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3D Printing in Pharmaceutical Industry

Mahima Patidar[1], Dr. Maina Chouhan[2]

Address of Corresponding Author[1]: Ms Mahima Patidar, M. Pharm. Pharmaceutics Scholar, Bhupal Nobles' College of Pharmacy, Udaipur (Raj.), 313001, India Email: mahimapatidar2000@gmail.com

[2]Associate professor, Department of pharmaceutics, Bhupal Nobles' College of Pharmacy, Udaipur (Raj.), 313001, India

ABSTRACT

Three-dimensional (3D) printing has emerged as a disruptive technology in the pharmaceutical industry, enabling precise fabrication of personalized drug dosage forms and novel drug delivery systems. This additive manufacturing technique allows for the customization of drug combinations, release profiles, and tablet geometries, thus supporting patient-specific therapies and improving treatment outcomes. Major advantages of 3D printing in pharmaceuticals include enhanced dosing accuracy, on-demand manufacturing, reduced drug waste, and the ability to produce complex drug release profiles in a single dosage form. Various sorts of 3 D Printing technologies used are inkjet printers, thermal inkjet printers, fused deposition modelling, hot melt extrusion etc. Key applications range from personalized Medicine and implants to transdermal patches and paediatric medications. However, several limitations hinder widespread adoption, such as high production costs, limited scalability, regulatory uncertainties, and challenges in ensuring product stability and uniformity. Despite these challenges, the integration of 3D printing is poised to revolutionize pharmaceutical manufacturing by promoting a shift toward more flexible, patient-centered healthcare solutions.

Keywords: 3-Dimensional Printing (3DP), Drug Delivery, On-demand manufacturing, dosing accuracy, Personalized Medicine.

1. INTRODUCTION

Our era is marked by revolutionary innovations and swift technological progress. Within these developments, 3D printing technology and the pharmaceutical industry have demonstrated significant potential. The 3D printing (3DP) process is a relatively new concept in the pharmaceutical sector and is also known as additive manufacturing (AM), rapid prototyping (RP), or solid freeform technology. The use of 3D printing in personalized medicine to produce drugs that are customized for each patient's needs has a lot of unrealized promise. " The FDA's authorization of a 3D-printed drug in August 2015 reflects the increasing use of 3D printing technology in pharmaceutical production. 2 Research interest in 3D printed pharmaceutical goods has been increasing since that approval. [1,2,3,4,5,6,7,8,9,10]

Even while 3D printing has the potential to produce drugs with unique dosages, forms, and release profiles in the future, customized medicine demands that treatments be tailored to the individual characteristics of each patient. The need for more individualized treatments is highlighted by the emergence of personalized medicine, which is driven by improvements in our understanding of genetics and life styles. [11,12,13] One example demonstrated how tablets with different dosages may be made via 3D printing depending on the needs of the patient.

For instance, Polypills containing several drugs may help elderly people take them more consistently and reduce their medication load.[14] "Moreover, 3D printing has been utilized to develop quick-dissolving oral films designed to assist patients who struggle with swallowing.[15] " These applications show some of the unique ways 3D printing can be used to satisfy patient needs. In order to provide successful care, a pharmacist is constantly at the forefront of developing and delivering 3D-printed medication to patients in a range of healthcare settings through careful customization.[16]

3D printing is a revolutionary invention that has emerged as a disruptive force that can overcome these limitations. Because 3D printing enables the exact layer-by-layer deposition of active pharmaceutical components and the utilization of computer-aided design models, it has the potential to completely transform the pharmaceutical industry. This new approach opens up new options for customized therapy, customized dosage, and sophisticated pharmacological formulations.[17] Moreover, the precision control of 3D printing makes it possible to design drug delivery systems with distinct release profiles, ensuring accurate dosage and long-lasting therapeutic advantages.[18] Will 3D printing actually revolutionize the design of medications? Three-dimensional printing, also known as additive manufacturing, is a technical development that allows three-dimensional objects to be produced from digital models by stacking materials.[19] 3D printing has the potential to revolutionize the pharmaceutical industry by enabling effective prototyping, creating complex pharmacological structures, and opening the door for customized treatment. [19,20]

Monteiro et al. propose seven types of 3D-printing applications, each with advantages and disadvantages, depending on the materials and printing requirements.[21] Additionally, cutting-edge 3D-printed materials like composites, smart materials, ceramics, electronics, and biomaterials are

influencing the direction of pharmaceutical manufacturing.[22] Among these applications, we focus on a few key elements of new derivatives based on seven fundamental additive manufacturing (AM) 3D-printing technologies in our study. (Figure 1). Among these is stereolithography (SL), which uses ultraviolet light to cure the liquid resin layer and produce a solid item. "Vat Photopolymerization (VP) employs ultraviolet light to cure and solidify liquid resin layer by layer from a reservoir, while Material Extrusion (ME) involves pushing thermoplastic or bondable material through a heated nozzle, depositing it sequentially to form the desired structure, whereas material jetting (MJ) drops material droplets onto a substrate selectively. While powder bed fusion (PBF) uses an electron beam or laser to selectively fuse layers, direct energy deposition (DED) uses a focused energy source to melt the material and deposit it layer by layer. Finally, binder jetting (BJ), which sprays a binding agent to a bed of powder, is used to build layers.[22]

