

Proceeding Paper

# Tuning of Paroxetine 3D-Printable Formulations for Fused Deposition Modelling<sup>†</sup>

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**Abstract:** This work reports the preliminary development of paroxetine-containing formulations amenable to hot-melt extrusion coupled to fused deposition modelling-based 3D printing. Polymeric matrices were used alone, or added with processing enhancers (e.g., plasticizer and filler). The polymeric formulation containing paroxetine (30% *w/w*), hydroxypropylcellulose (54% *w/w*) and excipients (16% *w/w* of dicalcium dihydrate phosphate, magnesium stearate and triethylcitrate; 10:1:5 ratio) exhibited the most suitable behaviour to be extruded and 3D printed, proving that adjuvants are critical to ensure processing of the formulations.

**Keywords:** extrudability; filament; printability; 3D-printed tablet; fused deposition modelling (FDM); hot melt extrusion (HME); paroxetine (PRX)



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## 1. Introduction

Three-dimensional printing (3DP) has been the subject of an exponential interest in pharmacy by overcoming challenges of traditional manufacturing processes and allowing the production of patient-centric dosage forms [1]. Fused Deposition Modelling (FDM), the most widely used 3DP technique, requires the production of a drug-containing thermoplastic polymeric 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 [2].

The successful coupling of these two technologies depends on the concurrent extrudability of the raw materials and the printability of the filaments (FIL) obtained by HME, properties which are influenced by mechanical, rheological and thermal properties of materials [3]. Based on the selection of formulation and processing conditions, this work reports the preliminary development of 3D-printable formulations containing paroxetine (PRX) for HME coupled to FDM 3DP.

## 2. Materials and Methods

PRX (Lusifar, Lisbon, Portugal) was selected as a model drug; methylcellulose (MC) and hydroxypropylcellulose (HPC; HPC<sup>TM</sup> LF and HPC<sup>TM</sup> GF Pharm, Ashland Inc., Schaffhausen, Switzerland) and Soluplus<sup>®</sup> (SLP; Polyvinyl caprolactam-polyvinyl acetate-polyethylene glycol graft co-polymer, BASF, Ludwigshafen, Germany) were used as matrix-forming polymers. Dicalcium dihydrate phosphate (CaP) (Budenheim, Budenheim, Germany), magnesium stearate (MgSt) (Roic Pharma, Barcelona, Spain) and triethylcitrate (TEC) (Sigma Aldrich, Darmstadt, Germany) were used as adjuvants (F1-F8; see Table 1).

**Table 1.** Development and preliminary evaluation of PRX-based formulations regarding extrudability and printability in HME coupled to FDM 3D printing.

	Formulation Components (% w/w)							PRX	Extrudible <sup>1</sup> Temp. (°C)/Speed (rpm)	Printable <sup>1</sup> Temp. (°C)
	HPC GF	HPC LF	MC	SLP	CaP	MgSt	TEC			
F1	60	-	-	-	-	-	-	40	Yes (140/20)	No <sup>2</sup>
F3	-	-	-	60	-	-	-	40	Yes (160/20)	No <sup>2</sup>
F4	55	-	-	-	-	-	15	30	Yes (150/20)	No <sup>3</sup>
F5	-	55	-	-	-	-	15	30	Yes (150/20)	No <sup>3</sup>
F6	-	-	-	55	-	-	15	30	Yes (130/20)	No <sup>3</sup>
F7	54	-	-	-	10	1	5	30	Yes (120/10)	Yes (200/50)
F8	-	54	-	-	10	1	5	30	Yes (120/10)	Yes (200/50)

<sup>1</sup> Extrudability and printability represent the ability of the powder physical mixture and FIL to be successfully extruded and printable by HME and FDM 3DP, respectively. <sup>2</sup> High formulation viscosity and FIL too brittle. <sup>3</sup> FIL too pliable.

3D-printed tablets (TAB) containing PRX were prepared under the processing conditions described in Table 1, by combining HME (Notzek Pro single screw extruder, Notzek, Shoreham, UK) and FDM (3D printer Delta WASP 20 40 Turbo 2, Wasp, Massa Lombarda, Italy) technologies. Extrudability and printability of the different formulations were evaluated.

### 3. Results and Discussion

For the preliminary development of PRX-based formulations suitable for HME coupled to FDM 3DP, cellulose-derived polymers, such as MC (Tg = 184–197 °C) and HPC (Tg = 105 °C), and Soluplus® (Tg ≈ 70 °C) were selected [3]. The formulation containing MC (F2; Table 1) was the only unable to be extruded into FIL, since it requires higher temperature (>180 °C) and was thus excluded. The other polymers were successfully extruded by HME. Yet, these polymeric matrices generated non-printable FIL precluding FDM 3DP, due to surface irregularity and non-uniformity of diameter (closely related to the high viscosity of the formulation), thus preventing printer feeding. Mechanical properties of FIL proved to be inapt for 3DP since they were too brittle, rupturing inside the printing head, due to the forces applied by the extruding gear, which was ultimately responsible for blocking the printer.

3DP ability is directly influenced by the materials' properties [3] and processing conditions may be enhanced by addition of adjuvants. First, a plasticizer (TEC; 15% w/w) was used to reduce the polymer Tg and allow gentler HME temperature (F4-F6). Though obtained at lower temperatures, FIL were unable to be printed into TAB due to high ductility. Over-plasticization of the FIL caused permanent deformation along the printing head and feeding defects (mainly for F6, so SLP use was discontinued). To address this issue, TEC was decreased and replaced by the same amount of a filler (CaP). In turn, a small quantity of MgSt was added (F7-F8) to improve rheological properties of FIL. These HPC formulations were successfully extruded in PRX-loaded FIL apt to print TAB.

Fine tuning of formulations is proved crucial for optimal extrudability and printability.

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**Conflicts of Interest:** The authors declare no conflict of interest.

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