Advantages of combining cellulosic polymers and lipids in extruded 3D printing filaments. Part II: 3D printing (FDM) and printlets characterization

Vanessa Havenith[(1)], Ceren Yuece[(2)], Elsa Gattefossé[(3)], Veronique Henner-Kulkarni[(1)]

[1] SE Tylose GmbH & Co. KG, Kasteler Str. 45, 65203 Wiesbaden, Germany
[2] Thermo Fisher Scientific, Pfannkuchstr. 10-12, 76185 Karlsruhe, Germany
[3] Gattefossé, 36 chemin de Genas, 69804 Saint-Priest, France

Introduction

Fused Deposition Modeling (FDM) 3D printing is transforming pharmaceutical research by enabling personalized dosage forms and doses tailored to patient-specific factors such as age, height, disease state, and genetic influences on drug bioavailability.

Hot-melt extrusion (HME) is key to filament preparation for 3D printing. In the first part of this study (1), we demonstrated that adding lipids to low-viscosity Hypromellose at 100°C reduces processing temperature while preserving filament properties.

This poster presents the second part of the study: Various combinations of lipid excipients and TYLOPUR® 605 (Hypromellose 2910) were extruded, printed with an active pharmaceutical ingredient (API), and comprehensively characterized.

Materials

Two lipid excipients from Gattefossé (Saint-Priest, France) have been tested: Labrasol® (caprylocaproyl macrogol-8 glycerides EP), Gelucire® 48/16 (macrogol-32 stearate (type I) EP). TYLOPUR® 605 (5 mPas viscosity, 2% in water), a low-viscosity HPMC from SE Tylose GmbH &Co. KG (Wiesbaden, Germany) was tested due to its optimal printing property.

The API Acetaminophen, dense powder was supplied from Anqiu Lui'An Pharmaceutical CO., LTD. (Anqiu City, China).

Table 1: Sample compositions

Formula code	Acetaminophen (%w/w)	TYLOPUR® 605 (%w/w)	Gelucire® 48/16 (%w/w)	Labrasol® (%w/w)	Extrusion temperature (°C)
#3a	30	65	5	0	100
#3b	30	65	5	0	120
#7a	30	65	0	5	100
#7b	30	65	0	5	120
#10a	30	70	0	0	100
#10b	30	70	0	0	120

Methods

The formulations are described in Table 1.

Filaments were produced on a Pharma 11 twin-screw extruder (Thermo Fisher Scientific™, Karlsruhe, Germany) with a target diameter of the filaments of 1.75 mm which was controlled with the Thermo Scientific™ CaliCut post-extrusion system.

3D printing was performed on MakerBot Replicator 2X experimental 3D printer from UltiMaker with those parameters mentioned in Table 2.

Dissolution tests were conducted using a USP Apparatus 1 (basket method, n = 6) operated at 100 rpm in 900 mL of purified water, with absorbance measured at 242 nm for Acetaminophen.

X-ray test performed on a BRUKER AXS (D8-ADVANCE) powder diffractometer. Measurements taken from 5°-50° in 0.02° steps in 2Θ.

Table 2: 3D printing parameters

Parameter	1st trials
Printing temperature (°C)	180 – 190°C
Platform temperature (°C)	25
Infill (%)	75
1st layer printing speed (mms^{-1})	10
Infill printing speed (mms^{-1})	90
Traveling speed (mms^{-1})	150
Infill layer height (mm)	0.1
Shell thickness (mm)	0..2
Printing time (min)	~2
Printing structure	honeycomb
Printlet size (mm)	d-6; h-3
Printlet weight (mg)	84 to 105

Results and Discussion

3D printing

Filaments with 10% of lipids (see part I (1)) could not be 3D printed due to the elasticity and softness: they slipped through the gears of the printer. Filaments with 5% of lipids could successfully be printed.

The 3D printlets exhibited a uniform cylindrical shape with a slightly rough but homogeneous, layered surface characteristic (see Figure 1).

Printing temperature could be reduced with Labrasol® in the same way as the temperature could be reduced in the HME, for Gelucire® 48/16 it was not visible. The mean weight of the printlets for formulations 3a, 3b, and 7a was approximately 100 mg, whereas formulation 7b weighed about 85 mg.