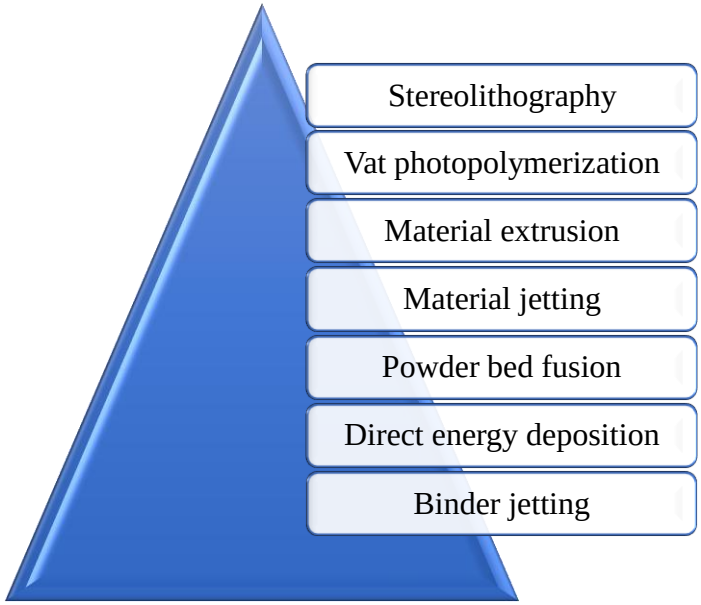

Figure 1: The seven am processes

2. THE HISTORY OF 3D PRINTING

The first public demonstration of 3D printing technology was conducted by Hideo Kodama of Nagoya Municipal Industrial Research Institute, who used photo-hardening polymer to manufacture a 3D plastic model. But the biggest breakthrough came in 1984 when Charles Hull, who would later co-found 3D systems, invented stereolithography. [23]

- 1980 – *Dr. Hideo Kodama* of Japan filed the first patent application for a rapid prototyping technology using a photopolymer-based system. This is considered one of the earliest documented attempts at 3D printing.[24]
- 1984 – *Charles Hull* invented the Stereolithography Apparatus (SLA), which uses UV lasers to cure photopolymer resin layer by layer to form 3D objects. This marked the birth of modern 3D printing.[23]
- 1986 – *Carl Deckard*, at the University of Texas, developed Selective Laser Sintering (SLS), a process that uses a laser to fuse powdered materials into solid structures. [23]
- 1989 – A patent was granted to *Carl Deckard* for his work on Selective Laser Sintering (SLS), further advancing the field of additive manufacturing. [23]
- 1990 – The Fused Deposition Modelling (FDM) technology was introduced by *Scott Crump*, co-founder of Stratasys. This method extrudes melted thermoplastic filament layer by layer to build objects. [23]
- 1992 – *3D Systems*, founded by Charles Hull, produced the first commercial SLA machine, making 3D printing accessible to industries for prototyping purposes. [23]
- 1993 – A 3D printing patent was granted to *Emanuel (Eli) Sachs* of MIT for a binder jetting process, laying the foundation for what would become one of the key 3D printing technologies. [23]
- 1996 – The first clinical applications of 3D-printed biomaterials were introduced for tissue regeneration, opening the door to biomedical and healthcare innovations. [23]
- 1999 – *Luke Massella* became the first patient to receive a 3D-printed bladder. The organ was created using a combination of 3D-printed biomaterials and the patient's own cultured cells. This groundbreaking procedure marked a significant milestone in regenerative medicine and tissue engineering. [23]

