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A Review on 3D Printing Technology in Pharmaceuticals

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ABSTRACT

Three-dimensional printing (3DP) is expected to be one of the most forward-thinking pharmacy advancements. Due of its potential advantages over tailoring medications in individually calibrated doses, the use of 3D printing technology in drug delivery systems has exploded in recent years. 3DP enables the precise deposition of pharmaceuticals and excipients, potentially altering drug design, manufacture, and use. It might range from preclinical events and clinical preliminaries to frontline medical care in terms of drug improvement. Despite the therapeutic and commercial benefits of 3DP technology, numerous specialised and administrative hurdles limit its use in pharmaceutical products. As a result, ongoing development and refining of 3DP approaches is required to overcome present limitations and work with patients. The many types of 3D printers and their applications in various fields of drug delivery are discussed in this overview. There is also a collection of recent studies in the field of pharmaceutical 3D printing for medication delivery applications. In addition to the intriguing opportunities, the analysis covers the technological and regulatory hurdles that stymie the adoption of such technology in the pharmaceutical and health-care industries, as well as suggested solutions.

KEYWORDS: *Drug delivery system; 3D printing; Individualized medicine; Pharmaceuticals; Novel technology*

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INTRODUCTION

3D printing technique appears to be a re-assessment in pharmaceutical manufacturing technology, as it differs significantly from existing bulk mass production methods. The usefulness of 3D printing in the pharmaceutical manufacturing product has the potential to minimize cost of the product manufacturing of pharmaceuticals from days to weeks Only a few hours. Enhancing the manufacturing process can result in a faster release of the medication of the product into the body. The Multifunctional drug delivery systems with the accelerated release characters, adjustable and designed dosage forms, implants and phantoms conforming to the specific patient anatomy, and cell-based materials for regenerative medicine are among the current breakthroughs.

In 2015 the first FDA Approved medicinal product, the researchers are carried out on 3D Printing technology for pharmaceuticals has trending the attention of many pharmaceutical scientists, due to its ability and the potential of making the complex structures and its geometrical characteristics. It is highly developed technology for manufacturing of self-dosage forms.

Three-dimensional (3D) printing technology is a way for developing pharmaceuticals and formulations that uses computer-aided designs (CAD) and printing settings to ensure that the medications that are printed are adjustable. Traditional pharmaceutical compounding, on the other hand, is the act of combining, mixing, or changing materials to make drugs in response to specific patient needs such as particular dosage forms, drug strengths, or excipients.

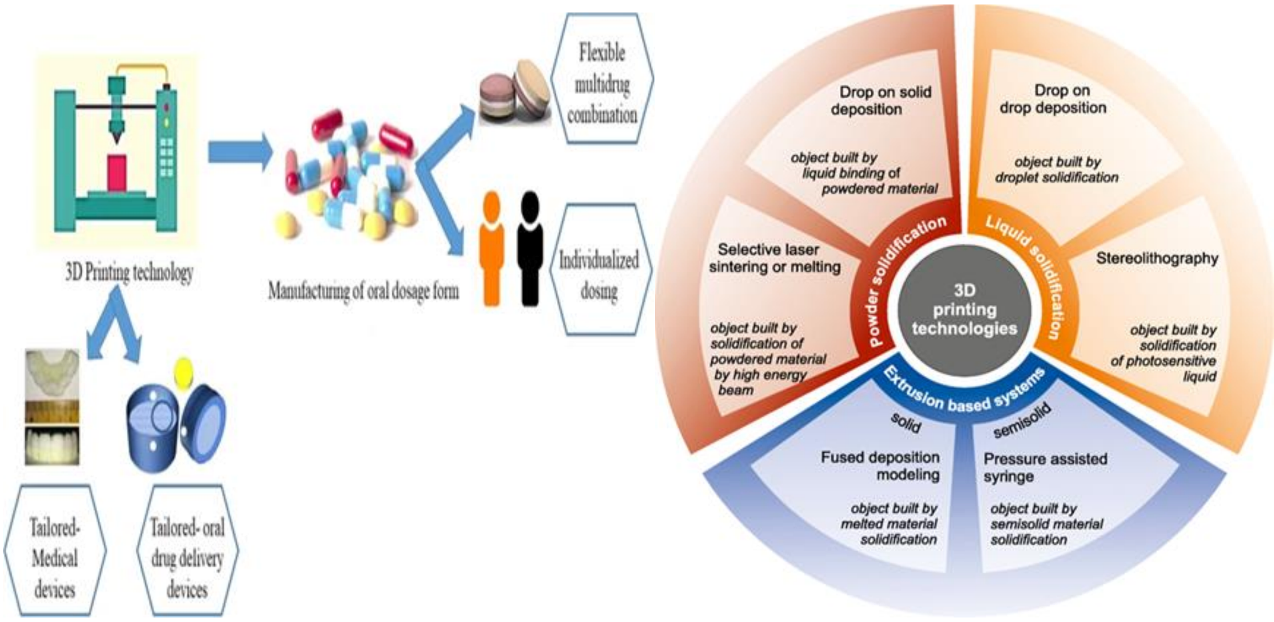

Figure 1 3-D Printing technologies

"The manufacturing of items through the deposition of a substance utilising a print head, nozzle, or other printer technology," according to the ISO. It has been widely used in tissue and organ engineering, diagnostics, disease modelling, and the production of medical devices. design and development of innovative dose devices in biomedical devices forms. It is used as a procedure in the pharmaceutical industry. utilising cutting-edge technologies to create digitally controlled and tailored environments by transforming a concept into a prototype additive manufacturing employing 3D computer-aided design (CAD) or a Magnetic Resonance Image (MRI)

On the one hand, this technology has a greater resolution than some other 3DP technologies, as well as superior mechanical strength and design flexibility, which allows for easy changes to some printing parameters, such as in fill. % of print lets required to achieve target medication release the printed dosage profiles forms. The biggest constraint, on the other hand, is the potential for drug degradation. This could happen if a large amount of heat is used. In many situations, Temperatures above 120°C are employed, which can cause medication degradation and deterioration, mechanical characteristics, physical stability degradation, filament ageing, and relatively the 3DP objects have a low resolution.

EVOLUTION OF 3 D PRINTING TECHNOLOGY: -

The concept of 3DP dates back to the early 1970s, when Pierre A. L. Ciraud outlined a method of applying powdered material and then solidifying each layer using a high-energy laser. Meltable materials such as plastics or metals might possibly be employed for object preparation in this case. Ross Housholder introduced an idea of sand binding by different materials in a patent titled: BA moulding procedure for making a three-dimensional product in layers in the early 1980s, and Carl Deckard created a method of solidification of powdered bed by laser beam termed selective laser sintering (SLS).

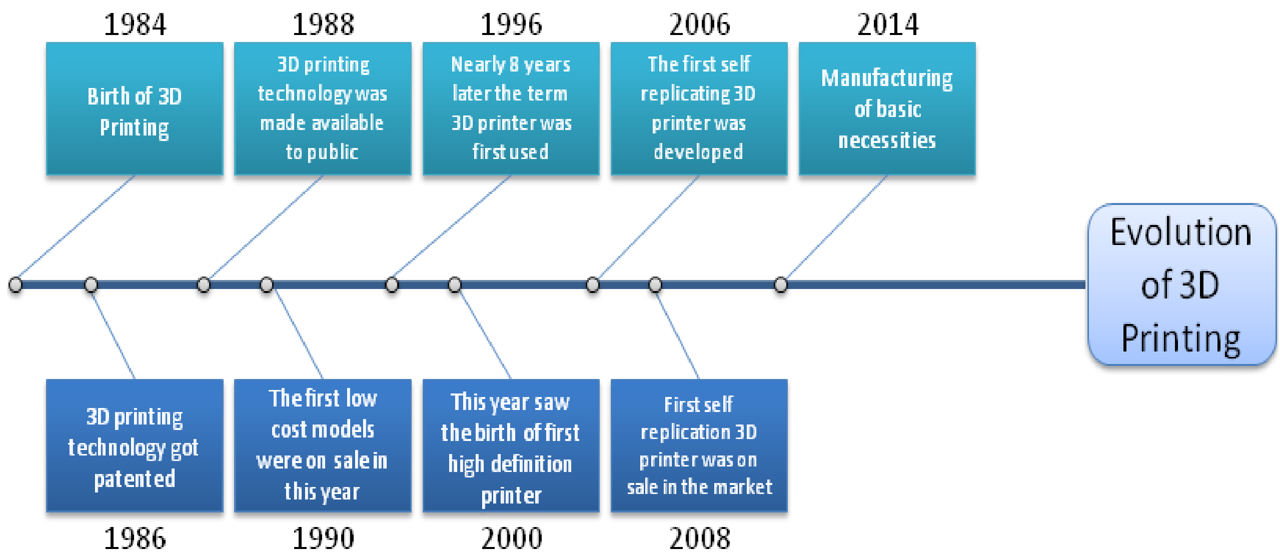

Figure 2 Evolution of 3D printing technology.

