3D-Printing of paracetamol tablets by fused deposition modelling

Gabriela G. Pereira[1], Ana I. Henriques[1], Ana I. Fernandes[2], Inês A. Santos[2], João F. Pinto[1,*]

[1] iMed.Ulisboa, Faculdade de Farmácia, Universidade de Lisboa, Avenida Professor Gama Pinto, P-1649-003 Lisboa, Portugal
[2] CiiEM, Instituto Universitário Egas Moniz, Campus Universitário, Quinta da Granja, Monte de Caparica, P-2829-511 Caparica, Portugal

jfpinto@ff.ul.pt

Introduction

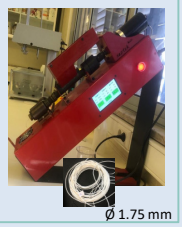
3D printing technology (3DP) offers the greatest potential to revolutionize the future of pharmaceutical manufacturing. Of the many techniques available, fused deposition modelling (FDM) has been the most used technique supporting the potential of the technology to prepare unit dosage forms[1]. FDM is a technique based on the deposition of successive layers of thermoplastic materials after softening / melting[2]. The challenges related to the use of the technique are mainly related to the scarcity of adequate filaments composed of pharmaceutical grade materials (e.g. polymers with appropriate characteristics) and processing related parameters (e.g. moisture exposure and content) that besides extrusion, enable printing[3].

This study was designed to develop and manufacture 3D printed tablets containing paracetamol (as a model drug) by FDM.

Materials and Methods

Paracetamol-loaded filaments production
- HME -

Notzek Pro, single screw extruder



Ø 1.75 mm

3D-printing of cylindrical tablets
- FDM -

DeltaWASP 2040 Turbo 2

Processing parameters
- Extrusion temperature (200°C)
- Extrusion rate (20mm/s)
- Printing speed (150mm/s)
- Layer height (0.50mm)
- 100% infill

Storage stability
- Desiccators -

Tablet evaluation
- Dimensions
- Mass
- Drug content (UV)
- DSC
- XRPD

Table 1: Composition (%) of the mixtures used to produce filaments

	HPC	Soluplus	MgSt	Paracetamol
M1	54.0	15.0	1.0	30.0
M2	40.0	9.0	1.0	50.0
M3	54.0	14.0	2.0	30.0
M4	39.5	8.5	2.0	50.0
M5	52.5	12.5	5.0	30.0
M6	37.5	7.5	5.0	50.0

Results and Discussion

Paracetamol-loaded polymeric filaments (F1-F6) were successfully prepared by hot-melt extrusion (HME) from mixtures M1-M6 (Table 1).

Five from the six filaments could be printed using FDM to produce the 3D printed tablets, whose properties, such as mean mass, diameter and thickness are shown in Table 2.

Table 2: Properties of the 3D printed tablets

Tablets	Mass (mg)	Diameter (mm)	Thickness (mm)	Drug content (%)
T1	658 ± 48*	5.91±0.07	2.50±0.022	94.36 ± 2.35
T2	871 ± 61	5.97±0.04	3.00±0.014	95.70 ± 3.01
T3	295 ± 30*	5.95±0.05	1.50±0.014	104.13 ± 2.14
T4	821 ± 54	5.96±0.04	3.00±0.017	95.15 ± 2.20
T5	809 ± 47	5.98±0.02	3.00±0.029	97.08 ± 0.98

*tablets printed smaller for dose adjustment; n=10 for mass and dimensions; n=3 for drug content

Figure 1 presents the thermal events observed for the products obtained: physical mixtures (M1-M6), HME filaments (F1-F6) and the 3D-printed tablets (T1-T5). Mixtures containing higher drug fraction show the endotherm for paracetamol, which decreased or was absent in the filaments. Heat used in the manufacture of the latter has contributed to the production of the amorphous solid dispersions of paracetamol in the polymers. This was particularly evident when paracetamol was in a low fraction and polymers in high fractions in the formulation.

When tablets presented endotherms, they could be related to paracetamol that had suffered some degree of plasticization. Noteworthy is that FDM printing promoted instability of the amorphous dispersions.

Figure 2 shows the diffractograms of the different products complementing the data collected from the calorimetric studies and emphasizing the effect of heat on the production of amorphous tablets.

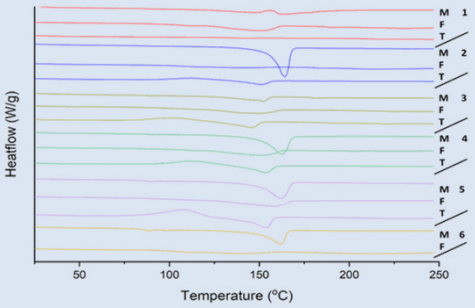


Figure 1: Thermograms from physical mixtures (M1-M6), filaments (F1-F6) and 3D-printed tablets (T1-T5)

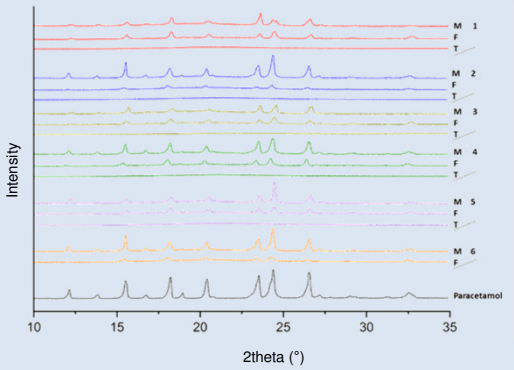


Figure 2: Diffractograms from physical mixtures (M1-M6), filaments (F1-F6) and 3D-printed tablets (T1-T5)

Conclusions

- The paracetamol-loaded filaments obtained by extrusion were successfully produced with appropriate characteristics for use in FDM 3DP.
- The use of heat in the production of both filaments and 3D-printed tablets promoted the production of amorphous dispersions.
- The combination of polymers and stearate improved the extrudability of the physical mixtures with Soluplus appearing to provide better amorphous systems than HPC.
- The processes still requires optimization, namely to reduce mass and drug content variation.

References

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*Member of: