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3D Printing in Pharmaceutical Technology: An Overview

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ABSTRACT

3D Printing is an additive manufacturing technique capable of producing various 3D drug products, medical devices from digital designs. This technology widely used in industries due to regulation and complex application, with 3D printing industries can create multiple version of the drug. This review aims to introduce 3D printing its history, advantages and various technique used in the fabrication of drug products. This review also described various applications and benefits of 3D printing.

INTRODUCTION

3D printing is the type of manufacturing technique in which the final object is formed by the successive addition of layers of material it builds a three-dimensional object from a computer-aided design (CAD) model. The 3D printing covers a variety of processes in which material is joined or solidified under computer control to create a three-dimensional object in this material is added together (liquid molecule or powder grains being fused) it is a standard tool in pharmaceutical industries. According to the United State Government Accountability Office (GAO), 3D printing produces 3D objects from digital models using layer by layer process. Nowadays, there dimensional printing is one of the fastest developing branches of technology. The 3D printing term is defined by International Standard Organisation (ISO) as Fabrication of objects through the deposition of a material using a print head, nozzle or another printing technology it has wide applications in various fields including automobile, pharmaceutical, aerospace, food, chemicals.

History of 3D Printing:

3D printing technology first comes in 1981, Hideo Kodama of Nagoya Municipal Industrial Research Institute his account on functional rapid-prototyping system using photopolymers. After three years later in 1984 Charles Hull made 3D Printing history by inventing Stereolithography then in1992 Charles Hull Company created the world's first stereolithographic apparatus (SLA) machine. That same year DTM produce the world's first selective laser sintering (SLS) machine. In 1994 model marks wax printer was released In 1997 development of engineered organs by 3D printing it brings a new advance in medicine first lab-grown organ is implanted in humans In 2000 the first inject printer is developed and same year Z corporation made first inject printer, In 2001 first desktop 3D printer was made by solid dimension. In 2006 as the first SLS (selective laser sintering) machine was developed. It was the outcome of the SLC that in 2008 the first person walks on a 3D-printed prosthetic leg. There was the biggest advancement in 3D printing technology when the RepRap project was launched in 2005, and in 2008 this project releases Darwin, the first self-replicating printer that can print many of its components. In 2009 first 3D bio-printed blood vessels were produced by Organovo. In 2011 3D printing technology first time helps to develop robotic aircraft, 3D printed cars, and even 3D printed silver and gold jewelry. In 2013Worlds the first 3D printed gun was designed, which fired successfully. In 2015 there was a groundbreaking advancement in the Pharmaceutical field as the first 3D printed drug

(Spitram) manufactured by Aprecia Pharmaceuticals was approved by USFDA. Spitram is produced by Aprecia using Zip Dose technology by utilizing a 3D printing platform that creates Orodispersible formulations of high-dose medications, designed to disintegrate in the mouth with just a sip of liquid.

Advantages of 3D printing:

- 3D printing helps to achieve formulation flexibility with a complex release profile.

- Faster Production: It is one of the most helpful advantages of 3D printing in which easier and quicker manufacturing of products the advantage of 3D printing technology can help the designers and professionals to make better decisions in selecting a better manufacturing process and will help to deliver great results.

- Single Step Manufacture: One of the biggest concerns for a designer is how to manufacture a part of efficiency as possible. Most parts require a large number of manufacturing steps to produce a product in 3D printing manufacturing of the product in one step.

- Better Quality: Traditional manufacturing methods can easily result in poor designs and therefore poor-quality prototypes. But 3D printing allows step by step assembly of the object, which designs better quality objects.

- Cost-Effectiveness: 3D printing is more affordable technology which deals with a low cost of labor, machine operation cost and material cost.

- Unlimited Shapes and Geometry: Old methods of manufacturing rely on molds and cutting technologies to generate the desired shapes. Designing geometrically complex shapes can be hard and expensive with this technology. 3D printing takes on this technology. 3D printing takes on this challenge with ease and there is not much the technology can not do with proper support materials.

- Less Waste Production: CNC cutting and injection molding resulting in a lot of wasted resources. Both involve the removal of materials from solid blocks, unlike these two, 3D printing, only uses materials that are needed to create a prototype part- no more, no less. As a result, additive manufacturing creates very little waste and saves a company a lot of money.

