

**A REVIEW: 3D PRINTING IN SOLID DOSAGE FORMS****Aman Upadhyay<sup>1\*</sup> and Anoop Kumar Singh<sup>2</sup>**<sup>1</sup>Scholar of B. pharm 4th Year, S.N. College of Pharmacy.<sup>2</sup>Director, S.N. College of Pharmacy.Article Received on  
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Pharmacy.**ABSTRACT**

A final product is created using the layer-by-layer deposition of materials in a 3D printer in accordance with a digital model. Over the past ten years, a number of innovative technologies have been created to transform the traditional dosage schedule into individualised medicine. Building a suitable 3D model for applications like drug testing, sensing, testing, and organs-on-chip may also employ methods intended to customise dosing regimes. Numerous cutting-edge technologies have been developed during the past 10 years to change the conventional dose regimen into individualised medication. Both the

development of medicine delivery methods and the identification of new drugs employed 3D printing. This study aims to investigate different 3D printing techniques used to produce oral solid dosage forms. It's critical to comprehend which polymers work best for extrusion-based 3D printing of medicines and how their characteristics and interactions with active pharmaceutical ingredients (APIs) affect printing. Successful 3D printing of dosage forms or printed structures requires an understanding of the rheology of the polymer and API-polymer mixes. The production of oral solid dosage forms has been demonstrated to be suitable for the FDM, SLA, SLS, and PB-Inkjet printing processes.

**KEYWORDS:** 3D printing, Personalized medicine, polymers, pharmaceuticals, Active pharmaceutical ingredients.

**INTRODUCTION**

Numerous applications for additive manufacturing, often known as 3D printing, have been found across numerous sectors. It is a method that uses solid free form manufacturing and has practical uses in things like satellite and jet engines<sup>[1]</sup>, unmanned aerial vehicles<sup>[2]</sup>, sensors<sup>[3]</sup>, custom implants, and scaffolds for people who need to regenerate bone or other tissues.

Prosthetics, medical devices, and artificial organs have all been created using 3D printing.<sup>[4-6]</sup> Recently, 3D printing has attracted increasing interest in the pharmaceutical industry where it has been used to create various drug delivery systems and dosage forms, which have been referred to as printlets in recent reports.<sup>[7-9]</sup> Because of their ease of manufacture, nearly accurate dosing, and ease of painless administration without the assistance of a healthcare professional, oral solid dosage forms are the most widely used types of medications.<sup>[10]</sup> As a result, they produce good patient outcomes through good adherence and compliance. Oral dose forms produced via 3D printing have received a lot of attention from the pharmaceutical industry.<sup>[11]</sup>

The creation of digitally created items via 3D printing is based on the notion of layering. Wide variety of materials, including polymers<sup>[12]</sup>, ceramics<sup>[13]</sup>, metals<sup>[14-18]</sup>, wood<sup>[19]</sup>, and organic tissue<sup>[20]</sup>, might be processed using the method. A technique known as 4D printing may also produce 3D items using smart materials that have been pre-programmed to change in reaction to outside stimuli. Using external stimuli like heat, pH, light, or a magnetic field, programmable materials might undergo changes in shape and function.<sup>[21]</sup> When compared to conventional pharmaceutical methods, such as milling, mixing, granulating, and compression<sup>[22]</sup>, which lack production flexibility and process capabilities, 3D printing offers innovative benefits. It also opens up a wide range of opportunities for pharmaceuticals, including the creation of sophisticated, customised, and made-to-order items.<sup>[23]</sup> The majority of 3D printing systems have relatively similar operating principles. First, a CAD programme is used to create the product design, geometry, and part sizes. The output is then transformed into a machine-readable format and divided into printable layers. To construct the physical items, raw ingredients are transformed into powder, filaments, or binder solutions that are then applied one layer at a time. Finally, some items might need to undergo post-processing, which often entails the removal of support or extra materials. Depending on the raw materials, tools, and solidification technique, many 3D printed technologies are used to manufacture pharmaceutical products.<sup>[24]</sup>