- 2000 – MCP Technologies launched Selective Laser Melting (SLM), a method that employs high-powered lasers to completely melt and bond metal powders into solid parts. This process enabled the production of high-density metal parts with complex geometries. [23]
- 2003 – *Dr. Thomas Boland* filed the first patent for a bioprinting technique involving the deposition of viable cells using modified inkjet printing technology. This laid the groundwork for modern bioprinting techniques used in tissue engineering. [23]
- 2004 – *Dr. Adrian Bowyer*, a senior lecturer at the University of Bath, conceived the RepRap Project—an open-source initiative to develop a self-replicating 3D printer capable of printing most of its own components. This project democratized access to 3D printing and inspired the global maker movement.
- *Dr. Gabor Forgacs* patented a scaffold-free bioprinting technique that allowed for the direct printing of multiple types of living cells simultaneously. His innovation advanced the field of organ and tissue fabrication by eliminating the need for synthetic scaffolding. [23]
- Early 2000s (Date unspecified) – Aprecia Pharmaceuticals, based in Blue Ash, Ohio, USA, utilized Stereolithography (SLA) to fabricate orally disintegrating tablets, such as the FDA-approved Spritam® (Levetiracetam). Additionally, material extrusion (ME) methods were applied to produce drug-loaded scaffolds and implants for controlled drug release, showing the versatility of 3D printing in pharmaceutical applications. [25,26,27,28]
- 2005 – Z Corporation developed the first full-colour 3D printer, which utilized a binder jetting technique to produce multi-coloured objects. This advancement greatly expanded the visual and functional possibilities of 3D printed models, particularly for prototyping and presentation. [23]
- 2007 – The concept of selective layer customization and on-demand manufacturing of industrial parts gained traction. The first RepRap 3D printer, named *Darwin*, was released, marking a major milestone in the open-source hardware movement This was subsequently succeeded by well-known models such as the Mendel, Prusa Mendel, and Huxley. [23]
- 2009 – *Organovo Inc.* released data on the first fully bio printed blood vessels, demonstrating the potential of 3D bioprinting in creating functional human tissues for medical use. [23]
- 2011 – 3D printing was successfully applied to precious metals such as gold and silver, expanding the technology into the jewelry and luxury goods industries. The world's first 3D-printed car and a 3D-printed robotic aircraft were also introduced, showcasing applications in automotive and aerospace sectors. [23]
- 2012 – Extrusion-based bioprinting was used to fabricate an artificial liver, highlighting advancements in complex tissue engineering. A 3D-printed prosthetic jaw was successfully implanted into a patient, marking a breakthrough in maxillofacial surgery and personalized implants. [23]
- 2013 – *Solid Concepts* produced the first 3D-printed metal gun, demonstrating the capability of additive manufacturing to produce functional, high-strength metal components. [23]
- 2014 – Implementation of multi-arm bioprinters allowed for the integration of tissue fabrication with printed vasculature, a critical step toward the printing of more complex, viable organs. [23]
- 2015 – *Organovo* released data on the first fully bio printed kidney tissue, bringing the possibility of functional organ printing closer to reality. The U.S. FDA approved Spritam®, the first 3D-printed pharmaceutical drug, produced by *Aprecia Pharmaceuticals* using ZipDose® technology. This opened new avenues for personalized medicine and rapid drug delivery systems. [23]
- 2018 – A gastric floating drug delivery system was developed using riboflavin as a model drug. This system demonstrated an exceptional floating capability of up to 3 days, significantly enhancing gastrointestinal retention time. This innovation was achieved by merging different 3D printing techniques, showcasing the potential of additive manufacturing in creating highly sophisticated and personalized drug delivery systems. The successful design and performance of this system marked a major step forward in achieving optimum, controlled drug release, and opened new frontiers in pharmaceutics and personalized medicine systems.[29]
- 2023–Advances in drug-loaded implants and bioprinting. [23]

