Advances in 3D Printing for Pharmaceutical Sciences: Applications, Barriers, and Future Directions

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Abstract:

Three-dimensional (3D) printing, also known as additive manufacturing and introduced in the 1980s, has significantly transformed the pharmaceutical industry by enabling efficient, cost-effective production of complex and patient-specific dosage forms. In pharmaceutics, 3D printing facilitates the development of personalized medicines, polypills, and controlled drug delivery systems, offering advantages such as precise dosing, enhanced drug loading, design flexibility, and reduced material waste, making it particularly valuable for pediatric, geriatric, and orphan drug therapies. Various techniques including fused deposition modeling (FDM), stereolithography (SLA), binder jetting, and semi-solid extrusion are used to fabricate oral, transdermal, and implantable dosage forms, while emerging approaches like bioprinting and 4D printing are opening new possibilities for responsive and advanced therapeutic systems. Despite its strong potential, widespread commercial adoption remains limited due to challenges related to process reproducibility, material compatibility, scalability, and regulatory compliance, indicating that further technological refinement and regulatory clarity are essential to fully realize the promise of 3D printing in personalized and precise medicine.

Keywords: 3D printing; Additive manufacturing; Personalized medicine; Drug delivery systems; Regulatory challenges.

Introduction:

Three-dimensional printing (3DP), also known as additive manufacturing (AM), is a cutting-edge technology that fabricates three-dimensional objects in a layer-by-layer fashion using computer-aided design (CAD) files[1]. In recent decades, this technology has transformed multiple sectors, including aerospace, automotive, environmental monitoring, biomedical engineering, and, more recently, the pharmaceutical industry. Its introduction into the pharmaceutical domain has opened the possibility of converting conventional drug formulations into digital designs and subsequently manufacturing them as precisely engineered dosage forms.

The concept of 3D printing originated in the late 1980s, pioneered by Emanuel Sachs and colleagues at the Massachusetts Institute of Technology (MIT), Boston, USA, leading to the granting of U.S. Patent No. 5,204,055[2]. Initially developed for prototyping, 3D printing has since evolved into a highly versatile platform that supports both research and large-scale manufacturing applications. A significant milestone for pharmaceutics was reached in 2015 when the U.S. Food and Drug Administration (FDA) approved Spritam® (levetiracetam) — the first 3D-printed oral solid dosage form — designed to treat partial-onset, myoclonic, and generalized tonic-clonic seizures[3]. This approval highlighted the potential of 3D printing to create complex, highly porous tablets with rapid disintegration, which was previously difficult to achieve using conventional manufacturing techniques.

Compared to traditional methods such as direct compression or wet granulation, 3D printing provides unparalleled advantages: precise control over dose geometry, the ability to produce patient-specific and combination dosage forms (polypills), reduced material wastage, on-demand production, and minimized human error. These features make it especially promising for personalized medicine, where dose flexibility and individualized therapy are critical — for example, in pediatrics, geriatrics, and orphan drug manufacturing[4].

Furthermore, 3D printing enables the fabrication of intricate drug delivery systems, including sustained- or controlled-release forms, multi-layer tablets, and implants with tailored drug release kinetics. It has demonstrated potential to improve pharmacokinetic (PK) properties and enhance the solubility of poorly water-soluble drugs by enabling complex geometries and optimized surface-area-to-volume ratios. Beyond oral dosage forms, 3D printing is being explored for transdermal patches, microneedles, buccal films, and even drug-loaded scaffolds for tissue engineering.

However, certain challenges continue to restrict its widespread adoption. Key limitations include the development of pharmaceutically acceptable printable feedstock materials, achieving reproducibility and scalability, and ensuring compliance with regulatory standards such as Good Manufacturing Practices (GMP). Converting active pharmaceutical ingredients (APIs) and excipients into printable formulations with suitable rheological and thermal properties remains a crucial bottleneck. Moreover, the pharmaceutical industry and regulatory authorities must establish robust quality control strategies, process validation protocols, and guidance frameworks for 3D-printed products before large-scale commercialization can be realized.

Given these opportunities and challenges, this review aims to comprehensively explore the available 3D printing techniques (fused deposition modeling, binder jetting, stereolithography, and semi-solid extrusion), their pharmaceutical applications, technological constraints, and potential future directions. The discussion also highlights the integration of advanced fields such as bioprinting, 4D printing, and digital health technologies, which together hold the promise of revolutionizing patient-centered drug delivery and reshaping the future of pharmaceutical manufacturing.

3D Printing in Medicine: Technology Overview

Three-dimensional printing (3DP), widely recognized as additive manufacturing (AM), is a layer-by-layer fabrication process that transforms computer-aided designs (CAD) into physical objects with high precision. The process begins with digital model creation using software such as AutoCAD, Fusion 360, SketchUp, or SolidWorks. The digital file is then processed using slicer programs such as Cura, Slic3r, or Simplify3D, which convert the model into printer-readable G-code. During this step, critical parameters like layer thickness, infill percentage, print speed, and printing time are defined. Once the G-code is uploaded, the printer executes the instructions to create the desired structure.