Different environmental and genetic variables contribute to individual variability in treatment response to the same targeted medicine. Novel technologies, such 3D printing, have been developed to alleviate the challenges involved with routine pharmacological delivery (3DP). This method has the advantage of allowing for on-demand dose adjustments in accordance with the unit by altering the object's shape or other physical dimensions. Researchers are

investigating the customised oral drug delivery technology known as 3DP, or additive manufacturing, to create pharmaceutical goods with tailored dosages. Although additive manufacturing is not a new concept, it has found widespread use across several industries. The most common types of pharmaceuticals are oral solid dosage forms because they are quick to prepare, have almost exact dose, are straightforward to deliver, and do not need a healthcare provider's help. This method, which makes use of solid free form production, has practical uses.<sup>[24]</sup>

### **Applications of 3-D printing technology**

According to the business, one benefit of employing 3D printing in fast-melt production is that it may solve the so-called "dose ceiling," over which it becomes challenging to produce quick disintegration and a satisfactory tongue feel. In commercially available fast-melt technologies, lower-dosage (30 mg) products are typical, but the business claims that accurate dosing and quick dispersion for greater doses (> 50 mg) in a fast-melt administration is more difficult. Other characteristics, such as taste-masking or modulated release, can be accommodated using 3-D printing technology. For the goal of masking flavour, medication particles may be coated or encapsulated. Alternatively, the product's release properties may be changed to enable quick dispersion and a modified release profile. There is greater opportunity to create formulations that include numerous APIs into the powder mix since there are less restrictions on tablet size. Additionally, it is feasible to print some APIs with quick dispersion capabilities, for example, in a fixed-dosed combination product combining many APIs.<sup>[25]</sup>

It would be feasible to include anti-counterfeiting features, such as the printing of a company mark (e.g., name, brand, etc.), into the inner layers of the dosage form, by creating 3D-printed dosage forms layer by layer. Additionally, by precisely regulating droplet size and placement within the microarchitecture of a dosage form, 3D printing manufacturing may be able to print drug-loaded fluids onto an excipient powder bed to create (complex) immediate, extended, and multi-release dosage forms as well as enable printing drug concentration gradients. The creation of very powerful drugs may also be aided by the control and repeatability of droplet size provided by 3D printing production, since medication deposition via fluid can allow highly precise dosage and may have advantages over handling powders. By solving issues including batch-to-batch drug variability, excipient mix during implant production, and inconsistent internal design of implants, as well as improving drug release in

these systems, 3D printing technology may also be successful in implantable drug-delivery systems.<sup>[26]</sup>

### **3DP techniques**

The three primary categories of 3DP processes are extrusion-based printing systems, inkjet-based printing systems, and laser-based printing systems.<sup>[27]</sup>

#### **Laser-based 3DP is primarily of two major types**

1. Stereo-Lithography Apparatus (SLA)
2. Selective Laser Sintering (SLS)

#### **Stereo-lithography apparatus (SLA)**

SLA was one of the earliest 3DP technologies created by Hull in 1986, using radiation to trigger the photopolymerization of a few photosensitive polymers. Liquid polymers and plastic resins that may be photo-polymerized are often scanned using digitally controlled UV-Light emitters. After polymerization, the 3D printer produces a layer of solid resins with the same thickness as the polymer layer that came before it. Multiple layers of polymers fuse due to UV light's strong penetrating capacity. To create the dosage form's intended design, these cycles are repeatedly performed.<sup>[28]</sup>