Chuck Hull's first commercially available technology was stereolithography (SLA). Photo polymerization was used in this procedure. Scott Crump filed a patent for fused deposition modelling (FDM), a technique for preparing objects using thermoplastic material, at the end of the 1980s. In the 1990s, Emanuel Sachs, an MIT scientist, and co-workers patented Three-dimensional printing processes, which rely on binding material to combine specific regions of powder. The most significant advances in 3D printing for pharmaceutical and biological applications are discussed.

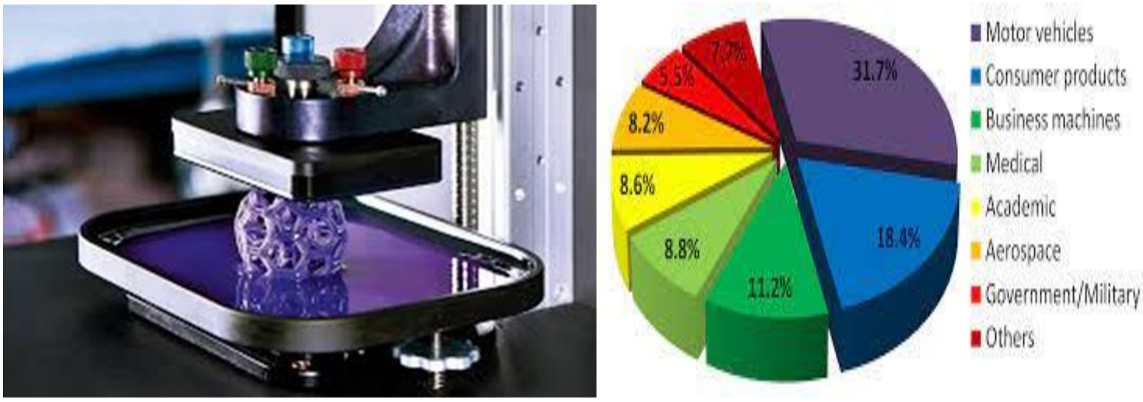

Figure 3. Evolution of 3D printing technology.

CLASSIFICATION OF 3D PRINTING TECHNOLOGY

3D Printing techniques are classified into main 4 types that are Raw material in liquid form, Raw material in solid form, Raw material in powder form and Raw material in sheets form. Further that they are sub classified into different categories .In first class stereo lithography, polyjet 3D printing and DLP printing. In solid form there are fused deposition modelling, fused filament fabrication and multijet modelling. In powder form there is selective laser sintering, direct metal laser sintering, laser powder forming and binder jetting. The last class can be classified as laminated object manufacturing, paper lamination technology and selective deposition lamination**.**

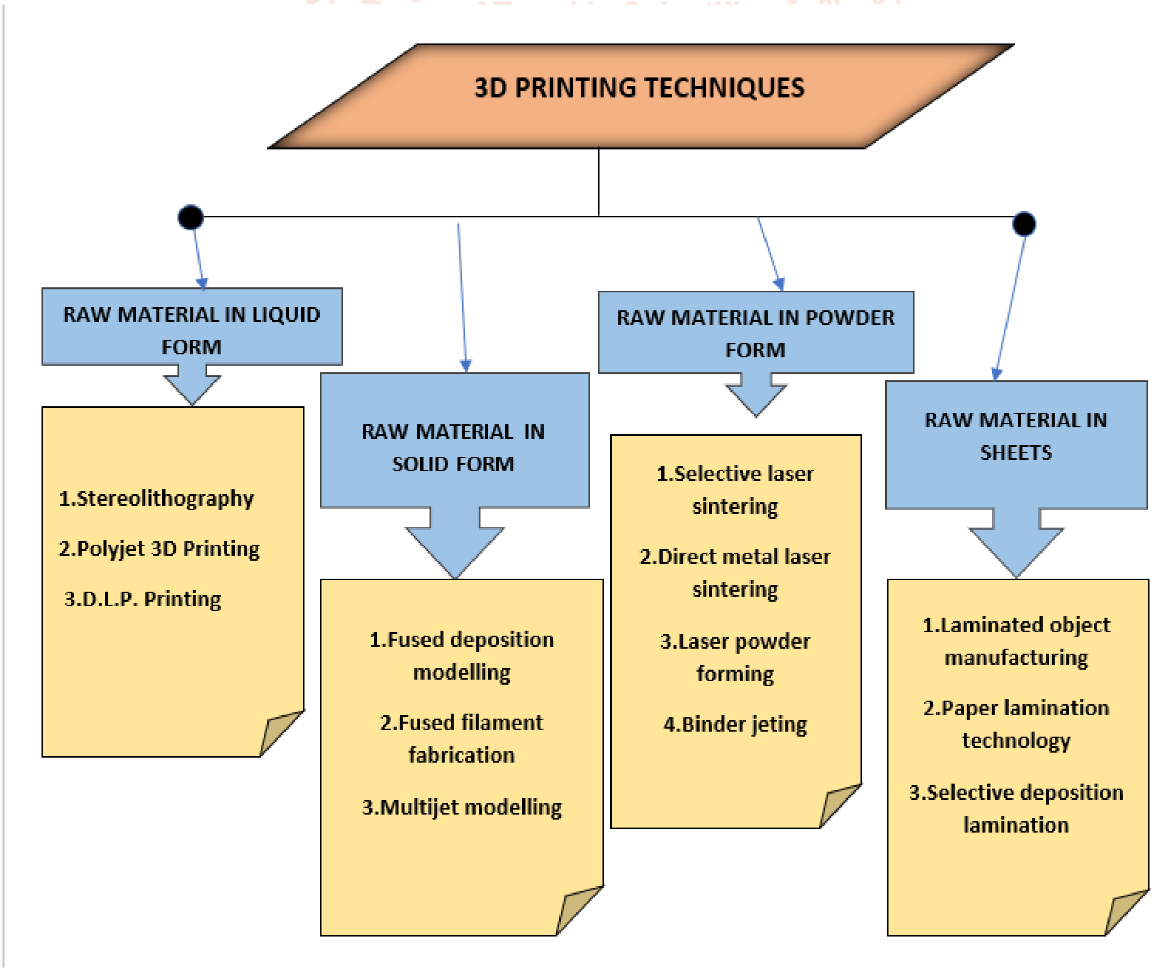

Figure 4 Classification of 3D printing.

A. Raw material in liquid form-

1. Stereolithography: -

Stereolithography is a 3D printing technique that involves layer-by-layer solidification of liquid resin using photo polymerization. When focused on a tank filled with photosensitive resin, an ultraviolet or other light source produces crosslinking and generates a polymeric matrix. After each layer has been dried, the platform is lowered and a new layer of uncured polymer resin is applied in a bottom-to-top build technique, deposited on top of the cured layer for the next curing,

Another method includes curing the resin layer through a clear plate at the bottom. a light source from underneath illuminates the resin tray. Then the curing of each layer, the platform is elevated, allowing uncured resin to fill the space between the platform and plate, allowing following layers to be cured in a top-down technique. The kinetics of the crosslinking reaction of resins are determined by the power of the light source, the speed of scanning, and the quantity of monomer and photo initiator, which influence the thickness of the cured layer as well as the curing time.

B. What are some of the benefits of SLA 3D printing?

1. SLA is capable of producing items with extremely high dimensional precision and fine detailing.
2. The excellent surface quality of SLA parts makes them perfect for visual prototypes.
3. Specialty SLA materials, such as transparent, flexible, and castable resins, are available.

This printing technology has the advantages of high resolution and speed, as well as minimised localised heating, making it suited for printing thermolabile pharmaceuticals. Furthermore, stereolithography's high-resolution capabilities allowed it to be used in the fabrication of high-quality microneedles patches, similar to those fabricated microfabrication techniques such as soft lithography, despite the fact that it was originally used to fabricate Nano and Micro patterns for micro electro mechanical systems. Another advantage is relevance in the realm of pharmaceutics is that this type of printing allows miscible components, such as excipients and APIs, to be entrapped in the polymeric matrix upon crosslinking.

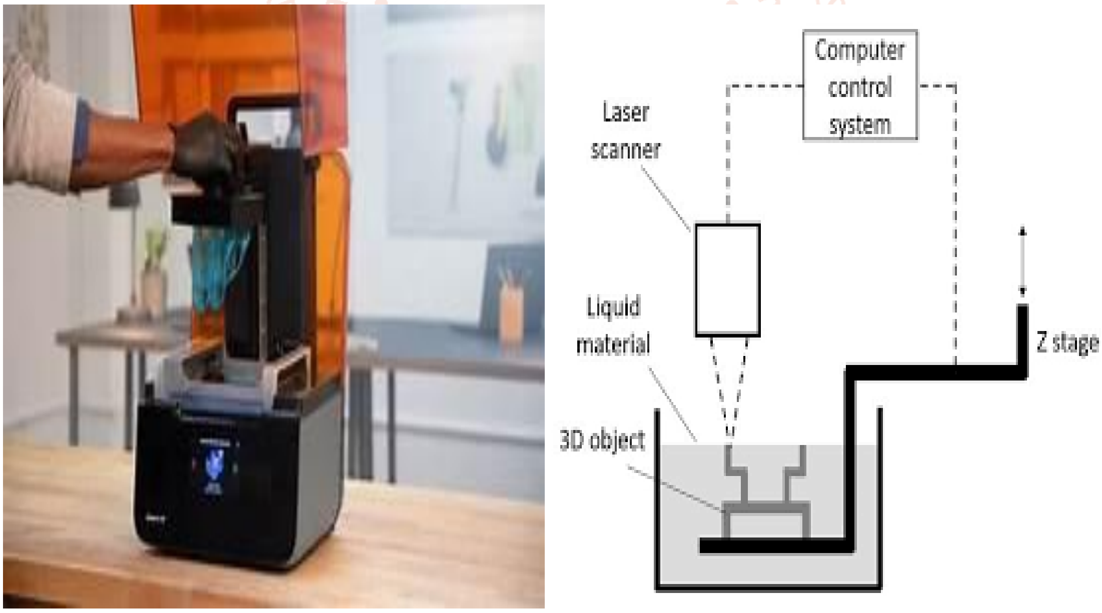

Figure 5. Stereolithography

2. Polyjet 3D printing: -

➢ How does Poly Jet Technology work?

