IJARSCT
International Journal of Advanced Research in Science, Communication and Technology
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
ISSN: 2581-9429
Volume 6, Issue 10, May 2026
Impact Factor: 8.2

# A Review - Advancement in Pharmaceutical 3D Printing: A Critical Analysis

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**Abstract:** *Three-dimensional (3D) printing, also known as additive manufacturing, is widely regarded as a transformative technology across various sectors. It holds promising applications in pharmaceutical production, particularly when personalized treatments are required.*

*Unlike conventional drug production methods, 3D printing offers distinct benefits for personalized medicine. It enables the efficient creation of formulations with intricate designs or tailored release profiles, and facilitates the swift production of limited drug batches.*

*Recent progress in 3D-printed pharmaceuticals represents a breakthrough in tailoring oral medications to individual patients, offering a safer and more efficient alternative to the traditional uniform treatment approach*

**Keywords:** Three-dimensional (3D) printing **,**Additive manufacturing**,** Transformative innovation, Pharmaceutical production, Personalized treatment, Conventional drug production **,**Personalized medicine, Formulation desig drug , release profiles**,** Small batch manufacturing

## I. INTRODUCTION

Pharmaceutical dosage forms have evolved significantly over time, beginning with the use of plant-based ointments, powders, and creams crafted by ancient Greek and Roman healers, and culminating in the development of compressed tablets by Dr. Robert Fuller in 1878.

3D printing has revitalized the pharmaceutical sector, enabling the creation of innovative drug formulations suitable for use both on Earth and in space. This additive manufacturing technique allows for a rapid and cost-effective development cycle in producing customized drug formulations.

3D printing enabled the rapid production of high-quality items through a streamlined manufacturing process. This on-demand approach significantly reduced both time and material waste.

The ongoing pursuit of innovative drug delivery systems aims to enhance the therapeutic performance of active pharmaceutical compounds, particularly large biomolecules like peptides and proteins, which often face challenges such as low bioavailability, poor solubility, and limited therapeutic range. 3D printing is a modern and rapid prototyping method that utilizes various material forms—such as powders, filaments, pellets, and granules—for fabrication.

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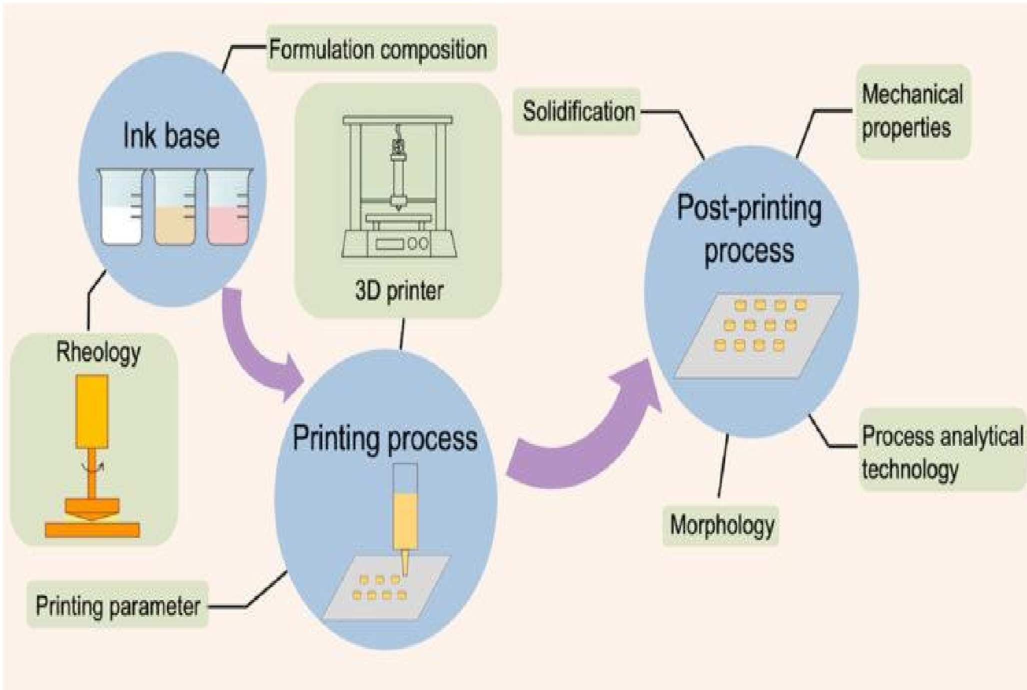


