Review Article

Three-dimensional printing in pharmaceutical technology – An overview of innovations

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ABSTRACT

Three-dimensional (3D) printing is an additive manufacturing (AM) technique competent of creating various 3D drug products and medical instruments from drug designs. SPRITAM was the first food and drug administration approved 3D printed drug product. It has advanced and inspired many researches in this field. Especially, the primary benefits of 3D printing are production of lot of medicines, each with specific dosages, shapes, sizes, and release features. 3D printer uses computer-aided design (CAD) model to execute rapid prototyping. In the age of personalized medicine, new platform required to produce the formulations with less toxicity, and to produce required action. This technology enables a flexible process for tailored dosing and drug combinations required. 3D printing is an AM technique that design formulations with CAD support. The objects can be designed by layering process with the help of computer-aided design (CAD). This technology allows the combinations in single dosage. Drugs are physically separated by layers and their release also adjusted individually. Different types of drug delivery systems such as implants, microchips, micro pills, fast-dissolving tablets, and multiphase release dosage forms have been developed using 3D printing technology. This review mainly focuses on the introduction, principle involved in 3D printing and focused on its working and types of materials used in creating the 3D objects. It also includes the achievement, advantages, and disadvantages embedded by 3D printing.

Keywords: Additive process, computer-aided design, rapid prototyping, three-dimensional objects, three-dimensional printing

Introduction

Three-dimensional (3D) printing has been around for many years, predominantly been used in manufacturing which has been playing unattainable role in healthcare medication and in pharma too. New possibilities in 3D printing may open up hilarious opportunities for pharmaceutical research and also in biotechnological applications. This technology impacts pharma business model. Pharmaceutical drug research and development (R&D) could be developed extremely by 3D printing. It could add a whole new dimension of possibilities to personalized dose and personalized medicine. It has been used by the manufacturing industry for decades primarily to produce product prototypes.[1] This concept seems like magic because this concept makes the field of pharma as easy desktop technology. A few strokes of printer, prescription medication, or medical device are available at our fingertips. Yet commonly known as "3D printing which seems to the unimaginable is indeed reality."[2]

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This review mainly focuses on the principle which involved during manufacturing process, the working of the printer, applications of 3D pharma technology, advantages, disadvantages of 3D printing, and achievements about this emerging technology which has a fabulous scope for new developments.[3]

What is 3D Printing

3D printing in pharma sectors an "adjuvant manufacturing" simply an additive manufacturing (AM) technology.[4] It is a process of making a 3D solid object of virtually any shape from a digital model which reacts object through a sequential layering process, under automated control. It reflects the simple fact that the technology shares the theme of a sequential layer of material addition of 3D envelope. Most popularly the term is used to cover a broad kind of AM techniques.[5]

Principle

The principle involved in 3D is "additive processes." In additive process an object is produced by establishing successive layers of material. It deposits a binder material onto a powder bed within inkjet printer heads layer by layer. It enables to produce complex shapes using less material than traditional manufacturing methods. It is an agile tooling used to describe the process to design and fabricate the AM of 3D printing methods to enable responses abruptly.[6-8]

Why Should We Focus on This[9,10]

a. Save amount of money in the prototyping process of several companies
b. Cost refers to only in hundreds and changes can be made instantly on computer
c. Waiting tends to be only hours/days but not years/months in case of prototype
d. Easy availability of personally customized products
e. Useful in drug testing purposes which revolutionize pharmaceutical R&D
f. Synthetic models lower the risk of trial failure
g. Revolutionary method saves time and cost by eliminating outcast designs
h. 3D printing could be a sustainable development in the developing world.