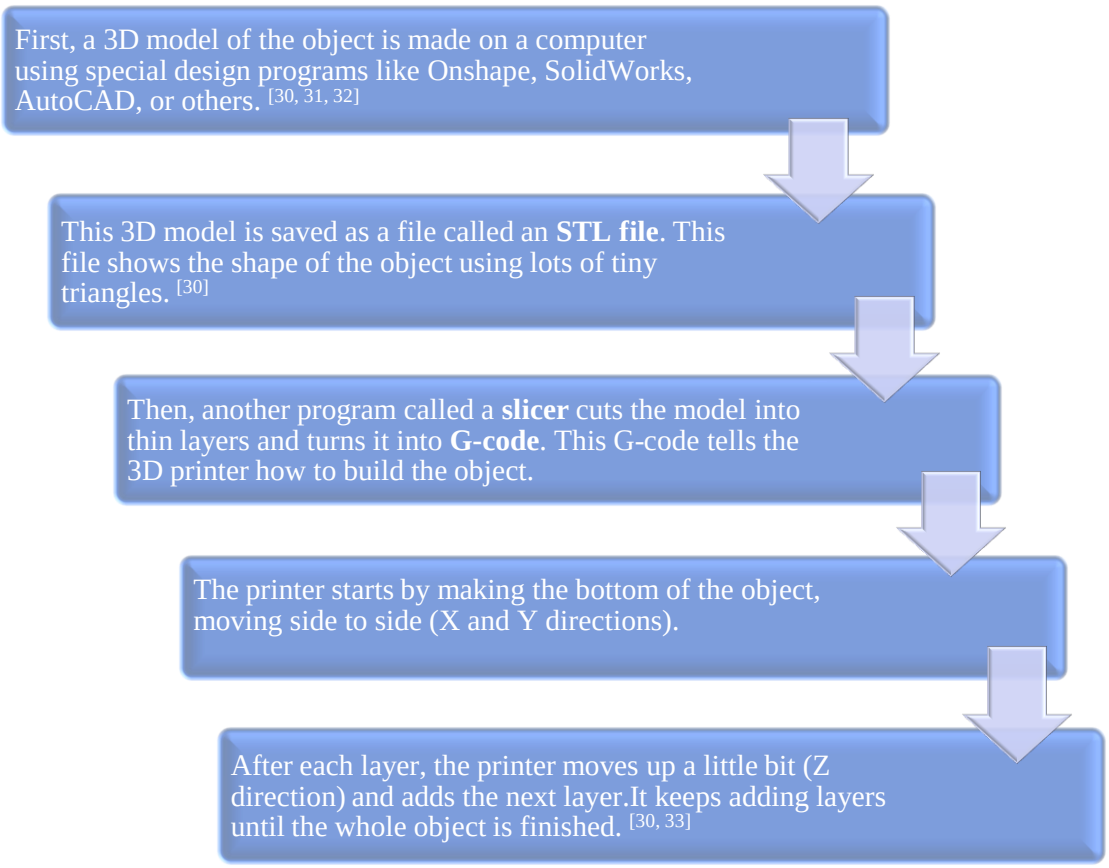

Figure 2: 3D printing procedure

3. 3D PRINTING PROCEDURE

Most 3D printing technologies work with STL file format. However, sometimes errors can happen when converting a 3D model into an STL file. To fix these errors, special software like Magics by Materialise can be used. There are also other file formats besides STL, such as AMF (Additive Manufacturing File Format) and 3MF (3D Manufacturing Format). These newer file types are useful because STL files do not include details like material type, colour, texture, or other important features.[34]

4. PROS AND CONS OF 3D PHARMACEUTICAL PRINTING

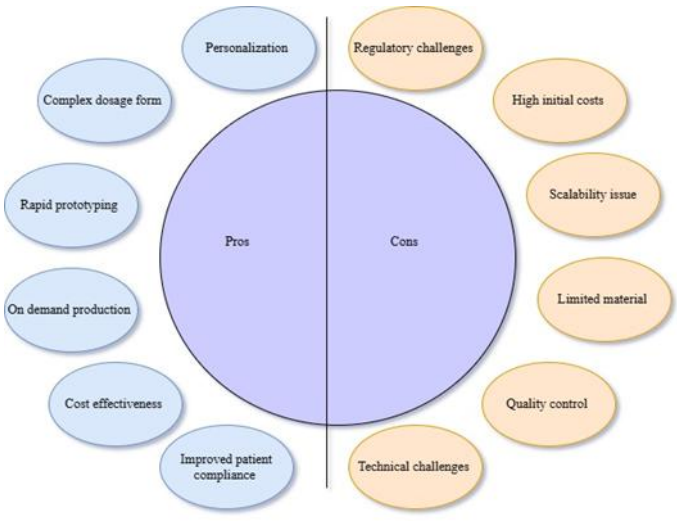

Figure 3: Pros and Cons of 3D Pharmaceutical Printing

The application of 3D printing in pharmaceuticals brings a range of benefits while also posing challenges, both of which play a crucial role in shaping it s impact on drug development and patient care (Figure 3).

pros

- A major transformative benefit of 3D printing in the pharmaceutical sector is its capacity to personalize medications. [35,36,37,38]
- This technology allows for precise manipulation of factors such as droplet size, drug release timing, dosage strength, and the combination of multiple drugs into a single form. [39,24,40]
- customization and consistency can lead to more effective and safer treatments, particularly for drugs with a narrow therapeutic index, where small changes in dosage can significantly impact outcomes. [37,41,42,43,44,45]
- 3D printing offers enhanced control over drug particle size, distribution, and formulation, which plays a key role in improving solubility and bioavailability. This is particularly beneficial for poorly soluble drugs, as 3D printing techniques can significantly enhance their dissolution properties, ultimately increasing therapeutic effectiveness. [26,46]
- The production of small batches is feasible with 3D printing, and the entire manufacturing process can be carried out in a single run. [47]

Cons

- Printer-related parameters significantly influence both the quality of the printed product and the overall cost of the printer itself. [48]
- Despite its potential, 3D printing in pharmaceuticals still faces several limitations that impact its current applications. For example, while it allows the fabrication of pill Molds and direct printing using drug powders as raw materials, different printing technologies—such as Fused Deposition Modelling (FDM), Stereolithography (SLA), and Selective Laser Sintering (SLS)—present their own specific challenges. [2849]
- The interaction between the drug ink and printer materials can affect the drug release rate, potentially altering therapeutic outcomes. [24,40]
- In terms of scalability, 3D printing currently falls short of the efficiency offered by traditional pharmaceutical manufacturing methods, making it less suitable for large-scale production and more applicable to specialized drugs or niche markets. [35,50,51,52] "An additional major drawback is the limited range of materials that are suitable for use in 3D printing."Many active pharmaceutical ingredients (APIs) and excipients commonly used in conventional manufacturing cannot be utilized with existing 3D printing technologies. Among these, the limited availability of suitable excipients poses a major challenge in the development of customized dosage forms. For broader adoption of 3D printing in pharmaceuticals, it is crucial to develop excipients that are biodegradable, biocompatible, non-toxic, and stable [36,37] Moreover, as dosage forms become increasingly complex, there is a growing need for continuous updates and improvements to modelling software used in their design and production.