This difference in weight influenced the total release profile of Acetaminophen (Figure 3B).

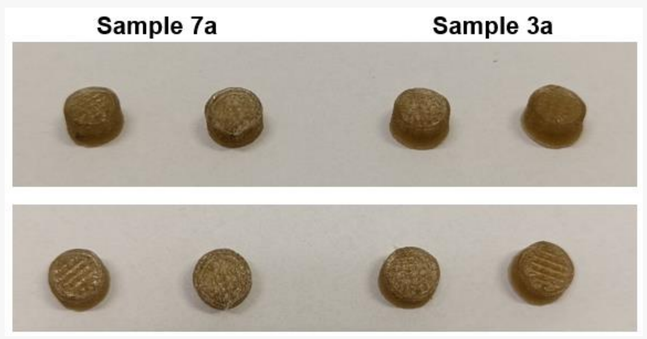

Figure 1: METT images of FF and NIF ASD-discs with different polymers and drug loads in 0.3 ml phosphate buffer (pH 6.8). Erosion time 60 min.

X-ray results

X-ray diffraction analysis was conducted on samples 3a, 3b, 7a, and 7b to determine the physical state of the active pharmaceutical ingredient. The resulting diffractograms are presented in Figure 2A. The data indicate that Acetaminophen remained in an amorphous state across all formulations, even after six months of storage in a closed container at room temperature (Figure 2B). These findings demonstrate that the extrusion and 3D printing processes successfully produced amorphous solid dispersions with notable long-term stability.

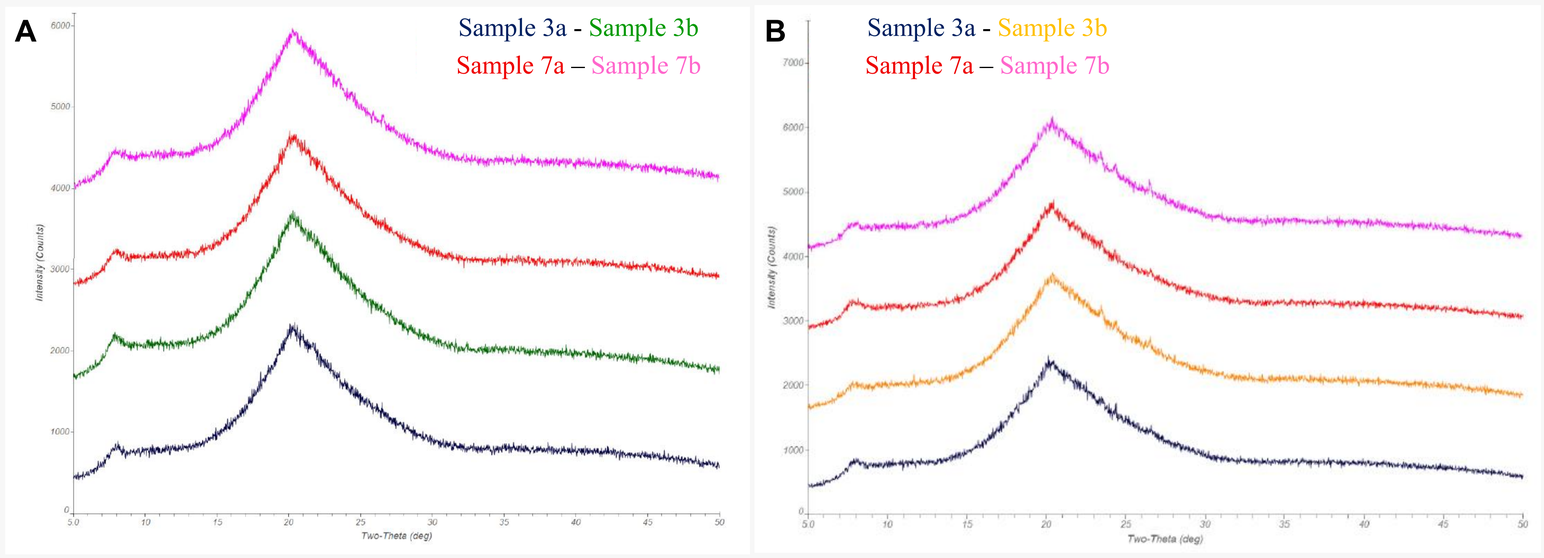

Figure 2: A) Samples 3a, 3b & 7a, 7b initial X-ray spectra. B) Samples 3a, 3b & 7a, 7b X-ray spectra after 6 month of storage in a closed container at room temperature.