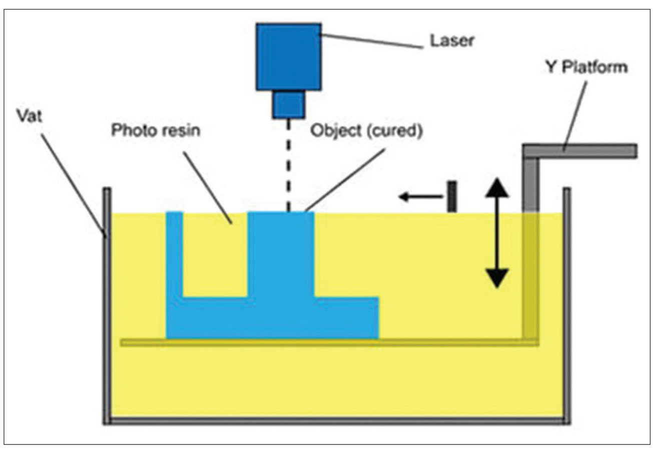

Figure 1: Vat polymerization

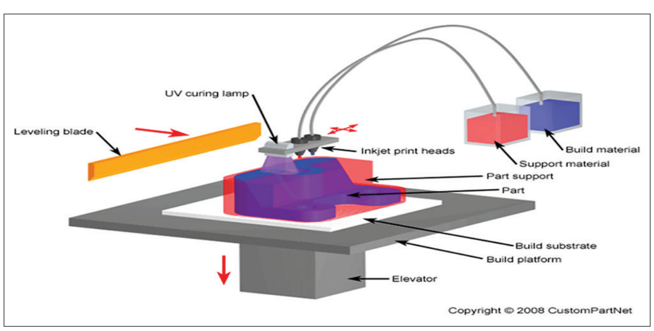

Figure 2: Material jetting

How It Works?

It starts with making a virtual design of the object we want to create. This bears a computer-aided design (CAD) file, which creates 3D modeling application, 3D scanner which can make a 3D scanner which can make a 3D digital copy of an object. American Society for Testing and Materials developed standards that classify the AM process into seven categories.[11-13]

1. Vat photopolymerization
2. Material jetting
3. Binder jetting
4. Material extrusion
5. Powder bed fusion
6. Sheet lamination
7. Directed energy deposition.

Vat polymerization

Commonly used technology is stereolithography (SLA). SLA is used for created models, prototypes, patterns, and production parts using photochemical process by which light causes chemical monomers to link together to form polymers. This technology employs a vat of liquid ultraviolet (UV) curable photopolymer resin and an UV laser to build the layers on object. This laser traces the pattern on the surface of the liquid which gets solidified by UV light [Figure 1]. Then, SLA elevator platform maintains thickness of 0.05 nm–0.15 nm. Resin blades sweep the section and recoat the fresh material. On this, a new surface layer of liquid is patterned joining the previous layer. It results the 3D one.[14]