#### **Selective laser sintering (SLS)**

One of the cutting-edge 3D printing technologies is SLS. This method involves drawing precise patterns on the surface of powders by stacking powder materials while employing focused lasers. The reservoir beds rise and the powder beds descend as the layers are sintered to create new layers, which are then layered on top of the older layers. To reach the desired dose designs, the technique is performed numerous times. A laser beam is utilised in the SLS method of 3D printing to fuse powder particles one at a time. The idea of selective laser sintering is based on the dispersion of layers of powder with a thickness ranging from 0.05 to 0.3mm, followed by the selective laser beam scanning of each layer.<sup>[29]</sup> The component or final structure is created by the sintered powder, whereas the support structure is created by the un-sintered surplus and eliminated during post-printing processing.<sup>[30]</sup> SLS is a one-step technique, which offers various benefits. Additionally, the use of additives to bind the item eliminates the need for lasers, which also have lower wavelengths and lower resolution, making it more efficient in terms of cost, time, and the environment. The process's high

temperature, brought on by the energy of the laser, might, however, result in the deterioration of the powder's active component.<sup>[31,32]</sup>

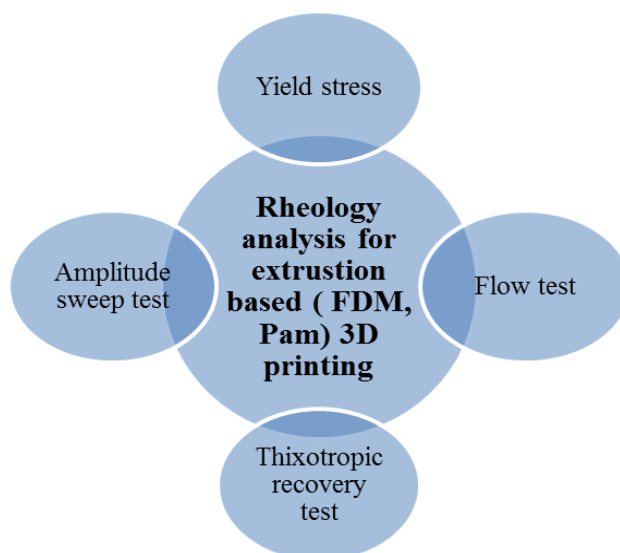
### **Printing-based inkjet (IJ) system**

The two technologies that make up IJ systems are continuous inkjet printing (CIJ) and drop-on-demand printing (DOD). Both IJ systems have a printer head and must regulate the speed, size, and interval of drop formations as well as fluid viscosity. CIJ technology uses a high-pressure pump to create a continuous stream of ink through an orifice that is between 50 and 80 micrometres in diameter, whereas DOD technology creates droplets that are between 10 and 50 micrometres in diameter and have a volume of 1 to 70 pL. Both thermal and piezoelectric crystal printer heads may be used with the DOD method. [34] With thermal DOD, also known as bubble jet printing, ink is heated locally and creates bubbles that discharge ink. The thermal DOD method is only compatible with volatile liquids, whereas the piezoelectric DOD method can be used with a wide range of liquids. Additionally, given that (1) the thermal method reaches temperatures of up to 300 °C, which may result in the degradation of drugs, and (2) the piezoelectric DOD method produces an acoustic pulse sufficient for the ejection of ink, the piezoelectric DOD method is preferred.<sup>[37]</sup>

### **Nozzle-based deposition systems**

Given that the most popular printing-based IJ approach has the disadvantages of having insufficient hardness, a rough surface, and low drug loadings[38], nozzle-based deposition devices might be a good substitute to get over those restrictions. Nozzle-based deposition systems mix the solid components with the binder beforehand and directly deposit the mixture through a nozzle to create a 3D object, as opposed to dropping the binder solution on a powder bed.<sup>[39]</sup> This method can be divided into two subtypes, named fused deposition modelling (FDM) and pressure-assisted microsyringes (PAM), according to the process with or without material melting, respectively.

