The Combined Effect of Potassium Carbonate and Nitrogen Sparging in Reducing Hydrochloric Acid Byproducts in Polymeric Bone Scaffolds

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INTRODUCTION: A common biopolymer for bone tissue engineering applications, poly (propylene-fumarate) (PPF) is commonly synthesized using methods such as traditional transesterification or an addition of a nitrogen blanket. However, a byproduct produced from these methods, hydrochloric acid (HCl), poses an issue in the biocompatibility of the polymer. This research introduces a potential synthesis method to reduce the effect of HCl using a nitrogen sparging method with the addition of potassium carbonate. Polymer's poly (propylene-fumarate) (PPF) and poly (1,2-butylene fumarate)(1,2-PBF) are synthesized to examine this method with intent for application in bone tissue engineering. We hypothesize that the nitrogen sparging combined with potassium carbonate will allow for greater neutralization of HCL which reduces the acidity of the polymers therefore increasing biocompatibility.

METHODS: This is a polycondensation reaction that reacts the carbonyl end groups of the fumaryl monomer with the hydroxyl end groups of butanediol (1,2 PBF) and propylene glycol (PPF), respectively, using a nitrogen sparging method with the addition of potassium carbonate to remove the byproduct HCl. Synthesis using nitrogen sparging has been shown to increase the polymer chain length, which increases mechanical properties. Nuclear magnetic resonance (C-NMR H-NMR) spectra was used to analyze the molecular structure of the synthetic biopolymer for confirmation of the removal of HCl in both PPF and 1,2 PBF. Cell viability tests were conducted using synthesized PPF and PBF via two-step transesterification, nitrogen sparging, and nitrogen sparging with the addition of potassium carbonate, respectively. In completion of the nitrogen sparging with the addition of potassium carbonate process, solid potassium carbonate is removed via centrifuge and vacuum filtration, leaving behind polymer.

RESULTS SECTION: NMR analysis was used to verify the molecular structure of PPF and 1,2-PBF for all synthesis methods used in this study. PPF and 1,2 PBF polymers via two-step transesterification, nitrogen sparging, and nitrogen sparging with the addition of potassium carbonate show significant peaks representing the fumarate group at 6.8-7.0 ppm on the H-NMR spectra. Peaks representing a side reaction produced from the byproduct was shown at 2.8-3.1 ppm and 4.7-4.8 ppm for the H-NMR spectra of PPF and 1,2-PBF synthesized via nitrogen sparging alone. Side reaction peaks for PPF and 1,2 PBF polymer via two-step transesterification and nitrogen sparging with the addition of potassium carbonate was absent. Live/dead cell viability assays confirmed that the reduction of acidity aids in cell viability.

DISCUSSION: PPF and 1,2-PBF polymers were successfully synthesized using a method of nitrogen sparging with the addition of potassium carbonate. The amount of HCl was significantly reduced using the nitrogen sparging with the addition of potassium carbonate method compared to the nitrogen sparging method alone. The reduction of HCl reduced the overall acidity of the polymers resulting in improved cell viability. Continuing research includes optimization of mechanical and rheological properties for 3D bioprinting of 1,2-PBF.

SIGNIFICANCE/CLINICAL RELEVANCE: We believe that this polymer synthesis method can aid in the use of 1,2-PBF as a potential material for 3D bioprinting of bone tissue scaffolds.

IMAGES AND TABLES:

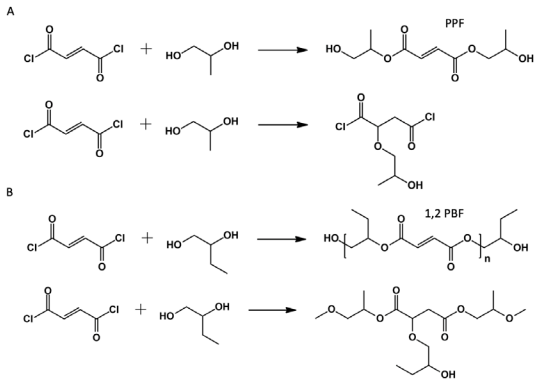

Figure 3:Desired reaction vs. the actual reaction where a side reaction occur due to an acid-catalyzed C=C bond saturation by an alcohol. A) PPF desired reaction (top) vs. actual reaction (bottom).B) 1,2-PBF desired reaction (top) vs actual reaction (bottom)

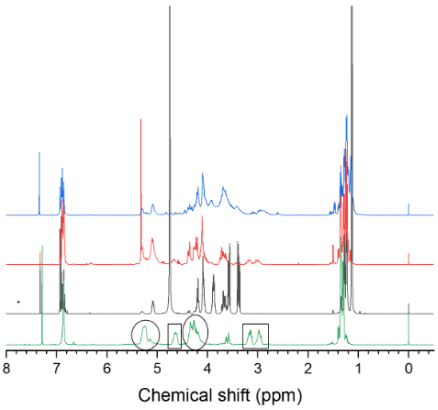

Figure 2: H-NMR spectra for PPF representing the fumarate group were present at 6.8-7.0 ppm on the H-NMR spectra. Peaks representing a side reaction produced from the byproduct was shown at 2.8-3.1 ppm and 4.7-4.8 ppm, respectively.

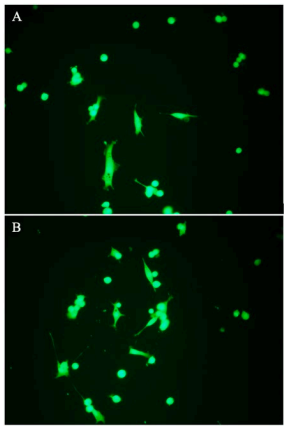

Figure 1:Cell viability testing of PPF (A) and 1,2-PBF (B).