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Abstract

Concept for a new 3D printing technique for multiple unit particle systems

L. R. Oldfield[1*], T. Auel[1], and A. Seidlitz[1]

[1] *Institute of Pharmaceutics and Biopharmaceutics, Heinrich-Heine-University, Düsseldorf, Germany*
[*] *Corresponding author, email: lee.oldfield@hhu.de*

Multiple unit particle systems (MUPS) are oral dosage forms often consisting of small pellets compressed into tablets. Those tablets rapidly disintegrate inside the stomach into small particles. Because of the small particle size (< 2 mm) they can pass the pylorus independently of the stomach contents. In contrast to monolithic non-disintegrating tablets, this may accelerate the emptying from the stomach, potentially leading to altered drug absorption kinetics [1]. However, the availability of marketed MUPS products is limited due to high production costs and the complexity of the manufacturing process. Conventional manufacturing of MUPS tablets includes a compression step that can damage the pellets and therefore might alter the pharmacokinetics [2]. To address these challenges, we propose a novel manufacturing approach for MUPS tablets using 3D fused deposition modeling (FDM) printing. This technique eliminates the need for compression. Additionally, FDM printing offers high flexibility and the ability to tailor medications to individual patient needs [3].

Our study implemented a dual extrusion process using commercially available polyvinyl acetate (PVA) and polylactic acid (PLA) filaments with an Ultimaker S3 FDM printer. Because of the printers two print heads we were able to load one print head with a water-soluble PVA filament and the second print head with a water-insoluble PLA filament. The printing process included two different printing steps. The water-soluble tablet shell was printed with the first print head, while the second print head subsequently incorporated the water-insoluble model particles. During the printing process, it was crucial to maintain a minimum distance between the particles to avoid collisions with the print heads and previously printed particles. We observed that particles tended to connect with each other when the print heads came into contact with them during printing, resulting in remelting of the PLA material and dragging it to the next particle. This phenomenon is unfavorable for the application of MUPS tablets as the connected particle aggregates were bigger than 2 mm and theoretically might not pass the pylorus in case of a fed state of the patient. However, by improving the printing process and the tablet design, we successfully printed 196 individual 1.4 mm small particles. The computer model of the tablet had a size of 22.6 x 8.5 x 6.0 mm. In future work, we plan to incorporate active pharmaceutical ingredient(s) (APIs) into the particles and fabricate pharmaceutical grade filaments by using hot-melt extrusion. Our findings demonstrate that FDM printing holds promise as a new manufacturing method for MUPS tablets, offering potential benefits in dose adjustment and personalization of medications. By modifying the tablet's height, size, or infill, the dose can be tailored to meet the specific needs of individual patients, such as low doses for paediatrics.

AUTHOR'S STATEMENT
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