FDM, which is also known as fused filament fabrication, describes a process in which a molten thermoplastic polymer filament is extruded through a high-temperature nozzle and deposited layer by layer with immediate solidification onto a build plate. FDM has been extensively studied in many fields, including pharmaceuticals, foods, and bioengineering.<sup>[41]</sup>

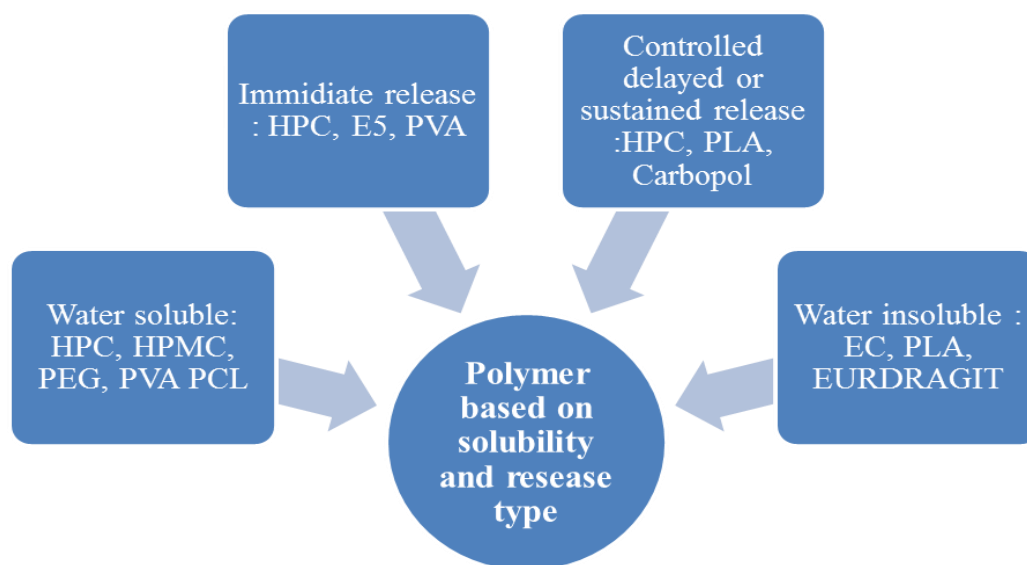


**Figure 1: Important rheological tests.**

### **Polymers used in 3D printing of pharmaceutical solid dosage form**

3DP creates innovative solid dose by combining several polymers and polymer types.

The two most often utilised polymers are polyvinyl alcohol (PVA) and poly vinyl pyrrolidone (PVP). The polymers used in 3DP are often divided into three categories: amalgams; non-biodegradable polymers like polylactic acid (PLLA); and biodegradable polymers like polyethylene glycol (PEG), polycaprolactone (PCL), etc. Polymer amalgams, like Eudragit RL PO and PLA, mix two or more polymers. There is a list of the polymers and mixtures of polymers that are utilised in 3DP. Non-biodegradable polymers and the mixtures of such polymers used in 3DP technologies to produce medicines.<sup>[42,43]</sup>



**Figure 2: Different types of polymers.**

### 3DP Solid dosage forms

For many years, researchers have used 3DP to create many products, including medicinal solid dosage forms. Levetiracetam (sprit am) is presently only offered in a single formulation on the market. In 2015, the FDA authorised sprit AM. The medication comes in four distinct strengths, namely 250 mg, 500 mg, 750 mg, and 1000 mg, and is designed as rapid dissolving tablets. Giomouxouzis et al. published a study in 2020 and using the FDM 3DP process in which they created diltiazem caplets utilising PVA and cellulose acetate (CA) as the ink polymers and used diltiazem as the model medicine. The physicochemical characteristics of the produced caplets are evaluated using thermal analysis techniques (TGA, DSC), and the morphological aspects are examined using X-ray diffraction (XRD) and scanning electron microscopy. Diltiazem inside the polymer has amorphized, according to the XRD study.<sup>[44]</sup>

