Inulin-*g*-P(D,L)LA and PCL 3D printed porous scaffolds for bone tissue engineering

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INTRODUCTION

3D printing (3DP) technologies, such as fused deposition modelling (FDM), are offering innovative opportunities in the field of tissue engineering (TE), thanks to the possibility to produce, in a highly controlled way, customizable scaffolds with complex shape, geometry, and architecture [1]. In recent years, the use of polymeric blends has been widely investigated as a promising strategy for bone TE applications [2]. In this work, we propose a method based on 3DP-FDM technology to realize customizable bone scaffolds starting from polymeric blends containing polycaprolactone (PCL) and the new grafted copolymer inulin-*g*-P(D,L)LA (INU-PLA) [3]. Specifically, the inclusion of INU-PLA in low weight percentages within PCL may allow maintaining PCL printability via FDM while increasing hydrophilicity and biodegradation, and hence bioactivity.

MATERIALS AND METHODS

Three polymeric films of PCL and INU-PLA in various weight percentages (2.5,5 and 10% w/w) were produced using solvent casting technique, cut into pellets, and then processed via hot-melt extrusion in form of filaments suitable for 3DP-FDM. The following step was dedicated to the design of scaffold digital model, the printing in optimized conditions via 3DP-FDM, and the preliminary characterization of scaffolds in terms of:

- size, using an electronic digital caliper,
- porosity, by liquid displacement method,
- morphology, 3D architecture and surface topography, by scanning electron microscopy (SEM),
- thermal proprieties, by differential scanning calorimetry (DSC),
- mechanical properties, using a texture analyzer,
- *in vitro* biodegradation profiles both in hydrolytic (in PBS pH 7.4 with 0.05% NaN_3– 37°C) and enzymatic conditions (in PBS pH 7.4 containing 0.5 mg/mL of *Amano Lipase* – 37°C), using an analytical balance and a gel permeation chromatography (GPC) system,
- *in vitro* hemocompatibility.

RESULTS

✓ The formulative choices as well as the selected techniques allowed to produce, with a high process yield (83-89%), homogeneous filaments, with a surface free of defects and a diameter (2.65-2.85 mm) suitable for 3DP-FDM.

✓ As the percentage of INU-PLA within the blend increased, an increase in surface wettability was highlighted.

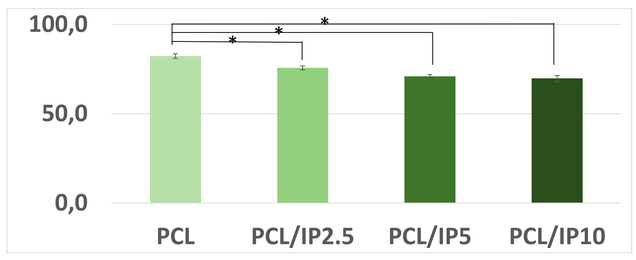

Figure 1. Water contact angle values of extruded filaments. *p<0.05 (Student's T test)

✓ All the filaments were successfully printed via FDM, obtaining porous scaffolds with size, 3D architecture and macroporosity values very close to those of the digital model.

	INU-PLA w/w%	Diameter (mm)	Thickness (mm)	Porosity (%)
S_PCL	0	9.61 (0.17)	4.65 (0.11)	62.83 (4.11)
S_PCL/IP2.5	2.5	9.60 (0.18)	4.76 (0.09)	62.16 (1.67)
S_PCL/IP5	5.0	9.25 (0.12)	4.70 (0.07)	65.86 (2.52)
S_PCL/IP10	10.0	9.31 (0.11)	4.68 (0.07)	62.05 (2.82)
Digital model		10	5	62

Table 1. Composition, diameter, thickness, and porosity of PCL and PCL/INU-PLA scaffolds