Poly Jet is a cutting-edge 3D printing method that creates smooth, precise parts, prototypes, and tooling. It can manufacture thin walls and complicated geometries using the greatest range of materials accessible with any technology, with microscopic layer resolution and precision down to 0.014 mm. ()

➢ **Polyjet's advantages: -**

1. Create smooth, detailed prototypes that accurately reflect the final product's appearance.
2. Make precise moulds, jigs, fixtures, and other production equipment.
3. Create detailed details, complicated shapes, and delicate characteristics.
4. For unequalled efficiency, combine the broadest range of colours and materials into a single model.

It's simple to see why more hospitals and academic medical institutes are incorporating 3D printing into their processes in an area where innovation saves lives. PolyJet printers like as the J5 MediJet and J750 Digital Anatomy are designed specifically for this purpose. PolyJet printing can be used to make realistic anatomical models that can be adjusted for a range of training applications. These adaptable models are easier to make and less expensive than standard training aids.

Surgery used to entail looking at scans on computer displays and imagining how the surgery would be performed without 3D printing. Patient-specific models can be generated with numerous materials and colours using PolyJet printing to closely resemble what the surgeon might see in a physical 3D model. The PolyJet printed models provide improved planning, potentially leading to faster surgeries and higher success rates.

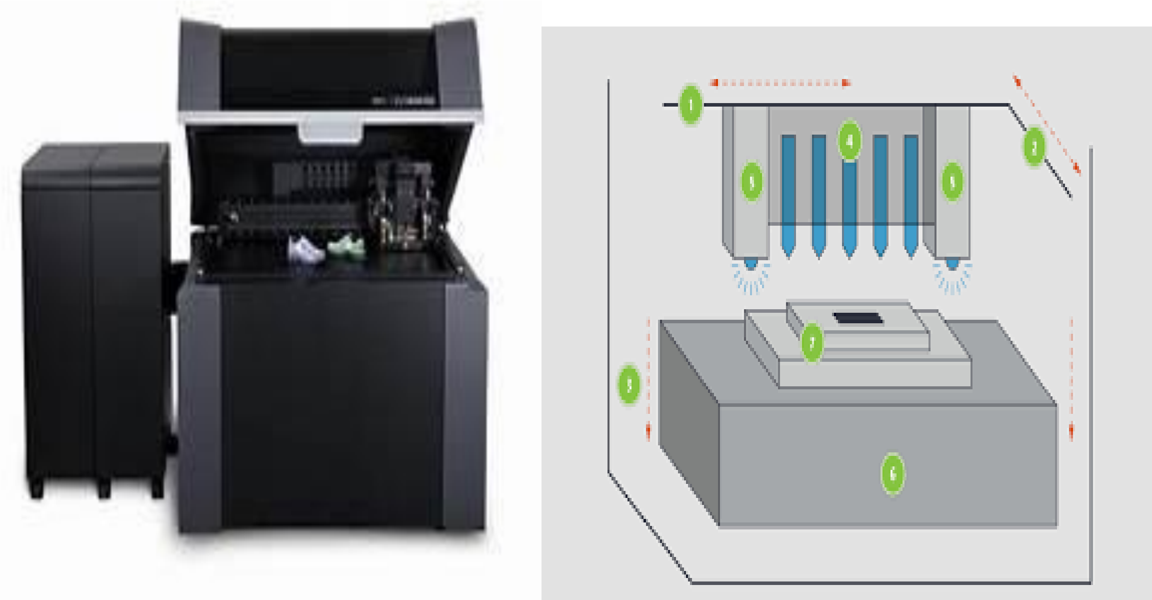

Figure 6. Polyjet 3D printing technique.

3. DLP Printing: -

Digital light processing printers are more efficient, quicker, and can print at a wider variety of wavelengths. DLP printers are adaptable to bespoke resin reservoirs and small volumes of photoreactive polymers, unlike laser-based commercially available SLA printers, which do not allow for the use of extremely small amounts of resins for printing. Despite DLP 3DP's potential for printing medical equipment and microneedle-mediated medication delivery systems, this technology has yet to be used in the manufacture of solid oral dosage forms. As a result, we intend to investigate the viability of using DLP 3DP in the production of solid oral dosage forms for the first time.

As a result, we intend to investigate the viability of using DLP 3DP in the production of solid oral dosage forms for the first time. We used theophylline as a model medicine and two typical photoreactive polymers, PEGDA and PEGDMA, to vary the polymer concentration in order to manufacture robust tablets with the least amount of polymer. We also created and made tablets with variable surface areas in order to obtain different drug release profiles. FTIR spectroscopy was also used to evaluate the drug's interactions with photopolymers.

➢ **The following are the key benefits of DLP technology: -**

1. rapid printing;
2. good laying precision;
3. several application areas;
4. printers are inexpensive.

DLP printers are widely available, making this technology attractive, particularly in personalised medicine. It's worth noting that DLP technology can be used to make dental models and various medication delivery implants. The biggest downside of photopolymerization methods is the high cost. The unreacted monomer and photoinitiator residues may cause cytotoxicity Compared to other methods, high drug loading has yet to be achieved in DLP printing due to its complexity important to give sufficient photopolymer content (which instantly decreases the chance of contamination) To obtain homogenous tablets, a larger number of other components is added.

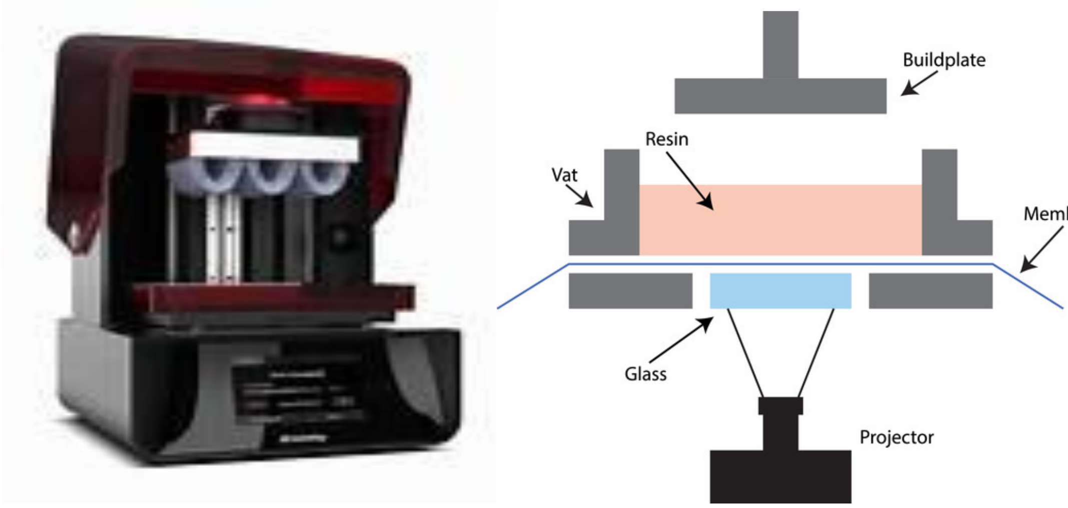

Figure 7. Digital light processing technique.

B. Raw material in solid form: -

1. Fused deposition modelling: -

FDM is a 3D printing technique that includes depositing molten polymer layers by layers onto a substrate to create a 3D object. The feeding of a polymer filament into the heated printer-head and nozzle of the 3D printer is used to deposit construction material. The melted semi-solid shape is extruded onto the printer platform after heating. The polymer is extruded along the x and y axes by the nozzle, and the stage is lowered to accommodate the next layer.

As a result, material accumulates along the z axis. CAD software is used to create the shape and size of the printed material. By adopting fused deposition modelling as a printing technology, common issues such as excess residual solvent in inkjet printing can be overcome. Despite the method's many advantages, such as its simplicity, low cost, and ease of accessibility, it has drawbacks, such as thermal deterioration of the material. components, inadequate drug loading, and delayed drug dissolution.

