

# **3D PRINTING IN PHARMACEUTICAL FORMULATIONS : FUTURE TREND IN PERSONALIZED MEDICINE**

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**Date of Submission** 15/04/25  
**Date of Acceptance** 02/05/25  
**Date Publication** 01/06/25

## **Abstract**

Additive manufacturing is also known as 3D printing. It is a relatively new technology that is currently attracting a lot of attention in the healthcare sector, particularly the pharmaceutical industry. With the help of additive manufacturing, 3D things of diverse geometries can be created layer by layer. 3D printing technology has emerged as a transformative tool in the pharmaceutical industry, offering many opportunities for personalized medicine, complex drug delivery systems, and on-demand manufacturing. By enabling precise control over drug composition, dosage, and release profiles, 3D printing allows for the creation of customized therapeutics tailored to individual patient needs. The capacity to customise medications with individually tailored doses, the ability to create sophisticated and complicated solid dosage forms, on-demand manufacture, and cost-effectiveness are some advantages of 3DP technologies over conventional manufacturing processes. The use of 3D printing is very common these days.

This article reviews the current advancements in 3D printing technologies for pharmaceutical use, discusses types and advantages of 3D printing, and highlights the future potential of this innovative approach to revolutionize drug development and delivery<sup>(1)</sup>.

**Keywords:** Additive Manufacturing, 3D printing, pharmaceutical industry, customization, on-demand manufacturing, Personalized Medicine, Tailored Dose

## 1. Introduction

Additive manufacturing (AM) commonly known as 3D printing (3DP), is a type of manufacturing in which an object is built up layer by layer. A few of the methods are vat polymerization, hot melt extrusion (HME), solid state extrusion (SSE), stereolithography apparatus (SLA), digital light processing (DLP), selective laser sintering (SLS), and binder jetting. Despite being widely utilized in other sectors like the automobile and aerospace, its use in the pharmaceutical sector is still in its early stages. AM is a revolutionary technique that is now extensively used in a range of fields and is simple to obtain because to the recent expiration of numerous AM patents. The transformation of the pharmaceutical industry to the era of personalised medicine has been accelerated by the application of AM. Even when the same amount of a drug is given, there may still be significant inter-individual variances in how the medication reacts<sup>(2)</sup>.

Customized medication may have a decreased risk of adverse effects or subtherapeutic benefits, as well as higher patient satisfaction and adherence, because these quantities are outside the therapeutic window. Individualised medicinal products also include dosage forms that are appropriate for specific populations, such as children, the elderly and patients with dysphagia, so that they can take their medicines. However, there may be a risk of incorrect dosing or the inconvenience or patient's ability to adjust regularly when changing available forms on the market by breaking and opening tablets. It is not feasible to use conventional manufacturing techniques in the individual dosing of patients due to their accuracy and complexity, however AM can be employed as an alternate production method through its very accurate, highly personalised approach.

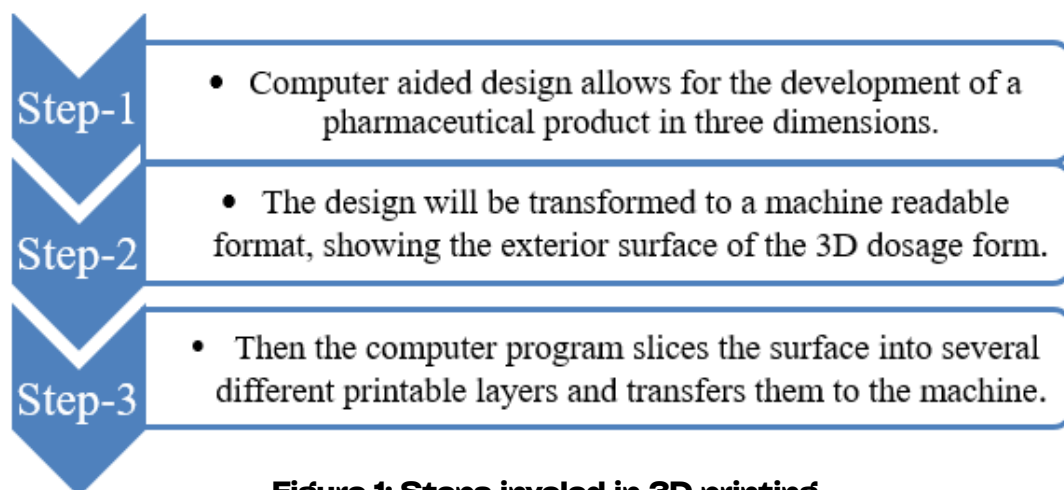
The ability of future AM technology to manufacture medicines in a manner which would make it simpler for people living in remote areas could also contribute to the availability of medicinal products. Additive manufacturing (AM) has its inherent limits, for example the scarcity of material to be used in pharmaceutical applications, the challenges faced by filaments which are so heavily packed with drugs that it is not possible to use them at large scale production<sup>(3)</sup>.

