Next generation gynaecological mesh implants: 3D printing and material-based strategies to enhance tissue-mesh integration

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Background: Pelvic floor dysfunction (PFD) is a common disorder among the female population, affecting one-third of women worldwide. Among the possible strategies employed for the management of these disorders, the surgical approach consists in the placement of a mesh, aiming to mechanically sustained the weakened tissues. However, the use of meshes has been often accompanied by the arising of severe immune reactions and fibrotic process, as well as infectious complications. Moreover, the mechanical mismatch between the tissue and the currently available devices is the main cause for tissue erosion. To address these issues, this research work focused on the production, via 3D printing, of polymeric meshes made of polycaprolactone (PCL) and polyvinylidene fluoride (PVDF) loaded with levofloxacin (LFX), aiming to produce antibacterial mesh implants with piezoelectric activity and the potential to improve tissue-mesh interactions.

Methods: Meshes of PCL and PVDF (5%, 10%, 16% w/w), loaded with LFX (0.5% w/w), were produced via melt-extrusion 3D printing. Powders were dry-mixed and then printed at high temperature in a honeycomb mesh structures. The employed materials were characterized according to their physicochemical and thermal properties. The morphology and the mechanical response of the as produced meshes were investigated. Finally, their drug releasing abilities, mechanical/drug stability under storage conditions and the degradation behaviour were also assessed for four and one months, respectively.

Results: Among the tested PVDF concentrations, 5% w/w was the most promising in terms of printability and mechanical response, thus being preferred for the remaining experiments. Materials' characterization showed that the manufacturing process did not alter the physicochemical properties of the employed polymers, moreover thermal characterization confirmed that no material degradation occurred during the printing process. Meshes possessed a macro-porous structure, with a pores' size of 1.20 mm, thus being suitable to allow cells infiltration. The computed mechanical properties were closed to the native ones, presenting a young modulus equal $E_{PCL/5PVDF/0.5LFX}$= 12.74 ± 0.26 MPa. The printed devices were able to release LFX for at least 72h, with an initial burst release and with 60% of the total drug released in three days. From the mechanical stability study, a small loss of mechanical properties was observed, with a final young modulus of $E_{PCL/5PVDF/0.5LFX(s)}$= 10.09 ± 0.05 MPa, along with some signs of degradations after 4 months of storage. Degradation studies highlighted a faster degradation behaviour for LFX-loaded meshes, with a young modulus post degradation equal to $E_{PCL/5PVDF/0.5LFX(d)}$ =15.2 ± 1.59 MPa.

Conclusions: The 3D printed meshes produced in this work proved to be a valuable option for the treatment of PFD, thanks to their macro-porosity, crucial to allow cells colonization, and to their mechanical properties. Additionally, the drug release studies highlighted the capability of the produced mesh implants to exert a more controlled release of LFX; however, still providing a fast action against bacterial infections thanks to the initial burst release observed.