



Made-on-demand, complex and personalized 3D-printed drug products

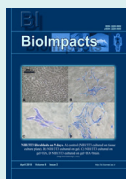
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Article Info



Article Type:
Editorial

Article History:

Received: 18 Jan. 2018

Accepted: 1 Mar. 2018

ePublished: 10 Mar. 2018

Keywords:

3D printing

Layer-by-layer fabrication

Made-on-demand drugs

Personalized medicines

Summary

Layer-by-layer fabrication of three dimensional (3D) objects from digital models is called 3D printing. This technology established just about three decades ago at the confluence of materials science, chemistry, robotics, and optics researches to ease the fabrication of UV-cured resin prototypes. The 3D technology was rapidly considered as a standard instrument in the aerospace, automotive, and consumer goods production factories. Nowadays, research interests in the 3D printed products have been raised and achieved ever-increasing traction in the pharmaceutical industry; so that, the first 3D printed drug product was approved by FDA in August 2015. This editorial summarizes the competitive advantages of the 3D printing for the made-on-demand, personalized and complex products, manufacturing of which establish opportunities for enhancing the accessibility, effectiveness, and safety of drugs.

Author's Biosketch

Professor Khosro Adibkia (Pharm.D., Ph.D.) is a Professor of Pharmaceutics in Tabriz University of Medical Sciences. He has received Ph.D. from Tabriz University of Medical Sciences in Pharmaceutics. He spent a six month (2007-2008) research fellow at Gent University in the field of Pharmaceutical Nanobiotechnology. He has authored over 100 publications in various areas of nanotechnology and pharmaceutics (H-index=19). He has also achieved outstanding research awards from Iranian Ministry of Health and Education. He is the winner of the Rhazes Research prize (one of the most valuable prizes in Iran) at 2008 as well. Furthermore, he has been selected as a Member of the Iranian National Elites Organization since 2008. In the recent years, he has focused on the preparation and physicochemical evaluation of novel drug delivery systems.



A controlled drug release behavior can be designed by drug delivery systems (DDSs) that enhance the safety and effectiveness of various drugs, providing patient compliance and convenience by establishing drugs with excellent distribution and absorption. Recent attempts in the drug delivery field included the development of targeted/smart DDSs,^{1,2} and formulations of DDSs with sustained-/controlled-release behavior(s).³⁻⁵ Different materials have been used in DDSs and the material inventory is continuously expanding especially in the targeted/ controlled delivery areas. In parallel with the advancement of new materials for DDSs, new procedures and techniques of material fabrication have been developed. This approach provides alternative methods for controlling the release behaviors by the controlled distribution of drugs within a given polymeric compound instead of designing another new host substance. Nowadays, numerous attempts have

been made to produce the 3D, from macro to nanoscale systems, made of thermoplastic⁶ and thermoset⁷ polymers; polyelectrolytes;⁸ hydrogels⁹ and powders¹⁰ that could be used in the tissue engineering¹¹; complex microfluidics devices¹² and DDSs.¹³ Various strategies have been used to accurately produce the 3D structures, including ink-jet deposition, material jetting, extrusion-based 3D printing, powder bed fusion, stereo-lithography (also known as photo-polymerization), pen-based 3D printing and 3D-printed molds. These techniques have widely been used in the pharmaceutical industry. Nevertheless, directed energy deposition, laminated object manufacturing and electro-spinning are examples of the methods that are not assembled with the 3D printing methods and are applied in drug product manufacturing.¹⁴

The 3D printing is a time-saving method with good flexibility and unique manufacturing abilities, which uses a computer-aided design (CAD) to produce drug



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products. In other words, layer-by-layer fabrication of the desired dosage forms is carried out based on a CAD model by using suitable drug materials.¹⁵ The 3D printing is discerned from the traditional manufacturing processes by three attributes, i.e., the complicatedness of product, individualization, and on-demand formulation. Unsurprisingly, these features impel the advancement of the 3D printed drug compositions.

Increase in the product complicatedness

Due to the possibility for a drug release behavior to be affected by a drug products structure, new opportunities are created in DDSs by manufacturing complex 3D structures. In this regard, the US FDA has approved a 3D printed drug (SPRITAM[®]) with an entire porous structure (bound powders without using compression), which permits a super fast disintegration of levetiracetam tablets (up to 1000 mg in seconds when taken with a sip of water).¹⁶ Dissolution rate enhancement strategies include high surface area objects printing¹⁷ and amorphous dispersions printing by hot melt extrusion-based printers.¹⁸ Potent active pharmaceutical ingredients may also be manufactured with advanced production options of the 3D printing methods. In addition to the ability to create immediate-release formulations using 3D printing, products with modified release behavior can be developed by these techniques. The complexity enhancement of the 3D printed products could critically control the drug targeting and release kinetics.¹⁹⁻²¹

Personalization

In comparison with the traditional processes, the 3D printing approach seems to simplify the personalization, in large part because the physical equipment modification is harder than the digital design modification. Besides, the automated 3D printing may have imperceptible operating costs. Briefly, individualized, multiple and small batches could be economically fabricated by the 3D printing process, including personalized implants medicines to improve the patients' compliance. In this way, the amount of delivered drug to a patient can be tailored based on the patient's metabolism and weight.²² Another aspect of dosing individualization is the multi-medication printing to bring together all medications of a patient into one daily dose.²³ Personalized drug administration considering population variation in the drug metabolism and patient anatomy have also stated by the researchers.^{24,25} Implants personalization and drug-loaded implants permit their printing that meet the patients' anatomical characteristics.^{26,27}

On-demand manufacturing

Products with various qualities can be produced by the 3D printer within minutes like a home ink-jet printer.²⁸ Public health could be beneficiaries of on-demand manufacturing via various methods, including direct printing of drugs onto the patients, printing timely or other resource

strained conditions (as for instances emergency rooms, disaster regions, ambulances, operating rooms, military operations and intensive care units), and low stability drugs printing for an urgent consumption.²⁹⁻³¹ While on patients printing seems to be imaginative, jetting and extrusion methods have been conducted to make the on-demand scaffolds and gels for the tissue engineering³⁰ and wound healing.³¹ The drug product formulation by the conventional methods need an automotive manufacturing techniques, while the 3D-printed products could be generated with minimum effort by a simple 3D printing system, which may enable faster formulation and optimization of a drug product during drug development.

In conclusion, the 3D printing as an automated layer-by-layer production method has the capability of producing on-demand, personalized and complex products. As discussed, researchers have innovated various 3D printing techniques to enhance the drugs efficacy, safety, and tolerability. The US FDA approved 3D-printed drug has proven the commercial and industrial feasibility of this technology. Finally, it should be noted that many health-related authorities encourage the development of science and technologies to establish manufacturing procedures (for instance, tablet printing) and complex dosage forms for improving clinical outcomes.

Ethical approval

Not applicable.

Competing interests

There is none to be declared.

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