## 2. STEPS INVOLVED IN 3D PRINTED FORMULATION:

Additive manufacturing, often referred to as 3D printing, is a multistep process which begins with the creation of an electronic file using computerised CAD design aided and concludes with actual three dimensional solid objects. Although there will be certain variations between the various 3D printing methods, production using any method is required for a total of 8 stages.

The first phase is computer-aided design (CAD), which uses reverse engineering tools like laser and optical scanning or solid modelling software to produce a 3D solid or surface representation. Using a Computer Aided Drafting System to convert 3D Solid Representation into STL File is also part of the 2nd stage.

This computation is based upon a STL file, which displays external closed surfaces of the original CAD model in layers. The 3rd step involves sending an STL file to your printer, and further modifying it in order to ensure its proper dimensions, location as well as orientation for construction. In phase four, the machine configuration of build parameters such as materials restrictions, energy sources, layer thickness, timing and etc. is complete. The fifth stage is to construct the physical model. The next steps are to remove the created printlet from the printer, perform any necessary post-processing such as cleaning, and then apply the finished 3D printlets.<sup>(4)</sup>



**Figure 1: Steps involed in 3D printing**



**Figure 2: 3D printing Process**

## 1.TYPES OF 3D PRINTER

Different 3D printing technologies have been created with various purposes. 3D printer classified into six categories Because each technology and machine has a specific use, there is no dispute over which performs better. A growing number of products are now being made using 3D printing technology, which is no longer just utilised for prototyping. The different type of 3D printer are:



**Figure 3: Different types of 3D printing**

### 3.1 Binder jetting

A liquid binding agent is selectively applied to combine powder particles in the rapid prototyping and 3D printing technique known as binder jetting. The layer is created by the binder jetting method, which jets chemical binder onto the dispersed powder. The production of casting patterns, raw sintered products, or other comparable large-volume items from sand would be the application of binder jetting. Binder jetting is also quick, easy, and affordable because powder particles are cemented together. Binder jetting can also print very huge goods, which is its final advantage<sup>(5)</sup>.

### 3.2 Directed energy deposition

A more difficult printing method frequently used to fix or add extra material to existing components is called directed energy deposition. Directed energy deposition can manufacture high-quality objects and has a high degree of control over the grain structure. In theory, directed energy deposition works similarly to material extrusion, but the nozzle can travel in any direction and is not fixed to one axis. Additionally, the method can be used to ceramics and polymers, but it is most frequently utilised with metals and metal-based hybrids, in the form of either wire or powder.

### 3.3 Materials extrusion

Plastics, food, and live cells could all be printed in multiple colours and materials using material extrusion-based 3D printing technology. This method has a relatively low cost and is commonly utilised. Additionally, this procedure can create product components that are fully functioning. The first illustration of a material extrusion system is fused deposition modelling (FDM). FDM was created in the early 1990s and employs polymer as its primary material. FDM uses heated thermoplastic filament that is extruded to manufacture parts layer by layer from the bottom to the top. The following are FDM's business operations: I. A thermoplastic is heated until it becomes semi-liquid and is thenlike a scaffold. For instance, the FDM technique creates 3D bone models using hard plastic material<sup>(6)</sup>.

### 3.4 Materials jetting

A 3D printing technique called material jetting selectively deposits construction material drop by drop. In material jetting, a printer sprays droplets of a photosensitive substance that solidifies while being exposed to ultraviolet (UV) light, layer-by-layer constructing a part. Material jetting also produces products with great dimensional precision and a very smooth surface finish. Material jetting offers multi-material printing and a large selection of materials, including polymers, ceramics, composites, biologicals, and hybrids.