In 2019, Glutei et al. manufactured tablets and filaments of pramipexole dihydrochloride monohydrate using FDM as the 3DP technique and EudragitEPO + POLYOXTM WSR N10 and Eudragit EPO + POLYOXTM N80 as polymers. To evaluate the qualities of the manufactured filaments and tablets, scanning electron microscope (SEM), differential scanning calorimetric (DSC), and filament disintegration tests were utilised. Selective laser sintering (SLS) was the preferred technology for 3DP in 2020, and ondansetron and anti-emetic medications were employed as model pharmaceuticals to make oro dispersible printlets using Collide VA-64 as the main polymer.<sup>[45]</sup>

Tabriz et al., 2021 created a brand-new solid dosage form (tablets) for rifampicin and isoniazid. The first line of therapy for TB treatment includes the use of both isoniazid and rifampicin. The preferred polymer for isoniazid is HPMC, whereas the preferred polymer for rifampicin is hydroxymethyl propyl cellulose acetate succinate (HMPCAS). To create a single tablet, the two medications are first printed on separate layers and then combined.<sup>[45]</sup>

Ibrahim M et al., 2019 employed PVA filaments as the preferred polymer in FDM as 3DP technology to create metformin tablets using HCl as a model medication. The metformin HCl solution is made with ethanol as a solvent and has a low water content (i.e., 10% v/v) to increase the drug's solubility. The PVA filaments are then immersed in a mixture of metformin HCl and ethanol for a predetermined amount of time.<sup>[46]</sup> To get the highest possible drug loading, the solutions are divided among many vials and swirled continuously for 1, 3, and 10 days. The produced metformin-PVA (ML-PVA) filaments are



physiochemically characterised using SEM, X-ray powder diffraction (XRPD), Fourier Transform Infrared Spectroscopy (FTIR), DSC, and dissolution investigations.

Similar to this, FDM 3DP is used to create drug-loaded filaments of ciprofloxacin HCl + PVA in another work by Saviano M et al., 2019. To create the physical blends, the dried powders of the medicine and the polymer are combined.<sup>[47]</sup> Dibutyl sebacate is then added to the mixture of the drug and the polymer to improve the drug's adherence to the pellets and to speed up the extrusion procedure. To feed the extruder, drug-loaded filaments with a diameter of 2.85 mm and 0.15 mm produce flat-faced cylindrical printlets.<sup>[48]</sup>

### **3D printing for organ-on-chip application and drug sensing**

It is crucial to test the medications in a model, such as the often used animal models, after developing oral dosage forms. The full physiology of a human organism, however, is frequently not replicated by the animal model. Using animal models to research cell-cell interactions is difficult as well. Using an animal modelling society is also raising more ethical questions. Scientists have created 3D models known as organ-on-chip systems, which have the capacity to not only mimic the cellular/tissue level in its microenvironment but also to act as a methodically analytical tool for disease progression, thanks to the current advancement in micro fabrication techniques like photolithography and 3D printing. For a definition, artificial living organ technology strives to develop artificial living organs that can imitate the physiological reactions of real organs. This technique provides a space for in-vivo-like cell manipulation, sensing, and drug testing.<sup>[49]</sup>

### **Stereolithography**

A laser beam is used in the stereo lithography 3D printing technique to polymerize liquid resin layer by layer, solidifying it. When focused on a tank containing a photosensitive resin, a UV or other light source produces cross-linking and creates a polymeric matrix. In a bottom-to-top build method, the platform is lowered following the curing of each layer and a fresh layer of uncured polymer resin is applied on top of the previous curing. Using a light source from below to cure the resin layer via a transparent plate in the resin tray is an alternate method. The platform is elevated and uncured resin is allowed to fill the space between the platform and plate after each layer has dried, enabling future layers to be cured top-down. The strength of the light source, the rate of scanning, the amount of monomer, and the amount of photo initiator all affect the kinetics of the cross-linking reaction of resins, which in turn affects the thickness of the cured layer and the curing time. The excellent



resolution, quick printing speed, and minimised localised heating of this printing technique make it appropriate for printing thermo-labile pharmaceuticals.<sup>[50]</sup>