The deposition process varies depending on the printing technology employed. Several techniques(fig no. 1) have been explored for pharmaceutical and biomedical applications, each with distinct advantages and limitations:

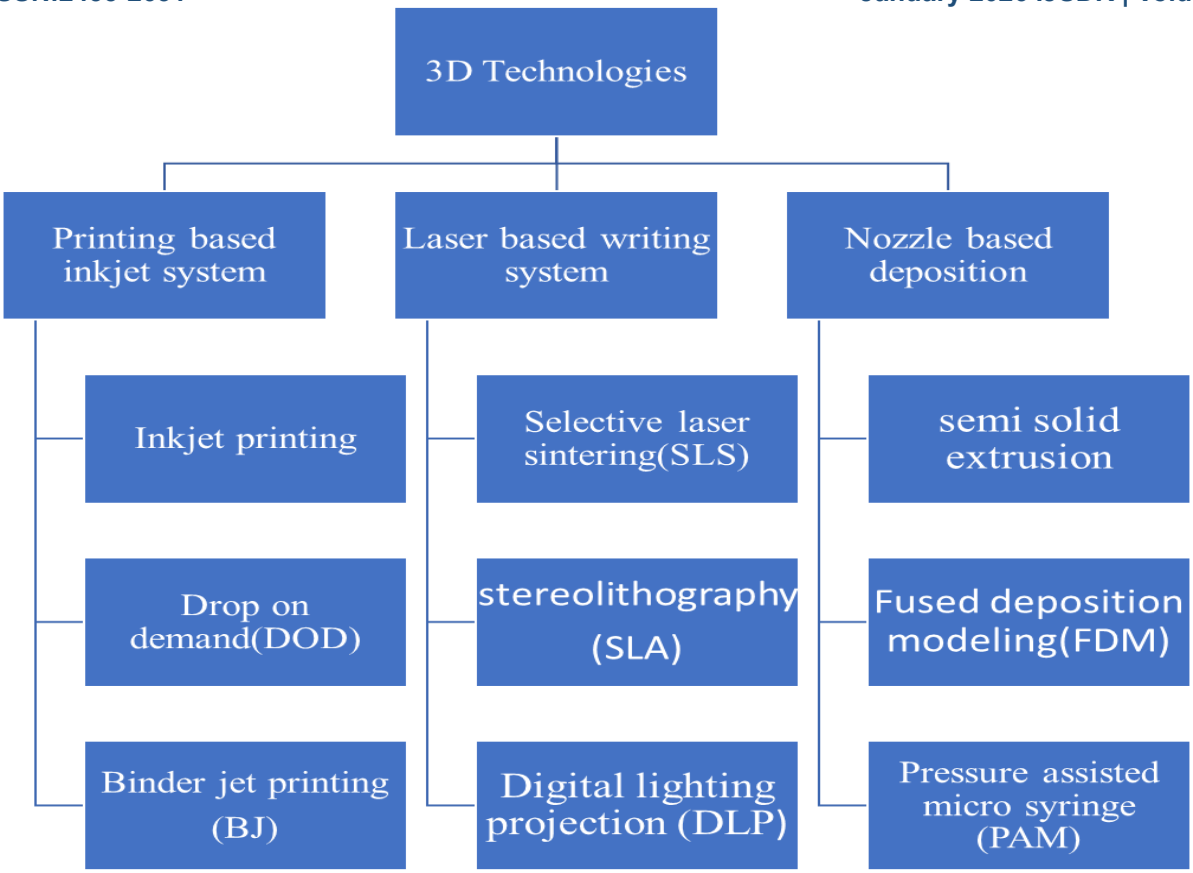

Fig no.1 Various 3D Printing Technologies Utilized in Pharmaceutical Drug Design (Source: Self-created figure.)

A)Inkjet-Based Printing and Binder Jetting

Inkjet 3DP is a mask-less and tool-free process that delivers droplets of solution or binder onto a substrate or powder bed with high precision. In binder jetting, successive layers of powder are selectively bound together using a liquid adhesive. This approach was instrumental in manufacturing Spritam® (levetiracetam), the first FDA-approved 3D-printed drug[7].

Drop-on-demand (DOD) printing, a variant of this method, generates droplets using either thermal or piezoelectric actuation. While highly accurate, thermal DOD requires heat (up to ~300 °C), restricting its use to thermally stable APIs[5,6](fig no.2)

Strengths: Enables dose precision, multi-drug polypills, and rapid disintegration tablets.

Limitations: Limited material compatibility, risk of API degradation with heat, and need for volatile solvents.

In pharmaceutical applications, binder jetting offers a unique advantage by allowing the incorporation of high drug loads without altering powder characteristics, as the liquid binder selectively solidifies particles while leaving unbound powder to support the structure. This method also enables the use of excipients that promote rapid disintegration or controlled release, depending on the formulation strategy. For example, studies have reported the development of highly porous dosage forms that dissolve within seconds, making them especially beneficial for pediatric and geriatric patients who face difficulty swallowing conventional tablets.

Another critical aspect of inkjet-based techniques is their capacity for spatially controlled deposition, which facilitates the fabrication of polypills with compartmentalized APIs. This precision opens possibilities for combination therapies where drugs with different release

profiles can be integrated into a single tablet. Furthermore, binder jetting eliminates the need for compression forces, reducing the risk of damaging fragile biomolecules such as peptides and proteins. Despite these advantages, challenges remain in optimizing droplet–powder interactions, binder spreading, and post-processing steps like drying and sintering, which can influence drug stability and uniformity of the final product.

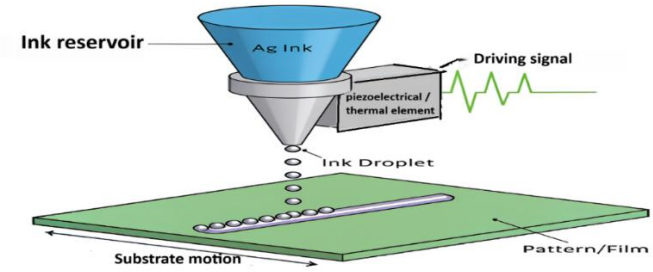

Fig no.2 Inkjet based printing (Source: Self-created figure.

B)Selective Laser Sintering (SLS)

SLS employs a high-energy laser, typically a CO_2 source, to fuse powdered particles layer by layer[8]. This process allows the production of objects without additional support structures, as the unused powder bed supports the part during printing.

Advantages:

High resolution and mechanical strength.

Suitable for heat-tolerant thermoplastic carriers.

Eliminates post-processing like drying.

Challenges:

APIs must withstand elevated temperatures.

High equipment cost and relatively slow throughput.

