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A REVIEW: NOVEL APPROACH OF 3D PRINTING IN DRUG DELIVERY SYSTEM

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ABSTRACT
Three-layered printing (3DP) takes into account the production of different calculations using PC helped plan and different cycles and materials for favored purposes, for example, drug prescription conveyance medication. The FDA's (2015) endorsement of printed medication gives a rare chance for the advancement of novel synthetic compounds and innovation for the administration of illness. This paper talks about a portion of the advantages, disadvantages, issues, and feelings on Polymer and mixtures of drug grade used in drug conveyance frameworks are 3DP.

KEYWORDS: 3D Printing, Drug Delivery, Pharmaceuticals.

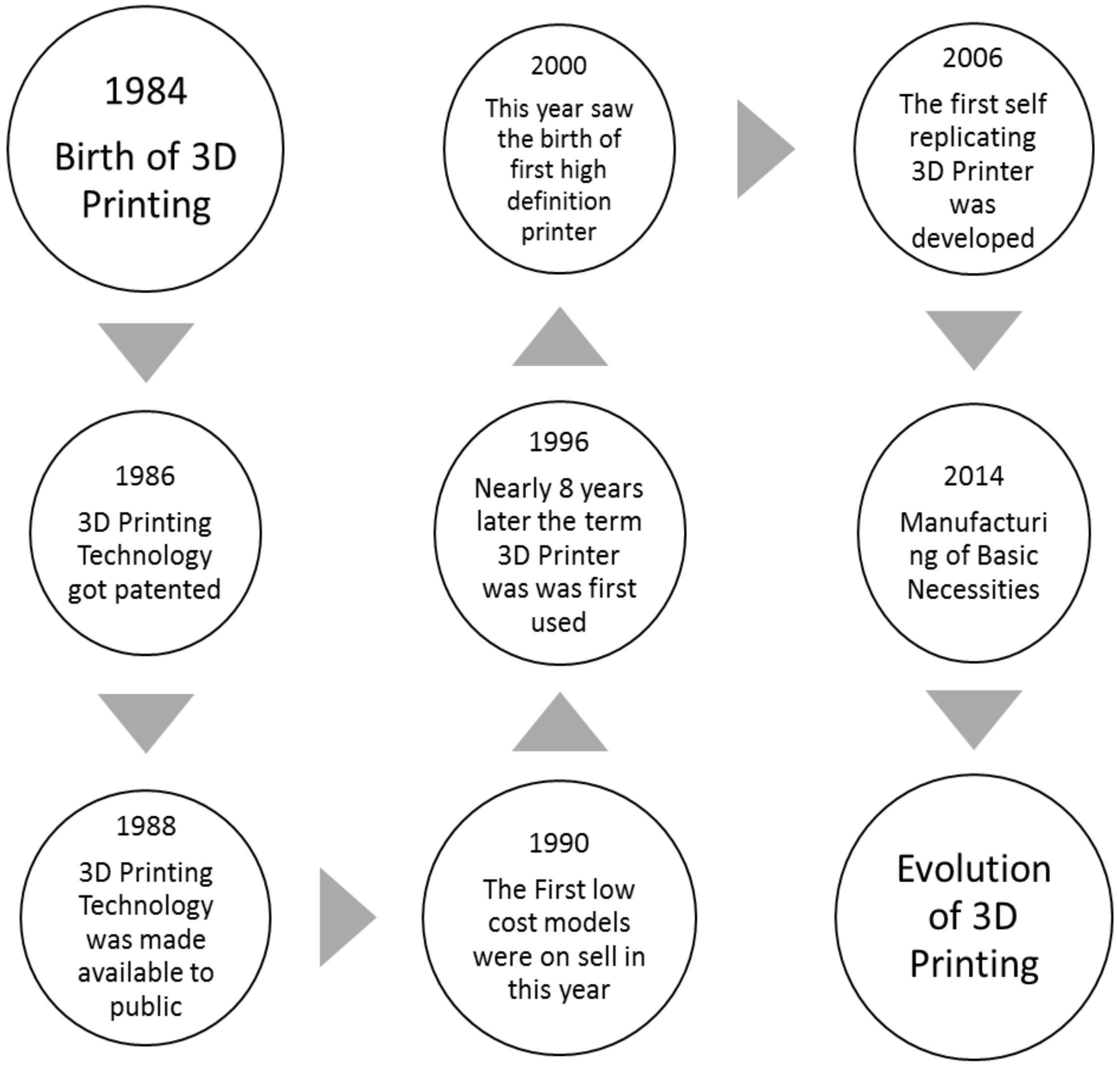
INTRODUCTION

Approaches, frameworks, innovations, and Drug conveyance alludes to the most common way of shipping a drug substance in the body on a case by case basis to deliver its designated helpful activity securely. From quick delivery oral dose structures to focus on discharge drug conveyance frameworks, the idea of medicine conveyance has developed significantly over the course of time. Controlling the medication release profile to adjust absorption, distribution, metabolization, and elimination of the drug quickly became a key aspect in optimising product efficacy and safety, as well as patient compliance.[1] In the drug delivery field, versatile therapeutic systems designed to produce customized combinations of drugs, drug doses, and release kinetics have gained traction, owing to the benefits that personalized pharmaceutical treatments would provide.[2]