### **Incorporating APIs into polymer filaments for 3D printing**

#### **Solvent immersion**

As active pharmaceutical ingredients (API) are not commercially accessible, filaments made from pharmaceutical grade polymers must be manufactured. Commercially accessible filaments like PLA, PVA, and PCL offer the right mechanical characteristics for printing, but successfully loading APIs into these filaments is still difficult. The first commercial filaments used for FDM printing of oral dosage forms were soaked in volatile solvent solutions to add APIs. Guyanese et al. created filament with amino-salicylic acid by soaking commercial PVA filament in ethanol that has been soaked with medication. As a result, the medication was able to passively diffuse into the filament and get stuck after drying. The percentage drug content recorded for this approach was quite low, recording 0.004% for 4-ASA and 0.001% for the less soluble 5-ASA, despite the fact that it was inexpensive, straightforward, and required no heating.<sup>[51]</sup>

#### **Hot melt extrusion (HME)**

Recently, the primary method for making API-loaded filaments was hot melt extrusion (HME). Pelletizing and grinding commercially available filaments coupled with the active ingredient(s) before a hot melt extrusion is one HME-based approach of medication inclusion. The grinding procedure is crucial since it guarantees that the polymer and API (powder) have equal particle sizes. Pellets and drug powder together would result in inadequate drug loading and encapsulation. PVA filaments were crushed into a fine powder and then passed through a sieve with a mesh size of 1000 m to create tiny, cylindrical pellets that were about 2 mm long. These pellets were used to print budesonide tablets. A single screw extruder was used to extrude a combination of the powdered polymer and budesonide. With strong mechanical strength and a larger proportion of drug content, these filaments are suited for printing and manufactured using this technology. HME offers the additional benefit of being able to increase the bioavailability of medications that aren't very soluble. As was previously indicated, the FDM method may also employ HME to produce customised filaments, thus it is not limited to using commercial-grade polymer filaments. The majority of extruders on the market are single screw extruders, which do not combine well enough to produce homogeneous contents for bespoke filaments.<sup>[52]</sup>

### Strategies and approaches for personalisation of printlets

Personalized dosage forms, dosages, implants, and other goods were produced using 3D printing in many medical and pharmaceutical applications in an effort to increase patient compliance and adherence. The creation of multi-layered tablets with one or more APIs in each layer is only one of the numerous ways that customization may be done. This would be the perfect method of treating individuals who have co-morbid conditions and polypharmacy. Polycarp is a fixed dosage combination therapy for co-morbid cardiovascular conditions that was previously documented in trials. The main drawback of this invention, however, is that the dosages are set and difficult to adjust using the traditional compaction approach. A multi-material 3D printer can be used to create multi-layered dosage forms (shown in FIG. 5a), and in situations where the printer technology is not set up for multi-material printing, adjustments can be made to the existing printer. By using the SLA method of 3D printing, Robles-Martinez et al. created a six-layered polypill containing naproxen, paracetamol, caffeine, aspirin, chloramphenicol, and prednisolone. The physical properties of the polypills, as well as the impact of geometry and the addition of excipients on the rate of drug release, were assessed. Due to the lack of commercial availability of the hardware and software required for multi-resin printing, various modifications are made to allow for periodic manual resin replacement and programme redesign.<sup>[53]</sup>

### Benefits of 3D printing solid dosage forms

#### On-demand manufacturing

Utilizing 3D printing technology makes it simple to quickly fabricate high-quality products. 3D printing on demand can be especially helpful in cases where there are time and material constraints, in the development of drugs for rapid optimization, and in the production of pharmacological products with poor stability. Due to the accessibility of desktop printers, this is increasingly likely. Low stability medication inkjet printing has already been documented, and 3D printing as a method of producing low stability pharmaceuticals has been suggested.<sup>[54]</sup>

