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OVERVIEW OF 3D PRINTING TECHNOLOGY IN PHARMA INDUSTRY

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ABSTRACT

The pharmaceutical industry is advancing at an incredible rate. Novel drug formulations for targeted therapy have been developed all thanks to advances in modern sciences. Even so, the manufacturing sector of novel dosage forms is minimal, and the industry continues to rely on traditional drug delivery systems, particularly modified tablets. The use of 3D printing technologies in pharma companies has opened up new possibilities for printed products and device research and production. 3D Printing has slowly progressed from its original use as pre-surgical imaging templates and tooling molds to produce one-of-a-kind instruments, implants, tissue engineering scaffolds, testing platforms, and drug delivery systems. The most significant advantages of 3D printing technologies include the ability to produce small batches of drugs with custom dosages, forms, weights, and drug release profiles. The production of medicines in this manner could eventually contribute to the realization of the principle of personalized medicine. The biomedical industry and academia have also embraced 3D printing in recent years. It offers commercially available medical devices as well as a forum for cutting-edge studies in fields such as tissue and organ printing. This mini-review provides an overview of 3D printed technology in medicines.

KEYWORDS: 3D printing, drug delivery, manufacturing, modified tablets, implants.

INTRODUCTION

Three-dimensional printing (3DP) is a growing industry that has simplified, made accessible, and inexpensive rapid prototyping and small-scale manufacturing, and is utilized in the aerospace, automobile, biomedical, dental, defense and industrial, commercial, and consumable sectors.[1] There are several possible applications for 3DP, including ophthalmology, which can significantly affect the way patients are being treated in the future for different conditions.[2] 3DP medical applications are increasingly expanding and the health care sector is expected to revolutionize. The implementation of 3DP in medicine will bring many advantages, for example, the development and personalization of medical devices, medicines, and appliances; economic efficiency; improved productivity; democratic architecture and production; and strengthened cooperation.[3]

In a range of medical uses, including dentistry, anatomic models, medical instruments, tissue models and engineering skins, and medication formulations, 3DP technology is currently employed. To date, 3DP has been most commonly used for the dental market and the hearing aid industry. This may be because finished goods are small and need to be designed for patients, rendering these industries receptive to 3DP.[4] Figure 1 shows the different applications of the 3DP technology.

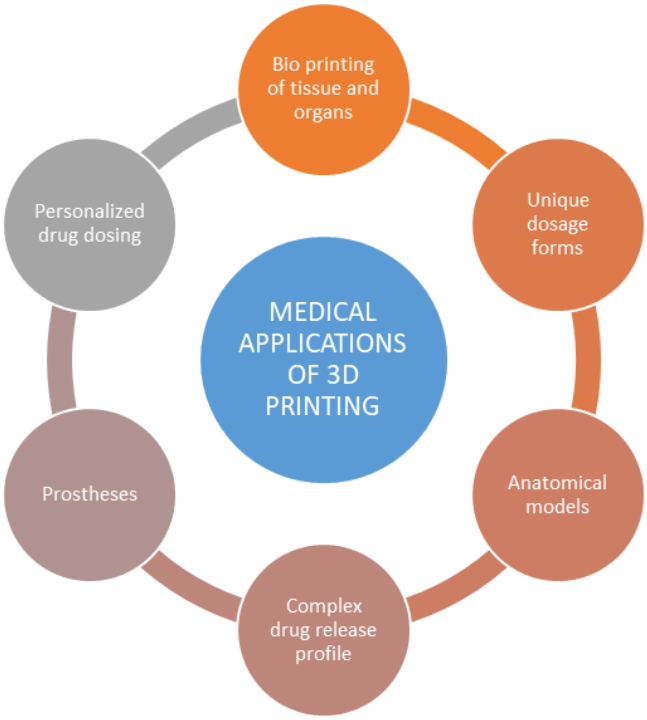

Figure 1: Medical applications of 3D printing technology.

3D PRINTING PROCEDURE

First, an object's simulated 3D modeling with applications of digital design, such as Onshape, Solidworks, Creo parametric, Autocad, Autodesk, etc

The digital model is then modified to the electronic file format (.STL) that stands for stereolithography or standard tessellation language

In terms of the surface of the 3D model (.STL) image, triangle facets provide detail

The.STL file has been transformed into G file, with the aid of specialized software slicer installed in a 3D printer which slices the design into a series of 2D horizontal cross-sections

The printer head can now be shifted to the base of the 3D object in the x-y axis. The print head will now shift into the z-axis, sequentially deposit the layers of the content you like, thereby producing a full 3D object

Maximum 3DP technology numbers are file format compliant (.STL). Few mistakes can arise when the 3D models are converted to a digital file.STL; tools such as Magics (Materialise) may be used to correct the mistakes during the conversion. STL has no detail about material type, color, texture, characteristics, and other characteristics.[5]