3DP is gaining popularity in pharmaceutical formulation development as a viable strategy for overcoming some of the challenges associated with traditional pharmaceutical unit operations. Drug loading, drug release, drug stability, and pharmaceutical dosage form stability can all be affected by milling, mixing, granulation, and compression. 3D printing technology has allowed for unprecedented flexibility in the design and manufacture of complex objects that can be used in both customized and programmable medicines.[3]

History of 3D Printing and its Development

- Hideo Kodama, a Japanese inventor, was the first to record 3D printing using the additive process in 1981. He developed a product that used ultraviolet lights to harden polymers and solidify them. This is a first step toward stereolithography.[4]
- Charles Hull invented stereolithography, a process similar to 3D printing that uses technology to create smaller versions of objects for testing before investing time and money in creating the actual product. Layer by layer, the object is printed, rinsed with a solvent, and hardened with an ultraviolet light. The 3D models are created using computer-aided design (CAD).[2]
- SLS (Selective Laser Sintering) is a more advanced form of 3D printing. Objects are created using additive manufacturing and a powder polymer (typically nylon). SLS employs a laser to fuse the powder together, layer by layer, to produce more complex shapes than SLA.Scott Crump's Fused Deposition Modeling (FDM) is the most prevalent 3D printing technique. Because it is the most widely employed used form of the technology, it is referred to as “desktop 3D printers.” To create an object, the printer melts a thermoplastic cable and squeeze out it layer by layer.[5]
- Over the last thirty years, 3D printing has evolved and improved. SLA, SLS, and FDM demonstrate the evolution of 3D printing and how it became a critical tool in manufacturing. It allows to make almost anything by simply saving it as a computer file.



Advantages[5]

1. Accurate and precise dosing of powerful drugs administered in small doses.
2. Reduces production costs by reducing material waste.
3. Narrow therapeutic window.
4. Medication can be tailored to a specific patient based on genetic differences, ethnic differences, age, gender, and environmental factors.
5. Superior drug loading capability when compared to traditional dosage forms.
6. Treatment can be tailored to improve patient adherence in the case of multi-drug remedy with multiple dosing regimens.
7. Appropriate drug delivery for difficult-to-formulate active ingredients, such as those with low water solubility.
8. Various materials can be used in 3D models. It makes it very simple to create prototypes for a broad scale of projects in a variety of industries.
9. Products with an excellent surface finish are manufactured.

Disadvantages[5]

1. At the moment, 3D printing method is constrained by size constraints. When using 3D printers, very large objects are still not possible.
2. The cost of purchasing a 3D printer is still prohibitively expensive for the average householder. Multiple types of 3D printers are needed to create different types of items, and printers that can design in colour are more priced than printers that can only print in monochrome.
3. As with any new technology, manufacturing jobs will be lost. This major drawback could have a major impact on the economies of third-world countries, particularly China, which rely on a large number of low-skilled jobs.
4. At the moment, 3D printers can work with about 100 different raw materials, but this is insufficient when compared to the vast array of raw materials used in traditional manufacturing. More research is needed to develop methods for making 3D printed products more durable and robust.

TYPES OF 3D PRINTING

Selective Laser Sintering[5]

Selective laser sintering (SLS) is a high-speed sintering manufacturing process that uses powder coated metal additives. It is commonly used for rapid prototyping. As a heating source, a continuous laser beam is used to scan and align particles in sizes and shapes that have been predetermined in the layers. The scanned layers' shape is identical to different sections of models created using computer-aided design or stereolithography files. After scanning the first layer, the second layer is scanned and placed over the first, and the procedure is continued until the product is complete.

A high-powered laser is used to fuse microscopic particles of plastic, metal, ceramic, or glass powders together into a mass with the appropriate three-dimensional forms. Laser selectively fused the powdered material by Scanning the 3D model's cross section or layers by the 3D modelling Programme on the surface of the powder bed, lowering the powder bed by one layer thickness.