➢ **Advantages of fused filament modelling: -**

1. Budget-Friendly
2. Reusable Filament
3. Printing from a Cloud Server
4. Less complicated
5. Simple Ergonomics

Sun and Soh demonstrated an alternative method for achieving complicated drug release in 2015. Tablets with complex release profiles can be made utilising a sequential casting method using a typical FDM 3D printer to develop designs for drug cores. Although this method can produce unique release profiles, the multistage drug casting process that follows pattern printing lacks important 3DP benefits including flexibility and efficient production. Drug compatibility with solvents and polymeric additives can also limit its applicability because pharmaceuticals are disseminated in UV-activating polymeric solutions for casting.

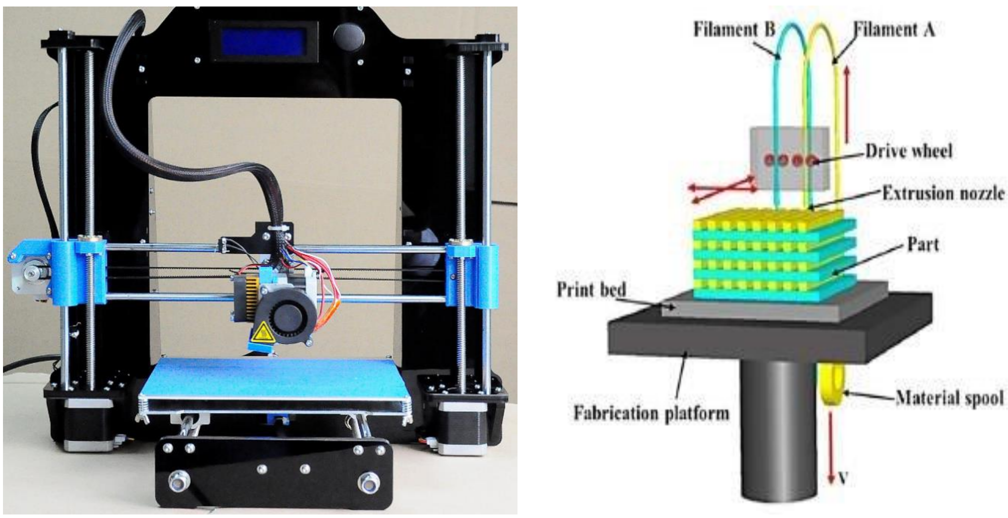

Figure 8. Fused deposition modelling technique

2. Fused filament fabrication:-

FDMTM (fused filament fabrication), often known as FFF, is a commonly utilised technology. It has had a significant price reduction during the last decade. This method also has a number of advantages over other 3D printing technologies, such as being user-friendly and requiring less maintenance. The final product's post-processing processes A filament is melt-extruded in a conventional FFF 3D printer. through a controlled movement of a nozzle with a particular diameter in three-dimensional space to create a 3D geometry. The physical state of thermoplastic polymers changes when heated from when fully melted, it goes from solid to semi-solid to liquid. The ideal printing temperature is determined by the substrate. The rheological properties of the melt and the thermal properties of the polymer.

Many common thermoplastics, wood and metal-infused thermoplastics, and even food is among the materials available (such as chocolate).

C. **Advantages of Fused filament fabrication: -**

1. The cheapest printer technology.
2. The cheapest materials.
3. It's simple to switch materials.
4. Printing with a variety of materials is possible.
5. Many firms provide printers and supplies.
6. Building your own printer is relatively simple and Printing is quick.

The filament is commonly made using the hot melt extrusion (HME) process, which is a well-known polymer processing technique. This technology is used to manufacture a variety of items. HME is based on the physical properties of materials changing when they are heated. This method employs a motor-driven screw-based extrusion mechanism housed in a barrel. Following the recent explosion of the FFF market, HME technology was heavily exploited to generate the feedstock material for these 3D printers, which is a filament with a diameter ranging from 1.75 mm to 3.00 mm.

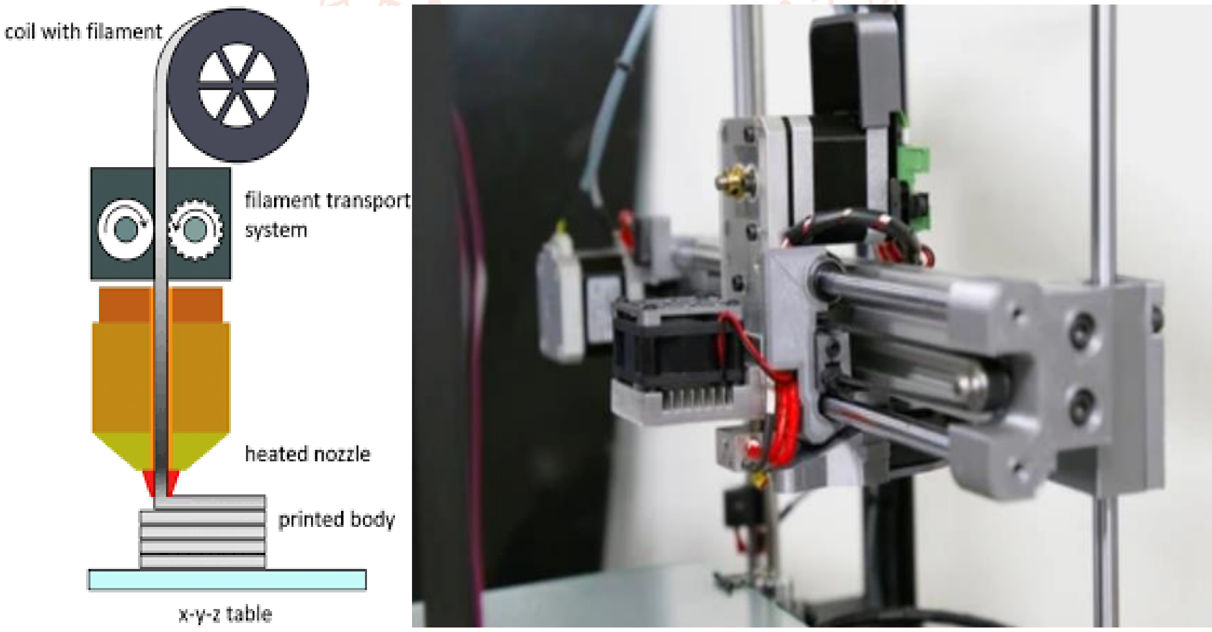

Figure 9 Fused filament fabrication

3. Multijet modelling: -

MultiJet Printing (MJP) is an inkjet printing technique that use piezo printhead technology to layer-by-layer deposit photocurable plastic resin or casting wax materials. MJP is utilised to create finely detailed parts, patterns, and moulds for a wide range of applications. These high-resolution printers are inexpensive to buy and run, and they use a meltable or dissolvable support material to make post-processing easier. This also enables support removal almost hands-free and allows for thorough cleaning of even the most delicate features and internal cavities without causing damage.

MJP printers produce smooth, high-resolution hard plastic items with complex geometries in a short amount of time. UV bulbs and photopolymer materials are used in the printing process. With layer thicknesses as low as 16 microns, MJP printers provide the highest Z-direction resolution. Selectable print modes allow users to choose the best resolution and print speed for their application, making it simple to discover the right mix. For many applications, MJP parts have a smooth surface quality and can attain accuracies that rival SLA. Plastic materials' durability has increased in recent years, making them appropriate for several end-use applications.

MJP printers have the advantage of providing easy and economical access to high-quality prototypes and indirect manufacturing aids. MJP printers are excellent for direct investment casting applications in the jewellery, dentistry, medical, and aerospace industries, where digital operations save time, labour, and money. MJP wax printers also provide a digital alternative to traditional lost-wax casting procedures, removing time-consuming and expensive processes while seamlessly integrating with existing casting methods and materials.

➢ **Advantages of multijet printings are: -**

1. Fast printing processing.
2. Economical 3D printed parts across industries,
3. MJP delivers true-to-CAD part accuracy in a variety of plastic, elastomeric, composite, and wax materials.
4. MJP is a fantastic option for: - a. medical equipment that require USP Class VI and/or
5. Rapid tooling patterns, dies, and moulds, Patterns for investment casting

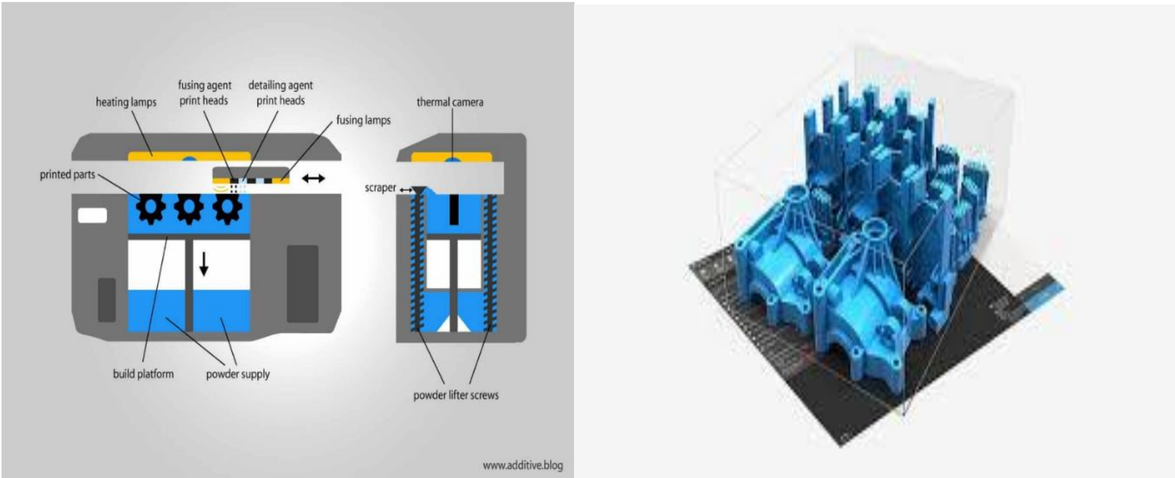

Figure 10. Multijet modelling.