5. TYPES OF 3D PRINTING

A diverse range of 3D printing technologies has been developed, each serving distinct functions. As defined by ASTM Standard F2792 [53], these technologies are classified into seven categories: binder jetting, directed energy deposition, material extrusion, material jetting, powder bed fusion, sheet lamination, and vat photo polymerization. There is no definitive superiority among these methods, as each is optimized for specific applications. Today, 3D printing has evolved beyond its original role in prototyping and is increasingly employed in the production of a wide array of end-use products.[54]

5.1. Fused Deposition Modelling

Fused Deposition Modelling (FDM) is a widely used technique in 3D printing, particularly known for its simplicity and cost-effectiveness.This material extrusion-based additive manufacturing method uses thermoplastic polymers as raw materials, typically in the form of filament. These materials are softened or melted using heat during the printing process to fabricate objects layer by layer.[55]

In FDM, the polymer filamentpotentially infused with drugs for pharmaceutical applications is heated and extruded through a nozzle. The nozzle, which usually has a standard diameter of 0.4 mm (though it can be reduced to 0.2 mm for finer resolution), moves in three degrees of freedom (DoF) according to pre-programmed G-code instructions. The extruded molten filament solidifies as it is laid onto the build platform, gradually constructing the intended structure.[56]

This precise layer-by-layer deposition enables the fabrication of complex geometries and customized dosage forms. The resulting printed objects can feature a hollow, shell-like structure, which may be either partially or fully filled depending on the intended application. [57, 58,59, 60]

Advantage:

- Simple setup: Requires less complex equipment and is relatively easy to operate.
- Cost-effective: Economical in terms of materials and operation.
- Material versatility: Compatible with a wide range of pharmaceutical polymers and drug compounds. [61,62,63,64,65]

- Design flexibility: Capable of producing complex dosage forms tailored for personalized medicine, improving patient compliance.

Disadvantages:

- Thermal sensitivity: Potential degradation of active pharmaceutical ingredients due to high processing temperatures. [66,67]
- Lower resolution: Produces less detailed structures compared to other 3D printing technologies like SLA (stereo lithography).[68]
- Surface finish and mechanical limitations: Results in coarser surfaces and structural weaknesses at the junctions of printed layers.
- Drug release issues: Drug molecules may become trapped within the polymer matrix, leading to slow or incomplete drug release [69]

One of the primary concerns associated with this printing technique is the risk of drug degradation due to the elevated temperatures used during extrusion and printing."However, this issue can be mitigated by selecting appropriate excipients that enable low-temperature printing. [70,71]

Fused Deposition Modelling (FDM) typically operates at temperatures ranging from 120 °C to 250 °C, making it suitable for processing polymers such as polyvinyl alcohol (PVA), polylactic acid (PLA), hydroxypropyl cellulose (HPC), and various types of Eudragit.[72] Studies focused on immediate-release 3D-printed formulations—particularly those using polyvinylpyrrolidone (PVP) and Eudragit EPO—have demonstrated successful printing at relatively lower temperatures, typically 110–135 °C. These materials are specifically selected for their ability to extrude efficiently at these reduced temperatures.

However, aside from Eudragit E and HPC, most of these polymers are not ideal for immediate-release dosage forms due to their slower drug release profiles. [73]

Examples of dosage forms produced using FDM include:

- Oral tablets
- Scaffolds
- Implants

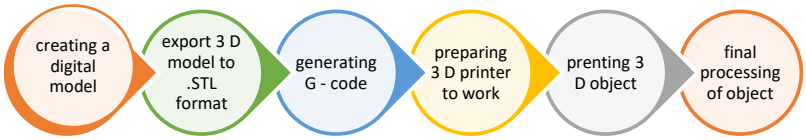

Figure 4: Process of FDM

5.2. Semi-Solid Extrusion

Semi-Solid Extrusion (SSE) is a material extrusion technique that builds 3D structures through the layer-by-layer deposition of gels or pastes. Upon extrusion, the material hardens—either through cooling, solvent evaporation, or chemical curing—allowing each new layer to be supported by the one below. [74]

The key distinction between SSE and other material extrusion methods, such as Fused Deposition Modelling (FDM) or Direct Powder Extrusion (DPE), lies in the form of the feedstock. SSE uses semi-solid or semi-molten materials, while FDM relies on solid filaments and DPE uses powdered materials. [75,76,77,78]