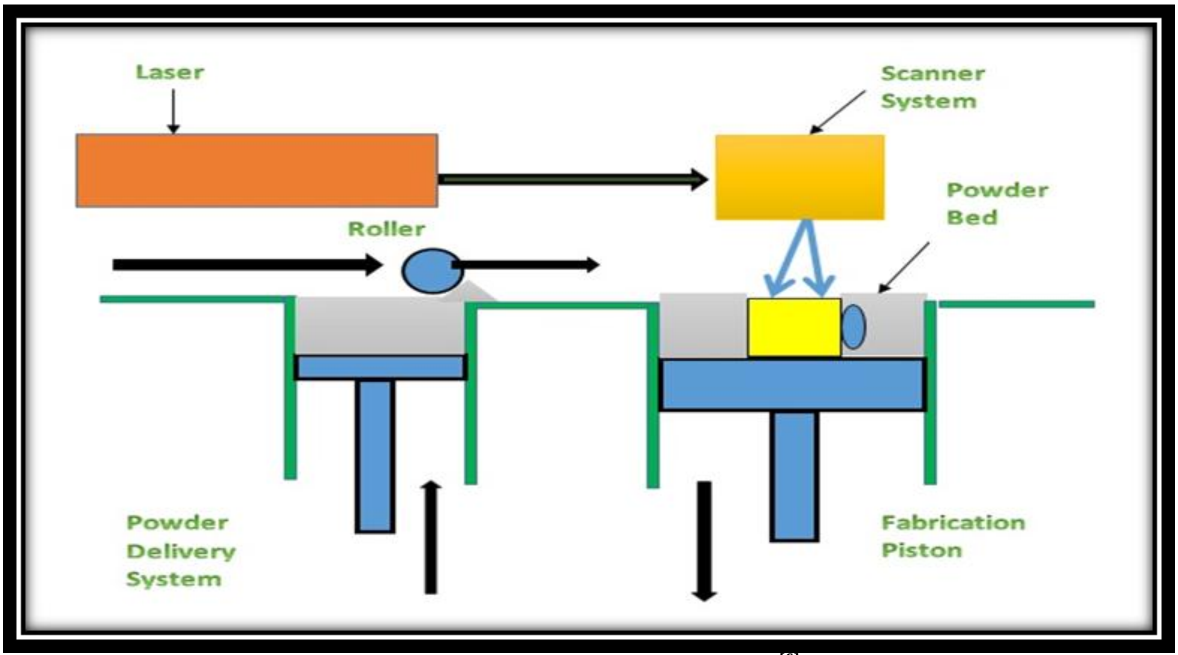


Figure 1: Selective Laser Sintering.[6]

SLS (selective laser sintering) is among the most popular methods for making recent and sophisticated methods offered for the manufacture of solid dosage forms. SLS is a one-step manufacturing process that produces 3D things by selectively sintering powder particles in layers using a laser.

Fused Deposition Modeling[5]

Modeling of Fused Deposition Printers are far more common and less economical than Selective Laser Sintering. A print head similar to that of an inkjet printer is used in a fused deposition modelling printer. Rather than ink, the print head releases beads of heated plastic as it travels, allowing the item to be built up in thin layers.The process is repeated indefinitely to precisely shape each layer and control the quantity and place of each since the substance is heated to fuse or bond to the layers below. Each layer of plastic hardens as it cools, gradually forming the solid object as the layers are added. Depending on the complexity and cost of a Fused Deposition Modeling printer, enhanced features such as multiple Print heads may be included. In Fused Deposition Modeling printers, plastics can be used. In fact, 3D Fused Deposition Modeling printed parts are frequently made from the same thermoplastics used in traditional injection moulding or machining, so they have comparable stability and durability.and mechanical properties.

Fused deposition modelling (FDM) is now a type of simulation a low-cost extrusion-based 3D printing technology capable of depositing materials layer by layer to produce solid shapes. This review paper seeks to offer an overview of the use of FDM-based 3D printing in the development of novel medication delivery systems.

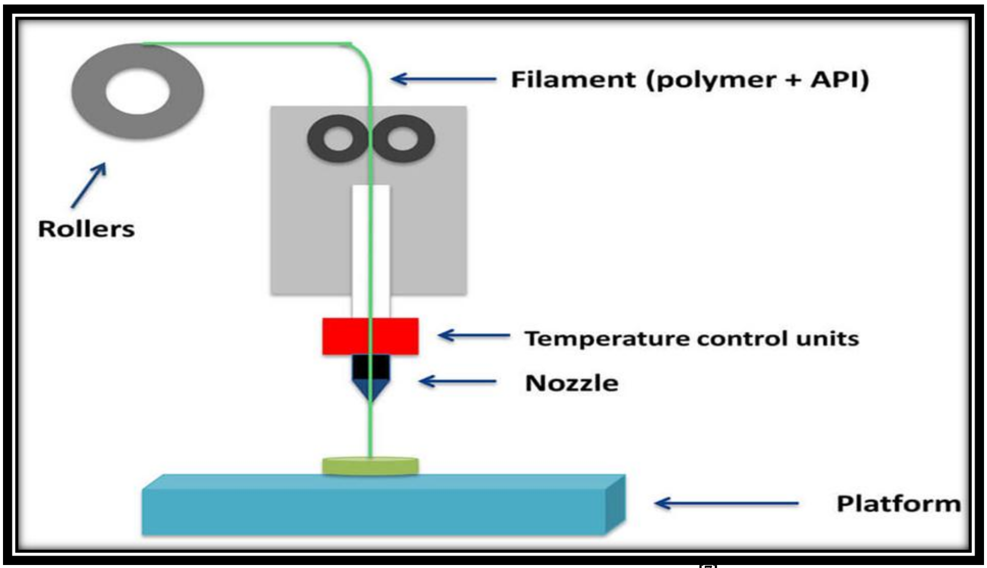


Figure 2: Fused Deposition Modeling.[7]

Fused deposition modelling (FDM) is a low-cost extrusion-based 3D printing technology capable of depositing materials layer by layer to produce solid shapes. This review paper seeks to offer an overview of the use of FDM-based 3D printing in the evolution novel medication delivery systems.

Inkjet Printing[5]

The same computer-assisted inkjet printing process is used in this approach to personalised medicine. It was altered for pharmaceutical use by substituting the ink with pharmaceutical solutions containing medications and the regular paper with edible substrates.