**PRINCIPLE OF 3D PRINTING MEDICATION:**

**Designing (Modeling):** A digital model of the object is created using computer-aided design (CAD) software.

**Building (Printing):** The 3D printer follows the digital design and builds the object layer by layer using chosen materials.

**Post-Processing (Finishing):** Once printing is complete, any support structures are removed or dissolved to reveal the final product.

**3D PRINTING MEDICATION TECHNOLOGY**

**1.Inkjet-style 3D printers**

Inkjet-based 3D printers operate by dispensing liquid in the form of tiny droplets. These systems are categorized into two main types: drop-on-demand and continuous jet printers.Inkjet printing typically refers to technologies that use digital patterning mechanisms to precisely deposit tiny liquid droplets onto a surface. In pharmaceutical applications, carefully formulated drug mixtures combined with compatible excipients—collectively referred to as 'ink'—are layered drop by drop onto a designated substrate to create dosage forms. Powder-based 3D printing techniques are foundational in the field of pharmaceutical production. These methods rely on the targeted fusion or adhesion of powder particles to fabricate solid dosage forms. This category is primarily defined by two leading approaches.

**2. Extrusion-Based 3D Printing [7–8]**

Extrusion stands as the most prevalent form of 3D printing technology. In this method, materials are pushed through computer-controlled nozzles to form structures. Unlike binder jetting, which relies on a powder bed, extrusion techniques can operate on a wide range of surfaces. Various substances—such as molten polymers, viscous pastes, colloidal suspensions, silicones, and other semi-solid materials—can be used in this process. One widely adopted extrusion technique is fused filament fabrication (FFF), which has been specifically applied to produce tablets containing Guaifenesin, an active ingredient used as an expectorant.

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**3. Stereolithography 3D printers**

Stereolithography (SLA) 3D printers work by shining ultraviolet (UV) light onto a liquid mixture that contains a light-sensitive polymer and a drug. The UV light causes the liquid to harden and form solid layers, gradually building up the 3D object. A digital mirror device controls the process by triggering a chemical reaction in the light-sensitive material, causing the exposed area to solidify into a gel-like form.

**4. Fused Deposition Modelling (FDM)**

Fused Deposition Modelling (FDM ) , also known as Fused Filament Fabrication (FFF), is a widely used and cost-effective 3D printing method. In this process, a thermoplastic material is heated above its melting point inside the printer's nozzle and then extruded layer by layer to build the final object. Thanks to its unique features, FDM technology has become a popular method for producing a wide range of formulations. Fused Deposition Modeling (FDM) 3D printing enables the production of delayed-release tablets without needing an external enteric coating, and it also allows for customizing medication doses to suit individual patient needs.

**5. Selective Laser Sintering (SLS)**

Selective Laser Sintering is a 3D printing technique where a laser is used to heat and fuse powdered material—like plastic or metal—into solid layers, gradually forming a 3D object. In this process, a roller continuously spreads fresh layers of powder over the previously fused ones, gradually building the desired 3D structure. These printers use powdered polymers and drugs, avoiding the need for solvents or extrusion methods.

**6. Powder-Based Binding Method**

This approach involves using inkjet technology to apply a thin layer of powder—called a powder bed—while simultaneously releasing a liquid binder. The final product is created by printing a 2D pattern of ink, which contains both the binder and the active drug ingredients, onto the powder surface. Since powders and binder solutions are already widely used in pharmaceutical manufacturing, this method can be easily adapted to existing production systems. To build complex 3D structures, the binder is sprayed repeatedly onto new.