The working principle of Selective Laser Sintering is based on the precise delivery of thermal energy from a focused laser beam to a powder bed, which induces particle fusion in a layer-by-layer manner. A thin layer of powdered material, usually a pharmaceutical-grade polymer blended with an API, is evenly spread across the build platform using a roller or blade. The laser, typically a CO_2 source, is guided by a computer-aided design (CAD) file to selectively scan specific regions of the powder bed. When the laser energy is absorbed by the particles, localized heating occurs, raising the temperature of the polymer above its glass transition or melting point, which leads to partial fusion or sintering of adjacent particles.

Once the first layer is completed, the build platform lowers incrementally and a new layer of powder is spread on top. The process is repeated iteratively, with each successive layer fused to the previous one, until the complete three-dimensional structure is formed. The surrounding unsintered powder remains loose and serves as a natural support for the developing object, eliminating the need for external scaffolds. At the end of printing, excess powder is removed,

yielding a solid dosage form with tailored porosity, geometry, and drug distribution. By adjusting parameters such as laser power, scan speed, hatch spacing, and powder characteristics, the process enables fine control over the microstructure and performance of the final pharmaceutical product (fig no.3).

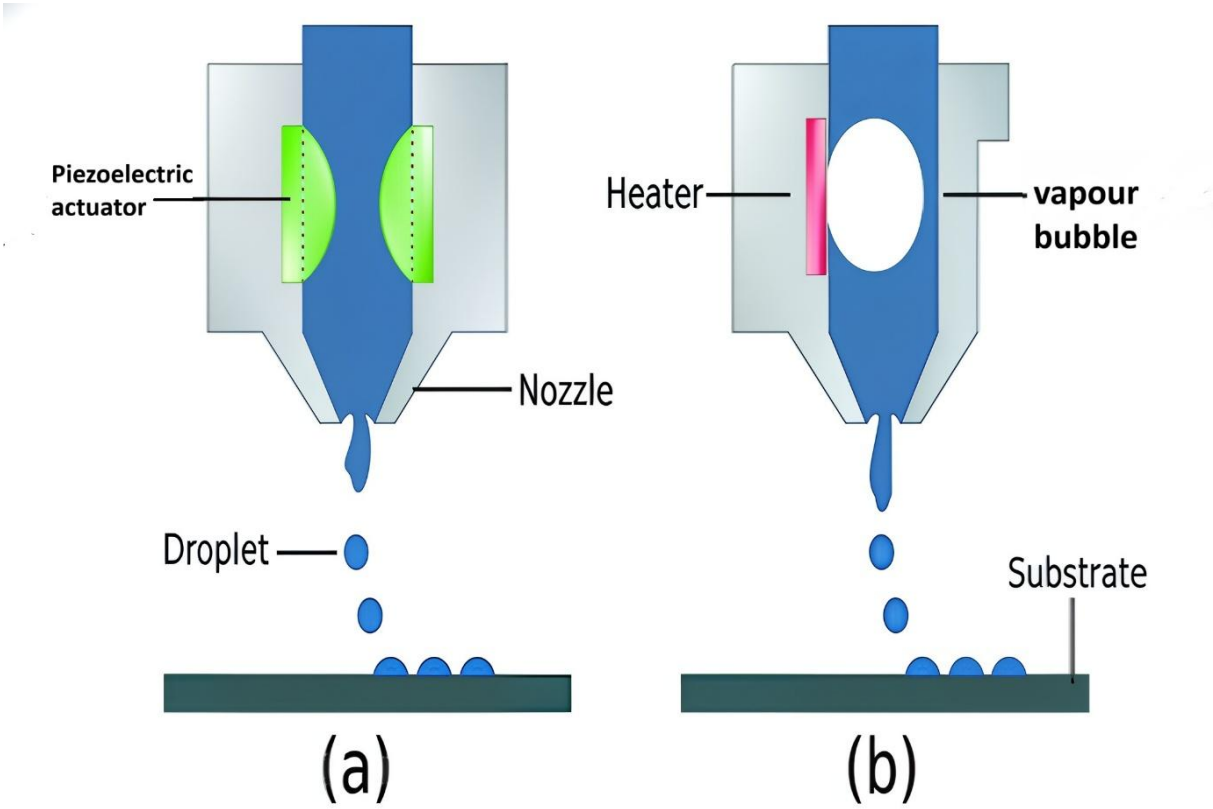

Fig no.3 Selective laser sintering (Source: Self-created figure.)

C)Stereolithography (SLA)

SLA is a photopolymerization-based process where a UV laser cures a liquid resin into solid layers with exceptional accuracy. Its ability to produce intricate designs makes it attractive for microneedle arrays, micro-patterned dosage forms, and drug-loaded scaffolds[9].

Key Benefits: Smooth surface finish, minimal thermal stress, high precision.

Drawbacks: Limited to photopolymerizable resins and requires post-curing steps.

The working mechanism of Stereolithography relies on the photopolymerization of liquid resins using a focused ultraviolet (UV) or visible light source (fig no.4) A vat is filled with a photosensitive resin, and the build platform is positioned just beneath the liquid surface. Guided by a computer-aided design (CAD) model, a UV laser selectively scans the resin surface, triggering polymerization in the exposed regions and solidifying the material layer by layer. After each layer is cured, the platform is incrementally lowered, and a fresh layer of resin is recoated, allowing the process to continue until the entire three-dimensional structure is

fabricated. Post-curing under controlled UV light is often required to ensure complete polymerization and to improve the mechanical strength of the printed device.

