3-D Printing In Pharmaceutical Field: A Review

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Abstract

The introduction section discusses the 3D printing technique and the manufacturing process. Additionally, it provides information on rapid prototyping and additive manufacturing. Different criteria are used to categorize 3D printers. Then, many applications are discussed, including those in the medical, healthcare and aerospace industries. The benefits and drawbacks of 3D printers are then covered. The way we create items and generate goods around the world may alter and improve dramatically as a result of advances in 3D printing technology. A solid three dimensional product can be created by printing out thin layers of an object that has been scanned or designed using computer-aided design software. The use of 3D printing spans the entire spectrum of human need.

Keywords: - 3D printers, Computer-aided design software, Solid three dimensional product, Additive manufacturing.

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INTRODUCTION

3-D Printing is one of the most technologies used to describe 3D-products. 3-D printing has shown a defined role in pharmaceutical field also, in past few years. Development of 3D-Printing Technology has changed the era and brought revolution in Digitalization in the pharmaceutical field, leading to non-digitalized medical products to digitalized medical products. Nowadays 3D-Printing has an extended application from drug development to pre-clinical Development, clinical trials to front line medical care.

History of 3D-printing

The very first development of concept of 3D-printing technology into pharmaceutical field was done by Massachuset Institute of Technology, Cambridge, MA, USA in early 90's. The very first patent on 3D-printing technology in pharmaceutical field was filed by Scott Crump. 3D printing technology was first developed in 1884, when Charles Hull invents Stereo lithography [1] In1994 Model Mark's wax printer was released. Aeromet in 1997 invented laser 3D printing. Development of engineered organs by 3D printing in 1999 brings new advances in medicine, as first lab-grown organ is implanted in humans. Object Geometries in 2000 developed the first inject printer, in the same year Z Corporation developed and manufactured first multicolour 3D printer. In 2001first desktop 3D printer was developed by Solid immersion. Year 2002 was found to be a revolutionizing year for medical science as first 3D printed functional kidney was engineered and developed which was able to filter blood and produce diluted urine in an animal. In 2006 there was a breakthrough in mass customization and on-demand manufacturing and developing of industrial parts and prostheses, as the first SLS (selective laser sintering) machine was developed. There was a highest advancement in 3D printing technology when the RepRap project was launched in 2005, and then in 2008 this project releases Darwin, the first self-replicating printer that is able to print the majority of its own components. In 2009 first 3D bio printed blood vessel was developed by Organovo. In 2011 3D printing technology for the first time developed robotic aircraft, 3D printed car, and even 3D printed silver and gold jewellery. Customized prosthetic lower jaw was developed for the first time in 2012 by Doctors and engineers of Netherland by using 3D printer, which was then subsequently implanted into an 83-year old woman. In 2013

World's first 3D printed gun was designed, which fired successfully(Av Plastics; A Brief History Of 3d Printing) In 2015 there was a ground-breaking advancement in the Pharmaceutical field as first 3D printed drug (Spitram) manufactured by Aprecia Pharmaceuticals was approved by USFDA. According to Wohler Report 2017 3D printing is currently a $6.063 billion industry, with $667 million (11% invested in medical applications. By 2027 3D printing industry is expected to grow into a $40 billion industry [2].

Applications of 3D printing

Manufacturing industries have been using 3D printers for more than decades, but mostly to make prototypes rapidly and cheaply. The majority are used as functional models, prototypes, and casting patterns, or for presentation models. As the technology is getting better and better more things are being printed as finished goods, around 28% of the output of 3D printers is now final products rather than prototypes, and this is expected to rise to 80% by 2020.Various applications of 3D printing but the focus of these applications is mainly on finished products [3]

Merits

- Personalized medicine or Tailor made medicine as per age, gender, environment, genetic variation.
- Targeted drug delivery
- Accurate & precise dosing of potent drug.
- As compared to conventional dosage forms, increase drug loading capacity.
- Production cost can be minimized as wastage of materials is less.
- Conventional drug delivery possess limitation such as poor water solubility & narrow therapeutic window, drugs can be overcome by 3D-Printing application,
- Treatment can be customized to improve patient adherence in case of multi-drug therapy with dose regimen.
- 3D printers capture minimal space & are affordable.

Demerits

- Powder printing clogging.
- Chances of modifying final structures because of storage condition adaptions & ink formulation effects.
- Printer related parameters & these effects printing quality.