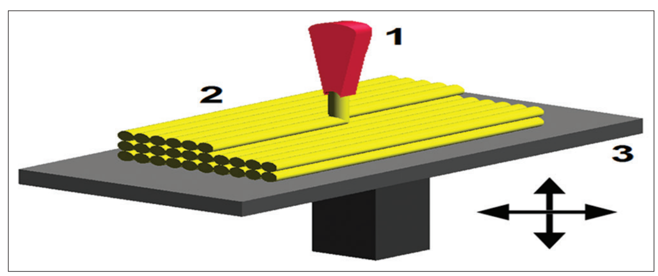

Figure 3: Material extrusion

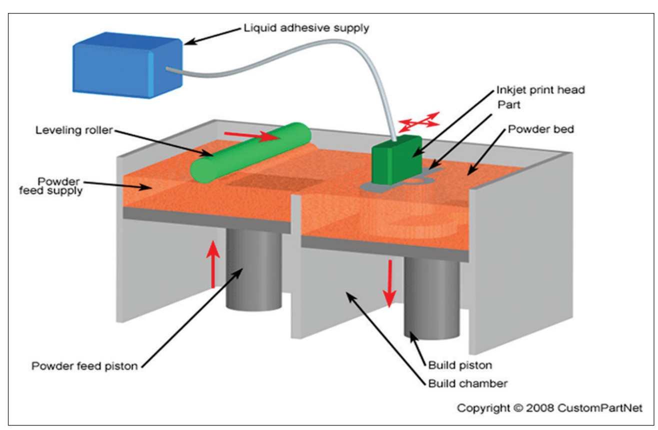

Figure 4: Binder jetting

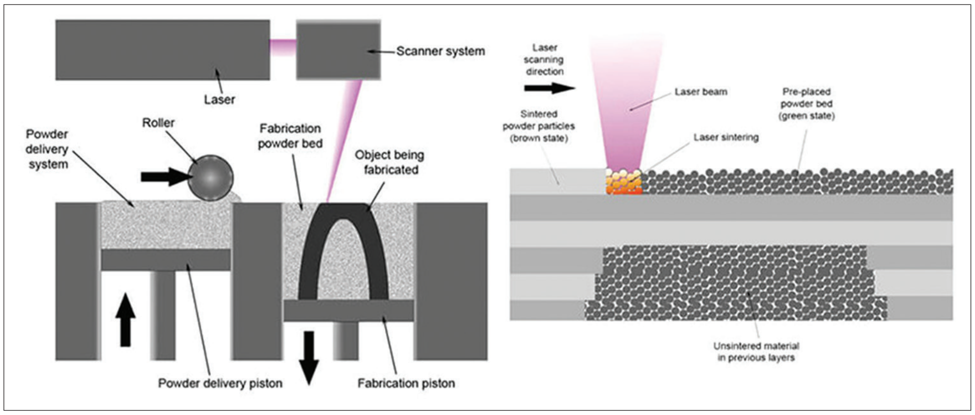

Figure 5: Power bed fusion

Material jetting

This process resembles to inkjet paper printer it is the only AM technology that can combine different print materials with in the same 3D printed model in the same print job. Completely processed models can be covered and used instantly without additional post-processing [Figure 2]. Material applied in the form of droplets through small diameter nozzle and layer by layer, which hardened by UV light making a 3D object.[15]

Material extrusion

Commonly used technology is fused deposition modeling material applied using a filament or wire estruses to nozzle, which turns the flow on and off and gets heated and melts the material and moves horizontally and vertically by computer-aided manufacturing. The melted material forms as layer and hardens immediately and results 3D object. In the case of complex shape, support material is also extruded [Figure 3]. The sacrificial material is later removed by hot water, water jet, or a solvent. Mainly used filaments are acrylonitrile butadiene styrene and polylactic acid (PLA).[16]

Binder jetting

It combines the principles of selective laser sintering (SLS) and material jetting. This includes powder-based material and a liquid binder [Figure 4]. The powder is spread in build chamber and a binder is applied through nozzles that glue the powder particles in the shape of a programmed 3D object.[17]

Powder bed fusion

Commonly used technology is SLS. This technology uses a high power laser to fuse small particles. The laser selectively fuses the powdered material by scanning the layers generated by programmed 3D object on the power bed. The SLS process uses an infrared laser beam to selectively scan powder material slightly above its normal temperature. After scanning, it maintains the thickness and then deposition of new layer of material is applied on top and then the process is repeated until the object is completed [Figure 5]. This is an advantageous technology over SLS and SLA because, no need of any support structure.[18]

