3D PRINTING IN PHARMACEUTICAL DOSAGE FORM DESIGN AND PERSONALIZED MEDICINE

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ABSTRACT

Three-dimensional (3D) printing has emerged as a transformative manufacturing technology that enables precise, customizable, and efficient production of pharmaceutical dosage forms. Unlike conventional batch-based manufacturing, 3D printing allows on-demand fabrication of personalized medications with tailored drug doses, release profiles, and geometric designs. In recent years, several 3D printing techniques—including fused deposition modeling (FDM), stereolithography (SLA), selective laser sintering (SLS), and inkjet-based printing—have demonstrated significant potential in producing tablets, implants, transdermal systems, and polypills with complex architectures [1–3]. Personalized medicine has benefited substantially from the capability to adjust drug combinations and strengths for individual patients, especially in pediatrics, geriatrics, and chronic disease management [4]. The approval of Spritam®, the first FDA-approved 3D-printed tablet, established a milestone that shifted 3D printing from theoretical research to practical pharmaceutical application [5]. This review systematically evaluates the role of 3D printing in modern dosage form development, its technological advancements, the challenges related to regulatory pathways, and its growing importance in precision and personalized medicine.

1. INTRODUCTION

Pharmaceutical manufacturing has traditionally relied on large-scale, standardized production processes that lack flexibility for individualized therapy. However, the rise of personalized medicine and the need for patient-specific dosing have highlighted the limitations of conventional techniques. Three-dimensional printing (3D printing), also known as additive manufacturing, has introduced a paradigm shift by allowing layer-by-layer construction of drug products with precise control over geometry, porosity, drug loading, and release kinetics [6]. Advanced computational modeling integrated with 3D design software enables researchers to modify tablet architecture, surface area–to–volume ratios, and internal channels, thereby enhancing dissolution and drug delivery characteristics [7].

Among its advantages, 3D printing facilitates combination products ("polypills"), pediatric doses, and modified-release formulations to meet patient-specific requirements [8]. Materials such as polymer filaments, photopolymers, powders, and printable inks allow flexibility in fabricating solid, semi-solid, and even implantable dosage forms [9]. Furthermore, the increasing availability of pharmaceutical-grade excipients compatible with 3D printing technologies has accelerated its adoption in both academic and industrial research environments [10].

The introduction of Spritam® (levetiracetam)—manufactured using Aprecia's ZipDose® technology—marked the first instance of a 3D-printed drug approved by the U.S. Food and Drug Administration (FDA), validating its safety, scalability, and pharmaceutical quality [5]. Since then, interest has grown in utilizing 3D printing to address unmet needs in tailored therapies, including dose titration, patient compliance, and personalized drug combinations.

This systematic review explores the technological foundations of 3D printing, evaluates its impact on pharmaceutical dosage form development, discusses its role in personalized medicine, and identifies current challenges and future directions in additive manufacturing for drug formulation and delivery.

2. 3D PRINTING TECHNOLOGIES, DOSAGE FORMS, AND PHARMACEUTICAL APPLICATIONS

3D printing encompasses several additive manufacturing techniques, each with distinct mechanisms, material requirements, and pharmaceutical applications. These technologies enable precise control over the structural

architecture of dosage forms, allowing modulation of drug release, dose strength, and dissolution behavior. By utilizing digital design software and computer-aided manufacturing, researchers and formulators can fabricate patient-specific medications with high reproducibility and minimal material waste [11].

2.1 Fused Deposition Modeling (FDM)

Fused deposition modeling (FDM) is one of the most commonly explored methods for fabricating oral solid dosage forms. In FDM, thermoplastic polymer filaments—often loaded with drug during hot-melt extrusion—are melted and deposited layer by layer to create a solid structure [12]. Polymers such as polyvinyl alcohol (PVA), polylactic acid (PLA), and hydroxypropyl cellulose (HPC) are frequently used due to their thermal stability and extrusion properties [13].

FDM allows the creation of tablets with complex internal geometries, enabling immediate-release, controlled-release, and multi-compartment drug delivery systems [14]. However, drug stability remains a concern, as elevated processing temperatures can degrade thermolabile molecules, limiting the range of drugs suitable for this technique [15].

2.2 Stereolithography (SLA)

Stereolithography utilizes a focused ultraviolet (UV) laser to selectively cure a liquid photopolymer resin, forming highly precise dosage forms with excellent resolution [16]. SLA is particularly advantageous for producing structures with intricate channels, micro-porous networks, and high surface-area configurations that enhance dissolution and drug release [17].

Pharmaceutical-grade photopolymers remain limited, posing challenges regarding biocompatibility, toxicity, and regulatory acceptance. Nonetheless, recent developments in biodegradable photopolymers and photo-crosslinkable hydrogels have expanded SLA's potential for fabricating personalized oral films and implantable drug delivery systems [18].

2.3 Selective Laser Sintering (SLS)

Selective laser sintering (SLS) employs a laser to fuse powdered materials, such as polymers or active pharmaceutical ingredients (APIs), into solid structures without the need for solvents or binders [19]. This technique permits rapid fabrication and enables high drug loading compared to FDM and SLA. Additionally, SLS-printed tablets often possess high porosity, leading to superior disintegration and dissolution performance [20].

SLS has been explored for immediate-release, floating, and orodispersible formulations. Its solvent-free nature minimizes concerns about residual solvents and enhances compatibility with moisture-sensitive drugs [21].