TYPES OF 3D PRINTING TECHNOLOGY

The processes traditionally used by the pharmaceutical industry such as milling, grinding, granulation, and compression often give rise to inconsistent finishing quality in accordance with factors such as drug packing, drug release, drug stabilisation and pharmaceutical dose stability. In contrast, 3DP has strategic advantages as a powerful tool technology such as increased efficiency of R&D, enhanced security, effectiveness and accessibility of medicines.[6] 3DP technologies are the most widely used in medical applications. A short discussion continues on each of these technologies:

I. Inkjet Printing System

In this system, in regard to pharmaceutical application the solutions of drug in place of ink and sheets of palatable material in place of general paper are used.[7] It further is classified into continuous inkjet (CI) and drop-on-demand (DOD) printing.

II. Continuous Inkjet (CI) printing

In this case, ink circulates via opening of size fifty to eighty µm diameter continuously in availability of pump with greater pressure. Fluid ink gets deranged into drops at already decided pace, dimensions and particular intermissions by application of piezoelectric crystal.[8]

III. Drop-on-demand (DOD) printing

Drops of dimension 10-50 µm in diameter are produced in DOD printing. Similar to CI printing piezoelectric crystal is applied and thermal heads are also utilized as printing heads in this kind. Fluidized ink temperature gets raised to 300 degree Celsius which leads to build up of bubbles that leads to forcing of ink to print. Usage of this technique is only for vaporous fluids.[9]

Upon Utilization of piezoelectric crystal for DOD printing, the crystal alters swiftly that leads to immediate alteration of volume. Pressure pulse is formed to escape out the ink.[10] Piezoelectric head can be utilised for distinct kind of fluids unlike thermal heads.[9]

IV. Thermal inkjet printing

It heats the ink fluid using a micro-resistor to create a steam bubble that covers and forces the ink to drop out from the dust after expansion. Exempt drug preparation/solution is dispensed into 3D scaffolds and this technology can be used.[11]

V. Nozzle Based Printing

This system has advantages over the drawbacks such as utilisation only in case of lower dosage of therapeutics, not upto the mark rigidity, issues in various layer printing of inkjet printing system.[8,12] Binder in solution form is assorted with solid constituents such as drugs and polymers in case of this technique. A three-dimensional object is formed upon transferring the assortment through a nozzle and following layers are transferred.[13]

VI. Pressure-assisted Micro syringes (PAM)

In this case, fluid matter of appropriate resistance to flow is forced out by micro syringe. Similar to inkjet system, micro syringe is able to proceed and fluid is ejected with assistance of pressurised air. Sophisticated drug delivery systems are made possible by PAM.[14] Akin system in which piston is utilised has emerged which delivers the printing component not by pressurized air but by stepper motor.[15]

VII. Fused Deposition Modelling (FDM)

The method consists of selecting the Polymer you want that is melted and pushed into a cloud of moving heated dust. The polymer is layer by layer on a 3-axis (i.e. x-y-z) basis, which provides the exact structure of machine-assisted modeling models when solidified. This approach allows you to create several ways of dosing, such as implants, zero-order release tablets, etc.[16] Figure 2 shows the FDM 3DP in feasibility of manufacturing 3DP medicines.

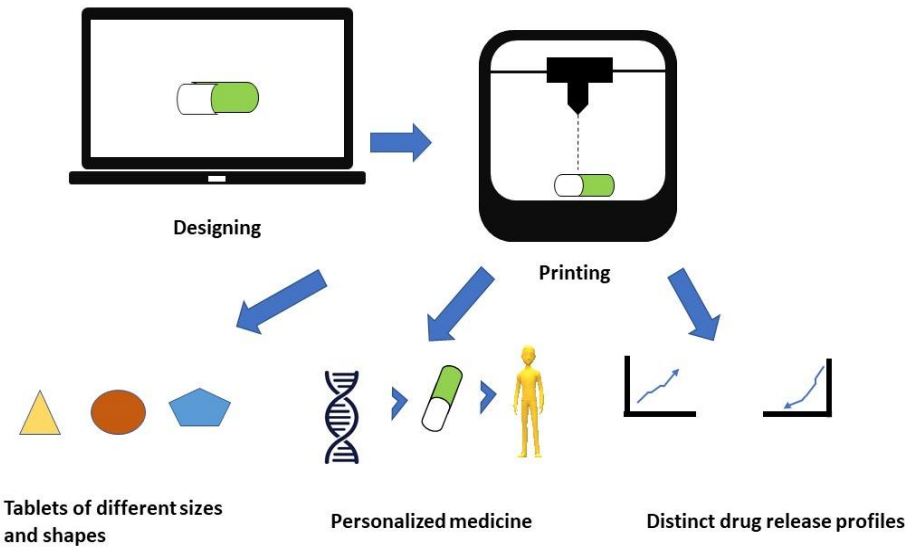

Figure 2: Researchers Explore FDM 3D Printing in Feasibility of Manufacturing 3D Printed Medications.[11]