Techniques used in 3D printing:

The formulation of solid dosage form requires a large number of processing steps like mixing milling granulation etc. The number of steps involved in preparation may increase the chance of batch failure. 3D printing can reduce the number of steps involved drastically requiring lesser regulatory and quality control issues. Following are the 3D printing technique used in manufacturing:

1. Binder Jetting:

The binder jetting process uses two materials; a powder fused material and a binder. The binder acts as an adhesive between powder layers. The binder is usually in liquid form and the built material in powder form. A print head moves horizontally along the x and y axes of the machine and deposits alternating layers of builds material and binding material. After each layer, the object being printed on its build platform.

Binder jetting steps -

- The powder material is spread over the build platform using a roller.
- The print head deposits the binder adhesive on top of the powder where required.
- The build platform is lowered by the model's layer thickness.
- Another layer of powder is spread over the previous layer. The object is formed where the powder is bound to the liquid.
- The unbound powder remains in position surrounding the object.
- The process is repeated until the entire object has been made.

2. Stereolithography (SLA) :

Stereolithography is a vat polymerization 3D printing process where photopolymer resin in a vat is selectively cured by a light source. Stereolithography builds accurate parts directly from 3D CAD data without tooling by converting liquid plastic (photopolymer) into solid cross-section using an ultraviolet laser. The part is created layer by layer, with each resin layer built on top of the next until the part is complete. This process is known as

photopolymerization. When the SLA part is complete, it is cleaned in a solvent solution to remove wet resin remaining on the part surface. Afterward, the part is put in a UV oven to cure it, completing the resin printing process.3D system (SLA) production 3D printer offers high throughput, build size up to 1524mm, unmatched part resolution and accuracy, and a wide range of print materials. Stereolithographic has a wider range of applications, including most demanding rapid manufacturing for highly accurate and durable prototype shape.

3. Fused Deposition Modeling (FDM):

Fused deposition modeling is a material extraction 3D printing process where a filament of solid thermoplastic material is pushed through a heated nozzle, melting it in the process. Fused Deposition Modeling, or FDM. They are also sometimes referred to as Fused Filament Fabrication or FFF. The way it works is that a spool of filament is loaded into the 3D printer and fed through to a printer nozzle in the extrusion head. The printer nozzle is heated to the desired temperature, whereupon a motor pushes the filament through the heated nozzle, causing it to melt. The printer then moves the extrusion head along with specified coordinates, laying down the molten material onto the build plate where it cools down and solidifies. Once a layer is complete, the printer proceeds to lay down another layer. This process of printing cross-sections is repeated, building layer-upon-layer until the object is fully formed.

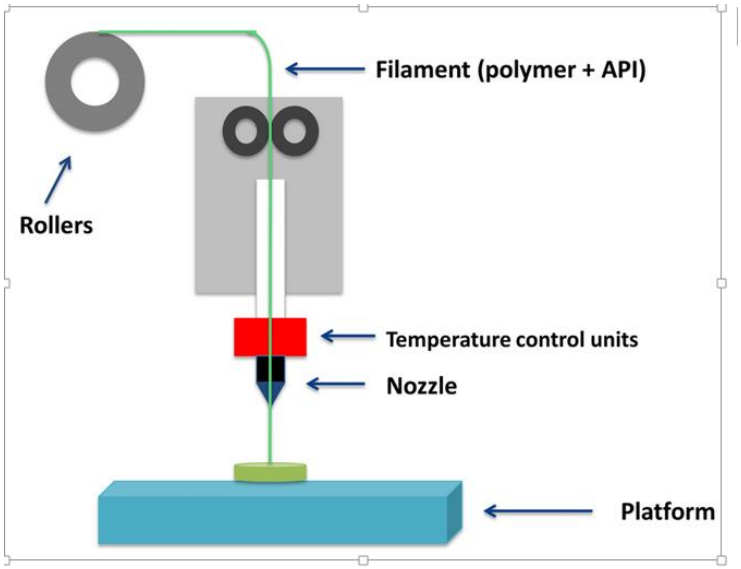

Figure No. 1: Fused Deposition Modeling

4 Selective Laser Sintering (SLS):

Selective Laser Sintering is a powder bed fusion 3D printing process where a thermal energy source will selectively induce fusion between powder particles inside a build area to create a solid object. First, a bin of polymer powder is heated to a temperature just below the polymer's melting point. Next, a recoating blade or wiper deposits a very thin layer of the powdered material typically 0.1 mm thick onto a build platform. A CO2 laser beam then begins to scan the surface. The laser will selectively sinter the powder and solidify a cross-section of the object. Just like SLA, the laser is focused on the correct location by a pair of galvos. When the entire cross-section is scanned, the build platform will move down one layer thickness in height. The recoating blade deposits a fresh layer of powder on top of the recently scanned layer, and the laser will sinter the next cross-section of the object onto the previously solidified cross-sections. These steps are repeated until all objects are fully manufactured.

