Photopolymerizable Elastomers for Tissue Engineering Application Based on Poly(ethylene glycol) and Diacid Monomers

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Introduction

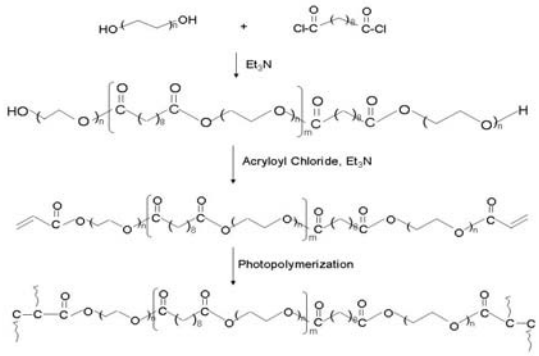
Poly (ethylene glycol, PEG) based macromers have been widely used in tissue engineering applications as hydrogel type biomaterials, mainly due to their well known hydrophilicity and biocompatibility [1,2]. In addition, PEG based biodegradable hydrogels have been reported [3]. Since then, PEG based materials have been even more attractive candidates for tissue engineering scaffolds and/or drug delivery systems [4,5]. However, the principle limitation to more extensive use of PEG hydrogels is their lack of mechanical strength [2]. Up to date, few non-hydrogel type biomaterials based on PEG have been investgated. The purpose of this study is to synthesize strong non-hydrogel type macromers based on PEG. We developed a new family of photopolymerizable macromers based on PEG and a variety of diacid monomers such as sebacic acid (aliphatic) and/or terephthalic acid (aromatic). These novel biomaterials have different properties from existing PEG based hydrogels, and can be useful for drug delivery vehicles and/or tissue engineering scaffolds.

Materials and Methods

Photopolymerizable PEG based macromers were synthesized by the reaction represented in Scheme 1. Briefly, fifty grams of PEG (m.w. : 200, 0.25 mol) was dissolved in 500 mL of anhydrous methylene chloride. Triethylamine was added and sebacic acid (0.225 mol) was subsequently added to the solution in an ice bath with vigorous stirring. The reaction mixture was stirred for 48 hr at room temperature, filtered, precipitated in petroleum ether and dried under vacuum. A total of thirty grams of the above described macromer was dissolved in methylene chloride, and other photopolymerizable macromers were synthesized by previously published methods [3]. The final elastomeric macromers were analyzed by gel permeation chromatography (GPC), FTIR-ATR, ^{1}H NMR and DSC. The PEG based elastomers were produced by photopolymerization. The disk shaped elastomers were immersed in PBS for 24 hr at 37 °C. After the swollen weight was measured, the samples were dried in vacuum for 24 hr and weighed. The swelling ratio was then calculated. The cytotoxicity of elastomers was evaluated up to 7 days by MTS assay using bone marrow stromal cells (BMSC) with a cell density of 20k cells/cm^2.

Results and Discussion

It is expected that PEG based materials are hydrophilic. Simple reaction between PEG and diacid monomers produces novel PEG based macromers, whose structures were deduced by analysis of their NMR and FT-IR spectra. The number-average molecular weight (Mn) of these macromers measured by GPC was between 3,000 – 6,000. DSC measurement shows that there is no glass transition temperature above 0 °C, indicating that these polymers are totally amorphous at 37 °C.



Scheme 1. Synthesis reaction for PEG-co-sebacic acid diacrylates and photopolymerization

Before crosslinking, these polymers are viscous liquids at room temperature. They are insoluble in water but soluble in most common solvents such as acetone and methylene dichloride. The swelling ratio of these prepolymers after soaking in PBS for 24 hr is 0.1-0.2. After photopolymerization, these polymers have elastomer-like behavior, similar to silicone rubber. The cytotoxicity test shows that these polymers are non cytotoxic, and they performed similarly to tissue culture polystyrene.

Conclusions

We developed a new family of photopolymerizable macromers based on PEG and diacid monomers. Their synthesis and post synthesis processing are straightforward. In addition, these materials can take advantage of such photopolymerization properties as spatial and temporal control of polymerization. It is also possible to fabricate these polymers as a three dimensional structures using solid free form (SFF) techniques. Preliminary results show that these polymers are non-toxic and have elastomeric properties. Therefore these novel biomaterials are expected to be useful for drug delivery systems and tissue engineering applications.

References

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