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The Application of 3D Printing in the Formulation of Personalized Drug Delivery Systems

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1. Introduction

the interest toward additive manufacturing is growing considering the formulation of personalized medicines [1]. 3D printing is commonly an additive process, which results in various layer-by-layer built objects. A vast number of methods are available beyond 3D Printing but there are only few of them which can be employed for tailored pharmaceutical manufacturing (e.g. Photopolymerization, Selective Laser Sintering (SLS) and Fused Deposition Modelling (FDM)) [2]. During these methods the number of unit operations is minimized, and the opportunity to fabricate every single printlet shaped according to the individuals' profile with only minimal human intervention can be the cause of the increased research activity in this field [3]. The additional benefit of this type of manufacturing is the capability of producing customized ways of medication for pediatrics, geriatrics and patients suffering from organ dysfunctions, avoiding the slightest chance of reaching toxic doses in their body. Several types of dosage forms were previously microfabricated including floating systems, pulsatile drug release tablets and zero-order release forms [4]. The first 3D printed orodispersible tablet was approved by the FDA in 2015.[5]

The objective of our study was to design and print biodegradable drug delivery systems. Commercially available filament materials were screened as well as the print settings were optimized. In addition, the influence of design parameters including wall thickness, morphology, number and size of pores on the drug delivery in case of model drugs was investigated. Moreover, the applicability of matrix polymers and gelling agents in the process of 3D printing was studied. There were some formulations aiming the study of dose proportionality, in order to expand the opportunities of personalized medication.

2. Materials and methods

the cylindric polygon models were designed with Autodesk® Fusion 360 (USA) and the objects were sliced with Ultimaker Cura 3.6 (Netherlands). After the design, an FDM printer (Creality Ender 3, China) equipped with 0.4 mm aluminium nozzle was used to print the objects. From the wide range of commercially available biodegradable filaments the water-insoluble polylactic acid (PLA) and the soluble polyvinyl alcohol (PVA) based filaments were chosen with several additives (e.g. PEG). The investigated printing parameters were the following: temperature of the extruder, bed temperature, printing speed, cooling fan performance, layer height and infill.

The dissolution profile of the model drug was examined in different pH media (1.2; 4.5; 6.8) recording also the particle size distribution of solid filaments.

Table 1 The critical print settings and the applied ranges

Print setting	Examined range
Nozzle temperature	170-250 °C
Bed temperature	50-110 °C
Print speed	5-40 mm/s
Cooling performance	30-100 %
Layer height	0.20-0.28 mm
Infill	0-100%

3. Results

as a result of this study, morphology of PLA and PVA based carriers were optimized via digitally enhancement and the proper print settings. According to the biorelevant dissolution studies, the PVA based printlets form colloidal dispersion in aqueous media without reference to H⁺ concentra-

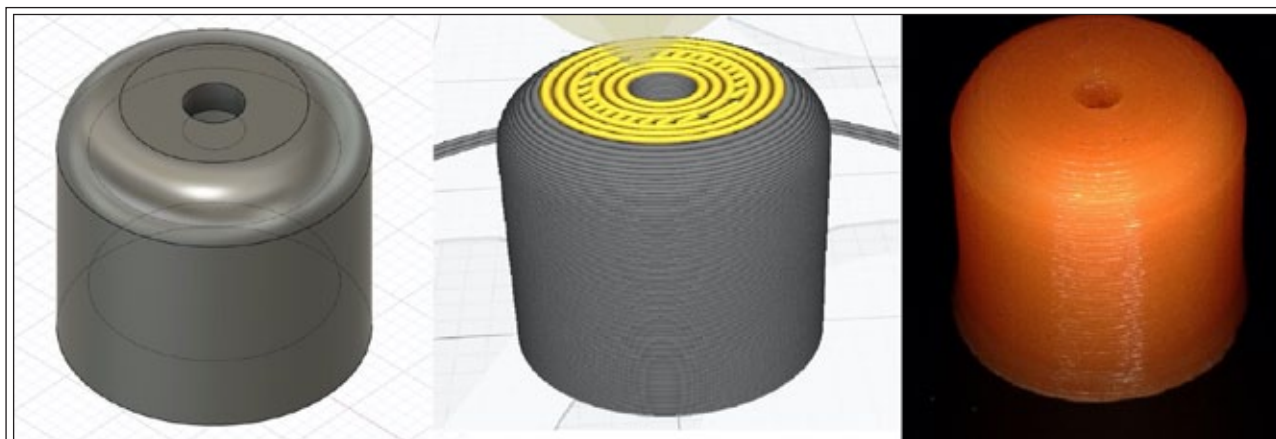


Figure 2 The three basic step of digital enhancement and printing of a CAD designed object



Figure 2 The PVA (white) and PLA (orange) filaments and the end-product carriers

tion. The drug release was significantly influenced by the morphology and layer characteristics of the carriers, the presence and number of pores and other excipients.

3. Conclusions

These adjustable properties lead to wide range of opportunities to precisely tailor the release profile of 3D printed drug delivery systems. The digital enhancement of the traditional pharmaceutical technology may offer better pharmacokinetic pro-

files specially formulated for the patient. The kinetic analysis of the dissolution data needs an approach involving dose proportionality calculations.

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