C. Raw material in powder form: -

1. Selective laser sintering: -

Light energy is used to bind powder particles together in SLS, an alternative laser process. The laser will be guided by the exact pattern entered into the computer in order to draw the specific free-forms from the powder bed. The goal is to achieve solid-state sintering with a local temperature between the material's melting point (Tm) and the highest porosity possible. This approach has just recently been studied in the pharmaceutical area. In 2017, SLS was used to create a solid paracetamol dispersion using Kollicoat® IR and Eudragit® L100-55. Candurin® Gold Sheen (3 percent w/w), an approved pharmaceutical absorbent excipient, was employed to boost the system's energy of absorption.

There was no evidence of deterioration. Thermograms and diffractograms in the Kollicoat® demonstrated paracetamol crystallinity, but no peaks in the Eudragit®. In the same fluid, Kollicoat® formulation permitted API dissolving in acidic conditions, whereas Eudragit® formulation only allowed for modest releases. Finally, it has been shown that as the drug content increases, the porosity decreases, requiring more time to release the complete loading process.

One year later, the same authors investigated the use of SLS to create a variety of shapes, including gyroid lattice. Again, different polymers (Eudragit® L100-55, Eudragit® RL, Ethylcellulose N7, and PEO) were used to treat paracetamol. Gold Sheen Candurin® was utilised. The length of dissolution was reduced in all formulations, which was attributable to an increased surface area once again. Within 10 minutes, PEO allowed for the fastest total release. This promising method allows for the creation of incredibly precise free-forms without the use of any support.

➢ **Compared to other technologies, laser powder forming has various advantages**.

1. The capacity to develop massive tools and components
2. It is very fast technique.
3. By using diverse metal alloys and composite materials is one of the advantages.

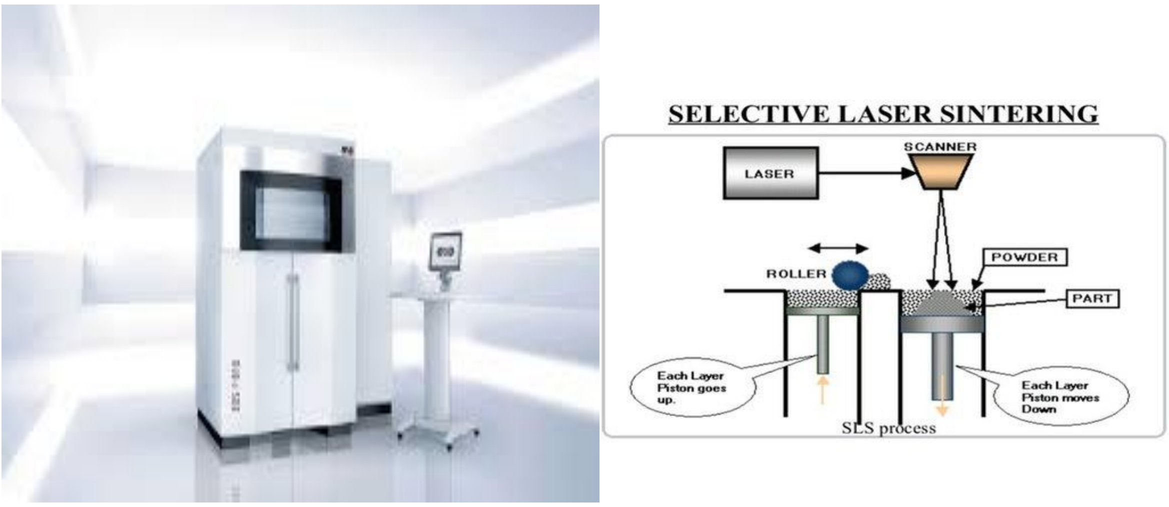

Figure 11. Selective laser sintering

2. Direct metal laser sintering

DMLS (direct metal laser sintering) is a metal 3D printing AM technology. By scanning a high-power laser beam through the metal powder (20 m diameter), which is free of binder or fluxing agent, the metal powder is totally melted. The final product has the same qualities as the source material. Fast Product Innovations (RPI) and EOS (Electro Optical System – Germany) invented direct metal laser sintering (DMLS) in 1994 as the first commercial rapid prototyping method to create metal parts in a single process. DMLS technology is well-known for being a leading technique in direct hard tooling, often known as direct tooling. The scanning of a high-power laser beam at 20 or 40 m layers sinters powdered metal devoid of binder or fluxing agent, with the option of bronze, steel, stainless-steel 316L, titanium, or Al-30 percent Si.

After that, the recoater arm sweeps over a new layer of powder, allowing a new layer to be sintered on top of the existing one. Because the pieces are created with a density of 95 percent, the DLMS technique does not require any further sintering of the parts. Support structures are required even when the layers are sintered. Heat treatment, support removal, shot peening, and other post-processing procedures may be required for parts.

Experiments currently reveal that powder qualities and process factors influence the properties of DMLS produced parts. Despite a lot of computational effort in recent years, the relationship between processing parameters and printed material qualities is still unclear [29]. The creation of melting pools and powder phase shift have been studied using computational fluid dynamics. To forecast the melting pool size, laser track, and residual stress, N'Dri et al. [30] provided an uncertainty quantification approach. Their research shows that simulation results are significantly reliant on particle conductivity and heat absorption accuracy.

- **Advantages of direct metal laser sintering are: -**

1. Larger Streamlined Production.
2. End-Product Precision.
3. Design Independence
4. Strong and versatile.

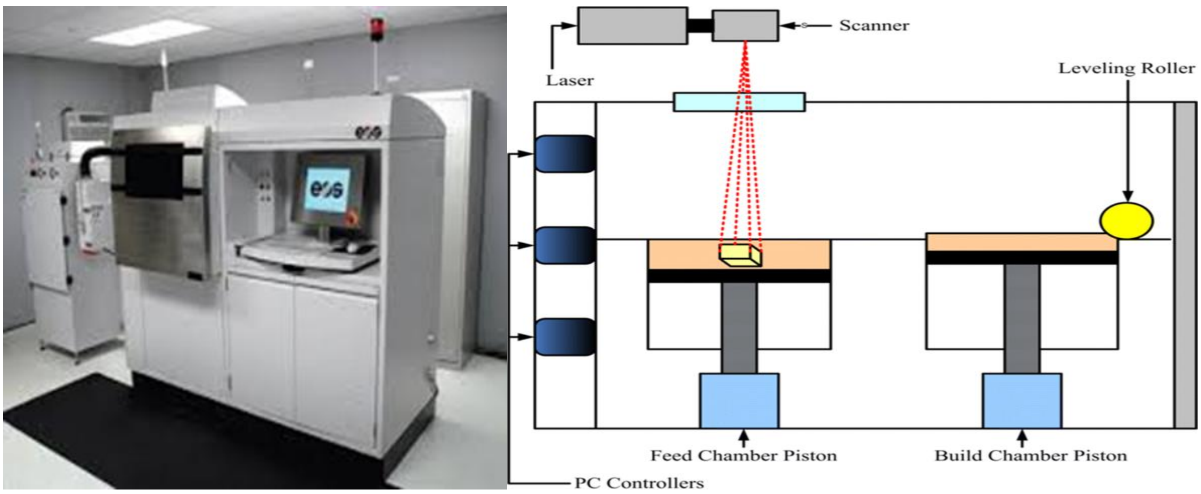

Figure 12. Direct metal laser sintering

3. Laser powder forming

The inkjet-powder bed 3DP technology, which was patented by MIT in 1989, involves applying liquid binder in successive layers to attach powder components together [2]. Its medical uses (implants, tissues, OSDF) were licenced exclusively to Therics Inc. under the Their Form TM trademark. Their Form TM application and related techniques have been thoroughly examined [4]. We provide a chronology of its evolution and significant milestones. Their Form TM's first pharmaceutical development focused on printing drug-loaded fluids onto an excipient powder bed to create (complicated) immediate, prolonged, and multi-release tablets (print drug approach). The limited selection and loading of active medicinal substances are its principal disadvantage (APIs).

The reason for this is that for reliable jetting and uniform drop creation with minimal satellites, print heads and ink must be well-matched acoustically for inkjet printing, especially drop-on-demand. Furthermore, parameters such as ink solvents and drying rate alter the solid state of an API following deposition (which affects bioavailability). As a result, developing an appropriate API-containing ink is an often over looked task. Printing binder solutions to consolidate API-containing powders into rapid dispersing tablets is an alternate strategy that is the foundation of Zip Dose®, Aprecia's Spritam® technology. This method simplifies ink composition (similar binders work with a variety of API powders) and enables the manufacture of high-dose drugs (Aprecia claims up to 1000 mg).