Adjusting the number of layers printed in a certain region or modifying the area to be printed are two ways to change the dose. The medicine and excipients are made to be printed as microdots on an edible substrate. Thermal inkjet printers and piezoelectric inkjet printers are the types of inkjet printers.

There are two types of printing-based inkjet systems: continuous inkjet printing and drop-on-demand printing. In continuous inkjet printing, liquid ink is directed via a 50-80 m diameter aperture, resulting in a continuous flow of ink. The liquid is made to flow and break into drops at regular intervals at a set speed and size using a piezoelectric crystal. These characteristics are controlled by an electrostatic field. As a result, to lessen electrostatic repulsion, the droplets are charged and separated by "droplets of guard." The charged droplets are directed to the substrate by the electrostatic field generated. Inkjet drug printing provides a significant advantage in terms of precise control over dose combination and drug release pattern. For efficient flow, ink jet printing requires certain characteristics in the starting materials, most notably particle size of 20 cP and surface tension of 30 to 70 nm/m.

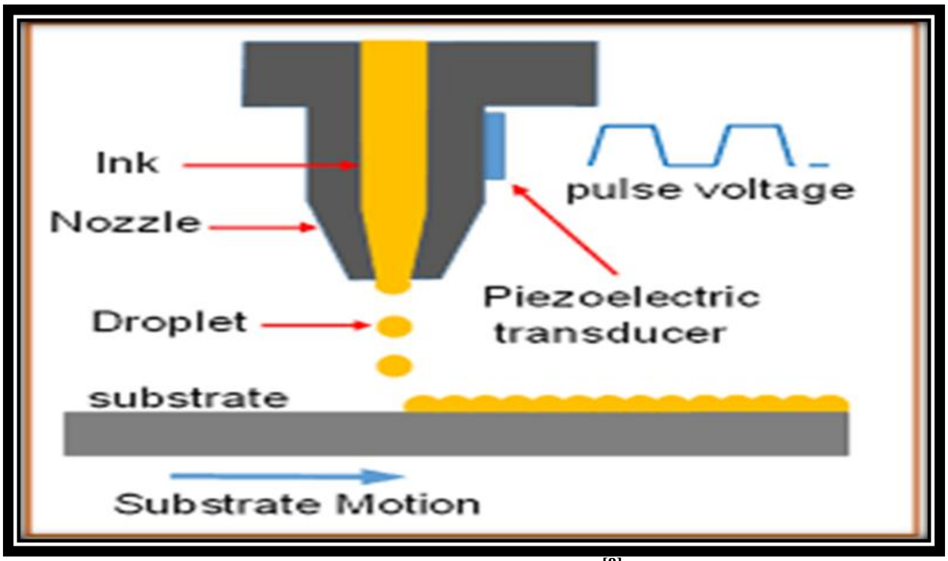


Figure 3: Inkjet Printer.[8]

Inkjet printing is a scaled technique for integrating pharmacologic agents with microscale or macroscale medical equipment, as well as embedding pharmacologic agents within drug delivery devices.

Stereo Lithography[5]

As the first 3D printing process, Charles Hull discovered it in 1988. During the printing process, photopolymer materials such as resin or acrylate that can be cured by UV laser were used. It's a popular and quick prototyping method that can create very detailed and accurate polymer parts. Stereo lithography creates an object layer by layer by tracing a laser beam on the surface of a vat of liquid photopolymer, which contains a movable stage to support the part being built. Wherever the laser beam strikes the liquid's surface, the photopolymer solidifies quickly. The platform is lowered using the layer thickness (usually 0.003-0.002 inch), and a fresh layer is generated on top of the previously finished layers. As a result of the material's self-adhesive characteristic, a three-dimensional object made up of multiple layers is totally constructed. During the fabrication process, objects having overhangs or undercuts must be supported by support structures during the fabrication process. These are either designed manually or automatically using a computer programme designed for rapid prototyping. When the part is finished, it is raised and drained from the vat. Surfaces with excess polymer are swabbed or washed. In other circumstances, the final cure is achieved by placing the part in a UV oven. The supports are removed from the part after the final cure, and the surfaces are polished, sanded, or otherwise completed.

