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Selection of Hydroxypropylcellulose Grade for Paroxetine 3D-Printable Formulations for Fused Deposition Modelling

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Introduction

Three-dimensional printing (3DP) has recently been attracting the attention of the pharmaceutical community since this technology gives the opportunity to personalize therapy according to patient's needs, re-centering medicines' design on the individual [1]. Fused Deposition Modelling (FDM), the most widely used 3DP technique, involves the prior production of a drug-containing polymeric filament by Hot-melt extrusion (HME), which is then melted and continuously deposited on a surface, layer by layer, building the 3D-printed dosage form [2].

The success of FDM for medicines customization depends on several factors, such as the choice of the adequate polymeric matrix, according to the intended drug release. Recently, **cellulose-derived polymers (e.g., hydroxypropylcellulose, HPC)** have been extensively studied for filament preparation by HME as they can modulate the drug release profile [3]. However, it is crucial to evaluate their properties since these matrix polymers have not been developed specifically for 3DP applications.

HPC grade	Viscosity (mPa.s)	Molecular mass (Da)	Usual pharmaceutical applications
Klucel GF Pharm	150-400	370 000	Controlled-release matrix
Klucel LF Pharm	75-150	95 000	Immediate-release binder/ Film-coating

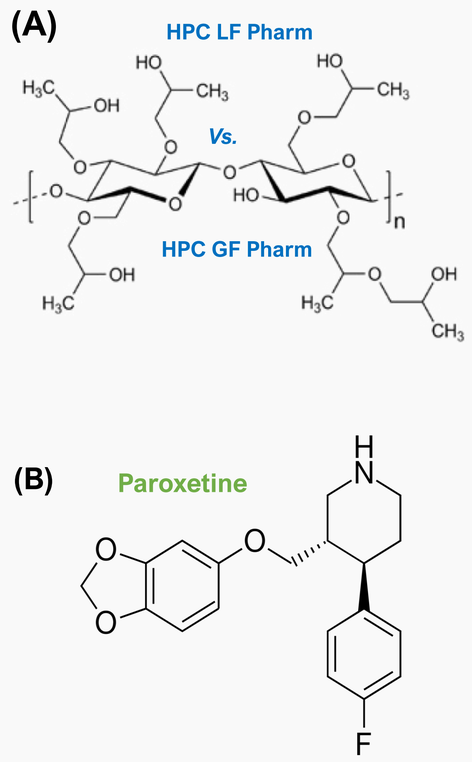
*HPC GF and LF grades were tested in this work.

Aim

Based on a comparative study of the drug dissolution profile, this work aims the **selection of the most suitable grade of HPC polymer** to modulate the release of paroxetine (PRX; used for the treatment of major depression, generalized anxiety and related disorders) from 3D-printed tablets obtained by HME coupled to FDM 3DP.

Materials & Methods

Tblets were 3D-printed by FDM from PRX-loaded filaments, previously manufactured by HME, and composed of two different polymeric formulations (HPC LF and HPC GF Pharm, Ashland.) [4]. In vitro dissolution of 3D-printed tablets was performed, and kinetic parameters were evaluated [5].



Chemical structures of HPC (A) and PRX (B).

Formulation

HPC LF Pharm (54% w/w) OR HPC GF Pharm (54% w/w)

Paroxetine (30% w/w)

Other excipients: 6% w/w of Calcium Phosphate, Magnesium Stearate and Triethylcitrate in a 10:1:5 ratio

Preparation of filaments

Filaments containing polymeric formulation 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.