Additionally, because ZipDose® is a raster layer production process, it may be readily scaled up by clustering numerous inkjet print heads to produce tablets in parallel. Customizing dose composition, on the other hand, is more challenging because different powder constituents must be carefully stacked between print passes. Finish machining may be required for the LPF process to produce more attractive items. Laser Powder Forming, unlike laser sintering, does not require a subsequent fire procedure. LPF technology is primarily employed in the manufacture of moulding tools. The process can also be used to create titanium metal components in the aerospace sector on a large scale.

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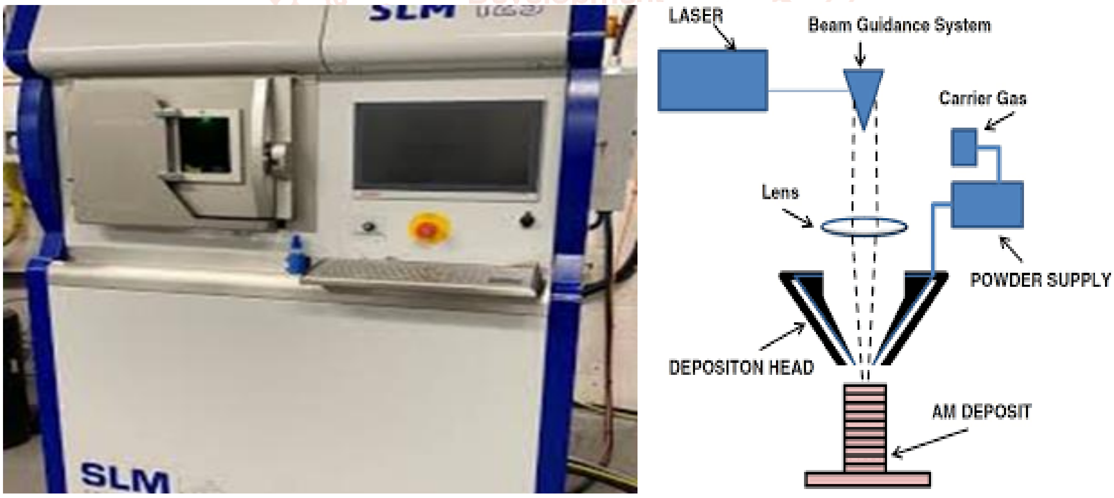

Figure 13 Laser powder forming

4. Binder jetting: -

Binder jetting refers to a group of additive manufacturing techniques. A binder is selectively placed into the powder bed in Binder Jetting, gluing these areas together one layer at a time to make a solid object. Metals, sand, and granular ceramics are among of the most typical materials utilised in Binder Jetting. Binder Jetting is utilised in a variety of applications, including full-colour prototypes (such as figurines), huge sand-casting cores and moulds, and the creation of low-cost 3D printed metal parts. With so many applications, it's critical for a designer who wants to make the most of Binder Jetting's capabilities to grasp the process's basic mechanics and how they relate to its primary benefits and limitations.

Accuracy and tolerance vary widely depending on the model and are difficult to anticipate because they are heavily influenced by geometry. Parts with a length of 25 to 75 mm, for example, shrink between 0.8 and 2%

following infiltration, while bigger parts shrink by 3 percent on average. The part shrinkage during sintering is roughly 20%. The machine's software compensates for shrinkage in the parts' dimensions, but non-uniform shrinkage might be a problem that must be addressed during the design stage in collaboration with the Binder Jetting machine operator.

The surface roughness of the generated items is an advantage of metal Binder Jetting over DMLS/SLM. After post-processing, metal Binder Jetted parts typically have a surface roughness of Ra 6 m, which can be decreased to Ra 3 m if a bead-blasting step is used. DMLS/SLM pieces, on the other hand, have a surface roughness of about Ra 12-16 m as-printed. This is especially useful for parts with complex interior geometry, such as internal channels, where post-processing is challenging. When compared to DMLS/SLM and Material Jetting, Binder Jetting creates metal parts and full-colour prototypes for a fraction of the cost. Because it is not limited by thermal effects, binder jetting can produce very big parts and complex metal geometries (e.g., warping).

➢ **Some key benefits are as follows: -**

1. Binder Jetting's manufacturing capabilities are ideal for small to medium batch production.
2. Due to their increased porosity, Metal Binder Jetting parts have inferior mechanical characteristics than DMSL/SLM parts.
3. Binder Jetting can only print rough details because the parts are brittle in their green condition and may shatter during post processing.
4. Binder Jetting has a limited material variety compared to other 3D printing methods.

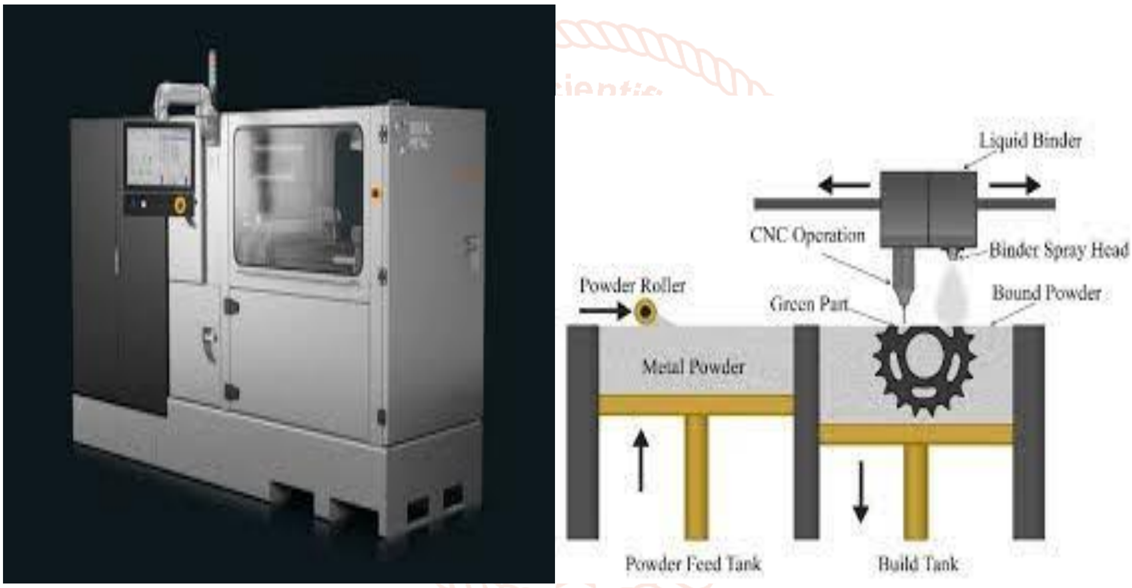

Figure 14. Binder jetting technique

D. Raw material in sheets: -

1. Laminated object manufacturing: -

LOM (laminated object manufacturing) is a 3D printing technique. Helisys Inc., situated in California, created it (now Cubic Technologies). Layers of plastic or paper are fused together using heat and pressure, then cut into the required shape with a computer-controlled laser or blade during the LOM process. While LOM isn't the most common 3D printing process today, it is still one of the quickest and most cost-effective ways to make 3D prototypes.

Helisys, Inc., which discontinued operations in 2000, produced the first LOM rapid prototyping system. Helisys' products are now sold, serviced, and supported by Cubic Technologies. Other companies specialising in LOM printing, such as Israel's Solido 3D and Japan's Kira, Inc., have closed their doors in recent years.

At least one company, though, is attempting to reintroduce LOM into the mainstream. Mcor Technologies Ltd., based in Ireland, sells professional 3D printers that use LOM technology to produce items on normal Letter/A4 paper. Architects, artists, product creators, and even doctors use its equipment to create cheap models and final things. LOM is still offered by various companies that also provide other 3D printing services, despite its lack of popularity compared to other methods of additive manufacturing**.**

A continuous sheet of material, such as plastic, paper, or (less typically) metal, is pulled over a build platform by a set of feed rollers in a LOM equipment. Adhesive is frequently applied to plastic and paper construction components. A heated roller is moved over a sheet of material on the build platform to melt its glue and press it onto the platform, forming an object. The material is then sliced into the required design using a computer-controlled laser or blade. Any surplus material is also sliced up in a crosshatch pattern by the laser, making it easier to remove once the object is fully created.

- **Advantages of this technique are as follows: -**

1. Large parts may be manufactured quickly and affordably.
2. No support material is required for delicate wood-like sections, which are generally weak and absorb moisture.

