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

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INTRODUCTION

Pelvic floor dysfunctions (PFDs) are a class of disorders widely diffused among the female population[1]. Their management may include the placement of a polymeric mesh to help sustain the weakened tissues[2]. Due to the significant number of mesh-related complications, and following the recent warnings and bans, and considering the withdrawal of several products from the market[3], finding new strategies to improve meshes outcomes and integration with the vaginal tissue is crucial.

AIM

To exploit the piezoelectric behaviour of polyvinylidene fluoride (PVDF), the antibacterial effects of levofloxacin (LFX), and the properties of polycaprolactone (PCL), to produce customizable resorbable meshes via melt-extrusion 3D printing with antibacterial effects and the potential to enhance tissue-mesh integration.

MATERIALS AND METHODS

1. Printing optimization

- Three PVDF concentrations (w/w) were tested, and 3D printed along with PCL and LFX (0.5% w/w): 16%, 10% and 5%.
- Meshes were printed with a honeycomb design.

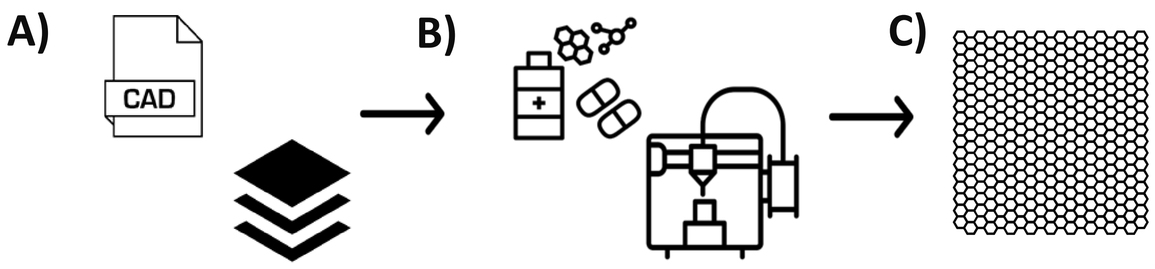


Figure 1: Workflow of the manufacturing process: A) creation of the design; B) 3D printing and inclusion of drug; C) final product.

2. Physicochemical characterization:

- Thermogravimetric analysis (TGA) and Differential scanning calorimetry (DSC)
- Fourier-transform infrared spectroscopy (FTIR), X-ray photoelectron spectroscopy (XPS), X-ray Diffraction (XRD) analysis

3. Morphological and mechanical characterization:

- Scanning electron microscopy (SEM)
- Tensile test and mechanical stability studies.

4. In vitro characterization:

- Drug release
- Degradation studies

RESULTS

Here will be reported the main results for meshes made with a PVDF concentration equal to 5% (w/w), as it proven to be the best among those tested.

1. Printing optimization

Table 1: Optimized printing parameters.

Material	Temperature (°C)	Pressure (bar)	Speed (mm/s)
PCL	130	6	0.6
PCL/0.5LFX	130	6.5	0.6
PCL/5PVDF	140	6.5	0.6
PCL/5PVDF/0.5LFX	140	6.5	0.6