**7. Zip dose**

zip Dose technology is the pioneering 3D printing method officially validated by the FDA for use in pharmaceutical manufacturing. In 2015, Aprecia Pharmaceuticals introduced Spritam—an oral formulation of the anti-epileptic drug Levetiracetam—as the first FDA-approved medication produced using this technique. This innovative approach allows for the incorporation

**Printing Materials in Pharmaceutical 3D Printing**

The choice of printing materials in pharmaceutical 3D printing plays a crucial role in determining drug release behavior, physical characteristics, stability, printer settings, and print quality. Each 3D printing method demands materials with specific attributes. Below are examples of substances commonly used in oral drug formulations via 3D printing.

**1. Lactose**

Lactose serves as a filler or diluent in techniques like powder bed printing and stereolithography (SLA). It contributes to better compressibility, enhanced physical stability, and improved solubility of active ingredients in printed tablets. Typically, lactose monohydrate combined with a binder is favored for powder bed printing, as the binder boosts the tablet's mechanical strength. Its high solubility makes lactose suitable for incorporating both hydrophilic and hydrophobic active pharmaceutical ingredients (APIs).

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**2. Polylactic Acid (PLA)**
PLA is a biodegradable polymer widely used in printing medical implants, scaffolds, and drug delivery devices. Approved by the FDA, it is considered safe for pharmaceutical use. PLA's thermoplastic nature makes it compatible with fused deposition modeling (FDM). Selecting the right molecular weight and grade of PLA, along with an appropriate plasticizer, enables filament production. PLA can be combined with various drugs and excipients to tailor drug release profiles, and its slow degradation rate makes it ideal for extended-release formulations.

**3. Polyvinyl Alcohol (PVA)**
PVA is a water-soluble thermoplastic polymer valued for its biodegradability, compatibility with biological systems, and ease of dissolution. It enhances the mechanical integrity and drug release characteristics of printed tablets. PVA is suitable for extrusion and inkjet printing methods. For instance, Goyanes and colleagues created customized oral caplets using FDM with PVA filaments containing paracetamol or caffeine. Kampanart's team used PVA to design tablet casings that regulate drug release and maintain buoyancy in gastric fluid for up to eight hours. PVA is also used in suppository forms, as demonstrated by Tatsuaki's group, who developed a dissolvable shell for controlled drug delivery.

**4. Hydroxypropyl Methylcellulose (HPMC)**
HPMC, a cellulose-derived polymer, is commonly employed in 3D-printed pharmaceuticals as a binder, filler, structural support, and agent for sustained release. It stands out for its solubility and low toxicity. HPMC is typically printed using extrusion techniques. Prashant and his team used HPMC and methyl cellulose to create biodegradable support structures, which could be dissolved post-printing. Yiliang's group utilized extrusion printing to fabricate semi-solid tablets at room temperature, embedding theophylline into HPMC-based hydrogels for prolonged drug release.

**5. Gelatin**
Derived from collagen found in animal tissues, gelatin is a natural biopolymer known for its compatibility with biological systems, biodegradability, and ease of processing. It has long been used in pharmaceutical formulations and can function as a bio-ink or printable material for constructing intricate drug delivery systems. Its flexibility, elasticity, and water affinity make it suitable for creating 3D-printed biodegradable excipients, such as gummy formulations of antiepileptic drugs for children using extrusion-based methods.

**6. Polyethylene Glycol (PEG)**
PEG is a multifunctional polymer used in pharmaceutical 3D printing due to its water solubility, biocompatibility, and biodegradability. It supports drug delivery and tissue engineering applications. Hsin-Yun Hsu employed drop-on-demand printing to produce naproxen/PEG 3350 solid dispersions, using PEG coatings of varying molecular weights to ensure accurate dosing and consistent API distribution within the printed structures.