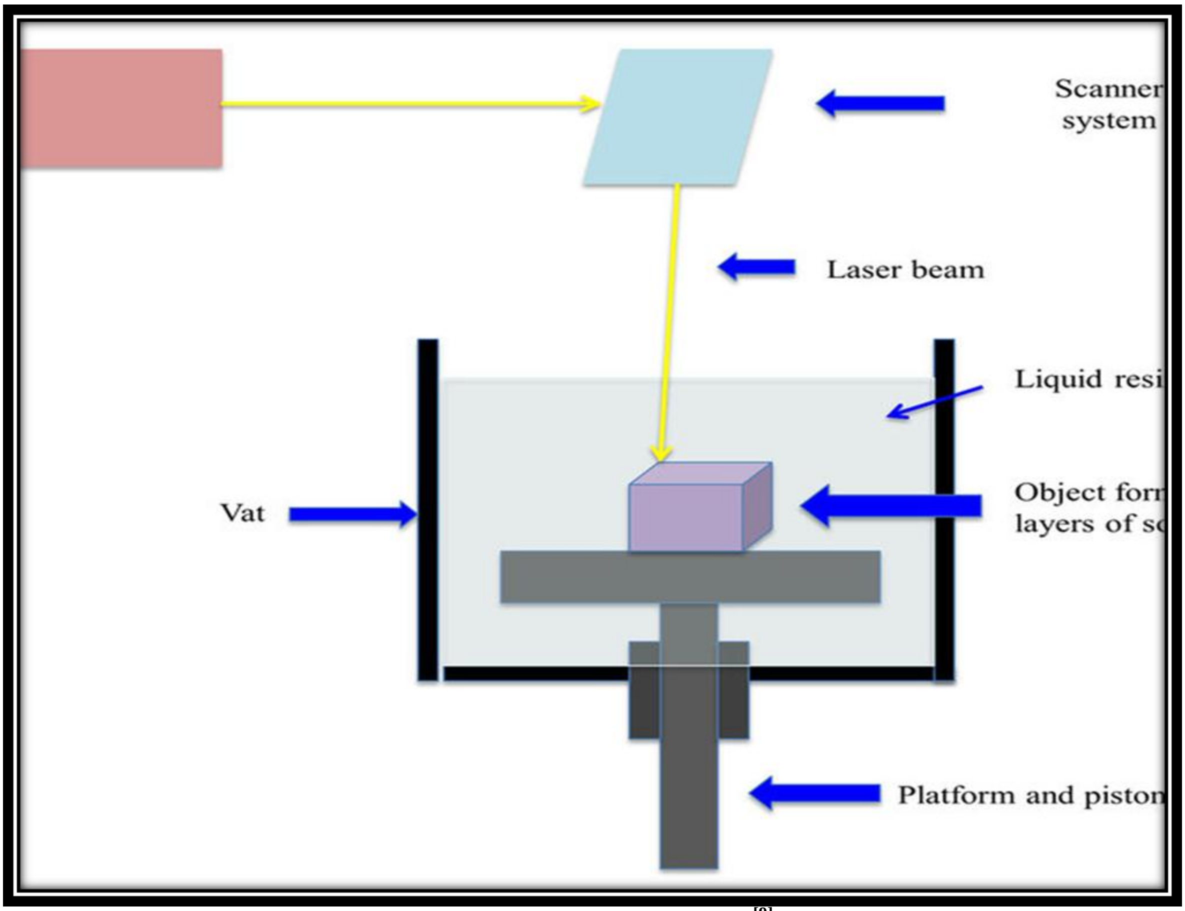


Figure 4: Stereo Lithography.[9]

New indwelling bladder devices for intravesical medicine administration were created using 3D printing and stereolithography (SLA). With various concentrations of lidocaine, elastic resin was employed to make two types of devices (hollow and solid).

Extrusion 3D Printing[5]

This technique not require any additional support material because the material is extruded from the automated nozzle onto the substrate. It is only used to make expect oral tablets containing Guaifenesin. Molten polymers, suspensions, semisolids, and pastes can all be extruded.

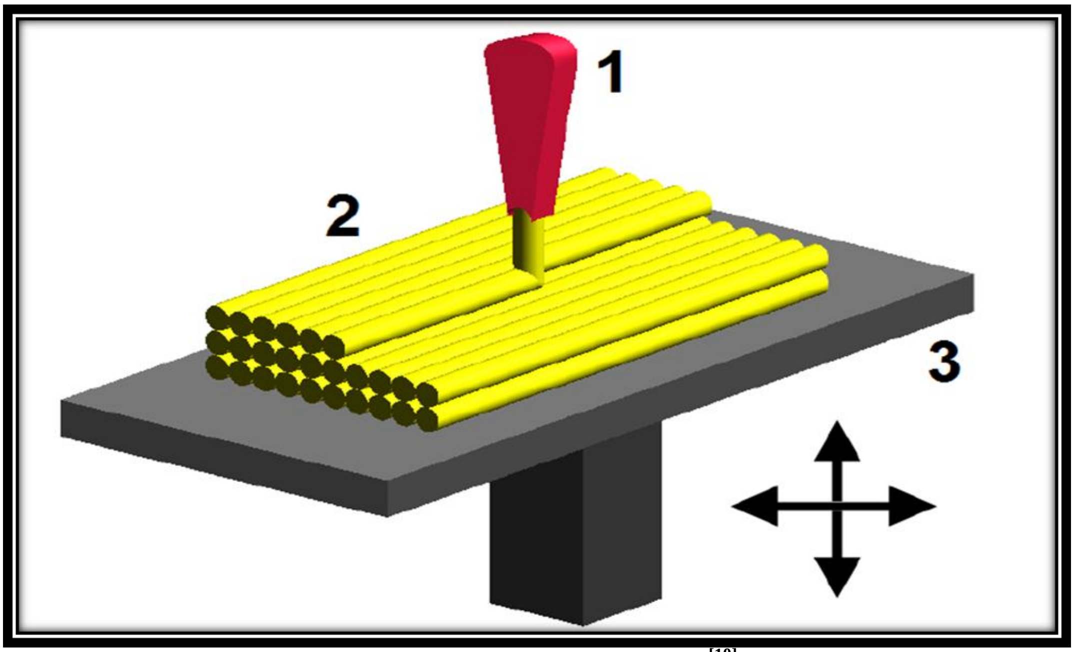


Figure 6: Extrusion 3D Printing.[10]

The initial step, regardless of the technology employed, is to design the object to be printed using computer assisted design (CAD) software. Semi-solid extrusion (SSE) is a material extrusion process that involves the successive deposition of a gel or paste to produce a 3D object.