Types of 3D printing

Varieties of 3D printing technologies have been developed with the different function. According to ASTM Standard F2792, ASTM catalogued 3D printing technologies into seven groups, including the binding jetting, directed energy deposition, material extrusion, material jetting, powder bed fusion, sheet lamination and vat photo polymerization. There are no debates about which machine or technology function better because each of them has its targeted applications. Nowadays, 3D printing technologies are no longer limited to prototyping usage but are increasingly also being used for making variety of products [4].

Binder jetting

Binder jetting is a rapid prototyping and 3D printing process in which a liquid binding agent is selectively deposited to join powder particles. The binder jetting technology uses jet chemical binder onto the spread powder to form the layer. The application of the binder jetting is would be producing the casting patterns, raw sintered products or similar large-volume products from sand. Binder jetting can print a variety of materials including metals, sands, polymers, hybrid and ceramics. Some materials like sand not required additional processing. Moreover, the process of binder jetting is simple, fast and cheap as powder particles are glued together. Lastly, binder jetting also has the ability to print very large products [5].

Directed energy deposition

Directed energy deposition is a more complex printing process commonly used to repair or add additional material to existing components [8]. Directed energy deposition has the high degree control of grain structure. The process of directed energy deposition is similar in principle to material extrusion, but the nozzle not fixed to a specific axis and can move in multiple directions. Furthermore, the process can be used with ceramics, polymers but is typically used with metals and metal-based hybrids, in the form of either wire or powder. The example of this technology is laser deposition and laser engineered net shaping (LENS) [6]. Laser deposition is the emerging

technology and can be used to produce or repair parts measured in millimetre to meters.

Laser deposition technology is gaining attraction in the tooling, transportation, aerospace, and oil and gas sectors because it can provide scalability and the diverse capabilities in the single system. Meanwhile, laser LENS can exploit thermal energy for melting during the casting and parts are accomplished subsequently [7].

Personalized medicine

The purpose of drug development should be to increase efficacy and decrease the risk of adverse reactions, a goal that can potentially be achieved through the application of 3D printing to produce personalized medications. Oral tablets are the most popular drug dosage form because of ease of manufacture, pain avoidance, accurate dosing, and good patient compliance [8]. However, no viable method is available that could routinely be used to make personalized solid dosage forms, such as tablets. Oral tablets are currently prepared via well-established processes such as mixing, milling, and dry and wet granulation of powdered ingredients that are formed into tablets through compression or molds. Each of these manufacturing steps can introduce difficulties, such as drug degradation and form change, possibly leading to problems with formulation or batch failures. In addition, these traditional manufacturing processes are unsuitable for creating personalized medicines and restrict the ability to create customized dosage forms with highly complex geometries, novel drug-release profiles, and prolonged stability [9]. Personalized 3D-printed drugs may particularly benefit patients who are known to have a pharmacogenetic polymorphism or who use medications with narrow therapeutic indices. Pharmacists could analyze a patient's pharmacogenetic profile, as well as other characteristics such as age, race, or gender, to determine an optimal medication dose. A pharmacist could then print and dispense the personalized medication via an automated 3D printing system. If necessary, the dose could be adjusted further based on clinical response [10]. 3D printing also has the potential to produce personalized medicines in entirely new formulations, such as pills that include multiple active ingredients, either as a single blend or as complex multilayer or multi reservoir printed tablets. Patients who have multiple chronic diseases could have their medications printed in one multidose form that is fabricated at the point of care. Providing patients with an accurate, personalized dose of multiple medications in a single tablet could potentially improve patient compliance [11].

Complex drug release profiles

The creation of medications with complex drug-release profiles is one of the most researched uses of 3D printing. Traditional compressed dosage forms are often made from a homogeneous mixture of active and inactive ingredients, and are thus frequently limited to a simple drug-release profile. However, 3D printers can print binder onto a matrix powder bed in layers typically 200 micrometers thick, creating a barrier between the active ingredients to facilitate controlled drug release. 3D-printed dosage forms can also be fabricated in complex geometries that are porous and loaded with multiple drugs throughout, surrounded by barrier layers that modulate release [12].

Orodispersible high dose medications

3D printing technology helps to produce Oro dispersible high-dose medications (up to 1000 mg) without using compression forces or traditional molding techniques. 3D printer stitches together multiple layers of powdered medication using an aqueous fluid to produce a porous, water-soluble matrix that rapidly disintegrates with a sip of liquid (Zip Dose Technology) [13].

Need of 3-D printing

The application of 3D printing in Pharmaceuticals can provide many benefits, including: cost-effectiveness; increased productivity; the democratization of design and manufacturing; and enhanced collaboration.