#### Dosage flexibility

Customizing medications to meet the requirements, preferences, and specific patient characteristics is an age-old concept that has exploded with the development of diagnostics. Pediatrics, where there is a large weight to age variance, would benefit most from dosage customization. Grouping the patient population based on certain biomarkers helps to control

the variability in therapy across people caused by variances in their histories, metabolisms, and demands. Personalization makes 3D printing more effective for management. In order to lessen non-compliance brought on by the prescription of many drugs, personalization and dosage customization would also be beneficial. Patients taking more than four drugs have a reported 35% medication non-adherence rate due to polypharmacy. According to research, polypharmacy is common among elderly people. It has been closely associated with unfavourable outcomes, such as bad drug responses, interactions, and medication non-adherence. Complex dosage regimens have been linked to poor adherence in the geriatric population, with older patients living in the community scoring between 43 and 100% in nonadherence. By using 3D printing to personalise dosage forms, it is possible to modify dosage and combination to suit the needs of each patient. Each patient's weight, age, and pharmacokinetics may all be taken into consideration while adjusting the dose.<sup>[55]</sup>

### **Improved quality dosage forms**

It is anticipated that using desktop printers in conjunction with computer-aided designs would improve control over the numerous variable parameters involved in 3D printing tablets. The printer system regulates crucial variables including scan speed, laser power, and temperature, resulting in great repeatability. In addition, compared to conventional techniques of formulation, 3D printing requires fewer processing steps for product manufacture. Stages including granulation, milling, compression, coating, and drying are necessary in the majority of traditional medicinal product formulations, and the more steps involved in these processes, the higher the risk of batch failure owing to increased likelihood of mistakes.<sup>[56]</sup>

### **Design flexibility**

The shape of tablets, caplets, and capsule shells is typically determined by the shape of the appropriate moulds in traditional medicine production techniques, however 3D printing enables creative product designs. Multiple active medications can be strategically included into preset portions or layers by carefully controlling the distribution of active components and excipients inside the dosage form. The content, macrostructure, and microstructure of a dosage form can all have a significant impact on how quickly a medication is released. For instance, designing a solid dosage form with a highly porous structure can speed up drug release by reducing the amount of time the dosage form needs to dissolve. Oral disintegration may be created to satisfy the needs of elderly, paediatric, and dysphasic individuals, with colours, forms, and flavours altered to suit the paediatric population.<sup>[57]</sup>

### Limitations of 3D printing techniques

Some 3D items' physical look may not be appealing to patients. When support materials are removed from FDM printlets or the porous structure of SLS printlets, certain printing processes yield printlets with rough or uneven surfaces. Products that patients find unsightly may lead to low patient compliance. Additionally, some 3D printing processes, including stereo lithography, call for the use of substances that can pose health hazards. A few carcinogenic concerns are thought to exist for the majority of authorised polymer resins and photo polymerization initiators. This limits the application of these techniques to the creation of oral dosage forms. Another significant drawback is the requirement for the use of lasers and other high-energy sources in techniques like stereo lithography and SLS printing, which might cause unstable medications to degrade. The usage of FDM printing may also be limited to pharmaceuticals and excipients that are thermally stable due to heat deterioration. The necessity for thermoplastic polymers and filament extrusion places restrictions on FDM printing. printing of tablets with a quick dissolve rate. The mechanical strength of printouts is compromised when utilising the powder bed printing technology, leading to high friability and poor hardness. The stereo lithography printing equipment is one expensive piece of printing equipment. In SLS, SLA, and powder bed 3D printing, post-printing procedures like curing and drying are necessary, which extends the print time.<sup>[58]</sup>

### Drugs classification

According to reports, several medications were added in the FDM 3DP formulations, and their application relied on the ailment to be treated. The most common types of medications utilised in the FDM 3DP formulations were analgesics like paracetamol and aspirin, anti-inflammatory medicines like acyclovir and prednisolone, and anti-hypertensive pharmaceuticals like nifedipine and carvedilol. One of the primary drawbacks of the FDM process, as mentioned in the introduction, was the drug degradation caused by the heated nozzle's temperature, which is proportional to the melting temperature of the polymers. According to Guyanese et al. and other scientists, it was important to choose the right medication and polymers to employ to create the 3D objects based on their physiochemical and mechanical characteristics in order to prevent this drug degradation during the extrusion process. To make this feasible, we chose to determine the melting point of the polymers employed in the included articles. Using these values, it would be possible to determine which medication would be ideal to include in the drug delivery system without running the risk of medication deterioration.<sup>[59]</sup>

