Mechanical properties as printability predictors of Paroxetine-loaded filaments by fused deposition modeling

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1. INTRODUCTION

Three-dimensional printing (3DP) is an innovative and emergent technology in the pharmaceutical sector with undeniable advantages over traditional manufacturing processes, namely in the customization of medicines.
Among several technologies, **fused deposition modelling (FDM)** is the most commonly used, involving the previous manufacture of a drug-loaded filament by **hot-melt extrusion (HME),** which is then molten and continuously deposited on a surface, layer by layer, building the 3D-printed dosage form [1].
To enable 3DP, the raw materials must have specific mechanical, rheological and thermal characteristics [2]. The **successful integration of HME and FDM** as a continuous pharmaceutical manufacturing process depends on a better understanding of the impact of environmental conditions (especially humidity) on the printability of formulations since these properties are highly influenced by the storage conditions of the materials [3].

2. AIMS

- To explore the **effect of environmental conditions on the mechanical properties** of Paroxetine-loaded polymeric filaments produced by HME.
- To evaluate the **impact of the mechanical properties on the printability** of Paroxetine-containing formulations for continuous HME-FDM manufacturing process.

3. METHODS

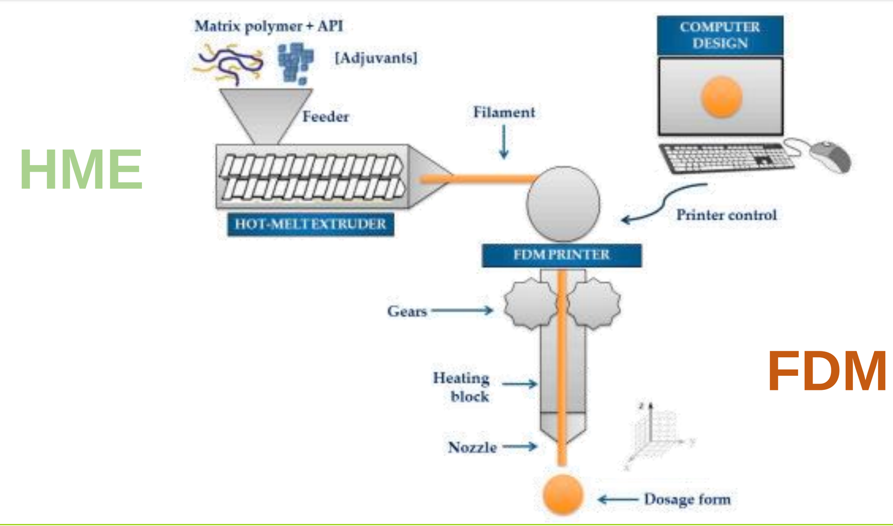
Formulation
PRX (30% w/w), HPC (54% w/w) and other excipients (16% w/w of a mixture made of CaP, MS and TEC in a 10:1:5 ratio)

Preparation of Filaments
Filaments containing polymeric formulation were prepared by HME (Notzek Pro single screw extruder, Notzek)

Stability of Filaments
Filaments were stored in stability chambers (Fitoclima D1200PH, Aralab) and dessicator inside open plastic bags, and re-examined at pre-defined times.