Binder Jetting[11]

Binder jetting is a fast prototyping and 3D printing technique that involves selectively depositing a liquid binding agent to connect powder particles. To build the layer, the binder jetting technique jets a chemical binder over the distributed powder. Binder jetting would be used to produce casting patterns, raw sintered goods, or equivalent large-volume items from sand. Metals, sands, polymers, hybrids, and ceramics may all be printed using binder jetting. Some materials, such as sand, did not require any extra processing. Furthermore, the Binder jetting is a simple, quick, and low-cost technique in which powder particles are bonded together. Finally, binder jettinghas the capability of printing extremely big items.

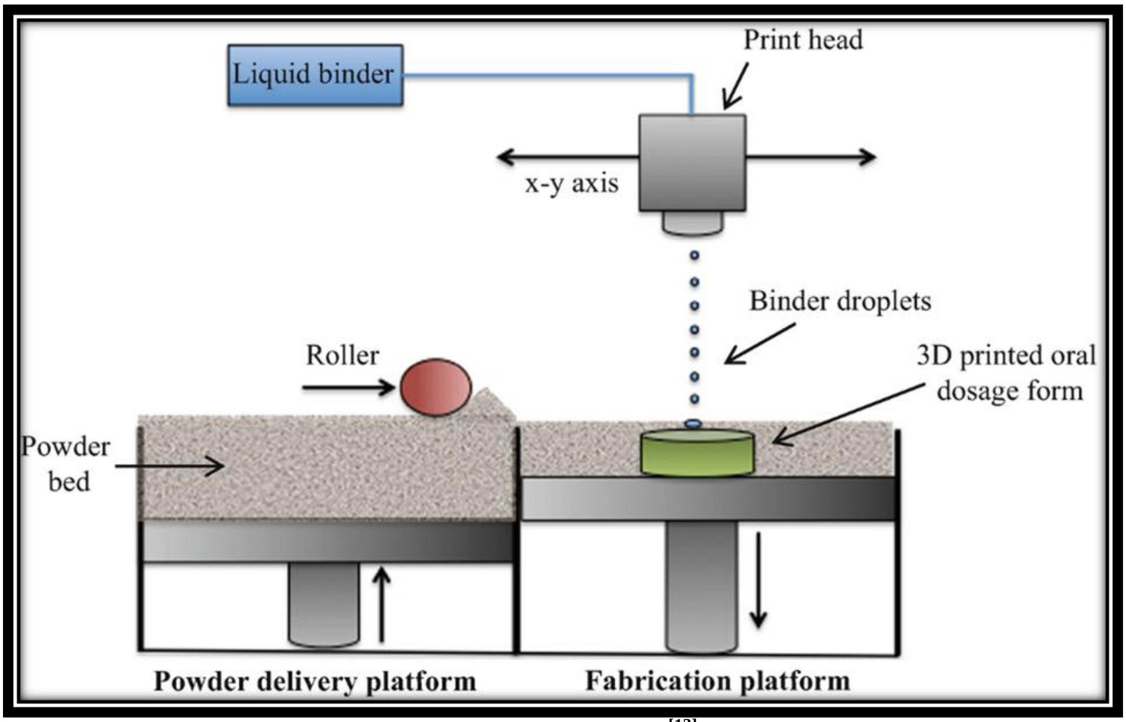


Fig 7: Binder jetting.[12]

This approach involved distributing pharmaceutical-grade powders repeatedly onto a build plate, then inkjet printing a liquid binder to selectively bind the particles in a specified pattern.

Directed Energy Deposition[11]

Directed energy deposition (DED) is a more difficult printing technique that is regularly used to restore or add material to existing components. Directed energy deposition offers a great degree of control over grain structure and may manufacture objects of excellent quality. In theory, directed energy deposition is comparable to material extrusion, except the nozzle is not locked to a single axis and can travel in various directions. Additionally, the technique may be utilized with ceramics and polymers, although it is most commonly employed with metals and metal-based hybrids. made with wire or powder Laser deposition and laser engineered net shaping are two examples of this technique. Laser deposition is a new technique that may be used to create or repair components with dimensions ranging from millimeters to meters. Because of its scalability and various capabilities in a single system, laser deposition technology is gaining momentum in the manufacturing, transportation, aircraft, and oil and gas industries. Meanwhile, laser LENS may use heat energy to melt metal during the casting process, resulting in finished components.[11]

The definition of directed energy deposition is "an additive manufacturing method in which concentrated heat energy is utilized to fuse materials via. At the Crossroads of Design, Manufacturing, and Surface Engineering. The Use of 3D Printing in Medicine.