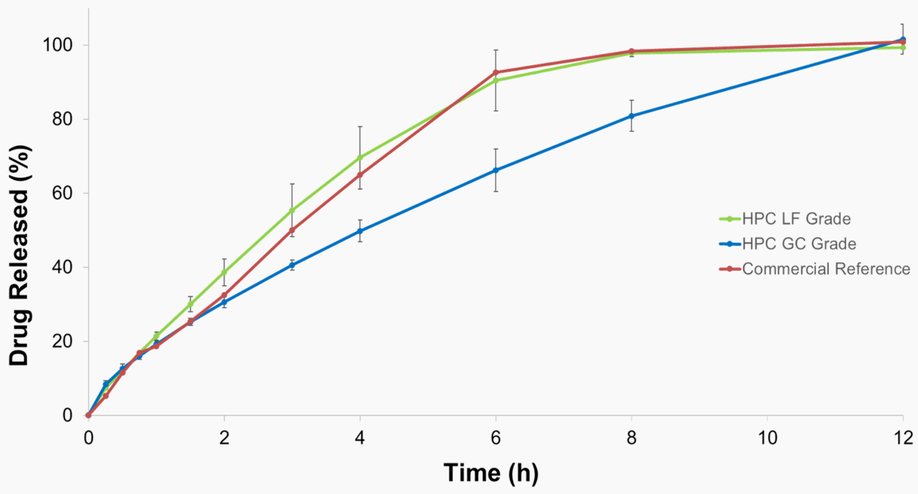
Printing of 3D tablets

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) and 60 mm/s printing speed.

Evaluation of 3D-printed tablets

Some kinetic parameters, such as the time required for 50% drug release ($t_{50\%}$) and the dissolution rate (DR), were calculated for both HPC-containing 3D tablets from dissolution testing.

Results



Dissolution profiles of 3D-printed PRX tablets prepared with HPC LF (green) and HPC GF (blue); commercial tablets obtained by a conventional manufacturing process (tabletting) (red) were used as a reference (n=3).

Dissolution parameters of 3D-printed tablets produced by HME coupled to FDM.

Formulation	$t_{50\%}$ (min)	DR (mg.min^{-1})	f_2	Similarity
HPC LF	2.681	0.184	71.46	Yes*
HPC GF	4.027	0.174	48.20	No

* Criterion defined for f_2: 50-100; (n=3).

The dissolution exhibited a profile typically associated with controlled release formulations related to the use of the HPC polymer in both formulations.

HPC LF Pharm

Release of ≥85% of PRX at ≈6h of the test, reaching the steady state (release close to 100%) after 8h.

The release profile was superimposable to that of the commercial formulation. The kinetics of drug release are amenable to adjustments leading to complete overlapping of the profiles, namely by modulating the polymer:PRX ratio or the adjuvants present in the formulation.

HPC GF Pharm

Slower release of PRX (↑t50% ;↓DR) when compared to the HPC LF-based formulation since more than 8h were required for ≥85% of the PRX to be released. The increase of HPC viscosity associated with the higher molecular weight of HPC GF, impaired the release of the drug.

The dissolution profile is not comparable with the commercial formulation, despite the f2 factor being close to 50.

Conclusions

This work supports the **selection of the HPC LF polymeric matrix as the best option**, among those studied, **to manufacture 3D-printed PRX tablets by integrated HME-FDM**, as a therapeutic strategy in the treatment of psychiatric diseases. 3DP is proven to be capable of mimicking the drug release of commercial formulations with the added value of possible customization, according to the patient needs.

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References

1. Alomari, M.; Mohamed, F.H.; Basit, A.W.; Gaisford, S. Personalised dosing: Printing a dose of one's own medicine. *Int J Pharm* **2015**, *494*, 568–577.
2. Zhang, J.; Feng, X.; Patil, H.; Tiwari, R.V.; Repka, M.A. Coupling 3D printing with hot-melt extrusion to produce controlled-release tablets. *Int J Pharm* **2017**, *519*, 186–197.
3. Pereira, G.C.; Figueiredo, S.; Fernandes, A.I. Pinto, J.F. Polymer selection for hot-melt extrusion coupled to fused deposition modelling in pharmaceutics. *Pharmaceutics* **2020**, *12(9)*, 795.
4. Figueiredo, S.; Pinto, J.F.; Carvalho, F.G.; Fernandes, A.I. Tuning of Paroxetine 3D-Printable Formulations for Fused Deposition Modelling. *Med Sci Forum* **2021**, *5(1)*, 17.
5. U.S. Department of Health and Human Services. Guidance for Industry: Dissolution Testing of Immediate Release Solid Oral Dosage Forms. Food and Drug Administration. 1993, Rockville, MD.