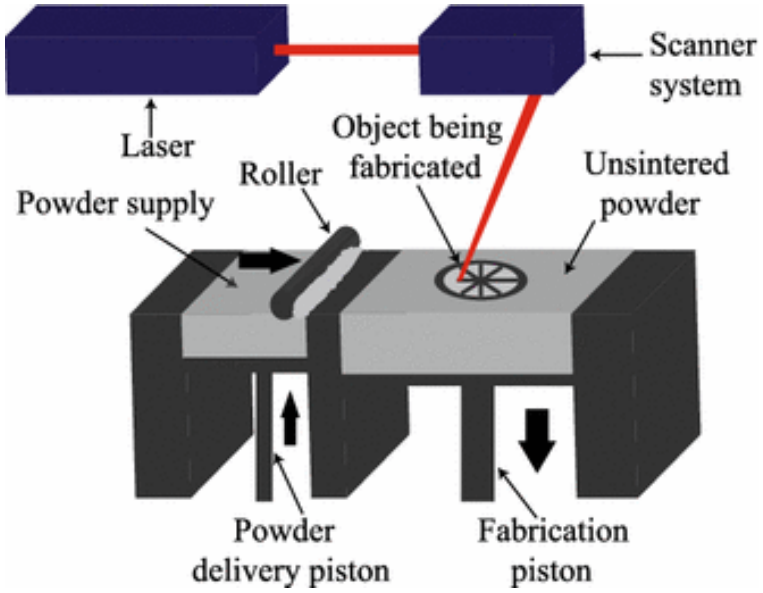

Figure No. 2: Selective Laser Sintering (SLS)

5 Material Jetting (MJ)

Material Jetting is a 3D printing process where droplets of material are selectively deposited on the build plate. Using photopolymer or wax droplets that cure when exposed to light, objects are built up one layer at a time. Material jetting works in a similar way to a standard inkjet printer. The print head jets hundreds of tiny droplets of photopolymer and then cures/solidifies them using an ultraviolet (UV) light. After one layer has been deposited and

cured, the build platform is lowered down the one-layer thickness and the process is repeated to build up a 3D object. Material jetting is different from other types of 3D printing technology that deposit, sinter or cure build material using a point-wise deposition. Instead of using a single point to follow a path that outlines the cross-sectional area of a layer, Material Jetting machines deposit build material in a rapid, line-wise fashion. The advantage of line-wise deposition is that Material Jetting printers can fabricate multiple objects in a single line with no impact on build speed. So long as models are correctly arranged, and the space within each build line is optimized, Material Jetting can produce parts at a speedier pace than other types of 3D printer. Objects made with Material Jetting require support, which is printed simultaneously during the build from a dissolvable material that's removed during the post-processing stage. Material Jetting is one of the only types of 3D printing technology to offer objects made from multi-material printing and full-color.

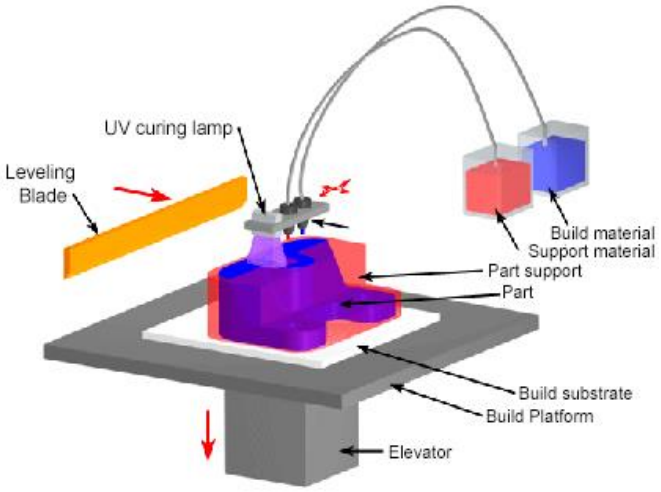

Figure No. 3: Material jetting 3D printing process

6 Powder Bed Fusion:

Powder Bed Fusion is a 3D printing process that produces solid objects, using a thermal source to induce fusion between metal powder particles one layer at a time. Powder Bed Fusion is a 3D printing process that produces solid objects, using a thermal source to induce fusion between metal powder particles one layer at a time. Most Powder Bed Fusion technologies employ mechanisms for adding powder as the object is being constructed, resulting in the final component being encased in the metal powder.