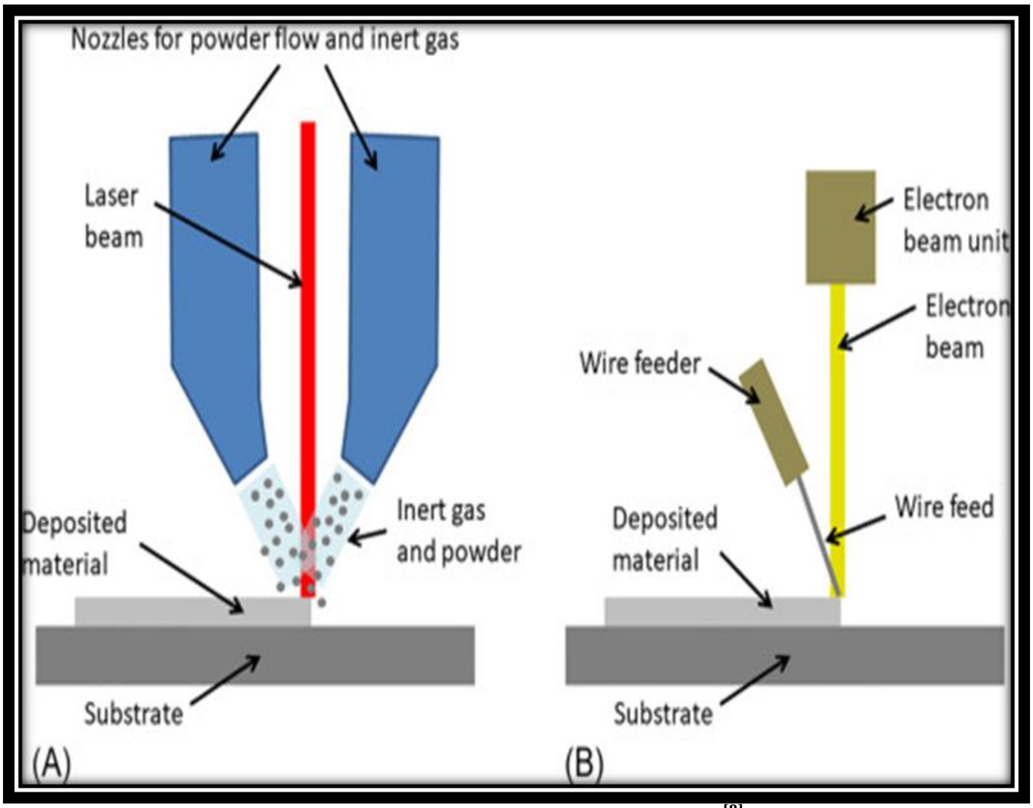


Figure 8: Directed Energy Deposition.[8]

Powder Bed Fusion[11]

The electron beam melting (EBM), selective laser sintering (SLS), and selective heat sintering (SHS) printing techniques are all used in the powder bed fusion process. This technique melts or fuses using an electron beam or a laser.the powder material combined Metals, ceramics, polymers, and other materials are examples of materials utilized in this process. hybrid and composite The common type of powder-based 3D printing is selective laser sintering (SLS). technology. In 1987, Carl Deckard invented SLS technology. SLS is a 3D printing technique that is currently in use. rapid speed, excellent precision, and a variable surface finish. Metal may be created using selective laser sintering. Objects made of plastic and ceramic.

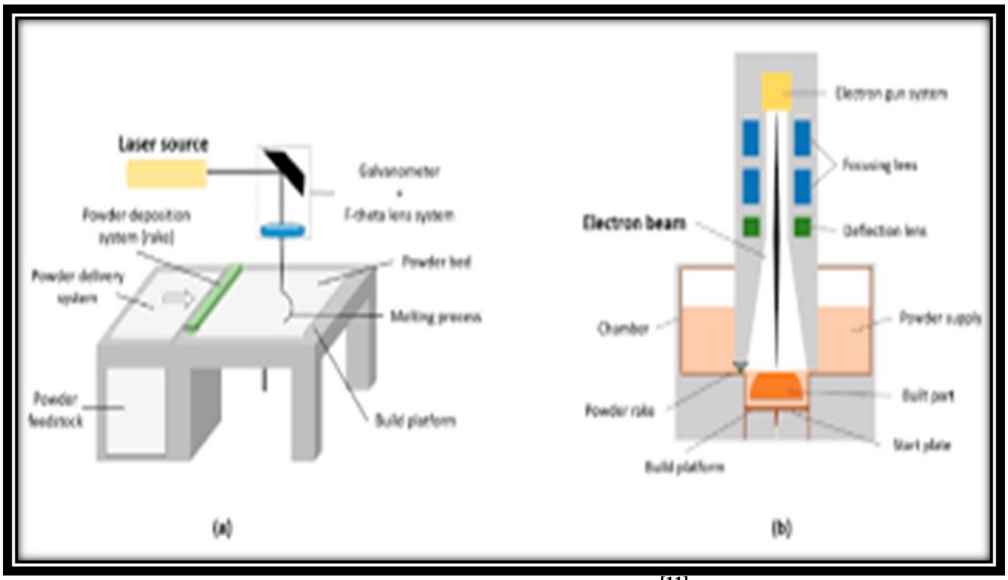


Figure 9: Powder Bed Fusion.[11]

Powder bed fusion (PBF) is a 3D printing technology that combines particles selectively into 3D objects using a power source.

