3D printing by fused deposition modeling of capsular devices for oral pulsatile release based on swellable/erodible polymers

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Purpose

To prepare swellable/erodible capsular devices for oral pulsatile release via 3D printing by Fused Deposition Modeling (FDM), starting from in-house produced filaments based on hydroxypropyl cellulose (HPC), and to explore the prototyping ability of the developed FDM process for the manufacturing of such devices by injection molding (IM).

Methods

FDM was carried out in a MakerBot Replicator 2, developing computer-aided design (CAD) files and using HPC-based filaments prepared by hot melt extrusion (HME). Dried HPC (12h, 40°C) and its blends with polyethylene glycol 1500 (2-10%w/w) were extruded by a twin-screw extruder (Haake MiniLab II, Thermo Scientific) equipped with a rod-shaped die (ø 2.00mm); extruded rods were calibrated and rolled up on a spool using a purposely-designed device. IM was carried out in a micromolding machine (BabyPlast 6/10P, Cronoplast SL) equipped with a capsule-shaped mold. The release performance of capsules filled with 80mg of acetaminophen (n=3) was checked by an adapted disintegration apparatus (800mL distilled water, 37±0.5°C, 31cycles/min; spectrophotometer λ=248nm).

Results

3D printing relates to processes employed for the manufacturing of objects of almost whatever shape starting from CAD files and based on the addition of materials layer by layer. In particular, FDM consists in the deposition of a thermoplastic polymer/polymeric blend, supplied in the form of a filament, in a semi-molten state to fabricate the desired item.

HPC-based filaments with appropriate cross section and diameter (1.75±0.05mm) needed to be prepared. A twin-screw extruder was coupled with an aluminium rod-shaped die and a pulling/calibrating device in-house produced. After adjusting the process parameters (e.g. screw and motor speed, extrusion temperature) suitable filaments to be loaded in the 3D printer MakerBot Replicator 2 were obtained. Not only the dimensions but also the mechanical characteristics of filaments were proved to affect the printer feeding. The plasticizer content in the HPC-based filaments was progressively reduced and a neat HPC filament was also prepared.

By developing suitable CAD files and adjusting printing parameters (e.g. temperature) with respect to the standard configuration of the MakerBot Replicator 2, prototype bodies and caps were successfully prepared, that could be assembled in perfectly sealed capsular devices. An intrinsic expansion of the polymer was observed and taken into account by modifying CAD files and, consequently, printer parts (tip). Capsular devices containing a tracer drug showed the expected pulsatile-release performance characterized by a reproducible ≈70min lag phase and a complete liberation of the filling formulation within 10min.

3D printed HPC capsules and IM ones with analogous design and composition were demonstrated in terms of weight, wall thickness, break-up behavior in aqueous fluids and release performance (Images 1, 2).

Conclusion

HPC based filaments suitable for FDM were produced and exploited to print swellable/erodible capsular devices with the desired pulsatile release performance. The application potential of FDM in real-time prototyping of IM processes was assessed.

CAD FILE		PRODUCT		WEIGHT, mg (cv)		THICKNESS, µm (cv)		BREAK-UP BEHAVIOR	LAG PHASE, min (cv)
cap	body	cap	body	cap	body	cap	body		
				102.07 (3.24)	129.07 (1.25)	709 (6.55)	717 (8.89)		68.5 (4.30)

Image 1: HPC capsular devices prepared by FDM: CAD files and main characteristics of printed prototypes

MOLD	PRODUCT		WEIGHT, mg (cv)		THICKNESS, µm (cv)		BREAK-UP BEHAVIOR	LAG PHASE, min (cv)
	cap	body	cap	body	cap	body		
			110.31 (0.37)	122.50 (0.17)	701 (3.32)	712 (8.60)		71.2 (16.32)

Image 2: HPC capsular devices prepared by IM: mold and main characteristics of molded prototypes