### **Combining 3D printing and nanotechnology**

Recently, research has started to be done on how 3D printing and nanotechnology may be combined to create oral formulations with better medicinal qualities. Similar to 3D printing, nanotechnology is an emerging method in pharmaceutical products. Nanocapsules, polymeric nanospheres, polymerosomes, drug nanocrystals, liposomes, and other nanotechnology-based pharmaceutical products offer numerous benefits and opportunities for creating medications with unique release profiles as well as for enhancing drug dissolution.<sup>[60]</sup>

### **Powder-based (PB) 3d printing**

A method for printing 3D objects using powder is known as powder-based (PB) 3D printing, often referred to as binder jetting or drop-on-powder. In this method, ink including a binder or only a solvent is jetted onto a flat printing bed using an inkjet head that may move freely in the X-Y direction. The printing bed slides down along the Y axis under the movement of the piston and a new layer when the powder mix on the printing bed is joined together and hardened by the binder.<sup>[61]</sup>

### **Clinical research and applications**

Following the FDA's 2015 approval of the first 3D-printed medication, Spritam, Trieste, Inc.'s T19 has now received FDA approval as an investigational new drug (IND) and has begun the clinical trial phase. The circadian pattern of rheumatoid arthritis symptoms is addressed by this medication. using the use of Melt Extrusion Deposition to design the tablet's 3D structure. With the use of 3D printing, the release of the medicine mixture may be precisely controlled. Approach to 3D printing that employs a laser's light energy to sinter (melt the surface) or fuse powder particles to make 3D solid things. SLS is superior to previous approaches in many ways since it doesn't use solvents and is very productive.<sup>[62]</sup>

### **Pharmaceutical Application**

Clinical trials are time- and money-consuming in the drug development process. The primary objective of the OoC field is to facilitate and advance evaluation in drug development and discovery. This ultimate goal has driven the creation of a large number of start-ups and spin-off businesses, which have moved the research community, mostly in academia, toward effective and trustworthy commercial availability on a product or service basis.<sup>[63]</sup>

Organovo Inc., based in San Diego, California, USA, has established a successful company as a contract research organisation that assesses investigational drug compounds on the 3D-

printed liver. This is one of the instances in the pharmaceutical manufacturing of the 3D bioprint OoC. Leading pharmaceutical corporations from across the world are now employing Organovo Inc.'s services, including Merck, Bristol-Myers Squibb, and Roche.<sup>[64]</sup>

## CONCLUSION

Growing interest in employing 3D printing to create customised dosage forms is a result of the need for such dosage forms and the advancements in additive manufacturing technology. The use of 3D printing in the production of pharmaceuticals is anticipated to bring about the much-needed upgrade to the traditional techniques of production, which are known to be inflexible and inefficient. In 2015, the FDA approved one of the 3D-printed solid dosage forms. FDM has received the most study out of all the 3D printing techniques and has shown to be more useful for producing medications. By opening the way for the development of potentially individualised medications, this technology has the potential to completely transform the pharmaceutical sector. A cutting-edge method called 3D printing makes it possible to create formulas that are specific to each patient, which lowers expenses and improves treatment compliance. Moreover, The most often utilised pharmacological form at the moment is an oral solid dose form. Due to the advantages of 3D printing over traditional tablet manufacture, it is now possible to modify medication release and increase drug solubility through formulation choice and unique structural design. Since the FDA authorised the first 3D-printed medicine in 2015, the use of 3D printing in the creation of oral solid dosage forms has skyrocketed.

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## Conflict of interest

The Authors declare no conflict of interest.

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