Selective Laser Sintering (SLS) 3D Printing of Medicines
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Purpose
3D printing is a new promising technology that allows the production of 3D objects, layer by layer, in three dimensions. Some 3D printing technologies have already been employed to produce personalized oral dosage forms containing drug, however, selective laser sintering (SLS) has not yet been investigated to produce drug loaded oral dosage forms due to the high energy input of the laser that might degrade the drug. The aim of this study was to manufacture immediate release 3D printed tablets (printlets) by SLS printing technology using a pharmaceutical grade excipient and three different drug loadings to evaluate the drug release properties. Potential drug degradation during the printing process was also evaluated.

Methods
Paracetamol USP grade (Sigma-Aldrich, UK) was used as a model drug. The polymer Kollicoat IR (BASF, Germany) was investigated. Candurin® gold sheen colourant (Merck, Germany) was employed to increase the powder absorbance of the laser of the printer. Mixtures of polymer, drug (5, 20 or 35% w/w) and colourant (3%w/w) were prepared with mortar and pestle. A new type of selective laser sintering (SLS) desktop 3D printer Sintratec Kit (Switzerland) using a blue diode laser was employed to fabricate the oral dosage forms. The selected 3D model was a cylinder 10 mm diameter x 3.6 mm height. Five printlets were printed at the same time.

Determination of the drug content of the printlets was obtained by HPLC. A high-resolution X-ray micro computed tomography scanner (SkyScan1172, Bruker-microCT, Belgium) was used to 3D visualize the internal structure, density and porosity of the printlets.

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
SLS 3D printer was found to produce printlets with a good degree of repeatability of weight and physical dimensions. Drug loading results for the 5, 20 and 35% theoretical drug loading formulations showed drug contents of 4.9%, 20.4% and 35.7 respectively, all of which are very close to the theoretical drug loadings. No other peaks other than paracetamol were present in the HPLC chromatograms, indicating that drug degradation did not occur during printing.

Dissolution tests conducted in a dynamic in vitro model, which simulates conditions of the GI tract, showed that drug release commenced during the gastric phase and was not affected by the pH of the media, indicating that the formulations were pH independent. Increasing drug content leads to more sintered/melted and less porous printlets that will require longer time to dissolve. These data confirm that it is possible to manufacture 3D printed oral dosage forms by SLS 3D printer using a pharmaceutical grade excipient with immediate release characteristics.

Conclusion
In this study, SLS 3D printer technology was successfully employed to produce oral dosage forms based on a pharmaceutical grade excipient with different dissolution profiles and without degradation of the drug. These results suggest SLS 3D printer can be used to make medicines, therefore widening the number of 3D printing technologies available to fabricate personalized medicines.