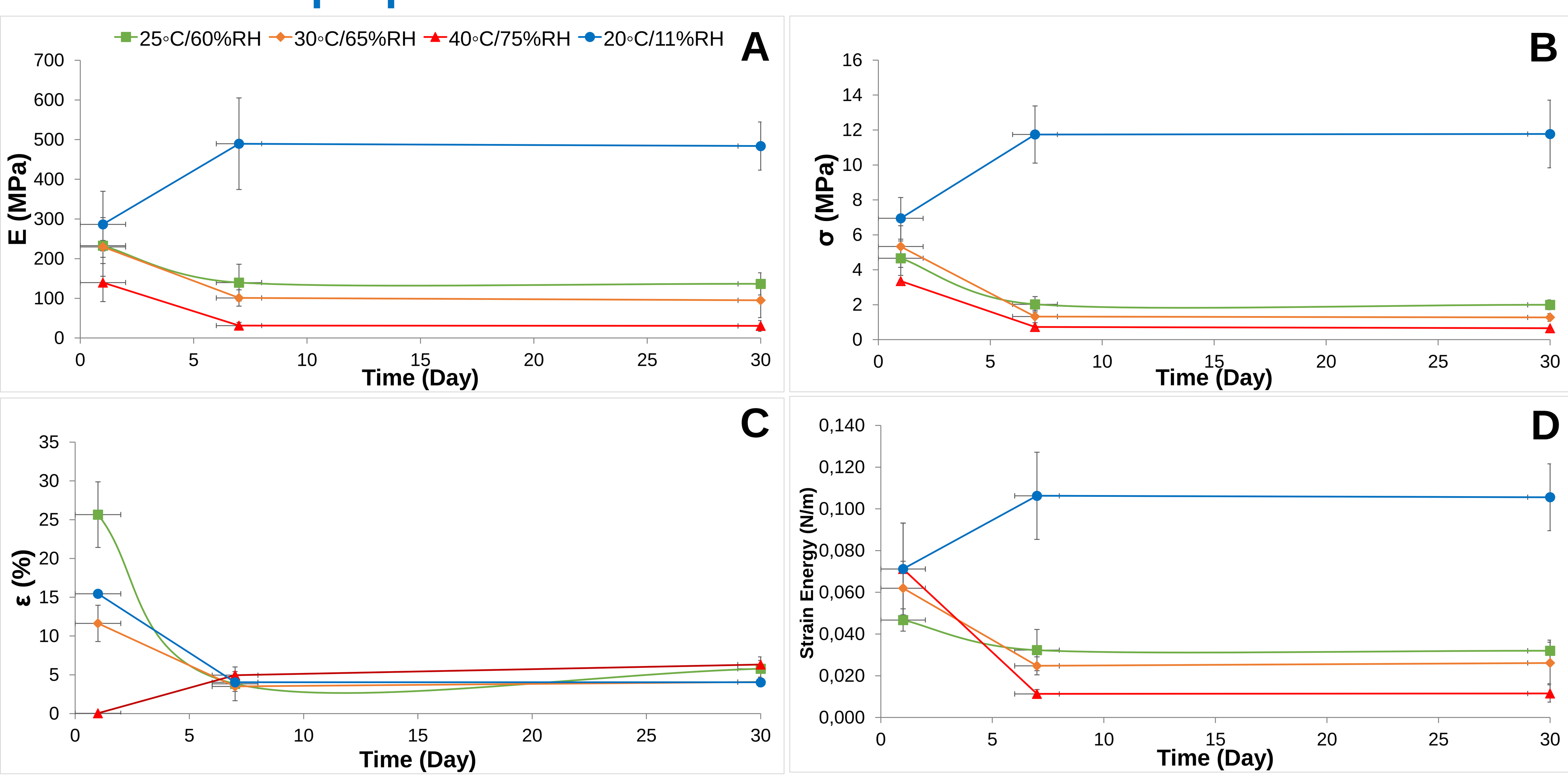
Evaluation of Filaments
Mechanical properties, moisture content and feeding/printing performance of filaments were evaluated for the different time points and conditions of storage.

Printing of 3D tablets
Whenever possible, FDM 3D-printed tablets were manufactured (3D printer Delta WASP 20 40 Turbo 2, Wasp, Italy) with printing temperatures of 200°C (extrusion) /50°C (plate).



4. RESULTS

Mechanical properties of filaments



(A) Young's (Elastic) modulus, (B) stress at maximum load, (C) strain at break and (D) energy strain over time and storage conditions.

High humidity (>60% RH):

Filaments became successively more ductile due to moisture absorption. The **increment of water content** promoted a **plasticization of the filaments**, supporting their plastic behaviour (breakage only occurs with significant deformation and making it inapt to feed the printer.