- In the literature, SSE is also referred to by various names, including:
  - Pressure-Assisted Micro syringe (PAM) printing [79,80,81]
  - Robocasting / Robotic Material Extrusion [82]
  - Cold Extrusion-Based Printing [83]
  - Hydrogel-Forming Extrusion [84]
  - Melting Extrusion / Thermal Extrusion [84,85]
  - Soft-Material Extrusion [84]
  - Melting Solidification Printing Process [86]
  - Direct Ink Writing (DIW) [87]
  - Hot-Melt Ram Extrusion [88]

- Hot-Melt Pneumatic Extrusion [89]
- Micro-Extrusion [90]

➢ Semi-Solid Extrusion (SSE) has been applied in the development of a wide range of pharmaceutical dosage forms, including [91]

- Immediate-release tablets
- Oro dispersible tablets
- Paediatric chewable gummies
- Controlled-release tablets
- Gastrofloating tablets
- Solid lipid tablets

One of the key advantages of Semi-Solid Extrusion (SSE) over solid extrusion techniques is its capacity to process a wider variety of materials, especially those that are sensitive to heat. Because SSE operates at lower processing temperatures, it helps maintain the stability and bioactivity of active pharmaceutical ingredients (APIs), which might otherwise degrade when exposed to the high temperatures required for melting solid material. [92]

5.3. Material jetting

According to ASTM standards, Material Jetting is a 3D printing process in which droplets of build material are selectively deposited in a layer-by-layer fashion.[93] In this method, a print head dispenses tiny droplets of a photosensitive material, which solidifies upon exposure to ultraviolet (UV) light, gradually forming the final structure.

Material jetting is known for producing parts with exceptionally smooth surface finishes and high dimensional accuracy. Additionally, it supports multi-material printing and is compatible with a broad spectrum of materials, including polymers, ceramics, composites, biological substances, and hybrid materials. [94]

5.4. Inkjet printing

Inkjet Printing is a droplet-based deposition technique that involves the precise placement of liquid formulations, including active pharmaceutical ingredients. The printer builds the 3D object by dispensing microscopic droplets of the formulation onto a substrate or previously deposited layers. This method offers high material versatility and is capable of producing high-resolution, high-quality prints, making it suitable for a range of pharmaceutical and biomedical applications.

5.5. Stereo Lithography

Stereolithography (SLA), discovered by Charles Hull in 1988, is a 3D printing technology known for producing highly accurate and detailed polymer parts. [23,95] SLA technology is primarily divided into two categories: laser-based systems and Digital Light Processing (DLP).[96]

SLA is an additive manufacturing technique that builds objects layer-by-layer by curing a photosensitive resin using a UV laser. The process relies on photo-polymerization, where a liquid resin is selectively solidified to form 3D structures. [97,98]

➢ SLA has been widely utilized in medical and pharmaceutical domains for various applications, including

- Tissue engineering
- Implantable device fabrication
- 3D-printed tablets containing multiple active ingredients
- Soft drug-delivery devices [99,100]
- One of SLA's key advantages is its exceptionally fine resolution, which enables the creation of intricate and complex structures.[101] Moreover, the minimal heat generation during printing makes it ideal for processing thermo-labile (heat-sensitive) drugs, as it avoids thermal degradation of active pharmaceutical ingredients. [102,103,104]
- The stereolithographic technique thus combines precision, biocompatibility, and gentle processing conditions, making it uniquely suitable for advanced pharmaceutical and biomedical applications.[105]

Principle of stereolithography

The core principle of SLA involves the full photo polymerization of a photosensitive resin upon exposure to ultraviolet (UV) light. A small layer of resin is solidified on the surface by low-power UV light (up to 1000mW) from a He-Cd/Nd: YVO4 laser.[106] The platform is a SLA machine's primary component. To form the 3D structure, the build platform is immersed in a vat filled with liquid resin. Another crucial component is the laser source. A computer is controlling it.After creating a 3D item, a solvent can be used to clean every component of the machine. The solvent can be used to remove any resinous materials from the surface.[107] The cleaned and completed 3D item is cured in a UV oven, and each layer of resin is scanned using a laser

process [108] with the aid of a CAD model. [109] When a pharmaceutical formulation with a higher water content is exposed to visible light irradiation, the drug release is significantly affected, increasing from 27% to 95% over the course of eight hours.[110]