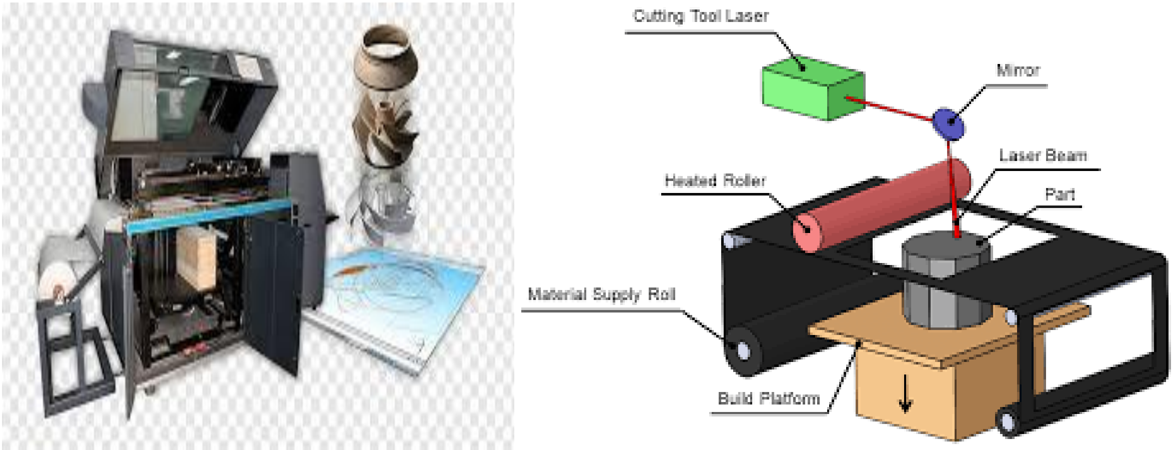

Figure 15 Laminated object manufacturing.

2. Paper lamination technology: -

Sheet lamination, also known as laminated object production or paper lamination. It employs foil instead of powder or wire to create an object. Helisys Inc. was the first to develop this AM method. Paper-based lamination, composite-based lamination, and selective lamination are three different types of sheet lamination procedures. Papers/foils are glued together layer by layer and precisely trimmed to the intended geometry to create the finished object in paper-based lamination.

For part construction, any sheet material that can be accurately cut with cutting equipment (laser or mechanical cutter) and bonded can be employed. Metal sheets, for example, can be utilised to create AM items. These objects are laser cut from flat metal sheets, then stacked and welded together to make a metallic 3D part. The thickness of the paper is normally between 0.07 and 0.2 mm.

A same idea applies to composite lamination, although reinforcement can be added to the buck material to improve the produced part's strength. Rather than using glue to join layers, the selective lamination procedure uses a binder that may be applied selectively in certain areas to construct the item. Metallic sheets are used as feedstocks in SL or laminated object manufacturing (LOM). It binds a stack of precisely cut metal sheets to build a 3D object using a localised energy source, usually ultrasonic or laser.

Ultrasonic additive manufacturing (UAM) or ultrasonic consolidation (UC), which was invented and patented by White, is the most widely utilised manufacturing process. The interfaces of stacked sheets are joined by diffusion rather than melting when ultrasonic waves and mechanical pressure are applied at room temperature to sheet metal stacks. Without employing any frictional force as a heat source, the stacked sheets are bonded layer by layer to produce a 3D object. The operation of UAM equipment is as follows: On a base plate, metallic sheets are spread out and layered.

To deliver ultrasonic vibration and pressure, a digitally controlled Sonotrode moves along the rolling direction. Because of the high-frequency vibration of the sonotrode, a fresh metallic layer is attached to the previously created structures. Frictional heat at the bonded interfaces raises the temperature of the consolidated region throughout this process. There is a short cooling period between each layer's production to eliminate residual thermal strains. The product is sliced off the base plate after all of the layers have been built and polished to increase the surface finish.

Advantages of paper lamination technology: -

1. Printing time will be reduced, but post-processing will be necessary.
2. Integration capabilities as hybrid manufacturing systems
3. Material handling is simple.
4. Parts made of ceramic (CAM-LEM) and composite fibre (SLCOM) are available.

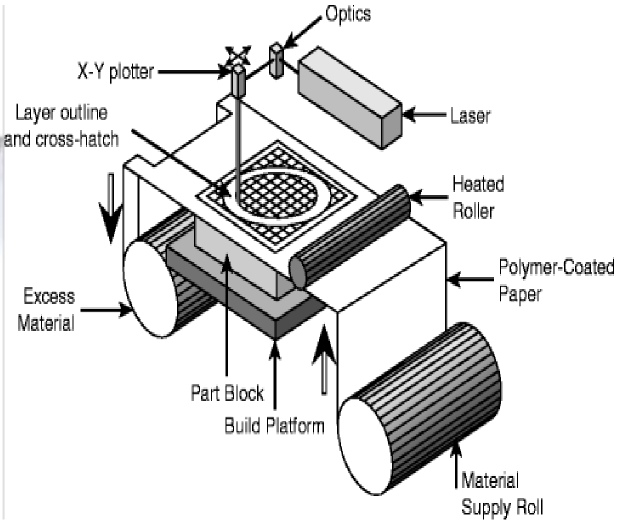

Figure 16 Paper lamination technology.

3. Selective deposition lamination: -

SDL is an additive manufacturing process in which sheets of material are bonded together to form an object, according to ASTM. This is a procedure for 3D printing. which is made from paper. The process of making laminated objects the method is straightforward. This is made up of glued adhesive-coated papers cut the shape successively with a heated roller layer-by-layer with the cutter The roller feeds from one side. To form the second layer, fold the paper after each layer is completed. Materials used for this having very less cost as we can shelf copy papers from any office.

SDL's final product has a wood-like look, allowing them to use wood finishing processes. It differs from LOM in several ways. A few things, mostly in terms of gluing technique. SDL is used. whereas LOM glues to the part that will form the final object glues the entire sheet evenly. Some of the most recent printers in SDL can create full-colour objects by colouring the exterior surfaces the cross-sectional edge. A study of steps is done to investigate SDL more thoroughly, which validates the name Selective deposition lamination.

1. Selected: The name includes the most crucial word. That is discriminatory. It's because the system provides more benefits. Selective gluing at work area & significantly lower at support area with simple access to support removal in another way The LOM method glues the entire sheet of paper. This causes issues with support removal.
2. Deposition: Applying adhesive droplets is an art. Paper cutting should be done after that. This is Unlike the LOM technique, where glue is used, consistently applied to the entire sheet.
3. Lamination: Lamination refers to building layered structure of sheets. The part built are made up of papers & are durable, they don't need to post process to increase strength. Parts made are not brittle in nature, that's why they didn't get break when dropped.

➢ **Advantages of SDL are: -**

1. Parts made are eco-friendly in nature.
2. Low running cost.
3. Does not require infiltration of printed parts.
4. No need for additional Support. It is Reliable process

Figure 17 Selective deposition lamination

Applications of 3D printing technology: -

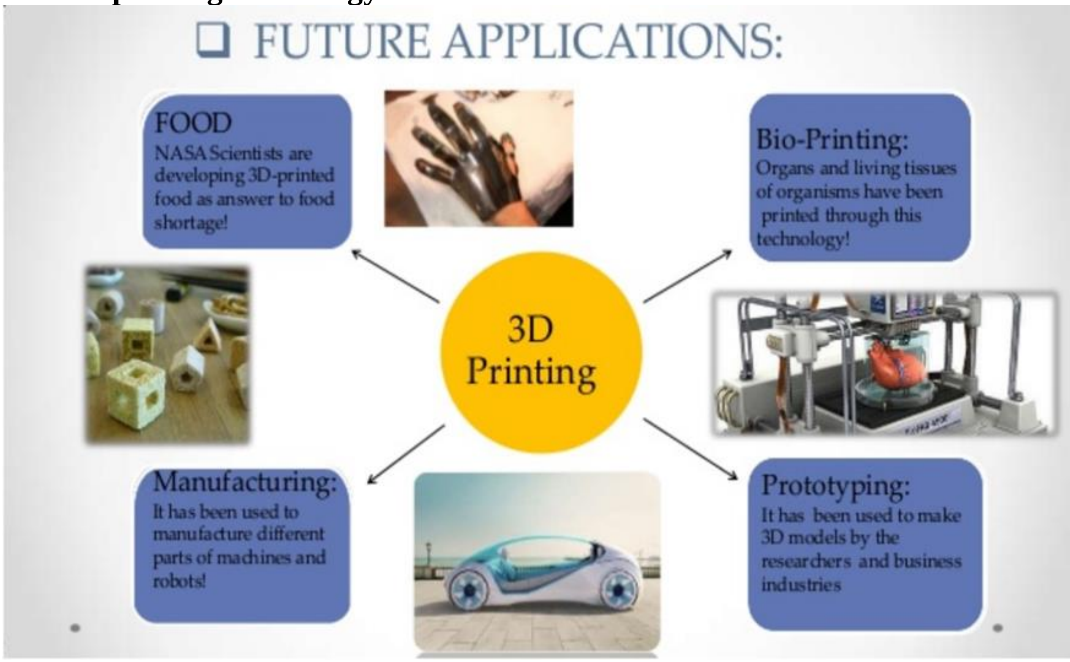

Figure 18 Applications in 3D printing technology

Table 1:- List of 3D printing technology applications in drug delivery: -

Drug name	Type of dosage form	3D printing type
Acetaminophen	Chewable Polypill with Ibuprofen made with gelatin and shaped as Lego TM-like bricks	Embedded (e-3DP)
Ascorbic Acid (Vitamin C)	Tablets of multiple sizes and the geometrics including cylinder, honeycomb with 1, 4, or 7 holes through the canter	Stereolithography (SLA)
Benzylamine	Oro dispersible Film with Multiple Layers	Semisolid Extrusion (Modified from FDM Printer)
Carvedilol Tablet	Tablet in the form of Ring, Mesh, Cylinder; Oro dispersible Film	UV Inkjet (Drop on Demand with UV Curing)
Delta-9-tetrahydrocannabinol (THC)	Oro dispersible Film (IR) with Cannabidiol (CBD) and QR coded Surface	Piezoelectric Inkjet printing of drug-containing ink/code pattern upon manually prepared substrate
Enalapril Polypill Tablet	Polypill Tablet with Hydrochlorothiazide	(IR) Fused Deposition Modelling (FDM) with 2 Thermal Nozzles
Fluorescein Sodium	Oro dispersible Tablet with 5-Aminosalicylic acid	Fused Deposition Modelling (FDM)
Glimepiride	Polypill Tablet of Glimepiride (IR) with Metformin (ER)	Fused Deposition Modelling (FDM)
Hydrochlorothiazide	Oro dispersible Film with Enalapril	Piezoelectric Inkjet
Ibuprofen	Chewable Polypill with Acetaminophen made with gelatin and shaped as LegoTM-like bricks	Embedded (e-3DP)

Figure 19 images of some 3-D printed medicines. Images of 3D printed medicines showcasing the opportunity for flexibility in formulation type, shape and color with 3D printing technology.