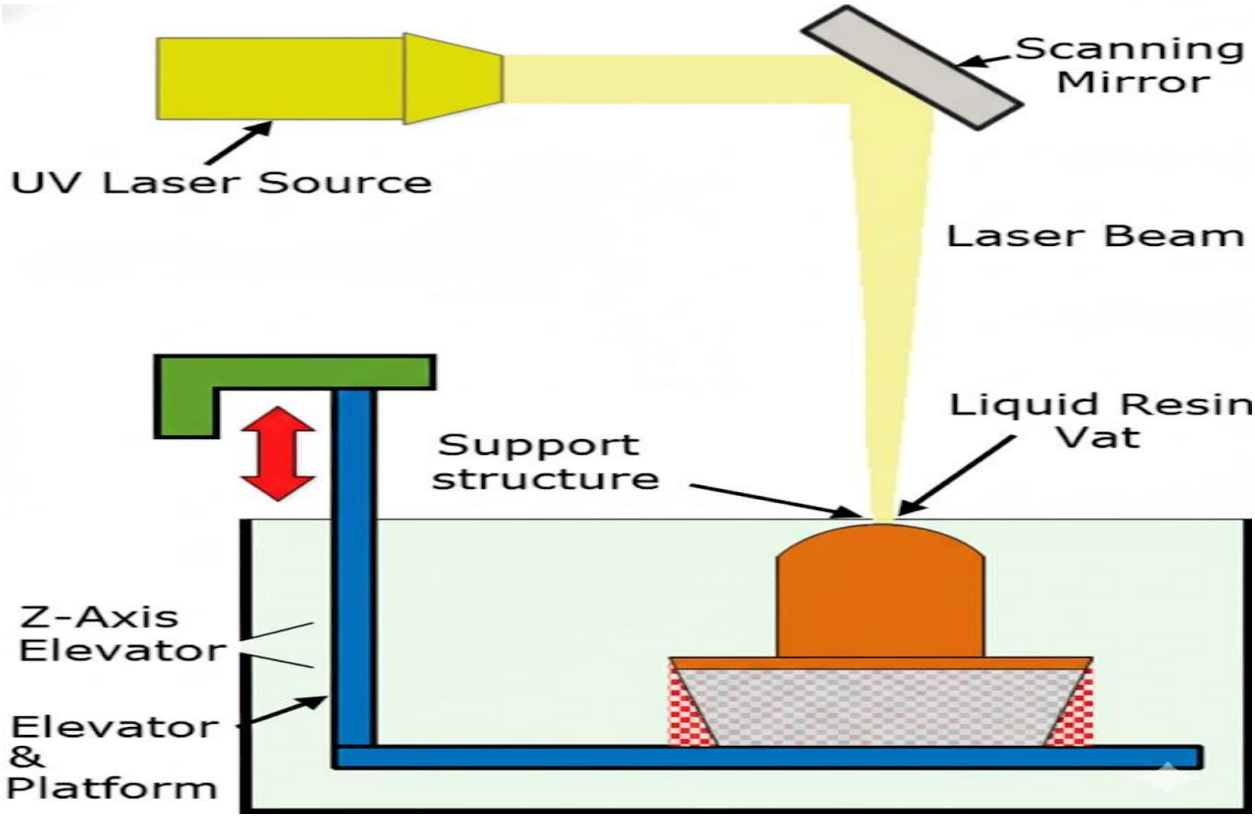

Fig no.4 Sterolithography (Source: Self-created figure.)

D)Digital Light Processing (DLP)

DLP uses a digital projector to simultaneously cure entire cross-sections of resin, significantly reducing printing time compared to SLA. It produces structures composed of small voxels, resulting in slightly rougher surfaces but higher throughput[10].

Applications: Used for drug-eluting devices and targeted delivery systems, such as esophageal rings releasing corticosteroids.

The working principle of Digital Light Processing relies on the projection of patterned light onto a vat of photosensitive resin to initiate photopolymerization. Unlike SLA, where a focused laser scans point by point, DLP employs a digital micromirror device (DMD) or similar optical system to project an entire cross-sectional image of the object simultaneously. This layer-wide curing process results in faster build times and reduced printing cycles. After each layer is cured, the build platform is lowered, and a fresh layer of resin is recoated, allowing successive images to be projected until the three-dimensional structure is complete. Post-processing, such as UV curing or washing to remove residual resin, is often necessary to achieve optimal mechanical stability and biocompatibility(fig no. 5)

Digital Light Processing (DLP) cures photosensitive resin layer by layer using a digital micromirror device (DMD) to project entire cross-sectional images simultaneously, allowing faster printing than point-scanning SLA. The build platform lowers after each layer, and fresh

resin is recoated, with precise light calibration and platform control ensuring uniform polymerization. Technologically, DLP integrates high-intensity UV or LED sources, microscale mirrors, and software controls to maintain accuracy and reproducibility. In pharmaceutics, DLP is used for micro-needles, drug-loaded scaffolds, and patient-specific implants, including multi-material designs for controlled or localized drug release. Limitations include the need for biocompatible, pharmaceutically safe resins and photoinitiators suitable for clinical use.

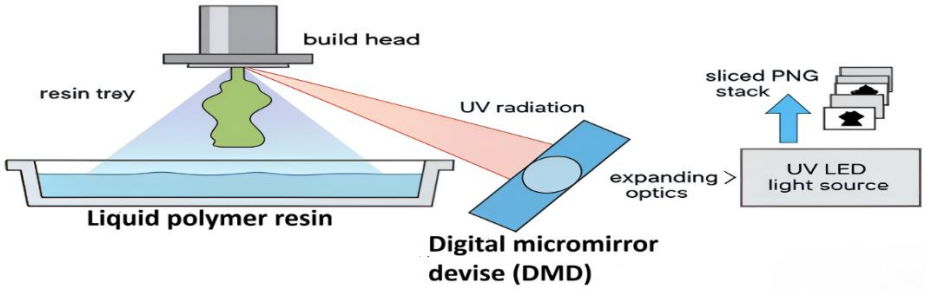

Fig no. 5 Digital light processing (Source: Self-created figure.)

E)Semi-Solid Extrusion (SSE)

SSE extrudes pastes, gels, or suspensions through a nozzle at room temperature, making it suitable for thermolabile drugs and biologics. This technique was utilized in one of the first hospital-based clinical trials to produce Printlets™, chewable dosage forms tailored for children with metabolic disorders[11].