**Categories of Pharmaceutical 3D Printing Systems**
The concept of 3D printing was pioneered and brought to market by Charles Hull in 1986. Since then, numerous printing techniques have emerged under the umbrella of "3D printing," which now encompasses a broad spectrum of technologies. Despite their differences, these methods typically follow a unified workflow for producing pharmaceutical printlets, often referred to as the "3 Ds of 3D printing." This framework outlines a clear path for integrating 3D printing into future clinical applications:
**Design**
Pharmacists begin by using computer-aided design (CAD) software to create the blueprint for the drug formulation. This includes defining the shape and size of the printlet to meet specific preclinical or clinical needs. Once finalized, the digital design is transferred to the chosen 3D printer.

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**Develop**

The next step involves preparing the printer with the appropriate "ink"—a mixture of the active drug and excipients. Key printing parameters such as resolution, temperature, and duration are configured based on the printer model, the properties of the drug, and the desired therapeutic effect.

**Dispense**

Finally, the printer fabricates the formulation layer by layer. Once printing is complete, the finished dosage forms are ready to be dispensed by the pharmacist for patient use.

**Applications of 3D Printing in Pharmaceutical :** 3D printing has emerged as a groundbreaking technology in the medical field, thanks to its flexibility and wide range of applications. It has revolutionized personalized medicine by enabling the creation of patient-specific models, medical devices, and implants. Whether it's crafting prosthetic limbs, repairing bones with orthopedic implants, or producing organs and tissues using bioprinting techniques—including organ-on-a-chip systems—3D printing offers unmatched precision and customization. In pharmaceutical manufacturing, it supports the development of advanced drug delivery systems, such as controlled-release formulations and combination tablets containing multiple medications layers of powder, stacking them one by one.

| Purpose | Dosage form | Technique used | Drug | Key Outcome |
|---|---|---|---|---|
| Advanced ocular delivery | Ocular inserts | FDM + Hot-melt extrusion | Ciprofloxacin HCl | 24-hour release, smooth surface, strong adhesion |
| | Ocusert | Nanovesicles + 3D printing | Ganciclovir | Noninvasive, prolonged release for eye infection |
| | Punctal plugs | Digital light processing | Dexamethasone | Safe and compatible for ocular use |
| Improved oral formulations | Immediate-release tablets | Melting solidification | Albendazole | Enhanced dissolution, stable nanocrystals |
| | Tablets | FDM | Hydrocortisone | Requires precise temperature and concentration control |
| | Dose titration tablets | 3D printing | Caffeine | Fast-release, consistent extrusion |
| Tissue regeneration | Skin scaffolds | 3D printing + electrospinning | Mupirocin | Strong antibacterial effect, fast healing |
| | Bone scaffolds | Solvent casting | Doxorubicin | Slow breakdown, long-term drug delivery |
| | Bone scaffolds | Fused filament fabrication | Inulin | High cell compatibility, strong bone regeneration |
| | Skin scaffolds | Bioprinting | Tacrolimus | Faster wound closure in vivo |
| Vaginal drug delivery | Intravaginal scaffolds | Microsyringe 3D printing | Metronidazole | Sustained release for 14 days, low toxicity |

**3D Printing for Drug-Loaded Ocular Inserts And Punctal Plugs :** The creation of personalized, patient-specific ocular inserts containing ciprofloxacin HCl was achieved using a combination of fused deposition modeling and hot-melt extrusion 3D printing techniques. Klucel™ hydroxypropyl cellulose—a biodegradable, biocompatible, and adhesive polymer—was selected for the printing process. An experimental design strategy was used to fine-tune the formulation and achieve the desired drug release profile tailored to individual needs.