2. Physicochemical characterization

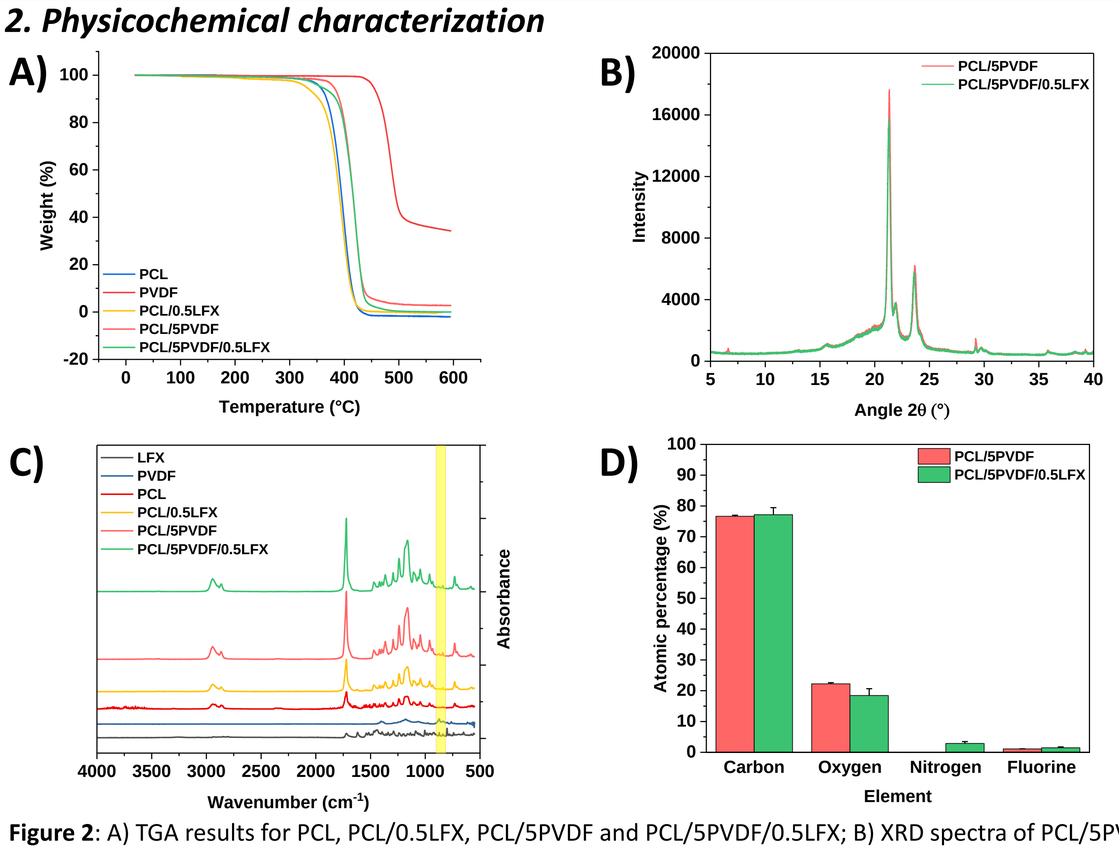


Figure 2: A) TGA results for PCL, PCL/0.5LFX, PCL/5PVDF and PCL/5PVDF/0.5LFX; B) XRD spectra of PCL/5PVDF and PCL/5PVDF/0.5LFX printed samples; C) FTIR spectra of LFX, PVDF, PCL raw powders and PCL/0.5LFX, PCL/5PVDF and PCL/5PVDF/0.5LFX printed samples; D) Atomic percentage of carbon, oxygen, nitrogen and fluorine found in PCL/5PVDF and PCL/5PVDF/0.5LFX samples.

3. Morphological and mechanical characterization

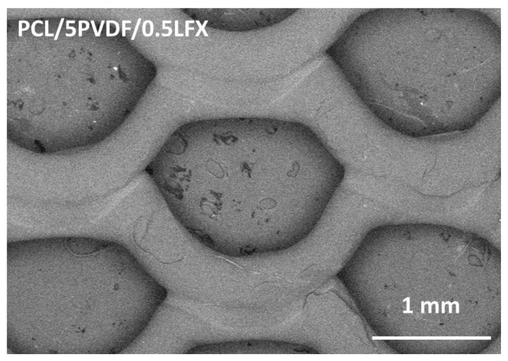
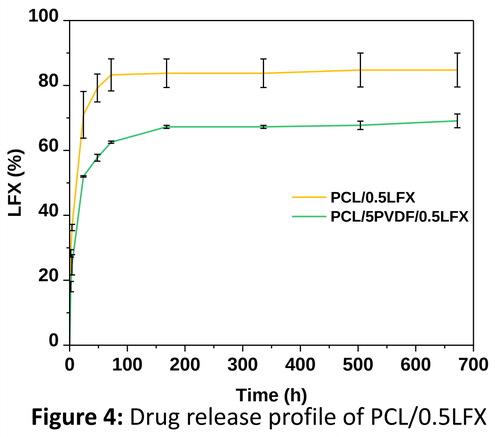


Figure 3: SEM image of PCL/5PVDF/0.5LFX honeycomb mesh. Samples were characterized by high shape reproducibility and macro-pores (≈1.2 mm).

Table 1: Meshes' mechanical properties. Results have been reported for Young Modulus (E) alone. Ultimate tensile strength (UTS) and Maximum elongation (ME) were also computed during the analysis stage.

Sample	E (MPa)
PCL	6.27±0.42
PCL/0.5LFX	8.71±0.18
PCL/5PVDF	8.63±0.26
PCL/5PVDF0.5LFX	12.74±0.26
Vagina $_{PreMen}$[4]	6.65±1.48
Vagina $_{PostMen}$[4]	10.26±1.10

4. In vitro characterization



- In the first three days PCL/0.5LFX and PCL/5PVDF/0.5LFX samples released 80% and 60% of the total encapsulated drug, respectively
- The degradation rate was accelerated by LFX
- During degradation, a mechanical transition to a more brittle behaviour was observed for all the samples.

Figure 4: Drug release profile of PCL/0.5LFX and PCL/5PVDF/0.5LFX samples.

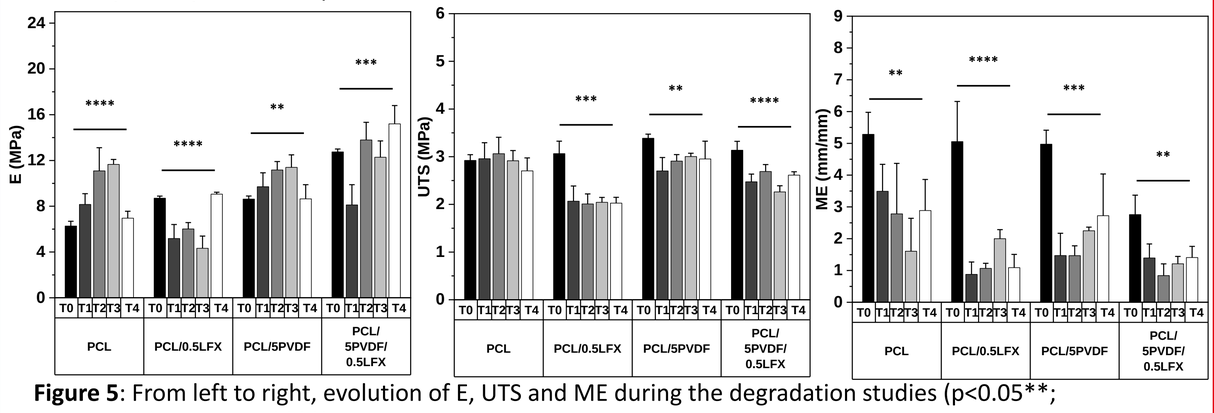


Figure 5: From left to right, evolution of E, UTS and ME during the degradation studies ($p<0.05$**; $p<0.005$***; $p<0.0005$****).

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

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