### 3.5 Powder bed fusion

The electron beam melting (EBM), selective laser sintering (SLS), and selective heat sintering (SHS) printing techniques are all parts of the powder bed fusion process. In this technique, the material powder is melted or fused together using a laser or an electron beam. Metals, ceramics, polymers, composite materials, and hybrids are a few examples of the materials employed in this procedure. The major type of powder-based 3D printing is selective laser sintering (SLS). SLS is a 3D printing method that works quickly, is highly accurate, and has different surface finishes. Metal, plastic, and ceramic can all be produced with selective laser sintering objects. SLS sinters polymer powders with a high intensity laser to create 3D objects. A head thermal print is used in the SHS technology, another component of 3D printing, to melt the thermoplastic powder and produce 3D printed objects. Last but not least, the material can be heated more effectively thanks to electron beam melting<sup>(7)</sup>.

### 3.6 Sheet lamination

In the 3D printing technique known as sheet lamination, sheets of different materials are bonded together to create an object's component. Laminated object manufacturing (LOM) and ultrasound additive manufacturing are examples of 3D printing technology that employ this technique. (UAM). The advantages of this technology are full-color printing capability, affordability, ease of material handling, and recycling of extra material.

## 4. MATERIALS USED FOR 3D PRINTING TECHNOLOGY IN MANUFACTURING INDUSTRY

To create consistently high-quality products, 3D printing requires high quality materials that adhere to strict specifications, much like any other manufacturing process. Procedures, demands, and agreements about material controls are developed between the suppliers, buyers, and end-users of the material in order to achieve this. Using a variety of materials, such as ceramic, metals, polymers, and their mixtures to create hybrid, composite, or functionally graded materials, 3D printing technology may create fully functional parts<sup>(8)</sup>.

### 4.1 Metals

The advantages offered by metal 3D printing have attracted a lot of attention in the manufacturing, aerospace, and automotive industries. Metal materials offer great physical qualities, making them suitable for application in a variety of manufacturing processes, including the printing of human organs and aerospace components.

### 4.1 Polymers

The manufacturing of polymer components, from prototypes to functional constructions with challenging geometries, is a common application of 3D printing technologies. Through the application of consecutive layers of extruded thermoplastic filament using fused deposition modelling (FDM), it is possible to create 3D printed objects such polylactic acid (PLA), acrylonitrile butadiene styrene (ABS), polypropylene (PP) ,polyethylene (PE). Due to their low cost, low weight, and processing flexibility, 3D printing polymer materials in liquid state or with low melting point are frequently employed in industry. The majority of the time, polymer materials played a significant part in biomaterials and medical device goods, frequently as inert materials, by supporting various orthopaedic implants mechanically and helping to ensure the devices functioned effectively<sup>(9)</sup>.

**Tabel 1: Different polymer used in 3D printing for pharmaceutical products**

S.NO.	Polymer	Drug Delivery System	Reference
1	Poly vinyl alcohol (PVA)	Tablet, Capsule, film	(Tagami et al., 2017; Wei et al., 2020)
2	Poly lactic acid(PLA)	Nanofiber	(Chi et al., 2020)
3	Polycaprolactone (PCL)	Tablet, Nanotube	(GV et al., 2017; Ho et al., 2017)
4	Hydroxypropyl methylcellulose (HPMC)	Matrix tablet	(GV et al., 2017; Ho et al., 2017)
5	Ethyl cellulose(EC)	Tablet	(Homaee Borujeni et al., 2020)

### 3.4 Ceramics

By optimising the conditions and setting up the good mechanical qualities, 3D printing technology can make 3D printed objects from ceramics and concrete without any cracks or pores. Ceramic is sturdy, long-lasting, and flame-resistant. Ceramics may be utilised in almost any geometry and shape because of their fluid state before setting, making them ideal for the design of new structures and buildings. Aerospace and the dental industries both benefit from ceramic materials. Examples of such materials include zirconia, bioactive glasses, and alumina<sup>(10)</sup>.