Dissolution test of 3D printlets

The impact of 3D printing and lipids addition are represented in Figure 3 A and B. Due to the bioavailability enhancement property, the incorporation of 5% (w/w) Labrasol® appears to enhance the dissolution of Acetaminophen in the filaments compared to both lipid Gelucire® 48/16 and lipid-free formulations (Figure 3A).

However, the 3D printing process results in reduced dissolution kinetics, likely due to the formation of a denser structure exhibiting increased gelation behavior (Figure 3B). This denser matrix slows the release of the API relative to the non-printed filaments. Nevertheless, the positive effect of lipid Labrasol® on accelerating dissolution is also evident in the corresponding 3D printlets.

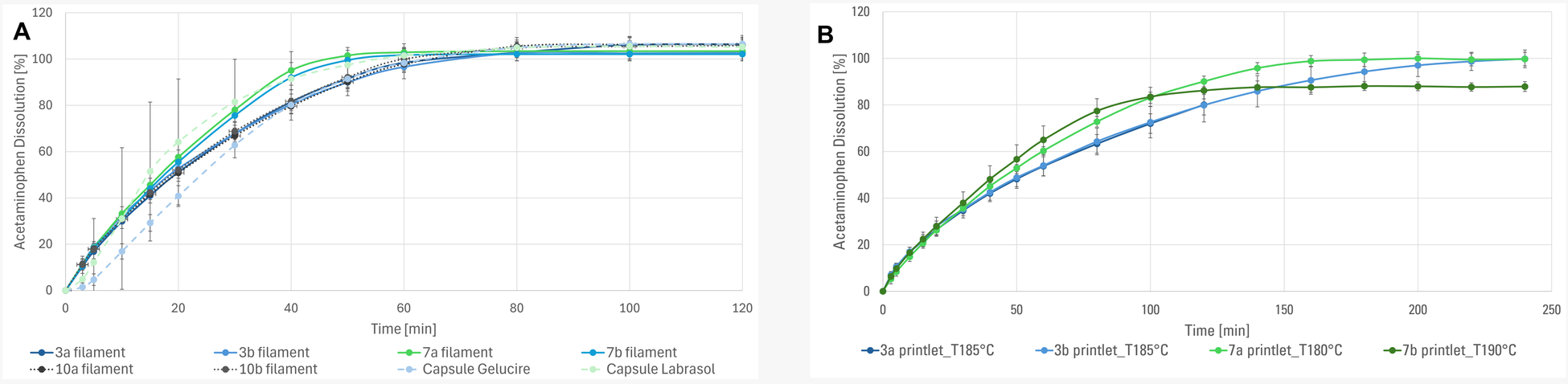

Figure 3: A) Acetaminophen dissolution of HME-filaments with and without plasticizer in purified water at 37° C. Capsules were filled with API, HPMC and plasticizer and measured in the same way as the filaments. B) Acetaminophen dissolution of 3D printlets with plasticizer in purified water at 37° C.

Summary

Three-dimensional printing (3DP) of Acetaminophen formulations was successfully accomplished. The incorporation of a plasticizer did not affect so much the 3DP processing temperature; however, a clear influence was observed during hot-melt extrusion (HME) (1).

The findings demonstrate that the increased density of the printlets leads to a reduced dissolution rate of Acetaminophen, attributed to the formation of a gel-like diffusion barrier during dissolution. Future studies will aim to optimize the dissolution profile to improve drug release characteristics to obtain immediate release with Acetaminophen besides a different API (BCS IV).

References

1. Advantages of combining cellulosic polymers and lipids in extruded 3D printing filaments. Part I: impact of lipids on processability – P. Caisse *et al* – ECP poster 2025.