Advantages: Room-temperature operation, compatibility with diverse excipients, suitability for biologics.

Limitations: Limited mechanical strength compared to FDM or SLA objects.

The working principle of Semi-Solid Extrusion (SSE) is based on the controlled deposition of drug-loaded pastes, gels, or suspensions through a nozzle to build three-dimensional structures layer by layer. The material is extruded either by pneumatic pressure, mechanical piston, or screw-driven systems, depending on the viscosity and rheological properties of the formulation. Each extruded layer is deposited on a build platform and may be partially solidified immediately or allowed to dry post-deposition, forming a stable three-dimensional dosage form. The extrusion parameters, including nozzle diameter, extrusion rate, and layer height, are critical for achieving accurate dimensions, uniform drug distribution, and reproducible dosage units(fig no. 6)

From a technological standpoint, SSE integrates precise extrusion control systems, build platform movement, and software-driven pattern generation to fabricate complex geometries and patient-specific dosage forms. The technique is compatible with a wide range of excipients and can incorporate thermolabile APIs or biologics without degradation, making it ideal for

personalized medicine. Advanced SSE systems may include temperature-controlled cartridges, real-time monitoring of extrusion flow, and automated layer alignment to improve reproducibility and mechanical fidelity. Despite its lower mechanical strength compared to FDM or SLA, SSE's versatility, mild processing conditions, and ability to create chewable or rapidly dissolving Printlets™ make it a valuable platform for hospital-based and on-demand pharmaceutical production.

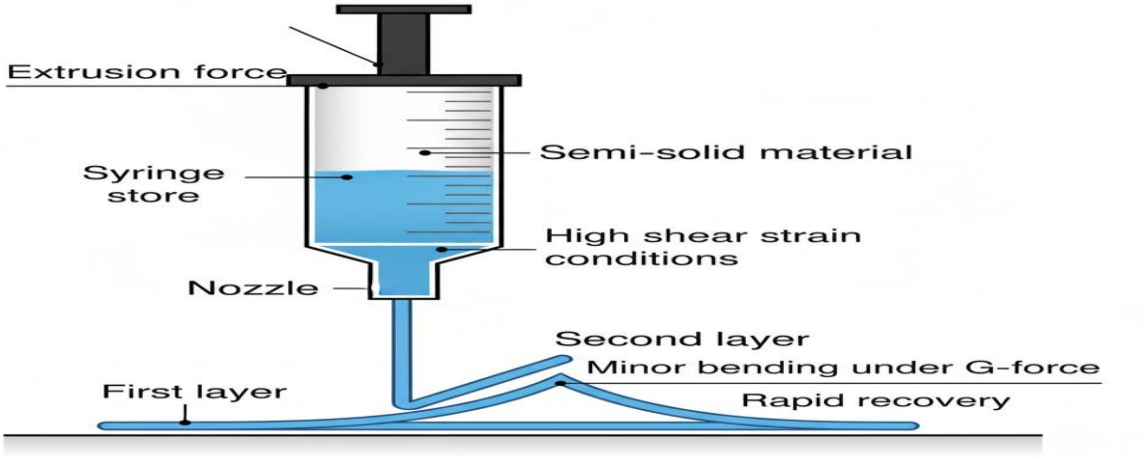

Fig no.6 Semi solid extrusion (Source: Self-created figure.)

F)Fused Deposition Modeling (FDM)

Also known as fused filament fabrication, FDM involves melting a thermoplastic filament and extruding it layer by layer. It is the most widely accessible and cost-effective technique.

Strengths: Simple, inexpensive, and compatible with various thermoplastics (e.g., PLA, PVA).

Limitations: Requires heat-stable APIs, may show slower drug release and dissolution, and risk of API degradation during processing[12].

Fused Deposition Modeling (FDM) operates by feeding a thermoplastic filament, often pre-loaded with APIs, into a heated extrusion nozzle. The filament is melted and deposited layer by layer onto a build platform according to a computer-aided design (CAD) model. Each layer solidifies rapidly upon cooling, forming a stable three-dimensional structure. Parameters such as nozzle temperature, printing speed, layer thickness, and raster orientation are critical for achieving accurate dimensions, structural integrity, and uniform drug distribution throughout the printed dosage form. By adjusting these parameters, FDM can produce tablets with tailored geometries, porosity, and release profiles(fig no. 7)

From a technological perspective, FDM integrates precise thermal control, stepper motors for filament feed and platform movement, and software-driven slicing algorithms that convert CAD designs into layer-by-layer printing instructions. The technique supports a variety of thermoplastics, including PLA, PVA, and Eudragit®, enabling customization of mechanical strength and drug release behavior. Advanced systems may incorporate multiple print heads for combination therapies or varying release profiles within a single tablet. Despite its heat-based limitations for thermolabile APIs, FDM's affordability, simplicity, and scalability make it a widely used platform for personalized medicine and experimental drug delivery research.