### 3.5 Composites

High-performance industries have been transformed by the outstanding adaptability, light weight, and tailorable features of composite materials. Carbon fiber reinforced polymer composites and glass fiber reinforced polymer composites are two examples of composite materials. Because of their high specific stiffness, strength, good corrosion resistance, and outstanding fatigue performance, carbon fiber reinforced polymers composite structures are widely employed in the aerospace sector. In addition, glass fiber reinforced polymer composites are frequently employed in a variety of 3D printing applications and have a wide range of prospective uses due to their high performance and cost-effectiveness.

## **5. ADVANTAGES OF 3D PRINTING OVER CONVENTIONAL SOLID DOSAGE FORM**

### **5.1 Conventional solid dosage form poses a certain limitation, such as Limited dosage flexibility**

- Need for proper flow properties in tablet formulation
- Poor dosage uniformity may be caused by compounds with poor solubility, low potency, or low density.

### **5.2 The tremendous benefits of 3D printing technology can overcome these certain limitation**

- Improved product complexity.
- High dose flexibility
- Formulation development suitability
- Low cost, simple manufacturing, and personalization appropriate for pediatric patients.<sup>(11)</sup>

### **5.3 Role of 3D printing technology in personalized treatment**

Pharmaceuticals are often mass-produced in a limited number of unique dose strengths depending on the optimum dose needed to have the desired effect in the vast majority of people. One dose obviously won't work for all patients, though. Their needs can change depending on a variety of reasons.

Due to the diversity among people of different races with variable metabolisms, traditional dosage forms cannot be given to all patients. Utilizing 3-D printing to create customised dose forms has a huge potential for use in the pharmaceutical industry. Customized treatment strategies for every patient are now possible because to modern pharmacogenomics research, computer and 3D printing technologies, and other breakthroughs. Genetic profiles will be used to choose and administer drugs, substitute safer chemicals for patient-specific allergies, and consolidate all of the patient's necessary prescriptions into a single pill. According to the patient's demands based on their age, race, or gender, pharmacists were now able to customise medications in terms of dosage, form, size, and dose combinations thanks to 3-D printing.<sup>(12)</sup> Additionally, this method offers the chance to create brand-new medicine formulations, which may be especially beneficial for patients with a variety of illnesses. For instance, a chemist could combine several active substances into one pill. Medication adherence may be greatly enhanced by reducing the patient's required dosage from ten to one. The technique that enables the 3D printing of pills into precise geometrical forms and sizes, which impacts the pharmacokinetics, was invented by MakerBot Replicator. The manufacturing of medications for customers is significantly



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### 6. CONCLUSION:

A physical model is created using digital data using the layer-by-layer, automated modern manufacturing technique known as three-dimensional printing. The goal is to essentially create a customised and personalised drug administration strategy. The use of three-dimensional printing

is crucial in the creation of many intricate medication delivery systems. Numerous research in recent years have noted improved 3-D printed pharmaceutical medicinal product safety, bioavailability, effectiveness, and acceptance. This strategy has proven to be a viable and useful way to administer medication to individuals who require a particular substance for individualised therapy.

After the first 3D printed tablet carrying the antiepileptic medicine levetiracetam under the brand name Spritam® produced by Aprezia Pharmaceuticals was approved, 3D printing technology advanced at an unusually rapid rate. Studies on topical dosage forms, implants, and solid oral dosage forms have demonstrated the 3D printing technology's enormous potential in the fields of pharmaceutical drug development and healthcare. In comparison to traditional manufacturing methods, this promising technology has many benefits, including increased product complexity, high dose flexibility, personalization appropriate for paediatric and geriatric patients, faster first-in-human (FIH) trials, on-demand and quick manufacturing with the potential for on-site preparation.

Additionally, this technology opens up new opportunities for the creation of multifunctional innovative drug delivery systems for personalised therapy. Using 3-D printing technology, several active pharmaceutical compounds can be combined into a single pill, improving patient compliance and promoting medication therapy adherence. It is feasible to acquire unquestionable benefits for the further growth of pharmaceutical medication delivery systems and suitable results at the industrial level by properly understanding the operating principles of various 3D printing techniques as well as their advantages and disadvantages.

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