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Synthesis of a proline-modified acrylic acid copolymer in supercritical CO_2 for glass-ionomer dental cement applications

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Abstract

Supercritical (sc-) fluids (such as sc-CO_2) represent interesting media for the synthesis of polymers in dental and biomedical applications. Sc-CO_2 has several advantages for polymerization reactions in comparison to conventional organic solvents. It has several advantages in comparison to conventional polymerization solvents, such as enhanced kinetics, being less harmful to the environment and simplified solvent removal process. In our previous work, we synthesized poly(acrylic acid-co-itaconic acid-co-N-vinylpyrrolidone) (PAA-IA-NVP) terpolymers in a supercritical CO_2/methanol mixture for applications in glass-ionomer dental cements. In this study, proline-containing acrylic acid copolymers were synthesized, in a supercritical CO_2 mixture or in water. Subsequently, the synthesized polymers were used in commercially available glass-ionomer cement formulations (Fuji IX commercial GIC). Mechanical strength (compressive strength (CS), diametral tensile strength (DTS) and biaxial flexural strength (BFS)) and handling properties (working and setting time) of the resulting modified cements were evaluated. It was found that the polymerization reaction in an sc-CO_2/methanol mixture was significantly faster than the corresponding polymerization reaction in water and the purification procedures were simpler for the former. Furthermore, glass-ionomer cement samples made from the terpolymer prepared in sc-CO_2/methanol exhibited higher CS and DTS and comparable BFS compared to the same polymer synthesized in water. The working properties of glass-ionomer formulations made in sc-CO_2/methanol were comparable and better than the values of those for polymers synthesized in water.

Keywords: Glass-ionomer cements; Proline-amide-modified polyacids; Free radical polymerization; Supercritical CO_2; Mechanical properties

1. Introduction

The high toxicity of some organic solvents in food processing, drug formulation and biomedical materials processing has created interest in developing new and clean routes for processing [1]. Supercritical (sc-) fluids such as sc-CO_2 and sc-water have been particularly of interest [2]. In the supercritical state, the physical properties of the fluids, such as density and viscosity, can simultaneously become between those of a gas and liquid phase [2]. Unlike that of liquid solvents, the density of supercritical fluids (SCFs) can be changed by altering the pressure and temperature of the fluid, and therefore the dissolution power can be changed. SCFs can have gas-like diffusivities, which have important implications for reaction kinetics, while having liquid-like densities, which allow the solubilization for many compounds [1–4].

Sc-CO_2 has been applied as a promising alternative to conventional organic solvents due to its relatively low critical temperature and pressure ($T_c = 31.1$ °C and $P_c = 7.2$ MPa), and its non-toxicity and inflammability [1–5]. Sc-CO_2 is an excellent non-polar solvent for many organic compounds. It has solvent power similar to a light hydro-

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carbon for dissolving most solutes; however, very polar molecules, such as amino acids, sugars and most inorganic salts, are usually miscible [4,5]. Interestingly, fluorinated or polysiloxane compounds are often more soluble in sc-CO_2 than in hydrocarbons; this increased solubility is important for polymerization reactions (such as biopolymers or scaffolds for tissue engineering). Organic compounds such as alkenes, alkanes, aromatics, ketones and alcohols up to ca. 400 amu are usually miscible in sc-CO_2; however, higher-molecular-weight polymers are generally not. Consequently, polar co-solvents or other agents are often added in order to overcome this problem [1–7].

It has been found that a processing route using a modified supercritical fluid can successfully be employed for the synthesis of novel polyelectrolytes (polymers) in glass-ionomer dental cement formulations. Such a route results in enhanced reaction kinetics of polymerization of the N-vinylpyrrolidone-containing polyacid [8]. Huang et al. [9] synthesized acrylic acid (AA)–itaconic acid (IA) copolymers in sc-CO_2/methanol mixtures and used them in formulations of glass-ionomer dental cements. Samples prepared in an sc-CO_2 mixture had higher compressive and flexural strength compared to samples prepared in water or a Fuji II (commercial cement) glass-ionomer control group, respectively. They also reported that the working properties of the cements made with polymers in sc-CO_2 mixtures were generally amongst the best observed [9]. By using sc-CO_2 it is possible to overcome some of the disadvantages of traditional polymerization reactions, such as long reaction times, low conversion rates and the need for time- and energy-consuming purification and separation procedures [9].