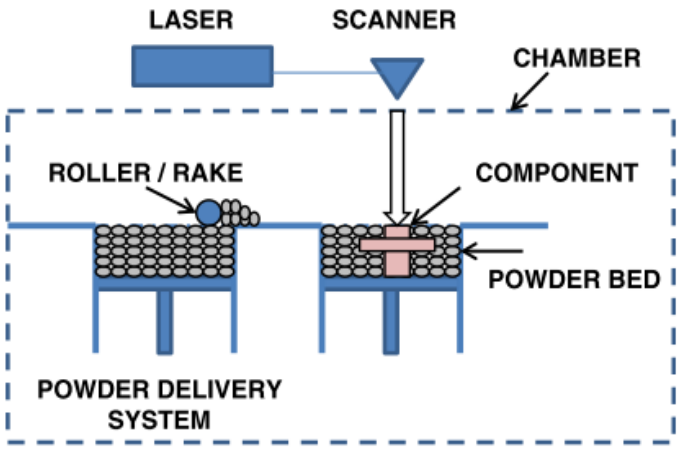

Figure No. 4: Powder Bed Fusion Process

Application Of 3D printing:

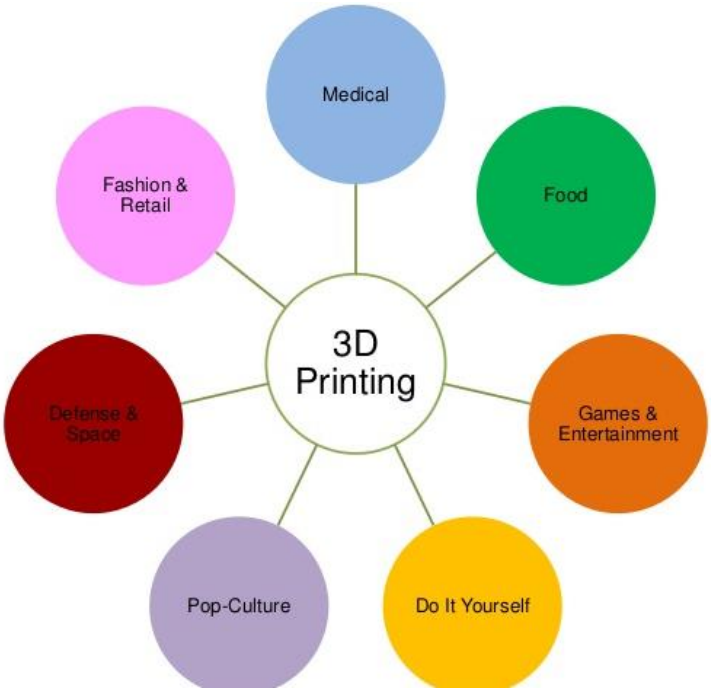

Figure No. 5: Applications of 3D Printing

1. Medical application of 3D printing:

The medical application of 3D printing is expanding rapidly to revolutionize health care. Medical use of 3D printing, both actual and potential, can be organized into different categories:

- Tissue and organ fabrication- 3D printing organ printing takes advantage of 3D printing to produce cells, biomaterials, and cell-laden biomaterials are individually or layer by layer directly creating a 3D tissue-like structure.

- Creation of prosthetics – 3D printing has been used successfully in the health care sector to make both standards and customized prosthetic limbs and surgical implants. This approach has been used to fabricate dental, spinal and hip implants.

- Implants and anatomical models-. The individual variance and complexities of the human body make the use of 3D printed models ideal for surgical preparation the use of 3D printing models for surgical training is also preferable to training on cadavers, which presents problems concerning availability and cost. 3D- printed neuroanatomical models can be particularly helpful to neurosurgeons by proving a representation of some of the most complicated structures in the human body.

2. 3D printing technology in pharmaceutical dosage forms:

The pharmaceutical applications of 3DP technology are focused on the oral solid dosage forms and transdermal delivery systems that seem to be undergoing relatively greater progress and are more suitable for wide applications of 3D printing.