Table 2: - Pros and cons of 3D Printing technology; -

3D Printers	Pros	Cons
1.Binder jetting	Minimal ink preparation. - Avoids contact between printer and drug formulation. - Minimal or avoidance of heat in processing. - Suitability in current FDA- approved 3D printed medicines	- Potential high cost. - Limited supply for pharmacy compounding application. - Requirement for post-printing drying.
2.Fused deposition modeling	- Very affordable. - Most commonly available. - Minimal ink preparation. - Avoids contact between printer and drug formulation. - Minimal or avoidance of heat in processing. - Suitability in current FDA- approved 3D printed medicines - Suitability for formulations with novel drug release designs. - Requires minimal post-printing processing	- Limited approved excipients. - May expose drugs to high temperatures. - Requirement for accessory equipment.
3.Semisolid extrusion	- Enhances formulation sterility and ease of cleaning. - Can avoid use of heat.	- Difficult to maintain viscosity and dispersal of ingredients. - requires a long post-printing time.
4.Embedded 3D printer.	- Combines benefits of FDM and semisolid extrusion. - Enhances ease of swallowing core FDM dosage form.	- Expensive. - Limited availability. - May require custom design

Perspectives and conclusion:-

3D printing, according to the FDA and others, has the potential to improve medication safety, strength, quality, precision, uniformity, and purity at a lower cost than traditional methods. traditional methods of production . Pharmaceuticals integration Compounding may be able to help with concerns about safety and quality. by enhancing automation, standardisation, and communication methods.Printed dosage forms, like other compounded medications,require investigation to ensure that the desired product characteristics have been achieved. a standard formulation has been successfully printed procedures. The requirement to examine each individual dosage formulation Medicine may postpone the much-needed implementation.In pharmacy using on-demand 3D printing technology To fully realise the potential of convenient analytical and predictive tools, more work will be required.Allow for customised medications The development of 3D printers and related programmes for pharmaceutical compounding, with built-in predictive and analysis capabilities, would improve the quality of research in this field.

Improve the acceptability of 3D printed dosage formulations in this area, and encourage any formulation adjustments needed for printability to be implemented USP-NF preparation standards take this into account.We feel that regulatory barriers for 3D printers in the United States are negligible.procedures involving non-sterile compounding This is because 3D printing has the ability to integrate into approved non-outsourcing compounding pharmacies' established processes The use of 3D printing technology in the formulation of non-sterile drugs will speed up the long-awaited process.Compounding process improvements for tailored precision medicationso be delivered in a timely manner in relation to the custom prescription.

Pharmacists, being the primary health-care professionals responsible for compounding, must constantly enhance relevant skills and practises in order to achieve the best possible patient outcomes. Customization and quality improvement of pharmaceutical compounding products Options will improve pharmacists' perspectives by requiring them to integrate their pharmaceutical expertise into interprofessional teams in order to improve medication therapy outcomes. The various types of printers have demonstrated that they may operate together to eliminate limits and increase benefits, including dosage forms that are now restricted to specific technologies.

The perfect 3D model A multi-printer customised for the future pharmacy could be used work with a variety of technology to get the most remarkable results Possibilities and release characteristics of dose forms. For the time being, pharmacists must choose their 3D printing technique mostly based on the lack of different multi-printer possibilities and studies using them on their 503A pharmacy's budget, the most therapeutically important pharmaceutical dosage forms and release patterns, and their ability to contribute compounding research to the technology. Patients with paediatric, elderly, allergy-related, or genetically unique medication metabolism may benefit the most. Reduced excipients, better flavour and appearance, or more well-implemented, customizable dosage and release characteristics. Increased drug compliance might be improved if high-quality tailored pharmaceuticals were more widely available. Unrelated to insurance coverage, therapy outcomes for all individuals battling with compliance.

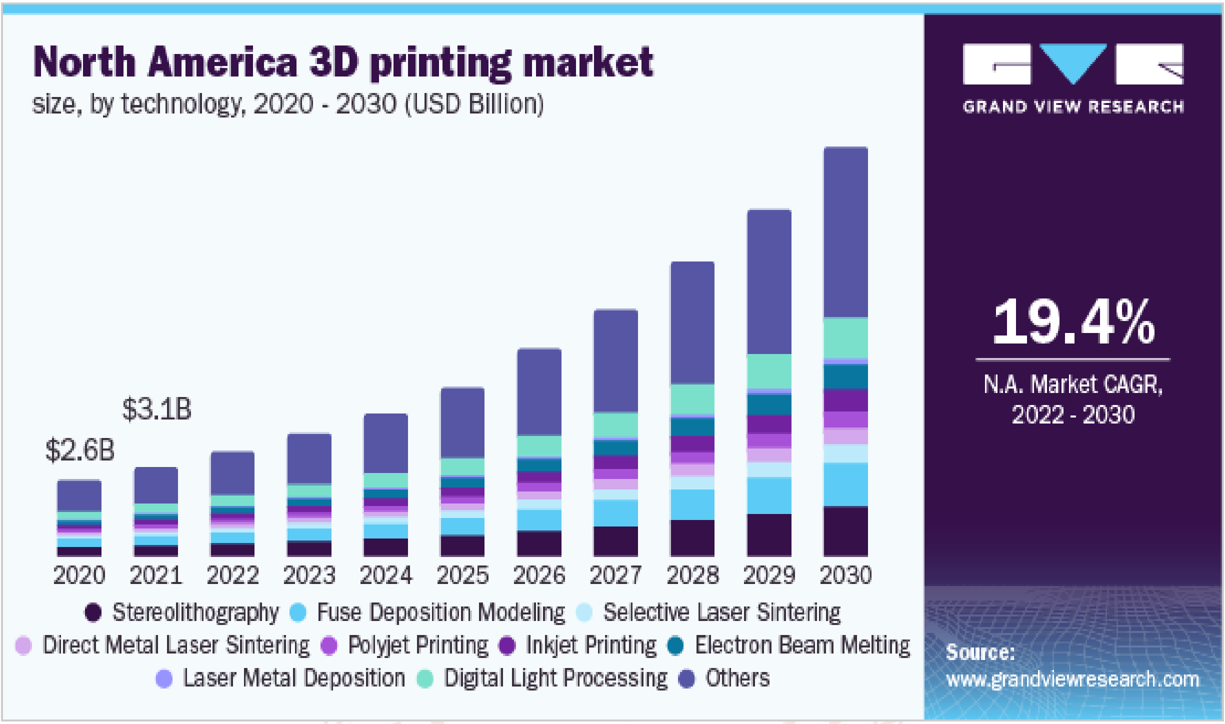

Figure 20. Overview of 3 D Printing market in upcoming years.

From 2022 to 2030, the worldwide 3D printing industry is predicted to develop at a compound annual growth rate (CAGR) of 20.8 percent. In 2021, 2.2 million 3D printers were shipped worldwide, with shipments predicted to increase to 21.5 million by 2030. The market is predicted to increase due to intensive research and development in three-dimensional printing, as well as rising demand for prototype applications from several industrial verticals, including healthcare, automotive, and aerospace and military.

To take advantage of the full range of benefits offered by 3D printing, more research is needed to develop efficient, effective medicine verification methodologies. To increase present compounding safety and allow processes to stay current, pharmacy schools must research efficient medication verification techniques up to date on potential dosage form alternatives. Training with 3D printers for compounding medicines should be part of pharmacists' professional growth. The Accreditation Council for Pharmacy Education should help promote this. PharmD programmes' standard curriculum requirements with training Compounding medications with 3D printing.

Installation services, consultancy solutions, and client support are all part of the deployment, as is resolving copyrights, licencing, and patenting issues. Manufacturers gain from 3D printing in terms of prototyping, structural and final product design, modelling, and time to market. As a result, manufacturing costs have decreased significantly, allowing manufacturers to provide superior products at more affordable pricing. As a result of these advantages, 3D printer demand is predicted to increase in the next year.

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