2.4 Inkjet and Binder Jet Printing

Inkjet printing and binder jetting are non-contact technologies that deposit droplets of drug-containing inks or binding agents to form layered structures [22]. These methods are well suited for low-temperature processing, making them ideal for thermosensitive APIs [23].

Inkjet printing supports precise micro-dosing, enabling custom dose titration for pediatric and geriatric patients. Binder jetting, on the other hand, allows rapid fabrication of porous tablets with fast disintegration profiles, as demonstrated in the manufacturing of Spritam® . The main limitations include limited material viscosity ranges and the need for post-processing to enhance mechanical strength [24].

2.5 Applications in Pharmaceutical Dosage Forms

3D printing has been successfully applied across a broad range of dosage forms, including:

Immediate-release and extended-release tablets: By modifying internal infill density, drug layers, and geometry.

Polypills: Combining multiple drugs into a single, patient-specific tablet with separated compartments [25].

Implants: Customizable shapes for localized and sustained drug delivery.

Transdermal patches and microneedles: Fabricated with precise needle arrays for enhanced drug permeation.

Oral films and chewable formulations: Useful for pediatric and dysphagic patients.

This technological versatility positions 3D printing as one of the most promising innovations for personalized dosage form design and advanced drug delivery systems.

3.1 Technical and Material Challenges

The performance of 3D-printed pharmaceuticals depends heavily on material characteristics, printer technology, and process parameters. One major challenge is the limited availability of pharmaceutical-grade printable materials, especially for techniques like SLA and SLS that require safe, biocompatible resins or powders [26]. Excipients used in traditional formulations are not always suitable for thermal or photopolymerization processes, complicating formulation development.

Additionally, process reproducibility is affected by factors such as printer calibration, printing temperature, laser intensity, and environmental conditions [27]. Minor variations may influence drug stability, mechanical strength, and dissolution rates. Another technical issue is drug degradation at high temperatures, particularly in FDM, where processing temperatures can exceed 200°C, limiting its compatibility with heat-sensitive APIs [28].

3.2 Quality Control and Manufacturing Consistency

Ensuring quality control remains a critical challenge, as 3D printing differs fundamentally from conventional batch manufacturing. The highly customizable, small-batch nature of 3D printing complicates standardized testing for hardness, friability, dose uniformity, and dissolution [29]. Moreover, multilayered or complex geometries may exhibit internal structural defects that are not easily detectable through traditional quality assessment techniques.

Advanced quality control methods—such as non-destructive imaging, real-time process monitoring, and in-process analytical technologies—are being explored to ensure uniformity and performance consistency of 3D-printed dosage forms [30].

3.3 Regulatory and Legal Barriers

The regulatory landscape for 3D-printed pharmaceuticals is still evolving. Because 3D printing allows on-demand and point-of-care manufacturing, regulatory agencies face challenges in defining standards for approval, validation, and post-market surveillance [31]. The U.S. FDA has issued general guidance for additive manufacturing, but specific guidelines for pharmaceutical dosage forms remain limited [32].

Key regulatory concerns include:

Ensuring consistent product quality across different printers and locations

Validating software used for 3D design and slicing algorithms

Establishing data integrity during digital workflow

Defining responsibilities in decentralized manufacturing models, such as hospitals or pharmacies using 3D printers

Legal issues related to intellectual property and the protection of digital drug designs further complicate global adoption [33].

3.4 Ethical and Patient Safety Considerations

Personalized medicine facilitated by 3D printing introduces ethical considerations around data privacy, patient-specific dosing, and accountability for errors. If a dosage error occurs during decentralized printing, determining liability—whether the healthcare provider, software developer, or printer manufacturer—is complex [34]. Additionally, the use of patient data for customized dose fabrication demands strong data protection frameworks.

3.5 Future Prospects and Emerging Innovations

Despite challenges, the future of 3D printing in pharmaceuticals is extremely promising. Advances in multi-material printers, 4D printing (structures that change after administration), and pharmo-printing AI algorithms are expected to improve customization and performance of drug products [35].

The integration of machine learning with 3D printing enables predictive modeling of drug release, mechanical strength, and optimal dosage form geometry. AI-driven design may significantly reduce formulation development time and improve therapeutic outcomes [36].

Moreover, regulatory agencies worldwide are exploring dedicated frameworks to support decentralized or point-of-care 3D pharmaceutical printing. Hospitals may soon produce personalized tablets for cancer patients, pediatric doses, or emergency treatments directly on-site, improving treatment accessibility and adherence [37].

CONCLUSION

3D printing has emerged as a groundbreaking technology that offers unprecedented flexibility in pharmaceutical dosage form design and personalized medicine. Its ability to fabricate patient-specific drug products—ranging from modified-release tablets to polypills and implants—marks a significant advancement over traditional mass manufacturing. Despite technical limitations, quality control issues, and an evolving regulatory environment, ongoing research and technological innovations are steadily addressing these challenges.

Looking ahead, the integration of artificial intelligence, advanced printable materials, and standardized regulatory frameworks will play a crucial role in expanding the clinical adoption of 3D-printed pharmaceuticals. As these advancements continue, 3D printing is poised to become a central tool in future precision medicine, enabling highly personalized therapies tailored to individual patient needs [39][40].

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