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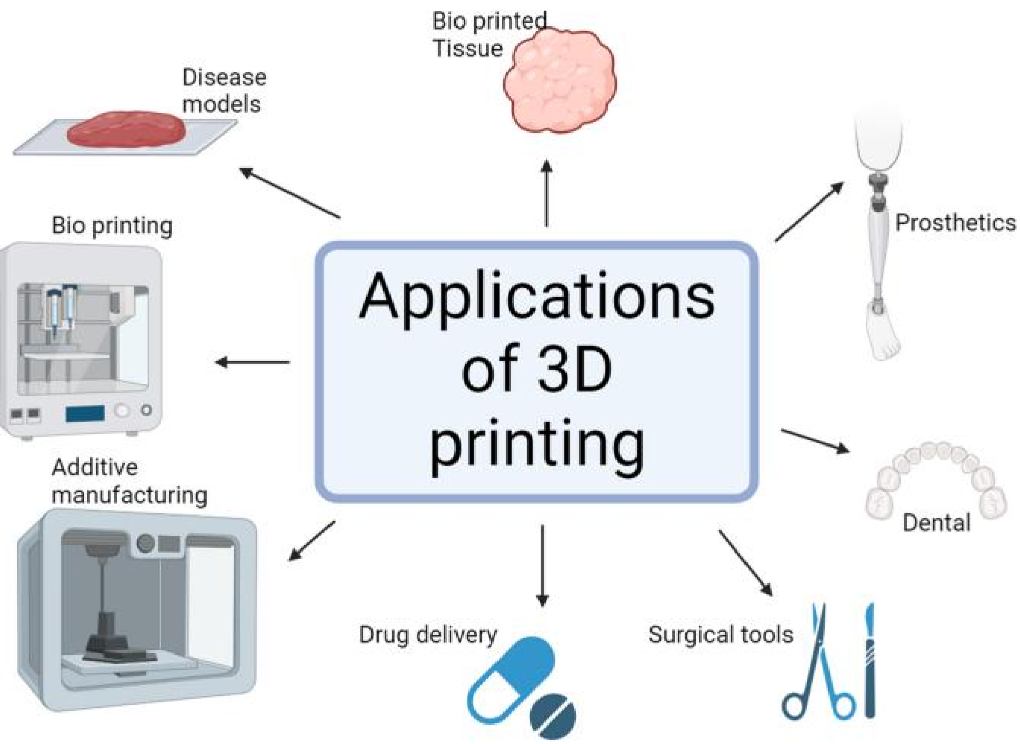


**Simplified Table: Applications of 3D Printing in Pharmaceuticals**

**Challenges in 3D Printing Technology**

3D printing in pharmaceuticals is still evolving, and there are several hurdles to overcome. These include fine-tuning the printing process, enhancing device performance for broader applications, choosing the right ingredients, and applying effective post-processing methods.

To make 3D-printed medicines more effective and expand their use in advanced drug delivery, improvements in design and production are needed.

**Importance of 3D Printing in Pharmaceuticals**

The integration of 3D printing into pharmaceutical science offers a wide array of advantages, including cost savings, enhanced efficiency, democratized design and production, and improved collaboration across disciplines.

**Cost Efficiency**

One of the most significant benefits of 3D printing is its ability to manufacture products at a lower cost. Unlike conventional drug production methods—which involve multiple complex steps like mixing, milling, granulation (wet or dry), compression, or molding—3D printing streamlines the process, reducing operational expenses and resource consumption.

**Improved Productivity**

Traditional drug manufacturing is often time-intensive due to its multi-step procedures. In contrast, 3D printing accelerates production by eliminating many of these stages. Alongside speed, the technology continues to evolve in terms of resolution, precision, consistency, and reliability, making it a more efficient alternative.

**Environmental Sustainability**

Compared to traditional pharmaceutical setups that require extensive infrastructure to produce even a single pill, 3D printing is more eco-friendly. It minimizes waste and energy usage, contributing to greener manufacturing practices.


DOI: 10.48175/IJARSCT-35730

**Democratization of Design & Manufacturing**

3D printing empowers broader access to drug design and production. It allows researchers, developers, and even small-scale innovators to participate in the creation of pharmaceutical products, fostering inclusivity and innovation.

**Future Outlook**

The future of 3D printing in pharmaceuticals holds transformative potential. Emerging applications may include:
Engineering novel dosage forms tailored to individual needs.
Creating optimized drug release mechanisms.
Developing new excipients to enhance drug stability.
Preventing incompatibilities in multi-drug formulations.
Supporting targeted delivery systems.
Preserving sensitive biological molecule .

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