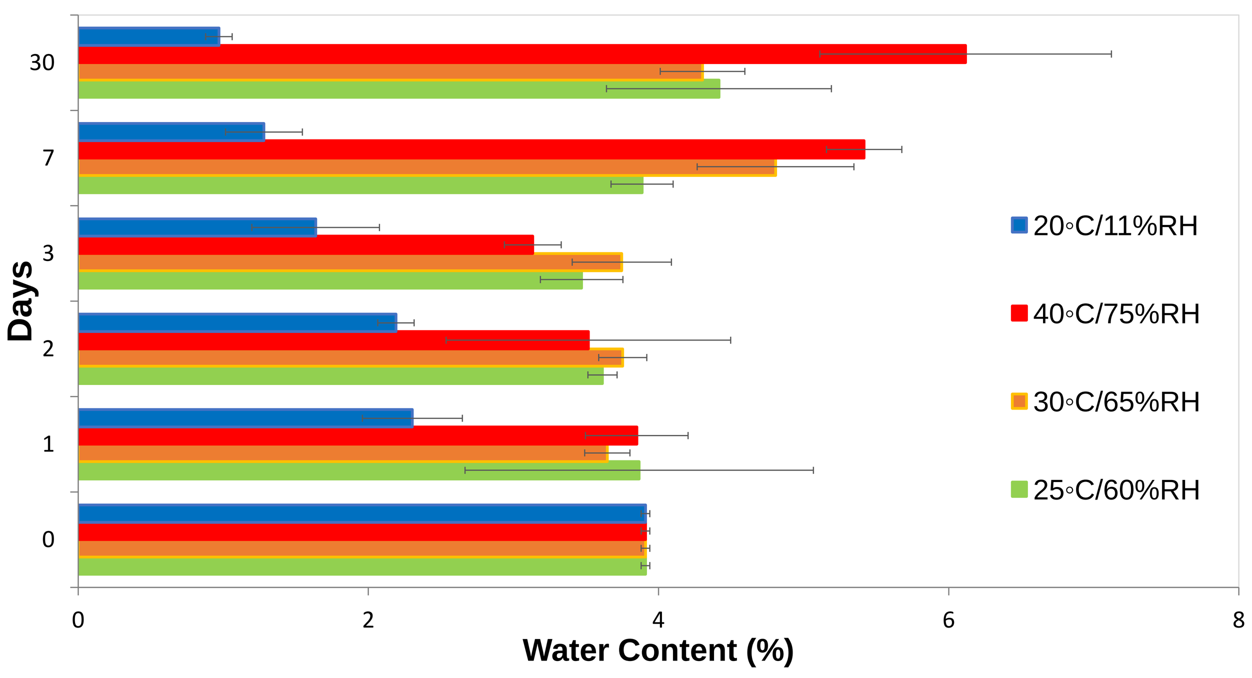
↓ Elastic modulus ↓ stiffness and stress at maximum load ↓ strain energy

Low humidity (11% RH):

Filaments became stiffer, making possible their proper feeding in the 3D printer head. These changes are the consequence of the **water loss during storage**, and they are more prominent **after 1 week of the HME** process.

↑ Elastic modulus ↑ stiffness & stress at maximum load ↑ strain energy

Water content of filaments



Increment of water content determined in the filaments during the stability studies for all environmental conditions.

Printability of filaments

Environmental Conditions →	Water Content →	Mechanical Properties ⇢	Printability
High Humidity	High moisture content (4-7%)	Filaments with remarkable ductility and flexibility	Non-Printable[1]
Low Humidity	Low moisture content (1-4%)	Filaments with proper ductility and stiffness	Printable[2]

[1]Filaments were not printable since the over-plasticization of the filaments caused permanent deformation along the printing head and feeding defects. [2]Filaments were printable after 1 week of the HME extrusion process.

5. CONCLUSIONS

This study corroborates that the **successful integration of HME and FDM technologies is highly dependent on the mechanical properties of the filaments** used in the production of 3D-printed dosage forms since they affect processability. In turn, it proves that **these characteristics are greatly influenced by storage conditions**, which must be carefully controlled during the continuous manufacturing process. **Complementary studies** to speed up the printability of filaments should be explored.

6. REFERENCES

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