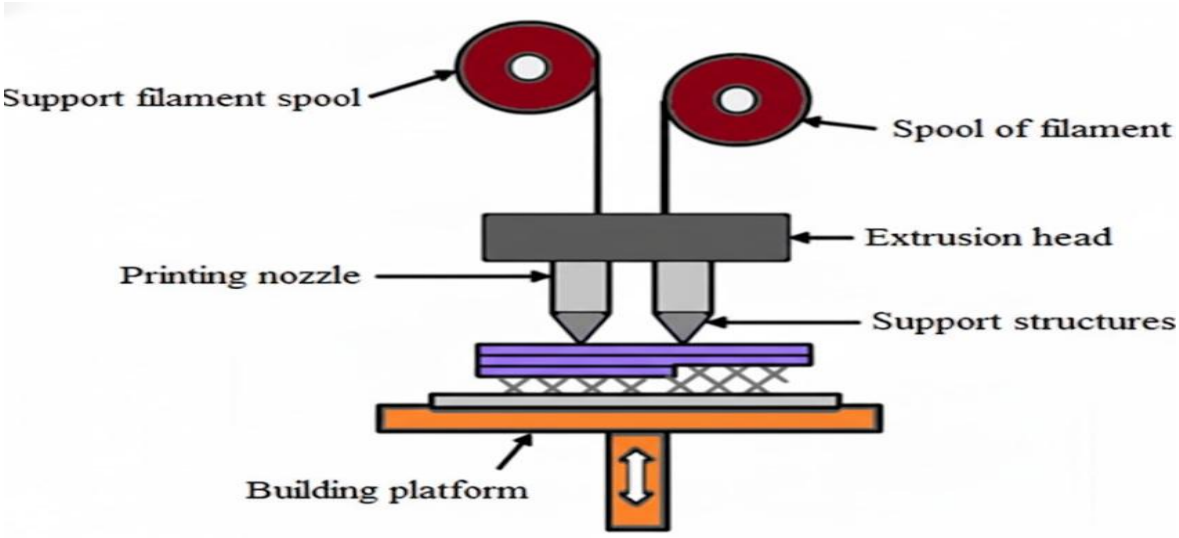

Fig no. 7 Fused deposition modelling (Source: Self-created figure.)

G)Pressure-Assisted Microsyringe (PAM)

PAM technology employs a micro-syringe and compressed air to extrude semi-solid materials in a continuous flow, achieving microstructures as fine as 5–10 μm[13].

Use Cases: Ideal for room-temperature processing of viscous formulations, production of personalized dosage forms, and deposition of heat-sensitive actives.

The working principle of Pressure-Assisted Microsyringe (PAM) involves the controlled extrusion of semi-solid formulations through a microscale syringe using applied pneumatic or mechanical pressure. The formulation, which may include pastes, gels, or suspensions loaded with APIs, is pushed continuously through the nozzle, allowing precise deposition of microstructures layer by layer. The flow rate, nozzle diameter, and platform movement are carefully adjusted to achieve high-resolution structures, with feature sizes as small as 5–10 μm. This precise control ensures uniform drug distribution and reproducible dosage forms, making PAM especially suitable for heat-sensitive or biologic drugs(fig no. 8)

From a technological perspective, PAM systems integrate pressure regulation, microsyringe precision, and computer-controlled stage movement to fabricate complex and patient-specific geometries. Advanced setups may include temperature-controlled syringes to maintain formulation rheology, real-time monitoring of extrusion flow, and software-guided path planning for intricate patterns. The ability to process viscous formulations at room temperature while achieving fine structural resolution makes PAM a promising platform for personalized medicine, customized implants, and on-demand production of pharmaceutical devices, bridging the gap between laboratory research and clinical application.

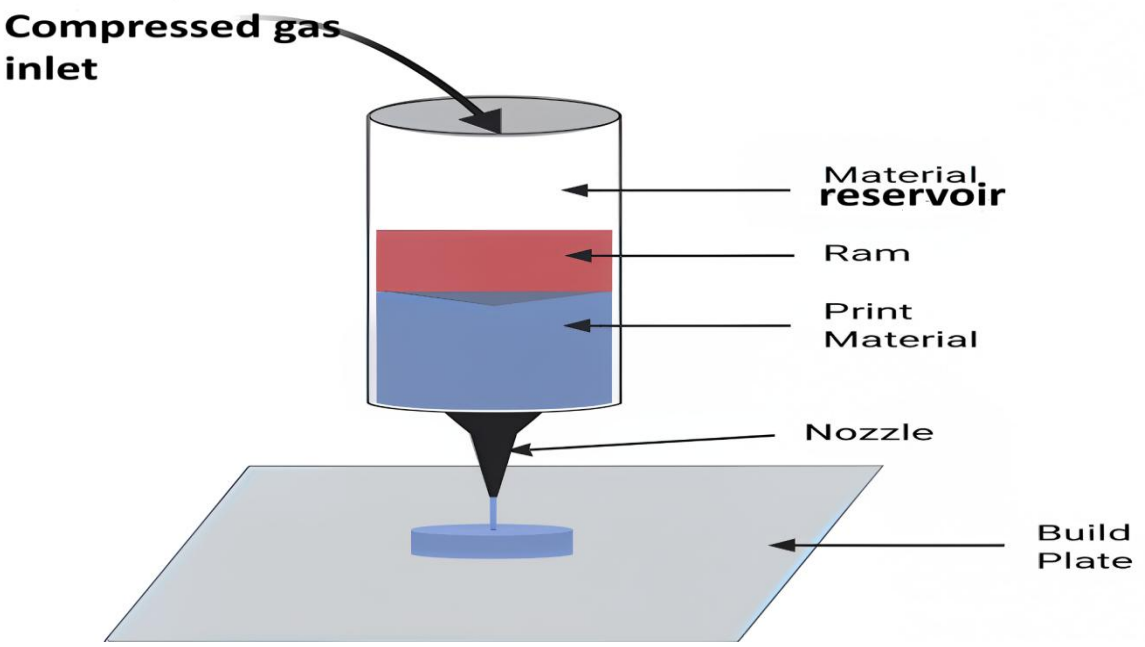

Fig no. 8 Pressure assisted microsyringe (Source: Self-created figure.)

Materials Used in 3D Printing and Their Applications in Medicine

Biodegradable Polymers

Biodegradable or bio-based polymers have gained significant attention as sustainable alternatives to conventional plastics due to their ability to naturally degrade in the environment. These polymers exhibit a balance of desirable properties such as mechanical strength, thermal stability, and good barrier performance, making them ideal for 3D printing applications. The adaptability of 3D printing enables the fabrication of complex structures with high precision using these polymers, providing an environmentally responsible solution[14]. Commonly used biodegradable polymers include polypropylene, polyhydroxyalkanoates (PHA), acrylonitrile butadiene styrene (ABS), polyamide, polycarbonate, polycaprolactone (PCL), polylactic acid (PLA), polyvinyl alcohol (PVA), and nylon.

