Production of bone scaffolds with hierarchical porous structure via 3D printing and Supercritical CO_2 leaching.

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Bone Tissue Engineering (BTE) strives to create artificial bones to replace or repair patient's defects. Currently, the aid provided by Additive Manufacturing (AM) techniques makes it easier to deal with the challenge of patient-specific devices. Fused Filament Fabrication (FFF), namely AM to process polymers, is suitable for BTE applications. It consists of feeding a filament to the liquefier, where it melts, injecting the molten material through a nozzle, and depositing layer by layer to obtain the final part. Despite the efficiency and accuracy of FFF, there are still many difficulties to overcome in prototyping. For instance, bone tissue features an interconnected, porous internal structure with hierarchical porosity spanning from the nanoscale to the microscale. FFF can reproduce features in the micrometrical scale, but features in the nanoscale cannot be obtained. To overcome this limit, FFF was coupled with the Supercritical CO_2-Assisted Leaching (SAL). In SAL, CO_2 in supercritical conditions diffuses into the polymer matrix, removing the porogen agent and allowing the formation of a foam. A blend of suitable polymer and a porogen agent was realized through melt-compounding. The scaffold was then created by FFF, and the porogen was subsequently removed via SAL. This procedure generates hierarchical porosity that enhances nutrient absorption and promotes cellular proliferation. Stearic acid (SA) was used as a porogen agent to create micropores. PLA is a biocompatible aliphatic polyester, proven to be a biodegradable, cost-effective, accessible material for printing scaffolds. Its performance is subordinated to the treatments and processes it undergoes before obtaining the final part. In this work, the FFF process, coupled with SAL, was optimized to enhance the mechanical properties of the scaffolds and achieve the required standards for BTE. To this end, the effects of nozzle temperature, flow rate, and initial crystallinity of the filament were explored in the FFF process. It was found that higher temperatures in the nozzle enhance the diffusion at the interface between adjacent layers, leading to a more stable part. Conversely, the increase in flow rate makes crystallization faster upon deposition and limits diffusion at the interface. The larger the crystallinity degree of the filament fed to the liquefier, the lower the mechanical performance is. Concerning SAL, the effects of temperature, pressure, and processing time on porosity dimension and distribution were assessed.

Keywords: *PLA, Bone Tissue Engineering, Fused Filament Fabrication, Supercritical leaching*