Stereolithographic (SLA) 3D Printing of Oral Modified-Release Dosage Forms
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Purpose
3D printing (3DP) is becoming an increasingly popular technology that provides the ability to fabricate structures of precise geometries. Stereolithography (SLA) is a type of 3DP technology in which the production of the object is based on the solidification of a liquid resin by photopolymerization. To our knowledge, there has been no demonstration on the use of SLA printing to manufacture drug-loaded oral dosage forms. Here, we manufactured drug loaded tablets by SLA with two model drugs (acetaminophen and 4-ASA) and evaluated the drug release profiles.

Methods
Polyethylene glycol diacrylate (PEGDA) and Polyethylene glycol (PEG) 300 were mixed in ratios of 90:10, 65:35 or 35:65 (v/v) with a photoinitiator at a concentration of 1% (w/v). Acetaminophen or 4-ASA was then added to the solution to a concentration of 5.9% (w/w).

Tablets were fabricated with a commercial Form 1+ SLA 3D printer (Formlabs Inc, USA). The selected 3D geometry was a torus, 11mm diameter x 4mm height, with a central hole of 3mm diameter.

Drug release from the 3DP tablets was determined in a USP II apparatus (Pharmatest, Germany) simulating the environment conditions of the fasted GI tract. Briefly, the tablets were placed for 2 h into 900 mL of 0.1 M HCl, which simulates gastric residence time, and subsequently into 950 mL of modified Hanks based dynamic physiological dissolution medium for 35 min (pH 5.6 to 7), which is converted by addition of 50mL of solution in 1000 mL of modified Krebs buffer (pH 7 to 7.4 and then to 6.5). The physiological buffers were pH controlled by an Auto pH™ system.

Results
The 3D printer was found to produce tablets with a high degree of repeatability of weight and physical dimension, difficult to manufacture by conventional production techniques. Drug loading of the tablets was similar to the theoretical drug loading, indicating no drug was degraded during the 3D printing process.

Dissolution tests conducted in a dynamic in vitro model, which simulates conditions of the GI tract, show that drug release commences in the gastric phase and continues during the intestinal phase for all formulations. Drug release is not affected by the pH of the media. Changes in the ratios of PEGDA/PEG play an important role in drug release rates, formulations with lower percentage of PEGDA showed faster release rates.

Conclusion
We have demonstrated the feasibility of using SLA 3DP to fabricate drug-loaded tablets and have shown that the release profiles obtained can be modified by careful selection of the composition of the tablet. SLA printing shows no drug degradation and so offers an alternative route to produce tablets incorporating thermo-sensitive drugs.

SLA 3D printing may be considered as an appropriate method to manufacture modified-release oral dosage forms, for industrial production or even for personalised dose.