In our previous work, we synthesized poly(acrylic acid-co-itaconic acid-co-N-vinylpyrrolidone) (PAA-IA-NVP) terpolymers in an sc-CO_2 mixture for glass-ionomer dental cements [8]. We observed that the mechanical and working properties (working and setting time) of glass-ionomer cements formulated from polymers made in sc-CO_2 mixtures were comparable and higher than for polymers prepared in water [8]. In addition, it has been hypothesized that having an amino acid with chemical structure similar to N-vinylpyrrolidone (which acts as a spacer group in the chemical structure of the glass-ionomer polyacid) would be advantageous [25]. Additionally, with the presence of more carboxylic acid and amide groups, there might be a greater probability of cross-linkage as well as formation of polysalt bridges, which should result in stronger final set cement. Therefore, in this study, a methacryloyl derivative of proline (a natural amino acid) was synthesized using the Schotten–Baumann reaction [10]. The product (1-methacryloylpyrrolidone-2-carboxylic acid) was used in a polymerization reaction with AA and IA in an sc-CO_2 mixture and also in aqueous reaction medium. These polymeric products were then used in glass-ionomer cement formulations, and the effects upon the mechanical and working properties of the glass-ionomer cements were investigated and compared to the samples prepared using polymers that were synthesized in water.

2. Experimental

2.1. Materials and equipment

All the chemicals in this study were of analytical grade and applied as received from Sigma Aldrich Chemical Co (Dorset, UK). L-Proline, methacryloyl chloride, sodium hydroxide, hydrochloric acid, ether, AA, IA and methanol were used for polymer synthesis. Carbon dioxide (99.95% purity; British Oxygen Company, Crawley, UK) was used as a solvent. The glass powders and all the polymeric liquids used in the experiments were from Fuji IX (GC International, Tokyo, Japan).

2.2. Syntheses of polymers

1-Methacryloylpyrrolidone-2-carboxylic acid (MP) was synthesized using the Schotten–Baumann reaction as described elsewhere [10–12].

2.2.1. Polymerization reaction in a supercritical CO_2 mixture

Free radical polymerization reaction carried out as discussed in our previous study [8]. Briefly, AA (27.4 ml), MP (5.8 g) and IA (6.5 g) were added to a 450 ml Paar autoclave in an 8:1:1 molar ratio, then 0.5 wt.% of 2,2′-azobis (isobutyronitrile) (AIBN) was added as the initiator. Methanol was used as the co-solvent of the reaction since the IA is not soluble in CO_2 solution; according to the methods of Moshaverinia et al. [8], Huang et al. [9] and Reighard et al. [13], in our case at least 4 mol.% of methanol in CO_2 was added to the other reagents to form a homogeneous solution prior to the addition of CO_2. The autoclave was briefly purged with CO_2 gas to remove any air before being filled with liquid CO_2 from the cylinder at 5 MPa (725 psi). The autoclave was then held at 20.7 MPa and 80 ± 5 °C, under continual stirring (250 rpm), for 4 h (an ISCO model 260D syringe pump used to reach the desired pressure). At the end of the experiment, the stirring was switched off and the CO_2 was released over a period of 5 min. The product was obtained as a pale red coloured viscous liquid. The product was washed and extracted with diethyl ether and dried using a vacuum oven. Yield was 80% overall based on dried mass of final product and expected formula.

2.2.2. Polymerization reaction in water

Initially 0.5 g of AIBN was dissolved in 50 ml distilled water in a 250 ml three-neck flask. In the next step, 27.4 ml of AA, 6.5 g of IA and 5.8 g of MP were measured and added dropwise (AA:IA:MP = 8:1:1 by mol). The solution was stirred with a magnetic stirrer (IKA Werke magnetic stirrer/heater, UK) and heated to 98 °C under continuous nitrogen purging. The polymerization was then allowed to proceed at that temperature for 12 h with continuous stirring under the blanket of nitrogen. At the end