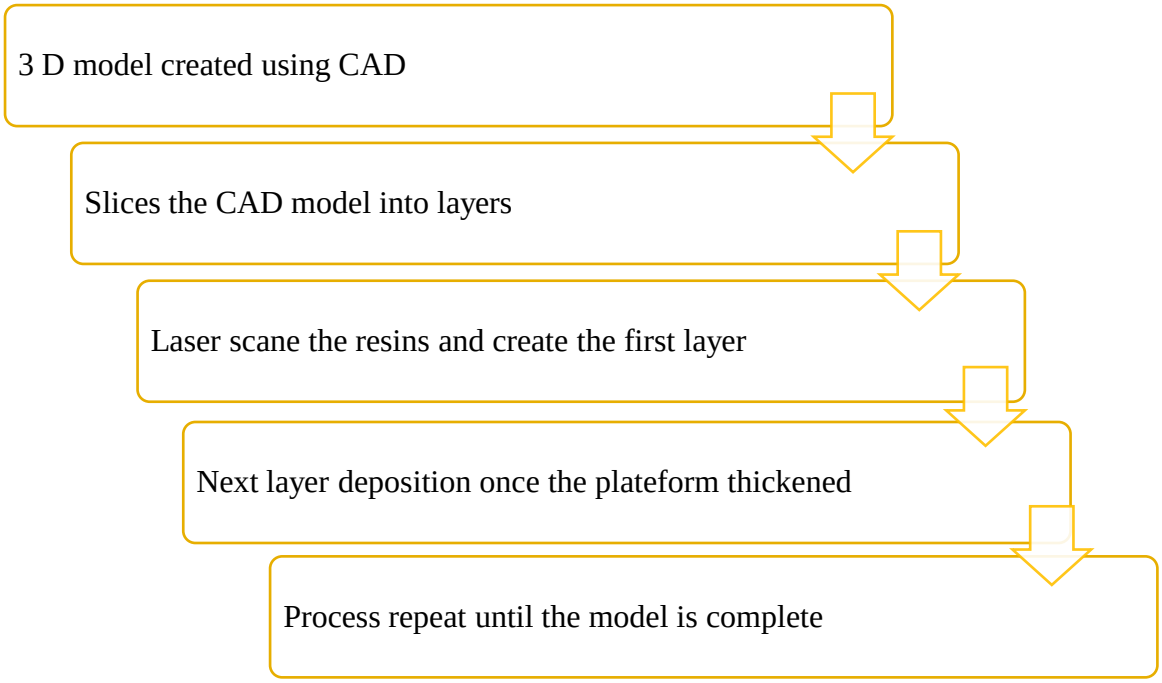

Figure 5: Process of SLA

5.6. Selective Layer Sintering

Selective Laser Sintering (SLS) is an advanced manufacturing technique that constructs components layer by layer using powdered metal materials. This method is commonly used for rapid prototyping. During the process, a laser beam sinters the powder particles, binding them together to form a solid structure. [39, 23, 69, 111]

SLS operates similarly to binder jetting, but instead of using a binder, a laser is employed to sinter the powder particles together.[112] The primary components of an SLS system include:

1. Spreading platform
2. Powder bed
3. Laser system [113]

A major benefit of SLS is its single-step production process, which eliminates the need for solvents. Additionally, because of its laser precision, SLS can produce high-resolution objects with excellent detail. [111]

5.7. Binder Jetting

Binder Jetting, also known as the drop-on-powder method, is an application of inkjet printing technology. This process involves the deposition of a liquid binder solution onto a layer of powder, which serves to bind the powder particles together. Binder jetting has been successfully used in the creation of pharmaceutical tablets and even multi-drug combinations in a single dosage form.[114]

The binding solution can act in several ways: it may dissolve a portion of the powder layer, evaporate and recrystallize, thereby solidifying the layers together, or a localized polymerization reaction may occur between the binder and the powder layer. [115,116] In some cases, certain binders may be removed after the printing process, resulting in a final product that does not contain the binder.[117]

5.8. Selective Laser Melting (SLM)

Selective Laser Melting (SLM) is similar to Selective Laser Sintering (SLS), but it fully melts the powder rather than just sintering it. This process results in denser and stronger structures. [118,119] SLM is commonly used in applications such as the production of implants and scaffolds.

6. APPLICATIONS OF 3D PRINTING FOR PHARMACEUTICAL

- **Solid Oral Dosage Forms (SODFs) Manufactured Using 3D Printing**

The most common solid oral dosage forms (SODFs) produced through 3D printing are tablets. With 3D printing technology, it becomes easy to design and customize tablets with various shapes, release profiles, and specific doses, including combinations of different medications.[120]

- **Polypills and Multi-Drug Combinations**

Pharmaceutical companies are increasingly using 3D printing to develop polypills, which are dosage forms containing multiple drugs within a single pill. This approach simplifies complex medication regimens, making it easier for patients to manage their treatments.[37]

- **Patient-Specific Dosage Forms**

Tailored 3D-printed dosage forms allow for precise customization, ensuring that patients receive the correct dose of medication based on factors such as age, weight, and medical condition. This personalized approach enhances the effectiveness of treatment, improving patient outcomes.

