Application of 3D printing in the formulation of solid pharmaceutical dosage forms for oral use with modified-release

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01 INTRODUCTION

The 'one size fits all' is a standard practice used in the pharmaceutical industry [1,2]. However, scientific progress is increasingly influencing the application of the completely opposite concept of 'personalized medicine' that takes into account the interindividual characteristics of patients. 3D printing, or additive manufacturing, is a new technology that fits into the framework of 'personalized medicine', given that it has shown promising characteristics in the development of solid dosage forms. One of the critical parameters for the success of personalized therapy for the patient relates to control over drug release profiles. Modified-release pharmaceutical forms include pulsatile-, extended-, and delayed-release formulations [3]. These formulations aim to reduce the dose, side effects, and increase compliance and efficacy. Utilizing the layer-by-layer fabrication process, 3D printing allows control of the parameters important for modification of the drug release profiles.

The aims of this research were to demonstrate the possibilities of 3D printing in the development of modified-release pharmaceutical formulations for oral use; as well as to present examples of 3D printing applications, focusing on examples published in the scientific literature, and investigational drugs approved by FDA for clinical testing.

02 METHODS

Data were collected by searching the Google Scholar and PubMed databases using the keywords '3D printed modified-release,' '3D printing,' '3D printing and formulations' and similar, as well as by analyzing the content of official websites of regulatory bodies. The methodology of this paper was based on a narrative review of the scientific literature through a search for these keywords.

03 RESULTS AND DISCUSSION

Among the most popular methods for producing solid pharmaceutical dosage forms using 3D printing are fused deposition modeling (FDM), stereolithography (SLA), semisolid extrusion (SSE), selective laser sintering (SLS), and powder-base 3D printing (PB), which can be seen in Figure 1. Depending on the 3D printing technology, modified-release can be achieved in different ways. Common factors across different 3D printing technique such as geometry, porosity, infill density, and the choice of excipients can play a key role in achieving modified-release of the active ingredient. As an example, higher infill density affects the slowing down of the release rate due to reduced porosity and surface area [4].

Xu et al, fabricated mini-sized oral pellets using SLA 3D printing [5]. The factors influencing the modified drug release from SLA-printed dosages include the size of the printed pellets and the presence of hydrophilic excipients such as polyethylene glycol 400. While larger pellets showed release influenced by both excipients and drug diffusion, smaller pellets allowed excipient-independent release, indicating that the drug release rate can be controlled solely by adjusting the pellet size.

In the study by Shaqour et al, 3D printing was applied to produce capsules containing ketoprofen-loaded pomegranate seed oil self-nanoemulsifying drug delivery systems. The release of the drug was influenced by the polymer used, capsule thickness, and the pH of the surrounding medium [6].

Given that the pediatric population represents a very specific group that often requires individualized therapy, Protopapa et al. applied 3D printing technology to produce mini-tablets with modified-release of hydrocortisone. Adjusting printing parameters such as temperature and pressure, along with varying the ratio of excipients Gelucire® 44/14 and Precirol® ATO 5, successfully modified the release profile of the active pharmaceutical ingredient [7].

A literature review revealed that there are three modified-release formulations of Triastek Inc. (T19, T20, and T21) that have received approval for clinical trials by the United States Food and Drug Administration (FDA), and were manufactured using 3D printing technology [8]. This represents a very important step towards implementing scientific practice into manufacturing, bringing innovative solutions to many patients and diseases.

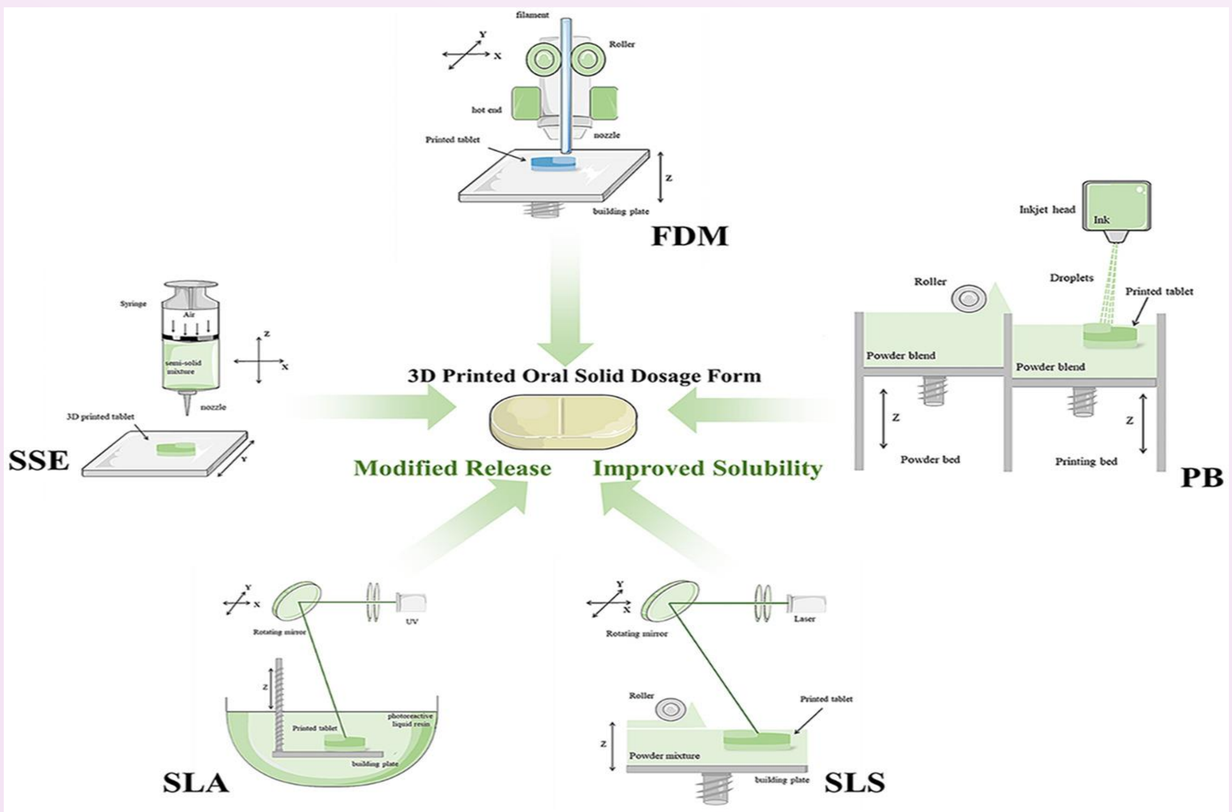

Figure 1. Main types of 3D printing technologies in production of solid oral dosage forms [4].

04 CONCLUSION

By combining different parameters such as polymer selection, infill density, geometric design, and various 3D printing technologies, it is possible to achieve modified-release of solid pharmaceutical dosage forms for oral administration. Various examples throughout the literature indicate the successful application of this technology to achieve the desired drug release profile. The start of approval of modified-release drugs obtained by 3D printing in clinical trials represents an important step towards personalized and patient-specific therapy.

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