

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Introduction

Hydrogels are a class of biomaterials the have shown great promise as a scaffold for tissue engineering. A hydrogel scaffold must initially be strong to survive the in vivo environment and protect encapsulated cells and nascent tissue while eventually degrading to increase pore size and allow and allow for full functional tissue formation. Polyphosphate class of biodegradable polymer systems based on their structural versatility and attractive physiological-chemical properties. The polyphosphates are a component of numerous biomaterials used for drug delivery and tissue engineering[1].

A polymer containing 2-methacryloyloxyethyl phospho rylcholine (MPC) units is an interesting synthetic polymer since the phosphorylcholine group in the side chain, which is one of the representative natural phospho lipids polar groups. As is known well, MPC polymers have excellent biocompatibility and blood compatibility due to the suppression of undesirable protein adsorption on the surface. In this study, novel phosphorylcholine hydrogel cross-linked methacryloyl-functionalized poly phosphates (PCPG) were synthesized as biocompatible and biodegradable tissue engineering scaffolds. Resulting physical properties and cytocompability was studied.

Experimental section

Poly(2-i-propyl-2-oxo-1,3,2dioxaphosphospholane-co-2(2-oxo-1,3,2-dioxaphosphoroyloxyethyl methacrylate) (IPP-co-OPEMA)) (PIOP) was synthesized by the method previously described[2].

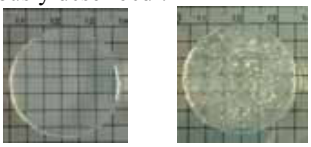
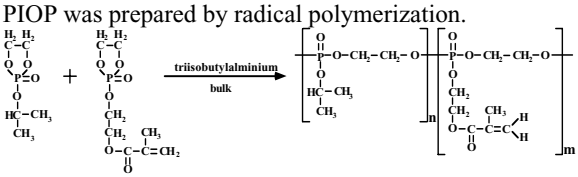


Figure 1. Morphology of hydrogel (G1) and porous hydrogel (G1A) were stored after 24 h in the water

PIOP (0.5 mol%), MPC (99.5 mol%), and 2,2-azobisisobutyronitrile (AIBN) (0.5 mol%) were dis solved in ethanol to synthesized PCPG hydrogels (G1) by radical polymerization. Porous hydrogels (G1A) were prepared by gas forming process using a combination of potassium hydrogen carbonate as an effervescent salt and citric acid to control porosity was shown in Figure 1. The physical properties was examined by oscillational mechanical analysis. The morphology of the dehydrated hydrogels was observed using a scanning electron microscope (SEM). Enzymatic degradation of hydrogel was incubated in non-and alkaline phosphatase (ALP) at concentration 72.5, 220 U/L in aqueous solution at 37°C. Mouse preosteoblastic cells (MC-3T3-E1) were cultured in hydrogels. Cell proliferation and viability test viable as qualitatively preformed by WST-1 cell viability assay and "Live/Dead" cell staining assay, respectively.

Results and Discussion

PIOP was synthesized by ring-opening polymerization of IPP with OPEMA. (scheme 1) The number averaged molecular weight of the PIOP was 10.9 KDa, and the number of OPEMA units in one PIOP molecule was 2.02. MPC cross-linked with the PIOP was prepared by radical polymerization.



Scheme 1. Synthetic route of PIOP

The porosities of porous PCPG were 94-98%. The elastic modulus and viscosity of the PCPG increased with cross-linking density. The morphology of the highly porous dehydrated hydrogels was fabricated using gas forming technique. This fabrication process enabled the homogeneous expansion of pores within the polymer matrices, leading to well-interconnected macroporous hydrogels and pore surface was denser with higher cross-linked PIOP. Enzymatic degradation of PCPG hydrogels were evaluated in ALP aqueous solutions. The dissolution time of non-and porous PCPG hydrogels were not different. The degree of degradation was dependent on the, the concentration of ALP was shown in Figure 2.

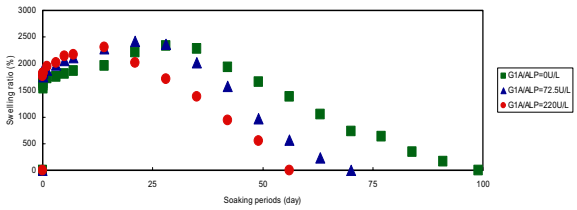


Figure 2. Enzymatic degradation of PCPG hydrogels

The PCPG hydrogels cross-linked with 0.5 % PIOP (G1) completely degraded in 60 days at concentration 220 U/L of ALP. In PCPG hydrogels, MC-3T3-E1 cells remain alive and their shape was relatively spherical. Cell proliferation in hydrogels was induced with an increase in the PIOP composition. PCPG porous hydrogels cross-linked with 2.5% PIOP, MC-3T3-E1 cells could be highly proliferated.

Reference

1) X.Y. Xu et al., *Biomaterials* 2002:23;3765.
2) Iwasaki Y et al. *Biomacromolecules* 2004:5;1110.