Natural Fillers as Reinforcing Materials

Polymers serve as a popular matrix material in additive manufacturing because of their low cost, chemical resistance, and easy processability. However, their relatively low modulus, tensile strength, and impact resistance can limit their performance in high-load applications. Incorporating natural fillers as reinforcement has emerged as an effective strategy to overcome these limitations. Nevertheless, these fillers may introduce challenges such as moisture absorption, reduced thermal stability, variable compatibility with polymer matrices, and inconsistency in chemical composition across batches, all of which can influence the quality of the final product[15]. Examples of natural fillers include chitosan, cellulose, and keratin.

Metals

Metal 3D printing represents a cutting-edge manufacturing technique in which objects are produced layer by layer from molten metal powders or wire feedstock. This process allows for precise control of part geometry and local mechanical properties by accounting for internal stress distribution. Studies have explored various aspects of metal-based additive manufacturing, including structural integrity and mechanical behavior. For

instance, experimental work on the buckling capacity of laser-printed metals highlights both the potential and current challenges of this technology. Metal-based 3D printing has also been used in fabricating electrochemical sensors, such as metal-plated electrodes for carbohydrate detection[16,17]. Commonly employed metals include titanium, zinc, stainless steel, and cobalt-chromium alloys[18].

Applications of 3D Printing in Medicine

1)Cardiovascular Diseases

Cardiovascular disorders remain the leading cause of morbidity and mortality worldwide, affecting over 523 million people and causing approximately 18.6 million deaths annually[19]. Traditional imaging modalities—CT, MRI, and echocardiography—are indispensable for diagnosis but are limited by their two-dimensional representation of complex anatomy. 3D printing bridges this gap by creating anatomically accurate models that improve visualization, surgical planning, and patient education. Examples of 3D-printed solutions for cardiovascular care include antiplatelet tubular grafts[20], artificial blood vessels[21], cardiovascular stents[22], and drug-loaded nanocomposites[23].

2)Cancer

Cancer continues to be a major global health challenge, responsible for a large proportion of deaths and treatment-related complications. Additive manufacturing plays an increasingly important role in oncology by enabling patient-specific tumor models that assist in diagnosis, drug screening, and therapy planning. These models—ranging from physical replicas to bio-printed tumor-on-chip systems—provide better insight into tumor biology and treatment responses compared to conventional 2D cultures. Notable 3D printing applications include cardiovascular implants[24], scaffolds[25], Fe–$CaSiO_3$ bio-scaffolds[26], and nanoparticle-loaded hydrogel systems[27] designed for targeted therapy.

3)Dentistry

Dentistry has rapidly embraced 3D printing due to its ability to produce highly precise, customized prosthetics and dental devices quickly. The technology has replaced conventional milling and plaster modeling for many applications, offering superior fit and improved reproducibility. Despite its benefits, studies have noted that 3D-printed crowns may still exhibit slightly poorer fit compared to those made using traditional methods, indicating a need for further optimization. Examples of dental applications include chlorhexidine-coated mouthguards[28], monolithic zirconia crowns[29], occlusal splints[30], dental implants[31], and custom dental crowns[32].

4)Diabetes

Diabetes mellitus is characterized by chronic hyperglycemia, which, if uncontrolled, leads to severe vascular complications[34]. 3D printing and bioprinting are increasingly applied to the development of biosensing devices and controlled drug-delivery platforms for diabetes management. Personalized microneedle arrays, electrochemiluminescence biosensors[35], self-nanoemulsifying tablets[36], 3D-printed glipizide tablets[37], orthopedic insoles[39], and bio-printed scaffolds[40] are examples of innovations targeting better glycemic control and patient compliance.

5)Orthopaedics

The growing prevalence of fractures, osteoporosis, and degenerative joint diseases has driven interest in patient-specific orthopaedic solutions. 3D printing enables the fabrication of implants, prosthetics, and surgical guides tailored to the patient's anatomy using imaging data such as CT or MRI scans[41]. These customized devices not only enhance surgical accuracy but also reduce operative time. However, high production costs, long processing times, and layer-related structural weaknesses remain key limitations. Orthopaedic applications include titanium implants[42], spinal[43] and pelvic implants[44], antimicrobial hydrogels[45], and custom finger splints[46].

Oral administration remains the most widely used and preferred route for drug delivery, particularly through solid dosage forms such as tablets. Tablets offer numerous advantages, including precise dosing, excellent chemical and microbiological stability, controlled drug release, and ease of self-administration. Their portability further enhances patient compliance and allows convenient on-demand use. However, conventional tablet manufacturing involves multiple steps—granulation, compression, coating—which are often time-consuming, labor-intensive, and limited in their ability to accommodate personalized therapy.

Three-dimensional printing (3DP) has emerged as a disruptive technology that enables the fabrication of oral dosage forms with complex geometry, variable architecture, and tailored drug loading. This advancement paves the way for a paradigm shift from the "one-size-fits-all" approach to patient-specific medicine. Using 3DP, researchers have successfully developed tablets containing a wide range of active pharmaceutical ingredients (APIs), including amitriptyline hydrochloride[47], indomethacin[48], ondansetron[49], clindamycin palmitate hydrochloride[50], carvedilol, and haloperidol[51], each optimized for individualized dosing and release profiles.

In 2015, Melocchi and colleagues pioneered the fabrication of the first 3D-printed capsular drug delivery devices using hot-melt extrusion (HME) to produce hydroxypropyl cellulose (HPC)-based filaments, which were subsequently printed into swellable and erodible capsules designed for pulsatile release[52]. These capsule prototypes consisted of three sections — two hollow cylindrical compartments and a central partition — with varying wall thickness and geometry to achieve controlled release. The systems demonstrated effective pulse-wise drug release within two hours, using model APIs such as acetaminophen[55], furosemide[53], metoprolol[54], nadolol, isoniazid, and norfloxacin[56].