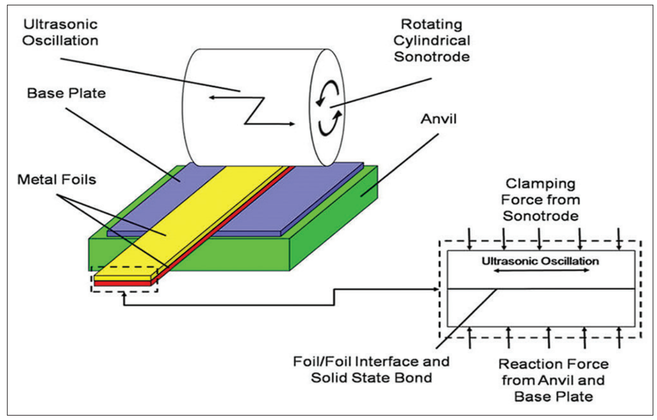

Figure 6: Sheet lamination

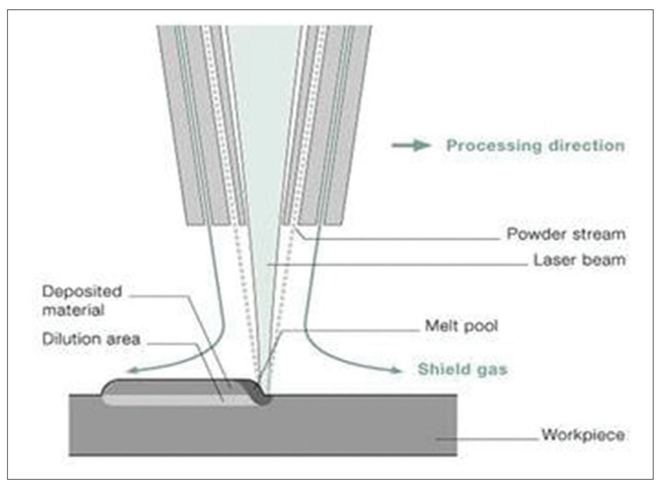

Figure 7: Direct energy deposition

Sheet lamination

It is used to produce colored objects in high detailed resolution. The precision of the results depends mostly on the thickness of the layered materials used [Figure 6]. It involves material in sheets which can be a polymer which bound together with external force.[19]

Directed energy deposition

Mostly used in the high tech industry and rapid manufacturing applications. This process enables the creation of parts by melting material as it is being deposited. In this focused thermal energy is used to fuse materials [Figure 7]. The device attached to multi-axis robotic arm and consists of nozzle deposits powder on surface and get melts by an energy source and finally forms a 3D dimensional solid object.[20-22]

Applications

1. Rapid prototyping: Used to create a real scale model of an object in short lead time, using CAD software
2. In the healthcare sector: Tools can be prepared for surgery and are made to measure the patient's body
3. Reconstituting bones and body parts in forensic pathology: Fingerprint examination, accident reconstruction, structural, and industrial accidents
4. Drug testing: Ability to fabricate complex geometries to achieve various drugs releasing kinetics
5. Personalized dosing: It uses digitally controlled devices for formulating active pharmaceutical ingredient (API) and excipients
6. Unique dosage forms: Capable of producing various 3D drug products and various customized dosage forms
7. Complex drug release profile: To fabricate fully customizable tablets that can deliver drugs with any type of releasing profiles
8. Low cost of production: It can decrease production time, costs, and allow testing of new product designs.[23-28]

Achievement

SPRITAM is the first drug manufactured using 3D printing process by Aprecia Pharmaceuticals Company approved by the US Food and Drug Administration SPRITAM (levetiracetam) for oral use in epileptic seizure. The formulation rapidly disintegrated with a sip of liquid.[29]

Advantages

a. Manufacturing of multiple dosages
b. Many from one: Manufacturing of multiple API from same raw material
c. All operations in a single machine
d. Drug dose at fingertips
e. Automation at fingertips
f. Zero skill manufacturing.[30]

Disadvantages

a. Human errors (placing wrong spool of the base material in printer)
b. Final product should undergo validation
c. Blueprint hacking
d. Scope for the manufacturing of illegal drugs
e. On exposure of the drug to laser, leads to lung diseases.[30]

Conclusion

This review concludes that the use of 3D printing for medical purposes today is beyond astonishing. It will be a revolutionary force in manufacturing technology and has a set of potential profit to society. It is highly efficient, reliable, time saving, and eco friendly. It has applications in wide variety of fields too.

Future

Hope this technology will change the nature of commerce so that users able to do much, own manufacturing rather than engaging from other people.

3D printing will change the manufacturing world it is really an exciting innovation is yet to come, yet to develop the ability to create materials at our fingertips.

Let's hope regulation can keep up.

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