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Effect of plasticizer content on the processability of paroxetine-loaded filaments by fused deposition modelling

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Introduction

Three-dimensional printing (3DP) is a novel approach to manufacture individualized medicines, representing an excellent opportunity to make a significant technological leap over traditional pharmaceutical manufacturing processes. The incorporation of 3DP in the pharmaceutical compounding landscape is expected to promote flexibility, efficiency, safety, and quality of existing medicines. Fused deposition modelling (FDM), the most used 3DP technique, involves the production of a drug-loaded filament, obtained previously by hot-melt extrusion (HME), which is then melted and continuously deposited on a surface, layer by layer, building the 3D-printed dosage form [1].

The successful integration of HME and FDM requires that both extrudability of the raw materials and printability of the HME filaments fabricated are attained, properties which are influenced by the mechanical, rheological and thermal properties of materials [2]. Previous studies demonstrated that environmental conditions (especially, humidity) play a key role in the coupling of these technologies, since they impact on the moisture content of the filaments and, consequently, on their mechanical properties and processability [3,4]. Besides atmospheric humidity, it is crucial to study whether the **composition of the polymeric formulation** (e.g., plasticizer content) can influence the printability of the filaments.

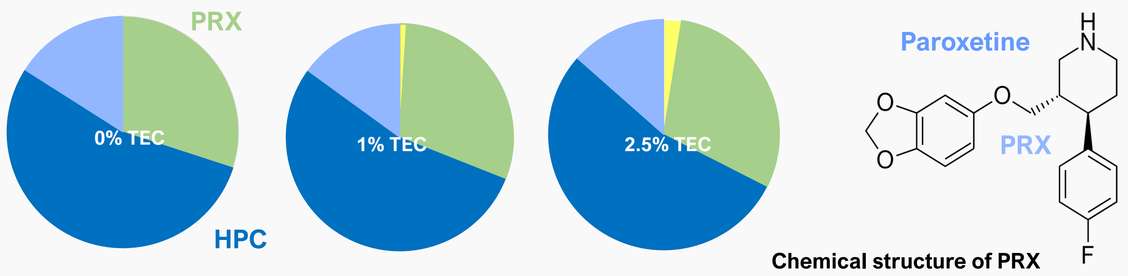
Aim

This work aims to **evaluate the impact of the plasticizer content** on the quality and printability of paroxetine-loaded polymeric formulations for integrated HME-FDM, by assessing the water content of the filaments and their performance during the 3DP process.

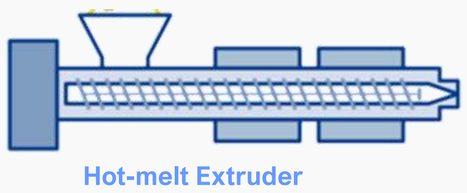
Materials & Methods

Filaments containing Paroxetine (PRX, 30% w/w), Hydroxypropylcellulose (HPC, 54% w/w) and other excipients (16% w/w of a mixture made of Calcium Phosphate, Magnesium Stearate and Triethylcitrate) were produced by HME. **Three different formulations containing HPC and different fractions of plasticizer** were evaluated.

Formulation



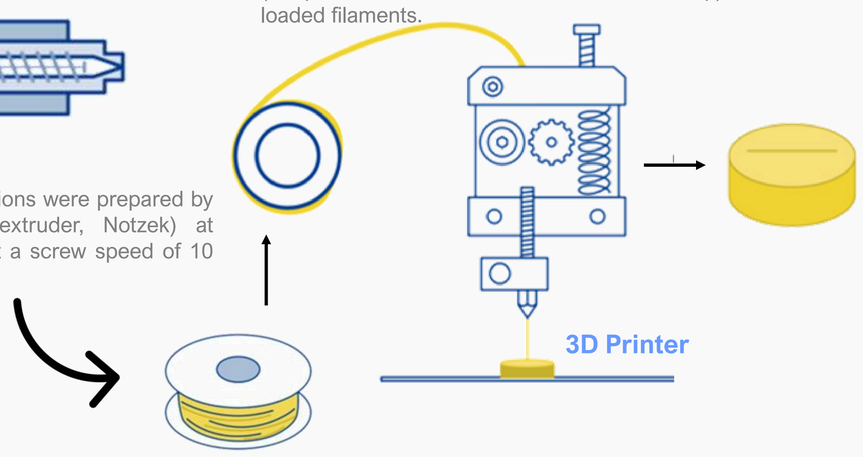
Preparation of filaments



Filaments based on different formulations were prepared by HME (Notzek Pro single screw extruder, Notzek) at temperatures of 120°C and 90°C, at a screw speed of 10 rpm.

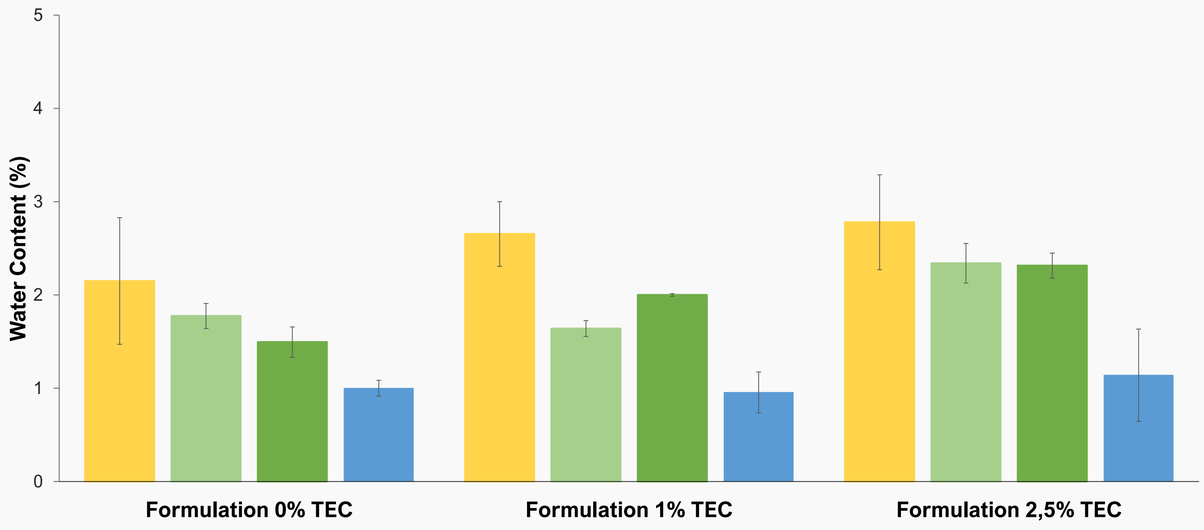
Printing of 3D tablets

Whenever possible, FDM 3D-printed tablets were produced (3D printer Delta WASP 20 40 Turbo 2, Wasp) from PRX-loaded filaments.



Moisture content and feeding/printing performance of filaments were evaluated for the different polymeric formulations, immediately after extrusion and after storage under specific conditions (room temperature (24°C) and humidities of 55%RH and 11%RH (desiccator).

Results



Variation of water content in the PRX-loaded products, throughout the manufacturing process and storage. PM Pre-Extrusion (yellow); Filament Post-Extrusion (light green); Filament stored at room temperature (dark green); Filament stored in a desiccator (blue).

Printability of the polymeric filaments containing different concentration of plasticizer during the storage.

Printability	0% TEC	1% TEC	2.5% TEC
After HME	**Yes**	No	No
After storage at room conditions	No	No	No
After storage at desiccator	**Yes**	**Yes**	**Yes**

The plasticizer content has shown a correlation with the water content, and it should be reduced and kept to the minimum fraction to allow double extrusion (HME).

- Higher moisture values were obtained for the formulations with high concentration of TEC.
- The printability of PRX-containing filaments was promoted by low water content (less flexibility of the filaments).

The reduction of the water content, promoted by the storage of the filaments at low RH, interacted with TEC showing a direct correlation.

- A more significant decrease in the water content of filaments made of 2.5% of TEC and stored in a desiccator was observed when compared to the results obtained from formulation without plasticizer.
- The plasticizing component can retain water molecules in the polymeric matrix and, consequently, make the filaments more ductile due to the higher moisture content.
- Storage the filaments under room conditions can originate a variable and unpredictable effect on their water content, regardless the plasticizer content.

Conclusions

This work reinforced **the importance of the plasticizer content in PRX-loaded blends** and in its downstreaming processability, allowing **optimization of the printing process**, namely by reducing holding time, and anticipation of the most satisfactory composition of filaments.

References

1. Zhang, J.; Feng, X.; Patil, H.; Tiwari, R.V. and Repka, M.A. Coupling 3D printing with hot-melt extrusion to produce controlled-release tablets. Int. J. Pharm., 519, 186-197 (2017).
2. Bandari, S.; Nyavanandi, D.; Dumpa, N.; Repka, M. Coupling Hot Melt Extrusion and Fused Deposition Modeling: Critical Properties for Successful Performance. Adv. Drug Deliv. Rev., 172, 52–63 (2021).
3. Figueiredo, S.; Fernandes, A.I.; Carvalho, F.G. and Pinto, J.F. Performance and stability of paroxetine tablets manufactured by fused deposition modelling-based 3D printing. J. Pharm. Pharmacol., rgab138 (2021).
4. Figueiredo, S.; Fernandes, A.I.; Carvalho, F.G. and Pinto, J.F. Exploring Environmental Settings to Improve the Printability of Paroxetine-Loaded Filaments by Fused Deposition Modelling. Pharmaceutics, 15, 2636 (2023).

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