Beyond tablets and capsules, 3D printing enables the production of drug-eluting implants with tunable porosity, mechanical strength, and drug release kinetics. Such implants offer promising applications in chronic disease management, post-surgical local drug delivery, and long-acting therapies. The ability to fabricate personalized implants according to a patient's anatomy and therapeutic requirements represents a major leap toward precision medicine (table no. 1)

Table 1. Clinical Trials Involving 3D Printing Applications in Medicine.

Sr No.	Trial ID	Sponser	Purpose/Aim	Ref No.
1	NCT05273060	Mayo Clinic	To evaluate the safety and effectiveness of using 3D printing technology compared to traditional planning methods in nasal reconstruction procedures.	85
2	NCT05741892	Insel Gruppe AG, University Hospital Bern	To assess how effective fracture reduction is in complex femur and tibia shaft fractures when patient-specific surgical guides are designed and 3D printed directly at the treatment site.	86

3	NCT05845099	Ain Shams University	To conduct a controlled clinical trial comparing patient outcomes between conventionally fabricated complete removable dentures (CRD) and those produced using 3D-printed CAD/CAM technology.	87
4	NCT06035211	University Hospital, Bordeaux	To assess how viewing and handling a 3D model of a patient's kidney with a tumor influences surgical planning and outcomes during nephron-sparing surgery.	88

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Table 2. Patented 3D printed pharmaceutical products, devices, and organs

Sr No.	Patent No.	Inventor	Title	Status	Ref No.
			Pharmaceutical products		
1	WO2020145898A1	Seng Han LIM, Wei Jiang GOH	Personalized tablets produced by 3D printing for customized dosing	Active	89
2	CN109125912B	Lei Yifeng	3D-printed microneedle patch for smart blood-glucose control	Active	90
3	ES2966388T3	Morten	Suspension-based process for precise and efficient 3D printing	Active	91
4	US11305480B2	Charles W. Hull	3D-printed hydrogel materials for biomedical use	Active	92
			3D printed devices		
5	CN108724712B	G.Wei	Porous implant produced using 3D printing for improved tissue integration	Active	93
6	CN108724713B	G.Wei	Mesh-structured implant fabricated by 3D printing for bone regeneration and delivery	Active	94
7	JP7045386B2	Wallace Anthony	Optical component manufactured through precision 3D printing techniques	Active	95
8	US10543638B2	DionysiosDouroumis	3D-printed stent designed for medical implantation and vascular support	Active	96
			3D printed organs		

9	EP2970896B1	Benjamin R	Development of engineered liver tissues and arrays using 3D printing for research and therapeutic purposes	Active	97
10	AU2017359330B2	Kapil BHARTI	Creation of vascularized human ocular tissue through 3D bioprinting for use in cell therapy and drug discovery	Active	98
11	EP3215603B1	Kelsey Nicole Retting	Fabrication of three-dimensional skin tissue structures and arrays using advanced bioprinting techniques	Active	99

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Commercially marketed implants often fail to address patient-specific variables such as anatomical differences, age, gender, and underlying medical conditions, leading to suboptimal therapeutic outcomes. Recent investigations have demonstrated that 3D-printed implants can provide more complex and programmable drug-release profiles compared to conventionally manufactured counterparts(table no.2) Additive manufacturing allows for the creation of miniaturized, less invasive, and highly site-specific implants, which can be tailored to match patient anatomy, thereby improving therapeutic precision and reducing adverse effects[57]. Examples of drugs successfully incorporated into 3D-printed implants include doxycycline[58], ciprofloxacin[59], diclofenac sodium[60], and lidocaine[61].

Another promising application of 3D printing in drug delivery is microneedle technology, which serves as an alternative to traditional hypodermic injections. Microneedles are typically arranged in arrays and measure between 25 to 2000 μm in height, allowing them to painlessly penetrate the stratum corneum for transdermal drug administration. Three-dimensional printing enables the production of microneedles with highly precise geometries and drug-loading capacities, allowing for personalized dosing and optimal mechanical strength. Moreover, the use of nanoscale-tipped microneedles facilitates enhanced skin penetration and enables targeted cell or tissue delivery. Multiple studies have demonstrated the successful 3D printing of microneedles for the delivery of insulin[62], diclofenac[63], 5-fluorouracil, curcumin, cisplatin[64], and fluorescein[65], among others.

Traditional drug delivery devices rarely account for individual variability in physiology and drug metabolism, such as differences in absorption rates during the menstrual cycle, menopause, or pregnancy. Such variability often necessitates adjustments in drug dosage or release kinetics. Three-dimensional printing provides a solution by allowing the fabrication of patient-specific drug delivery systems with customized geometry, drug loading, and release profiles. These personalized systems improve therapeutic efficacy, reduce dosing frequency, and enhance patient compliance, while also lowering the risk of post-treatment complications[66].

Recent advancements have extended 3DP applications to intravaginal drug delivery systems designed for hormone therapy and localized treatment of infections or malignancies. Researchers have successfully fabricated devices containing estrogen and progesterone[67], paclitaxel, cidofovir[68], chloramphenicol, and metronidazole[69], demonstrating their potential to deliver sustained, localized therapy with improved patient comfort and adherence.

Challenges

Void Formation

One of the major limitations associated with 3D printing is the occurrence of voids between the printed layers. Additive manufacturing processes are prone to developing additional porosity, which reduces interlayer adhesion and ultimately compromises mechanical strength. This phenomenon is particularly evident in

filament-based techniques such as Fused Deposition Modeling (FDM), where void formation results in anisotropic and suboptimal mechanical behavior. Research has shown that reducing the layer height in powder bed-based printing, particularly for alumina/glass composites, can minimize void formation by improving laser penetration and promoting better interlayer diffusion of ceramic particles[70].

Printer-Related Challenges

Geometric Restrictions:

Although 3D printing offers remarkable freedom in design, not all geometries are practically printable. