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REVIEW ARTICLE

# A Comprehensive Review of 3D Printing Applications in Drug Development and Delivery

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**Abstract:** Three-dimensional (3D) printing has emerged as a transformative technology in the pharmaceutical industry, offering unprecedented opportunities for personalized medicine and advanced drug delivery systems. This review explores the diverse applications of 3D printing in drug development and delivery, highlighting its potential to revolutionize pharmaceutical manufacturing. The primary 3D printing technologies employed in this field include fused deposition modeling (FDM), stereolithography (SLA), and powder bed fusion (PBF), each with unique strengths suited for different aspects of drug production. 3D-printed pharmaceuticals offer numerous advantages, including customized dosing, complex geometries for controlled release, and improved patient compliance. The technology enables the creation of personalized dosage forms, polypills, and novel drug delivery systems such as microneedle patches and implants. Additionally, 3D bioprinting shows promise in developing organ-on-a-chip models for drug testing, potentially reducing the need for animal studies. Despite its potential, the widespread adoption of 3D printing in pharmaceuticals faces challenges, including regulatory hurdles, material limitations, and scalability issues. As the technology continues to evolve, it is poised to significantly impact the pharmaceutical industry, advancing personalized medicine and improving patient outcomes. This review provides a comprehensive overview of the current state, challenges, and future prospects of 3D printing in pharmaceutical applications.

**Keywords:** 3D printing; Personalized medicine; Drug delivery; Controlled release; Bioprinting.

## 1. Introduction

The pharmaceutical industry is continually seeking innovative approaches to improve drug development, manufacturing, and delivery. In recent years, three-dimensional (3D) printing has emerged as a groundbreaking technology with the potential to revolutionize various aspects of pharmaceutical research and production [1]. This additive manufacturing technique, which creates objects layer by layer based on digital designs, offers unprecedented flexibility and precision in drug formulation and delivery [2]. The concept of 3D printing, also known as additive manufacturing, was first introduced by Charles Hull in the 1980s [3]. Initially applied in industries such as aerospace and automotive, the technology has since found its way into the medical and pharmaceutical fields, opening up new possibilities for personalized medicine and advanced drug delivery systems [4].

In the pharmaceutical context, 3D printing offers several advantages over traditional manufacturing methods. It allows for the production of complex geometries, precise control over drug release profiles, and the ability to create personalized dosage forms tailored to individual patient needs [5]. This level of customization is particularly valuable in an era where precision medicine is gaining prominence, as it enables healthcare providers to optimize drug efficacy while minimizing side effects [6]. The primary 3D printing technologies employed in pharmaceutical applications include fused deposition modeling (FDM), stereolithography (SLA), and powder bed fusion (PBF) [7]. Each of these methods has its unique strengths and limitations, making them suitable for different aspects of drug development and delivery. FDM, for instance, is widely used for its simplicity and cost-effectiveness, while SLA offers higher resolution and is suitable for creating intricate structures [8].

One of the most promising applications of 3D printing in pharmaceuticals is the production of customized dosage forms. Traditional tablet manufacturing processes are limited in their ability to produce a wide range of doses, often resulting in the need for pill-splitting or liquid formulations for precise dosing [9]. 3D printing overcomes this limitation by allowing for the precise deposition of active pharmaceutical ingredients (APIs) in various shapes and sizes, enabling on-demand production of patient-specific doses [10].

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Moreover, 3D printing facilitates the creation of complex drug release profiles through the manipulation of tablet geometry and composition. By designing tablets with specific internal structures or combining multiple materials, researchers can achieve controlled release patterns that are difficult or impossible to attain with conventional manufacturing methods [11]. This capability is particularly valuable for drugs requiring precise temporal control of release or those targeting specific areas of the gastrointestinal tract [12]. The technology also shows promise in improving patient compliance, especially for individuals with difficulty swallowing conventional tablets. 3D-printed formulations can be designed to rapidly disintegrate in the mouth or have unique shapes that are easier to swallow [13]. Additionally, the ability to combine multiple drugs into a single 3D-printed tablet (polypills) can simplify complex medication regimens, potentially improving adherence in patients with multiple chronic conditions [14]. Beyond oral dosage forms, 3D printing is being explored for the creation of novel drug delivery systems. For instance, 3D-printed microneedle patches offer a painless and efficient method for transdermal drug delivery, while 3D-printed implants can provide long-term, controlled release of medications [15]. These innovations have the potential to improve patient experiences and treatment outcomes across a wide range of therapeutic areas. Moreover, 3D bioprinting, a specialized form of 3D printing that uses cell-laden bioinks, is opening up new avenues for drug testing and development. By creating three-dimensional tissue models or "organs-on-a-chip," researchers can more accurately predict drug efficacy and toxicity in human tissues, potentially reducing the need for animal testing and accelerating the drug development process [16]. As 3D printing continues to evolve, it promises to reshape the pharmaceutical landscape, offering new solutions to longstanding challenges in drug development and delivery. However, the widespread adoption of this technology in pharmaceuticals still faces several hurdles, including regulatory considerations, material limitations, and scalability issues [17]

## 2. 3D Printing Technologies in Pharmaceuticals

### 2.1. Fused Deposition Modeling (FDM)

FDM is one of the most widely used 3D printing technologies (shown in Table 1) in pharmaceutical applications due to its cost-effectiveness and simplicity [18]. This method involves the extrusion of thermoplastic filaments through a heated nozzle, depositing the material layer by layer to create the desired structure. In pharmaceutical manufacturing, drug-loaded filaments are used to produce tablets with precise geometries and compositions [19]. Recent advancements in FDM for pharmaceuticals include the development of new drug-polymer combinations to enhance drug release profiles. For instance, Goyanes et al. [20] successfully printed tablets containing paracetamol using polyvinyl alcohol (PVA) as the polymer matrix. They demonstrated that by altering the infill percentage of the tablets, different release profiles could be achieved, ranging from immediate to prolonged release. Another significant development is the creation of multi-drug tablets using FDM. Khaled et al. [21] produced a five-drug polypill using a multi-nozzle 3D printer, showcasing the potential of FDM in creating complex, personalized medication regimens.

| Technology | Principle | Advantages | Limitations | Examples of Applications |
|---|---|---|---|---|
| Fused Deposition Modeling (FDM) | Melting and extrusion of thermoplastic filaments | - Low cost<br>-Wide range of materials<br>-High resolution | - High temperatures may degrade drugs<br>- Limited to thermoplastic materials | - Controlled release tablets<br>- Multi-drug combinations |
| Stereolithography (SLA) | Photopolymerization of liquid resin | - High precision Smooth surface finish | - Limited material options<br>- Potential toxicity of photopolymers | - Microneedles<br>- Hydrogels for drug delivery |
| Selective Laser Sintering (SLS) | Laser sintering of powder materials | - No need for support structures<br>-Wide range of materials | - High power consumption<br>- Potential thermal degradation | -Orally disintegrating tablets<br>- Porous drug delivery systems |
| Inkjet Printing | Deposition of liquid droplets | - Room temperature process<br>- Precise control of dose | - Limited to low-viscosity materials<br>- Potential nozzle clogging | - Personalized dosing<br>- Combination products |

### 2.2. Stereolithography (SLA)

SLA offers higher resolution and precision compared to FDM, making it suitable for creating intricate drug delivery systems [22]. This technology uses a laser to cure photopolymerizable resins layer by layer, allowing for the production of complex internal structures and highly detailed external features. Wang et al. [23] utilized SLA to fabricate microneedle arrays for transdermal drug delivery. The high resolution of SLA enabled the creation of sharp, precise microneedles capable of painless skin penetration and

efficient drug release. This application demonstrates the potential of SLA in producing advanced drug delivery systems that were previously challenging to manufacture. Moreover, SLA has been employed in creating hydrogel-based drug delivery systems. Kadry et al. [24] developed a photo-crosslinkable hydrogel loaded with prednisolone, demonstrating controlled release profiles based on the hydrogel's crosslinking density.

### 2.3. Powder Bed Fusion (PBF)

PBF technologies, including selective laser sintering (SLS) and binder jetting, have gained attention in pharmaceutical 3D printing due to their ability to work with a wide range of materials, including commonly used pharmaceutical excipients [25]. Fina et al. [26] used SLS to produce orally disintegrating printlets (ODPs) containing paracetamol. The resulting tablets showed rapid disintegration times and dissolution rates, highlighting the potential of SLS in producing fast-acting oral medications. Binder jetting has been explored for the production of complex release profile tablets. Infanger et al. [27] created a dual-component tablet with an immediate-release layer and a sustained-release layer using binder jetting technology, demonstrating the versatility of this method in creating multi-functional dosage forms.

## 3. Personalized Medicine and Customized Dosing

One of the most promising applications of 3D printing in pharmaceuticals is the ability to produce personalized dosage forms tailored to individual patient needs [28]. This approach aligns with the growing trend towards precision medicine, where treatments are optimized based on a patient's genetic profile, lifestyle, and specific health conditions. Goyanes et al. [29] demonstrated the feasibility of on-demand, personalized dose printing using FDM technology. They successfully printed warfarin tablets with doses ranging from 0.5 mg to 5 mg, showcasing the potential for precise dose adjustments that are not possible with conventional manufacturing methods. Furthermore, 3D printing enables the creation of personalized polypills, combining multiple medications into a single dosage form. Pereira et al. [30] developed a 3D-printed polypill containing three antihypertensive drugs (irbesartan, hydrochlorothiazide, and amlodipine) with distinct release profiles. This approach not only simplifies complex medication regimens but also allows for personalized combinations and doses based on individual patient requirements.

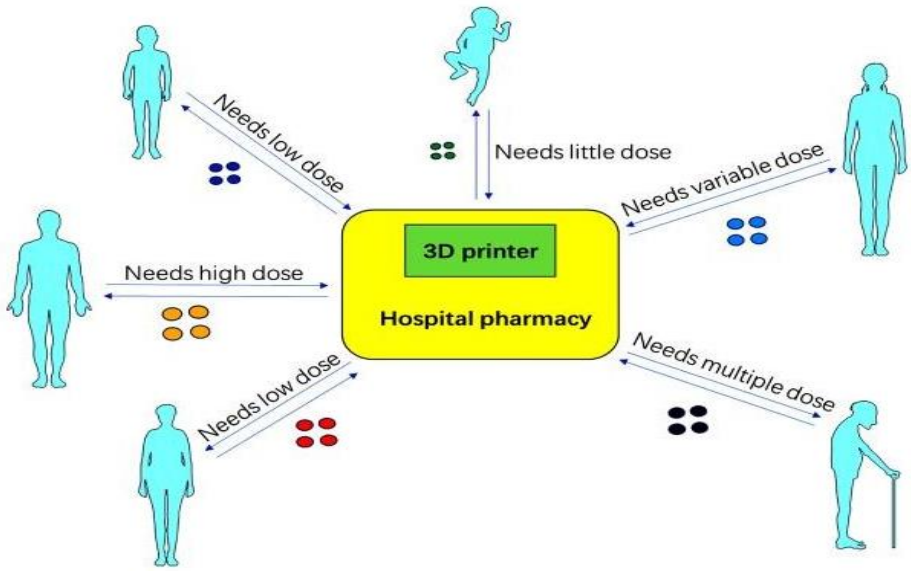


**Figure 1. 3D printing for personalized medicine**

### 3.1. Controlled Release and Complex Geometries

3D printing offers unprecedented control over tablet geometry and internal structure, enabling the creation of dosage forms with tailored release profiles [31]. This capability is particularly valuable for drugs requiring precise temporal control of release or those targeting specific areas of the gastrointestinal tract. Chai et al. [32] utilized FDM to produce tablets with varying internal structures, including honeycomb, grid, and ring designs. They demonstrated that by altering the internal geometry, drug release rates could be finely tuned, offering a novel approach to controlled release formulations. Similarly, Sadia et al. [33] explored the use of gyroid lattices in 3D-printed tablets to achieve zero-order release kinetics. The complex, interconnected channels of the gyroid structure allowed for consistent drug release over an extended period, showcasing the potential of 3D printing in creating advanced controlled release systems.

## 4. Novel Drug Delivery Systems

3D printing has enabled the development of innovative drug delivery systems that were previously challenging or impossible to manufacture using conventional methods [34].

### 4.1. Microneedle Patches

3D-printed microneedle patches offer a painless and efficient method for transdermal drug delivery. Pere et al. [35] used stereolithography to produce microneedle arrays loaded with insulin. The resulting patches demonstrated efficient skin penetration and controlled insulin release, highlighting the potential of this technology in improving the management of diabetes and other conditions requiring regular drug administration.

### 4.2. Implantable Devices

3D printing allows for the creation of customized implantable drug delivery devices. Genina et al. [36] developed 3D-printed T-shaped intrauterine systems (IUS) for controlled release of indomethacin. The ability to tailor the shape and size of the IUS to individual patients' anatomies represents a significant advancement in personalized contraceptive and drug delivery options.

### 4.3. Orodispersible Films

Ehtezazi et al. [37] utilized 3D printing to produce orodispersible films with complex geometries. These films demonstrated rapid disintegration times and improved drug dissolution rates compared to conventionally manufactured films, offering potential benefits for pediatric and geriatric patients who may have difficulty swallowing traditional tablets.

## 5. 3D Bioprinting and Drug Testing

3D bioprinting, which involves the deposition of cell-laden bioinks, has opened up new possibilities in drug development and testing [38]. By creating three-dimensional tissue models or "organs-on-a-chip," researchers can more accurately predict drug efficacy and toxicity in human tissues. Ma et al. [39] developed a 3D-bioprinted liver-on-a-chip model for drug toxicity testing. The model demonstrated metabolic activity and drug sensitivity profiles similar to those observed in vivo, suggesting its potential as a more reliable alternative to traditional 2D cell cultures and animal models in early-stage drug screening.