Increased cost efficiency

The most important benefit offered by 3D printing is the ability to produce items cheaply. Conventional method of drug manufacturing are less cost effective then 3D printing technology, because conventional method uses a lot of processes such as mixing, milling, dry or wet granulation, compression or molding etc. 3D printing can also reduce manufacturing costs by decreasing the use of unnecessary resources. For example, a pharmaceutical tablet

weighing 10 mg could potentially be custom-fabricated on demand as a 1 mg tablet. Some drugs may also be printed in dosage forms that are easier and more cost-effective to deliver to patients [14].

Enhanced productivity

3D printing technology is much faster than traditional method of drug manufacturing, which uses various processes such as mixing, milling, dry or wet granulation, compression or molding that makes it time consuming. In addition to speed, other qualities, such as the resolution, accuracy, reliability, and repeatability of 3D printing technologies, are also improving [15].

Environment friendly

3D printing technology claims to have more environmental benefits than traditional drug manufacturing methods which needs huge setup to manufacture a pill.

Democratization and collaboration

Another beneficial feature offered by 3D printing is the democratization of the design and manufacturing of goods [16].

Barriers and challenges

Post-processing: In many cases, 3D printer is unable to generate components with the desired accuracy and only produce products with nearly final shape. These products may then require a finishing operation, such as grinding or polishing, to produce the final product [17].

Limitations of materials

The choice of different raw materials as feedstock for 3D printers is still rather limited. There might be physical and technical limitations regarding the diversity of potential raw materials.

Massive job loss

3D printing technology will fall somewhere between the extremes of creating and destroying jobs. Currently, 3D printing serves as an indispensable tool for rapid prototyping, but as systems improve and become mainstream in manufacturing, 3Dprinting technology will likely replace unskilled human labour needed for subtractive manufacturing processes. At the same time, skilled jobs in CAD design, math, materials engineering, and automation oversight will become more valuable [18].

Regulatory concerns

Securing approval from regulators is another significant barrier that may impede the widespread pharmaceutical application of 3D printing. Only one dosage form printed by Aprecia pharmaceuticals has received the FDA's approval till this date. However, fulfilling more demanding FDA regulatory requirements could be a hurdle that may impede the availability of 3D-printed drugs on a large scale [19].

Applications of 3-D printing in health care

3D printing technology can used to print 3D skin, drug and pharmaceutical research, bone and cartilage, re placement tissues, organ, printing for cancer research and lastly models for visualization, education, and communication [20].

There are several advantages of 3D Printing technology for biomedical products which are:

- 3D printing technology can replicate the natural structure of the skin with the lower cost. 3D printed skin can be used to test pharmaceutical, cosmetics, and chemical products. Therefore, it is unnecessary to use the animal skin to test the products. Consequently, it will help the researcher to get accurate result by using replicate the skin.
- By using 3D printing technology to print drug can increase efficiency, accurate control of dropped size and dose, high reproducibility and able to produce dosage form with complex drug-release profiles [21].
- 3D printing technology is able to print cartilage and bone to replace bony voids in the cartilage or bone that caused by trauma or disease. This treatment is different options from using auto-grafts and allografts because this treatment focuses on to generate bone, maintain, or improve its function by using in vivo.
- 3D printing technology also can be used to replace, restore, maintain, or improve the tissues function. The replacement tissues produced by 3D printing technology have the interconnected pore network, biocompatible, appropriate surface chemistry and has good mechanical properties.

Printing technology also can be used to print out similar organ failure caused by critical problems such disease, accidents, and birth defects. Printing technologies are able to form highly controllable cancer tissues model and show great potential to accelerate cancer research. By using 3D printing technology, the patients can get more reliable and accurate data printout models can use in the learning process to help neurosurgeons practicing surgical techniques. By using 3D model, it can improve accuracy, can take the short time to the trainer when performing clinical procedure, and provides opportunities for training surgeons hands-on, as the 3D model is a simulation of a real patient's pathological condition [22].

Conclusion

Introduction part is about the 3D printing technique that what process is used for making it. It also tells us about the additive manufacturing process. Then it tells us about the different principle methods which can be used for 3D printer which includes stereo lithography, fused classified the 3D printers on different criteria. Then different applications are discuss which includes medical field, automobile and aerospace industries. Then the advantages and disadvantages of 3D printers are discussed. Advances in 3D printing technology can significantly change and improve the way we manufacture products and produce goods worldwide. An object is scanned or designed with Computer Aided Design software, then sliced up into thin layers, which can then be printed out to form a solid three dimensional product. As now we all know that 3D printing has application in all the stages of human need. 3D printing includes approximately 100 of materials now a days and the research is going on for increasing the range of material use in this technique.

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