A Non Free Radical, Single Step Synthesis Method for Poly(β-amino Ester) Hydrogels

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Statement of Purpose: Biodegradable polymers are gaining more attention due to their versatility in drug delivery applications. In recent years, poly(β-amino ester) (PBAE) have emerged as an exciting class of biodegradable polymers for drug delivery and tissue engineering [1]. PBAEs can be synthesized in a single step polymerization method by the reaction of amine monomers to diacrylates, without any byproducts. In prior studies, a wide range of poly(β-amino ester)s were synthesized by altering the chemical composition and diacrylate to amine molar ratio [2]. In prior studies, poly(β amino ester) hydrogel synthesis required free radical polymerizations to form the gel network, and this can result in the degradation of loaded agents, etc. In addition, some polymer functionalities (e.g., polyphenolic compounds) can react with free radicals and thus inhibit the polymerization process. In this work, we developed a simple method for poly(β-amino ester) hydrogel synthesis by a single step Michael addition reaction between diacrylates and primary diamines. We synthesized and studied the swelling and degradation properties of different types of poly(β amino ester) hydrogels, by varying the molar ratios of diacrylate to diamines. Further, different types of poly(antioxidant β amino ester) hydrogels were also synthesized and characterized through the reaction of antioxidant di/multiacrylate with primary/secondary diamine.

Methods: All hydrogel syntheses were carried out by the reaction of di/multiacrylate and primary diamine by a single step Michael addition reaction, at 50°C. The reaction kinetics of the polymerization were studied with the help of an ATR-FTIR setup (Varian 7000e FTIR spectrometer). The swelling properties of the hydrogels were investigated in different solvents at room temperature. The degradation properties of the hydrogels were observed in PBS (pH 7.4) at 37°C. Poly(ethylene glycol) diacrylate (PEG400DA) and diethylene glycol diacrylate (DEGDA) were purchased from Polyscience, Inc. Polyphenolic antioxidants quercetin and curcumin, acryloyl chloride, and three primary diamines (4,7,10-Trioxa-1,13-tridecane diamine, TTD; 2, 2' (ethylenedioxy) bis ethylamine, EDBE; and hexamethyldiamine, HMD) were obtained from Sigma Aldrich. For antioxidant systems, phenolic antioxidants were first functionalized with acrylate groups by reacting antioxidants with acryoyl chloride in presence of triethylamine. The PBAE hydrogels were synthesized by single step polymerization between thedi/multiacrylate and diamine at 50°C.

Results: The antioxidants were successfully functionalized with acrylate groups and characterized by FTIR and NMR spectroscopy. PBAE hydrogels with varying molar ratios of reactive diacrylate to diamine groups were also synthesized, and their swelling and degradation properties investigated. The swelling ability of the hydrogels depended on the hydrophilicity of the diacrylate and diamine (Figure 1). The degradation rate of PBAE hydrogel depends on the nature of the diacrylate, diamine, and their initial molar ratio during gel formation. Also, the degradation rate of poly(antioxidant β amino ester) hydrogel was found to be a function of initial antioxidant content (Figure 2).

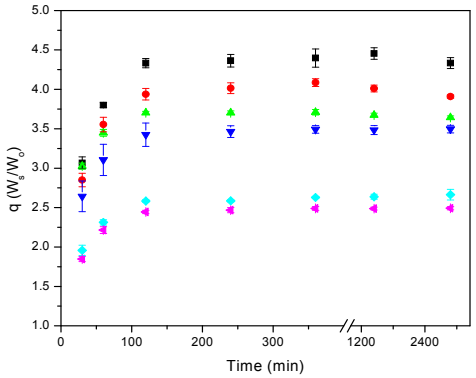

Figure 1 Swelling characteristics of 1.2:1 molar ratio of PBAE hydrogels in THF.

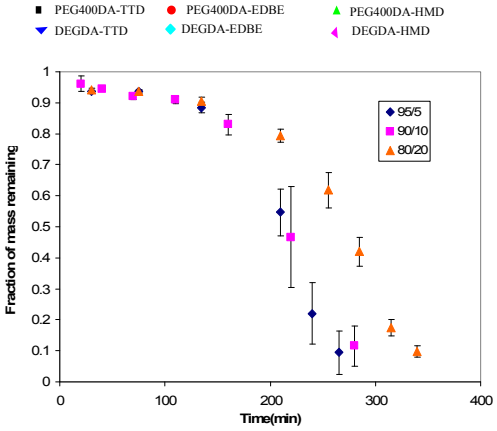

Figure2. Degradation profiles of poly(antioxidant β amino ester) hydrogels with different molar ratio of PEG400DA and curcumin diacrylate.

Conclusions: Poly(β-amino ester) hydrogels were successfully synthesized by single step polymerization method. The rates of degradation of the hydrogels are tunable by using appropriate diacrylate, diamine, and their initial molar ratio. Similarly, poly(antioxidant β-amino ester) hydrogel degradation rate depends on the initial antioxidant content as well as the hydrophilicity of the monomers. This novel single step synthesis will facilitate the formation of various poly(β-amino ester) hydrogel systems and their application for a variety of biomedical, pharmaceutical, and tissue engineering applications.

References:

[1] Burdick JA et al., J Biomed Mater Res A. 2008; 85A:731-741.
[2] Anderson DG et al., Adv Mater. 2006;18:2614-2618