Printfills: 3D printed systems using Fused Deposition Modelling and Injection Volume Filling

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CÁTEDRA IBEROAMERICANA-SUIZA DE DESARROLLO DE MEDICAMENTOS

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INTRODUCTION

- Fused deposition modelling (**FDM**) has a good potential for fabrication of dosage forms, but is unable to load temperature sensitive substances during extrusion due to the high processing temperature.
- Injection volume filling (**IVF**) technology was combined with FDM to incorporate drug solutions/dispersions at room temperature to the extruded scaffold during the printing process.
- Colon targeting remains a very promising area for the treatment of colonic diseases and protein delivery due to its unique physiological characteristics.

The aim of this work was to design and characterize colon-specific drug delivery systems manufactured in a simple and automated 3D printer combining two 3D printing technologies: FDM and IVF. This new kind of printed pharmaceutical dosage forms have been called printfills: printed systems filled with a liquid or semisolid.

MATERIALS AND METHODS

•Polylactic acid (Leon 3D, Spain)

• HPMC Methocel™ K4M (Colorcon Ltd., UK)

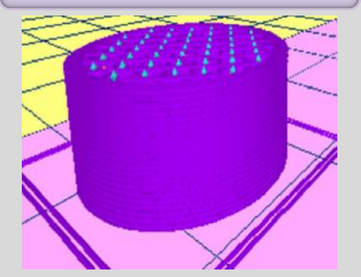
• Eudragit FS30D (Evonik, Germany)

• Anhydrous theophylline (Acofarma, Spain)

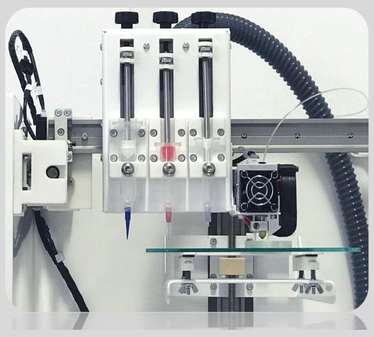
Drug Printable Ink

Hydroalcoholic gel (HPMC 1%)
+
Theophylline (20 mg/mL)

Designing Process



Regemat 3D v1 printer



3D Printing Process

FDM parameters + **IVF parameters**

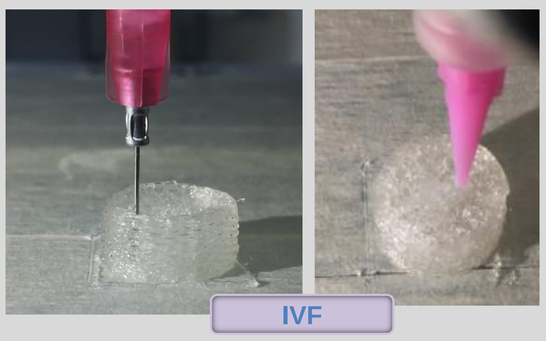
Layers: 21
Layer thickness: 0.35 mm
Feeding rate: 1.2 mm/s
Perimeter speed: 8 mm/s
Infill speed: 8mm/s

Deposit speed: 1µl
Retract speed: 1µl
Purge: 50 µl

Drug -Gel Injection

Eudragit FS30D injection: 350 µl

FDM



IVF

Technological and Biopharmaceutical Characterization

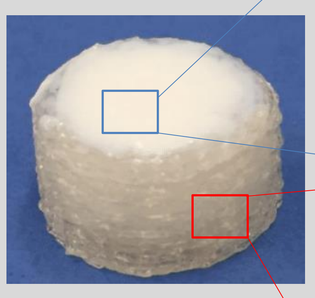
Scanning Electron Microscopy (SEM)

Microscopy Service of the CITIUS in the University of Seville by using a FEI TENEO electronic microscope

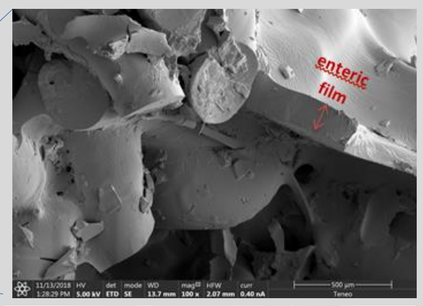
Dissolution test

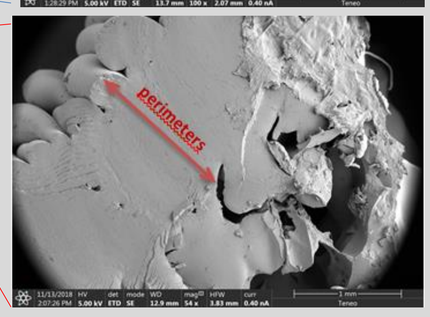
USP Apparatus II
Sotax AT7
UV-Vis spectrophotometer Agilent 8453

RESULTS AND DISCUSSION



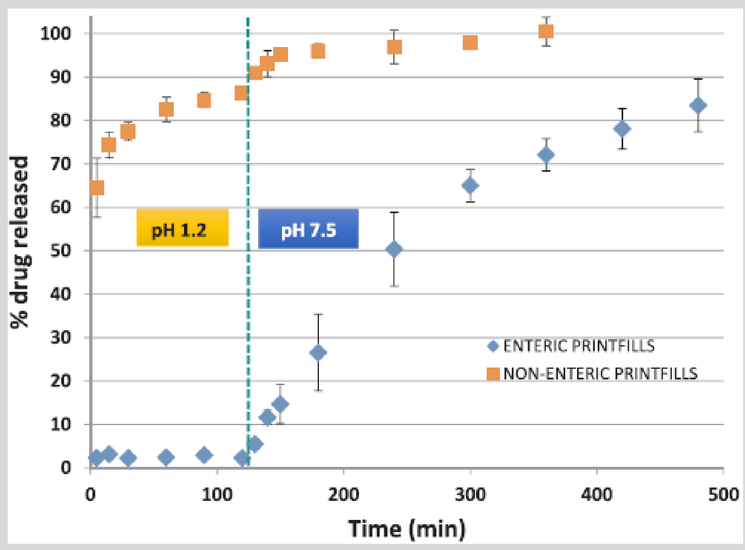
Printfill and SEM microphotographs of the perimeter and the enteric film.





The **homogeneous film of Eudragit FS30D,** presented on the top face of the printfill, provides a colon-specific drug delivery system

The **sealed scaffold** allows to keep the drug inside the system until the switch solution at pH 7.5 dissolved the enteric film.



Mean dissolution profile of printfills.

Results from drug release studies performed at different pH confirm the ability of printfills for **colon-specific drug delivery.**
After the lag time, drug is released with an intermediate kinetics between zero order and diffusional kinetics, as shown by Korsmeyer time exponent (n=0.8749).

CONCLUSIONS

- Pharmaceutical dosage forms have been manufactured for the **first time** with a 3D printer **combining Fused Deposition Modelling and Injection Volume Filling.**
- The integration of these two techniques allows an **easier incorporation of drug/excipient liquid systems** to the extruded scaffold **at room temperature**, avoiding other intermediate processes.
- In vitro studies show the ability for **colon-specific drug delivery** of the performed printfills thanks to the perfect sealing of the scaffold and the homogeneous layer obtained with the delaying release polymer.
- IVF technology complements FDM solving the main limitations of this technique and providing a **versatile platform for drug delivery**.

REFERENCE

[1] V. Linares, M. Casas, I. Caraballo, Printfills: 3D printed systems combining fused deposition modeling and injection volume filling. Application to colon-specific drug delivery, Eur. J. Pharm. Biopharm. 2019; 134: 138–143.

ACKNOWLEDGEMENT

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