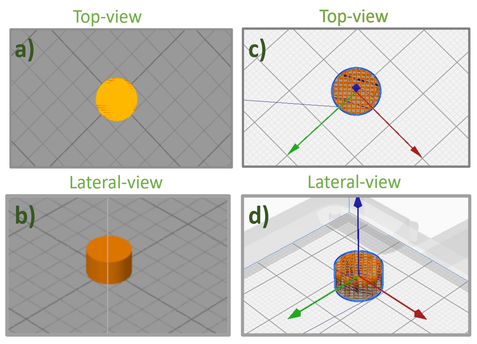

Figure 2. Scaffold CAD design **(a,b)** and sliced model **(c,d)**

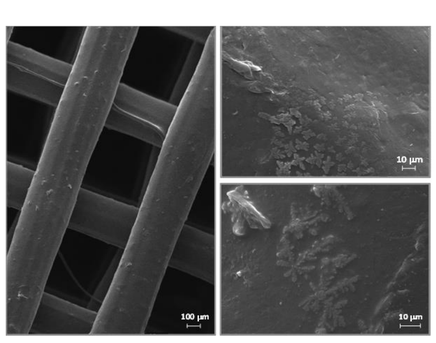

Figure 3. SEM micrographs of S_PCL/IP10 scaffolds

✓ Thermal investigation showed for all samples (extruded filaments and scaffolds) a melting temperature around 56°C, a crystallization peak at about 32-33°C, and a crystallinity degree of 48-49%, without significant variations among the systems with different composition.

✓ Scaffolds showed good mechanical properties: all tested samples showed a Young's Modulus in the range of 31-36 MPa and a compressive strength between 4.2-5.3 MPa, which are compatible with lower values of human cancellous bone [4].

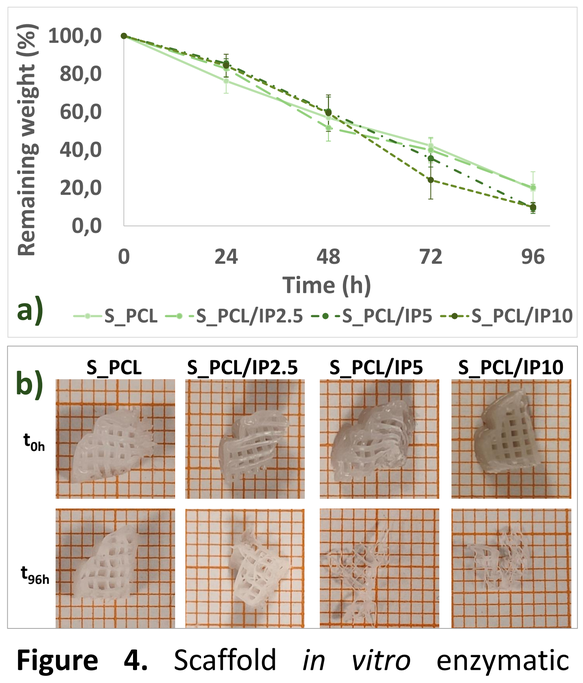

Figure 4. Scaffold *in vitro* enzymatic degradation profiles **(a)** and degraded scaffold images **(b)**

✓ Biodegradation studies showed a very slow degradation rate in hydrolytic conditions (mass loss 2-3% within 3 months, and a very slight decrease in molecular weight), while suggested that the presence of INU-PLA within the blend is able to speed up scaffold enzymatic degradation.

✓ All scaffolds have proved to be highly hemocompatible.

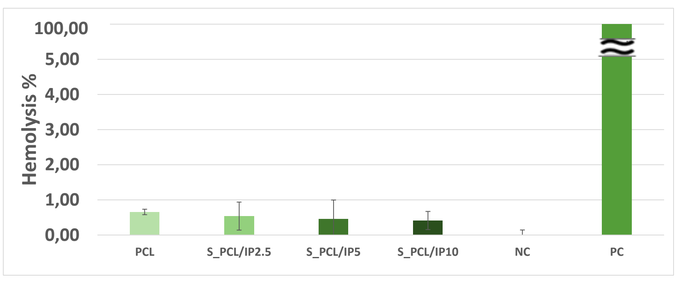

Figure 5. Scaffold hemolysis percentage

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CONCLUSION

✓ The results highlight the high potential of FDM in the production of scaffolds with predictable and reproducible internal architecture.

✓ The presence of INU-PLA within the PCL matrix doesn't affect either material printability, or scaffold mechanical properties, while it improves wettability and degradation profiles and therefore could allow improving bioactivity.

✓ Such results suggest that the inclusion of INU-PLA within the polymeric blend may be a useful tool to improve PCL features for the manufacturing of bone scaffolds.