- **Tablets:** Tablets and capsules are widely used in solid dosage forms. Tablets have been extensively examined for the feasibility of 3DP technologies in pharmaceutical manufacturing. Generally, tablets produced by 3DP methods can be categorized into two groups: single API tablets and multiple API tablets. 3DP technology was applied to fabricate simple immediate release (IR) tablets comprising a single API and multiple APIs can be loaded in a single tablet, called a polypill.

- **Microneedles:** Microneedles are a class of transdermal drug delivery systems, which has arrays of micron-sized needles on the surface of a matrix to enhance the skin penetration of biologically active molecules. Microneedles may be more effective to deliver macromolecules through the skin than traditional patches, due to its microstructure. Recent advances in high-resolution 3DP techniques fabricating small and tiny structures, accelerate the application of 3DP in manufacturing the microneedles.

- **Capsule:** a Capsule is a dosage form which encloses drug within a hard or softshell. Capsules are available in various sizes to enclose the required amount of drug as powder, granules, solution, emulsion and other formulations. 3D printing technique was successfully applied to fabricate an erodible capsule for pulsatile release of various drug formulations with varying sizes and thicknesses. It can be filled with various solid and liquid dosage forms such as powders, pellets, solutions, dispersions and other formulations.

3. 3D printing Technology in various diseases:

- **Cancer:** Cancer is a term used to describe disease caused by abnormal and uncontrolled growth of cells and which can invade other tissue and they can spread to other body parts via systemic circulation and lymphatic system. Advances in 3D printing technology have enabled the fabrication of in vitro models to understand tumor development and metastasis. It is particularly useful in engineering of the cell microenvironment as it allows precise spatial control of the cell organization and insertion of biomolecules Along with the basic structure, it is also capable of incorporating various cell types, polymers, vasculature, and micro-channels to mimic the tissues or organs.

- **Cardiovascular diseases:** Cardiovascular diseases are a group of disorders related to heart and vasculature and are difficult to manage and cure. The diagnosis and treatment traditionally depend upon 2D model Magnetic Resonance Imaging (MRI), angiography and echocardiography with limitation of inability to represent real size structure in 3 dimensions. 3D printer utilizes the extensive volume of data obtained from the imaging techniques to produce a replica of the cardiac structures the prepared 3D replica model helps in a detailed understanding of the cardiac anatomy and pathophysiology and accordingly plan treatment with a high degree of precision.

- **Diabetes:** Diabetes is a metabolic condition characterized by higher than normal blood glucose levels (normal pre-prandial: 72–108 mg/dl and post-prandial i.e. 2 h after eating: 140 mg/dl) caused by either lack of sufficient insulin production or inability to use the produced insulin. The 3D printing method has been extensively used in designing treatment approaches to diabetes. Major challenges of production of insulin-producing islet cells and a personalized dose of medicine have been designed by 3D printing.

4. Other Application of 3D Printing: 3D printing also in food, industries, automobile, space, art, and jewelry also in communication, education, and research, etc.

- In the food industry food is being developed by squeezing out food, layer by layer, into three-dimensional objects. A large variety of foods are appropriate candidates, such as chocolate and candy, and flat foods such as crackers, pasta, and pizza.

- 3D printing is used in automobile industries to designing cars also in designing various auto parts.

- In art and jewellery3D printing is used to manufacture molds for making jewelry, and even the jewelry itself. 3D printing is becoming popular in the customizable gifts industry, with products such as personalized models of art and dolls, in many shapes: in metal or plastic, or as consumable art, such as 3D printed chocolate.

- In education and research 3D printing, and open-source 3D printers in particular, are the latest technology making inroads into the classroom? 3D printing allows students to create prototypes of items without the use of expensive tooling required in subtractive methods. Students design and produce actual models they can hold. The classroom environment allows students to learn and employ new applications for 3D printing. RepRap, for example, has already been used for an educational mobile robotics platform. This is a various application of 3D printing.

CONCLUSIONS

3D printing can increase the quality of the product. It can print medicine in various shapes, sizes, doses and dosage forms with desired and prespecified characteristics. In pharmaceuticals, it helps design various dosage forms like tablets, capsules by 3D designing. It is capable of producing various medical devices, implants, anatomical models, artificial organs, etc. it is a more affordable technique. The continuous innovation and development in the 3D printing technique improve the quality of life.

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