- **Immediate- and Modified-Release Tablets**

3D printing (3DP) has enabled the production of formulations that dissolve quickly in the mouth, improving patient compliance and convenience. [121,122] Modified-release tablets, including delayed-release, controlled-release, sustained-release, and targeted-release forms, can also be manufactured using 3DP. Traditional modified-release tablets often experience a decrease in surface area during the absorption process in the gastrointestinal tract, leading to non-constant drug release. However, 3DP can overcome this challenge by creating tablets with complex geometries that support individualized release profiles or continuous sustained-release dissolution patterns. [123]

- **Pharmaceutical Research and Development**

Researchers use 3D Printing to develop experimental drug formulations and conduct preclinical studies on new pharmaceutical products.[124]

7. CHALLENGES OF 3D PRINTING DRUGS

Despite the advantages of 3D printing technology, many technical difficulties and obstacles urgently need to be overcame to promote wider application of DDSs. [125,126]

- **Considerations for regulation**

The laws governing 3D printing in the pharmaceutical industry are always changing. Concerns exist over the clearance process, quality control standards, and validation procedures for 3D-printed medications. To ensure the safety, efficacy, and quality of drugs made by 3D printing, regulatory bodies must create exact guidelines and standards.[127]

- **Quality Control and Assurance**

It can be difficult to guarantee the constant safety and quality of medications made using 3D printing. Drug release and dosage irregularities may result from variations in printing settings, materials, and procedures, which may have an impact on patient outcomes.[128]

- **Excipients selection**

Expense and Availability It can be costly to purchase and maintain 3D printing supplies and equipment. The high prices may be a barrier to entrance for smaller pharmaceutical companies.[129] Due to their distinct printing principles, all forms of 3D printing technologies have certain criteria for the excipients' qualities throughout the preparation phase. The printing procedure for FDM technology involves both heating and melting, therefore choosing an appropriate drug carrier is crucial. PVA is the most commonly reported carrier excipient; nevertheless, due to its relatively high melting temperature, it is not appropriate for use with thermally unstable medications like levetiracetam[130] or 4-ASA. [102]

A growing number of researchers have tried to integrate HME technology with 3D printing technology in recent years [131,132] or low-temperature 3D printing technology.[133] They have done this by preparing low-temperature printed filaments using excipients like PVP, HPMC, Kollidon, talc, and triethyl citrate to address drug degradation [134] and enhance drug loading.[135] The only excipients available for SLA and SLS technologies are photopolymers and laser sinter able materials, neither of which are on the FDA's generally recognized as safe (GRAS) list. To date, only a limited number of excipients have been used in 3D printing, most of which are expensive, potentially toxic, have strong odours, and require protection from light to avoid premature polymerization. Additionally, safe manufacturing is anticipated for the creation of drugs.

The viability of applying DOP and SSE technologies to a variety of active medications and excipients, including cheese, chocolate, hydrogels, and epoxy resins, is one of the significant associated benefits. Nevertheless, organic solvents would be related to both technologies. In DOP technology, organic solvents serve as the primary printing inks. The main purpose of the potential addition of organic solvents in SSE technology is to create a soft paste. Thus, the main drawback of some of the finished 3D-printed tablets is the presence of leftover solvents. There is a minimum acceptable residual level for each solvent, and the choice of solvents is restricted due to specific acceptability limitations for the solvents as stated in ICH guidelines Q3C

(R5). Multidisciplinary research must therefore be strengthened in order to overcome this constraint, for example, by creating new kinds of 3D printers.[136]

- **Expense and Availability**

It can be costly to purchase and maintain 3D printing supplies and equipment. The high prices may be a barrier to entrance for smaller pharmaceutical companies.

- **Additional regulatory obstacles**

Additional regulatory obstacles prevent 3D-printed medications from being approved. The implementation of 3D printing technology in healthcare is constrained by the lack of clear regulatory frameworks governing its production. Drug production has not been reviewed, despite the FDA issuing restrictions for the use of 3D printing in prosthetics and medical equipment. [137]

8. CONCLUSION:

3D printing has emerged as a revolutionary technology in the pharmaceutical industry, offering unprecedented opportunities for personalized medicine, complex drug formulations, and on-demand manufacturing. Unlike traditional methods, 3D printing enables the creation of highly customized dosage forms with unique performance characteristics tailored release profiles, multilayer structures, and patient-specific dosages that were previously difficult or impossible to achieve.

The ability to integrate these innovations into scalable, mass-produced pharmaceutical products holds the promise of enhanced drug efficacy and reduced side effects, ultimately leading to improved patient outcomes. As 3D printing technology continues to evolve alongside advancements in material science and the development of clearer regulatory pathways the pharmaceutical industry is entering a new era of precision and efficiency.

Looking ahead, the full potential of 3D printing lies in its ability to accelerate drug development, minimize waste, and deliver more targeted, effective therapies. With ongoing innovation and collaboration across sectors, 3D printing is poised to redefine the future of medicine.

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CONFLICT OF INTEREST

The author declares that there is no conflict of interest.

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