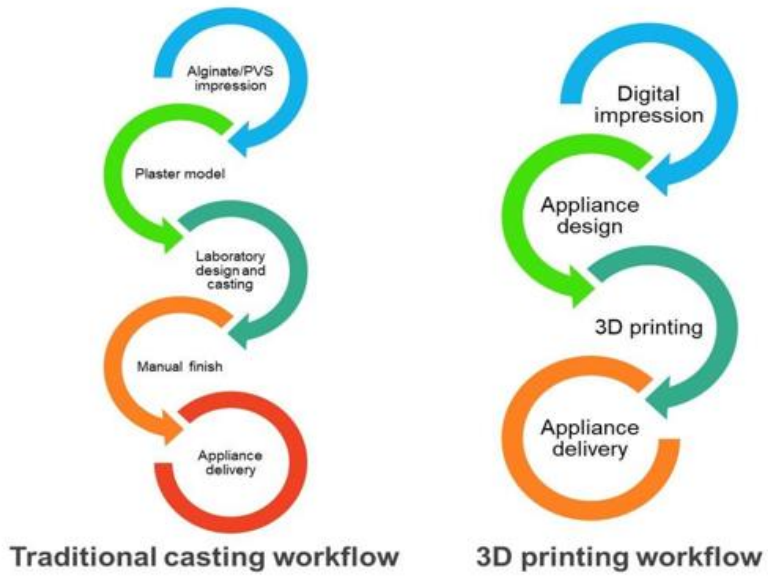


**Figure 2. Traditional casting versus 3D printing in drug manufacturing**

Similarly, Zhang et al. [40] created a 3D-bioprinted heart-on-a-chip platform for cardiotoxicity assessment. The model successfully recapitulated the structure and function of cardiac tissue, enabling more accurate prediction of drug-induced cardiotoxicity compared to conventional in vitro methods. These advancements in 3D bioprinting not only have the potential to accelerate the drug development process but also to reduce the reliance on animal testing, addressing both ethical concerns and the limitations of interspecies differences in drug responses.

## 6. Challenges and Future Prospects

Despite the significant potential of 3D printing in pharmaceuticals, several challenges need to be addressed for widespread adoption [41]:

### 6.1. Regulatory Considerations

The regulatory framework for 3D-printed pharmaceuticals is still evolving. Agencies like the FDA are working on guidelines for the approval and quality control of 3D-printed drugs, but many questions remain regarding Good Manufacturing Practices (GMP) compliance and product standardization [42].

### 6.2. Material Limitations

The range of pharmaceutically acceptable materials suitable for 3D printing is currently limited. Research is ongoing to expand the palette of printable excipients and to develop new drug-polymer combinations optimized for 3D printing processes [43].

### 6.3. Scalability

While 3D printing excels in producing small batches of personalized medications, scaling up to meet the demands of large-scale pharmaceutical manufacturing remains a challenge. Improvements in printing speed and multi-nozzle technologies are being explored to address this issue [44].

### 6.4. Quality Control

Ensuring consistent quality across 3D-printed pharmaceuticals, especially in on-demand printing scenarios, poses unique challenges. Advanced in-line monitoring systems and non-destructive testing methods are being developed to address these concerns [45].

Future prospects for 3D printing in pharmaceuticals are promising. Emerging areas of research include:

- 4D Printing: This technology involves 3D-printed structures that can change shape or function over time in response to external stimuli. In pharmaceuticals, this could lead to smart drug delivery systems that respond to physiological changes in the body [46].
- Bioprinting for Personalized Medicine: Advances in 3D bioprinting may eventually enable the creation of patient-specific tissue models for individualized drug testing, further personalizing drug selection and dosing [47].
- Continuous Manufacturing: Integration of 3D printing with continuous manufacturing processes could revolutionize pharmaceutical production, allowing for more flexible and efficient drug manufacturing [48].
- Advanced Materials: Development of new, biocompatible materials specifically designed for pharmaceutical 3D printing could expand the range of drugs that can be formulated using this technology [49].

## 7. Conclusion

Nanoemulsions have emerged as a promising and versatile platform in the fields of drug delivery, food science, and cosmetics. Their unique properties, including enhanced solubility, improved bioavailability, and controlled release capabilities, offer significant advantages over conventional formulations. The ability to encapsulate both hydrophilic and hydrophobic compounds, coupled with their stability and potential for targeted delivery, makes nanoemulsions particularly attractive for a wide range of applications. Recent advancements in formulation techniques, characterization methods, and the use of novel, biocompatible materials have further expanded the potential of nanoemulsions. From improving the efficacy of pharmaceuticals to enhancing the nutritional value and shelf life of food products, nanoemulsions demonstrate remarkable versatility and efficacy.

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