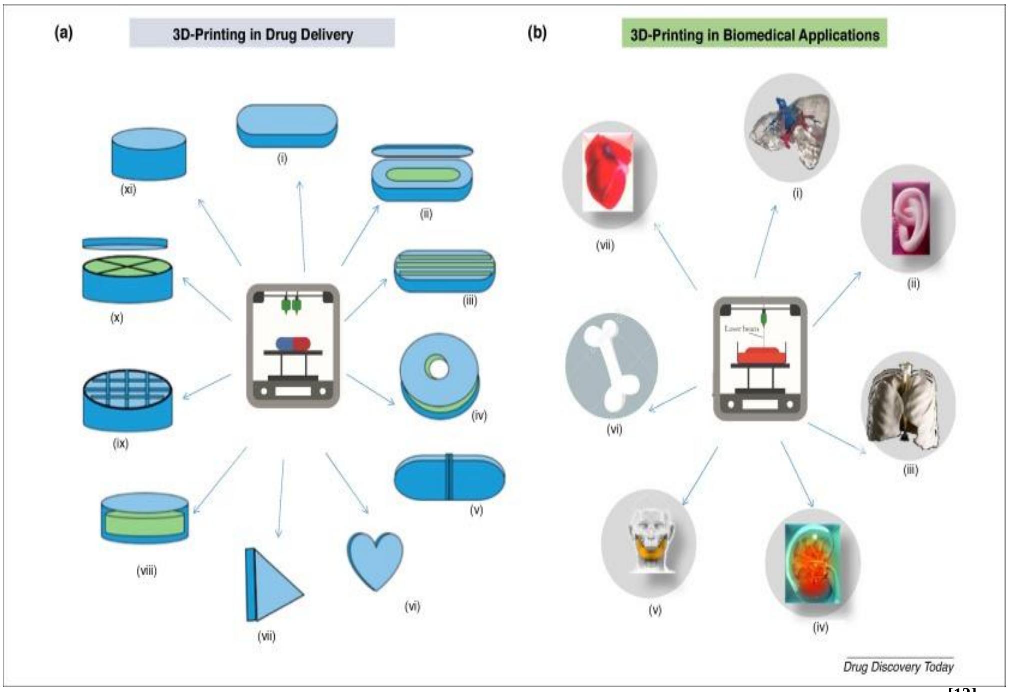


Figure 7: 3D Printing Technology for drug delivery and biomedical applications.[13]

Applications of 3D Printing[4]

3D printing has long been utilised in medical, with dental implants and personalised prosthetics being the first applications. Some of the current medical applications of 3D printing include tissue and organ manufacturing, prostheses, implants, and anatomical models, and pharmaceutical research encompassing drug discovery, delivery, and dosage forms.

Bio Printing Tissues and Organs

Organ printing employs 3D printing technology to layer by layer manufacture cells, biomaterials, and cell-laden biomaterials, resulting in 3D tissue-like structures. Researchers created a knee meniscus, a heart valve, a spinal disc, other types of cartilage and bone, and an artificial ear using 3D printers.

Customized Implants and Prostheses

Implants and prostheses that are made to order By turning X-ray, MRI, or CT scans into digital 3D print files, implants and prostheses in practically any shape are possible. This method has been used to create dental, spinal, and hip implants.

Anatomical Models

They provide a picture of some of the most complicated components in the human body, 3D-printed neuro-anatomical models can be very useful to neurosurgeons.

Dosage Forms and Drug Delivery Devices in 3D-Printed[14]

Pharmaceutical research and fabrication have employed a variety of approaches, with 3D printing being one of them due to the precise control of droplet size and dose, excellent reproducibility, and ability to construct dosage forms with complex drug-release profiles. 3D printing can also be used to standardise complex medication manufacturing procedures, making them easier and more viable. 3D printing technology may also play a key role in the advancement of personalised medicine.

Unique Dosage Forms

Inkjet-based or inkjet powder-based 3D printing are the primary 3D printing technologies used in pharmaceutical production. These technologies provide the ability to create an infinite number of dosage forms, which is likely to put conventional drug manufacturing to the test. Many novel dosage forms have already been created using 3D printers, including: Microcapsules, hyaluronic-based synthetic extracellular matrices, antibiotic-printed micro patterns, mesoporous bioactive glass scaffolds, Nano suspensions, and multilayered drug delivery devices are all examples of such materials.

CONCLUSION

3D printing has emerged as a useful and potentially transformative tool in the pharmaceutical industry, paving the way for personalized medicine centered on the needs of the patient. 3D printing technology is emerging as a new frontier for advanced drug delivery, with built-in flexibility that is well suited for personalized/customized medication. The pharmaceutical manufacturing style and formulation techniques will be transformed by 3D printing technology.

There is a growing body of research utilizing various types of 3DP. The capacity to generate individualised medicine is one of the key features shared by all available varieties of 3DP. Due to its ease of use, speed, and accessibility, it is increasingly pushing the development of medical equipment and pharmaceutical items on demand for patients in a clinical context. The capacity to adjust the release profile and dosing of a 3D printed tablet simply by changing the geometry using CAD, as well as the ability to include pharmaceuticals into FDM produced injectable devices or mesh implants using HME, expands 3DP's medical applications.

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