VIII. Laser Based Writing System

Hypothesis of photopolymerization is applied in this system which involves interplay of photo initiator and ultraviolet light that in turn leads to formation of free radicals.[17]

IX. Stereolithography

It is based on laser orientation print system and is solid fabrication technique. Ultraviolet beam of light as embodiment of laser is concentrated on fluidized resin for it to attain

firmness due to photopolymerization.[18] The Procedure continues until a three-dimensional structure develops. This method is quite precise that leads to production of three-dimensional structure of fine grade. So far, this technique has been utilised for formation of paracetamol and aspirin oral doses.[19,20]

X. Selective Laser Sintering (SLS)

The crushed material for printing new items is used in an SLS printer. A laser pulls the object outline into the powder and fuses it. Then a new powder layer is formed and the procedure is repeated one by one and builds each layer to create the product.[3] Varied drug delivery systems have been formed with assistance of SLS. For instance, miniprintlet of anti-pyretic drug paracetamol.[21]

Pharmaceutical Potentials of 3d Printing

The conventional techniques in pharmaceutical industry for example, milling and mixing lead to inconsistent outcomes in regard to grade of products in some cases in regard to loading and release of drug, whereas three-dimension printing has benefits such as enhanced research and development potency, better security and effectiveness and reach to drugs. The benefits of 3D printing are explained in following points.

a) Sophisticated distinctive shapes and designs

3D printing permits to produce tablets of varied complicated configurations, and maintains the precise amount of the drug ingredients in tablet, even small dosage such as 10^{-12} mole per tablet.[22] By use of traditional techniques of tablet manufacturing, partially filled tablet design is not feasible, but with 3D printing that is feasible.[23] Another studied utilisation of 3D printing is production of dosages with distinctive release profiles.[24] For instance, distinct configurations of medicines can assist to attain varied release profiles. Tablets with varied sophisticated release profiles have been prepared by utilisation of 3D printing such as immediate release and sustained release.[25]

b) Personalised drug delivery and tailored dosage

3D Printing has capabilities to fabricate personalized medicines which can be utilized in management for specific individual groups suffering from different ailments. Therefore, three-dimensional printing can play the role as effectual magic bullet for complicated disorders like Alzheimer's disease and malignancy in addition to infant populace and elderly populace.[8,26,27] For on location production, 3D printing bestows with pliability. On the other

hand, traditional techniques of production depend upon proper erection of heavy machinery.[28,29,30] 3D printing can also be utilised for producing multiple main constituent doses, as one mix or multiple layered tablets to decrease count of units of tablets taken as well as recurrence of dose by suffering individual every day.[31]

c) Mini-Dispenser Unit

Very less area is needed by 3D printers, that they can easily adjust in any surrounding. Also, these are cost effective and can be operated from far distant locations also by usage of computer software systems.[32] 3D printers bring the production of tablets nearby to sufferer by acting as a mini-Dispenser by permitting to produce sole items in solitary production operation.[33]

d) Faster disintegration

In case of 3D printing, the arrangement of powder collection in the tablet layout is distinctive relative to powder compression. 3D printing has shown the powder binding limited to peripheral in tablet arrangement in some instances, leading to less stiff powder in the middle which allows faster disintegration.[34,35]

CHALLENGE

Though 3DP technology has shown promising results in the delivery of drugs, the technology is still under development. The issues include process optimization, improved efficiency for multi-use systems, selection of suitable excipients, post-treatment methods, etc., which need to be tackled to increase the performance of 3DP devices and expand the field of use of new drug delivery systems.[36] SPRITAM is Aprecia Pharmaceuticals' only 3DP product for the treatment of epilepsy that received USFDA approval in the year 2015. However, the compliance with the regulatory specifications for 3DP products would be the obvious path for the widespread commercial pharmaceutical use of this technology. 3DP technologies will result in a massive loss of work for a vast range of manufacturing processes. As well as this drastic reality, it will establish a great work opportunity for qualified specialists in CAD technology, materials engineering, computer technology, mathematics, and technology automation.[37]

CONCLUSION

3DP in medicine can, in short, technique may be used to serve as a means to produce any kind of organ. In 3DP, the pharmaceutical industry may use a valuable and future medium

that leads to customized medicines that address the needs of the patients. It provides many benefits, including increased cost efficiency and production speed. The usage of the customization of nutritional products, organs, and medicines 3DP is predicted to play an important role in this movement to personalized medicine. The manufacturing method has been revolutionized by 3DP. It increases the manufacture of new materials and decreases lead time and tooling costs. The impact of 3DP in medicine today, though, remains limited but it will become an incredibly advantageous technique.

COMPETING INTERESTS

The author declared no competing of interest.

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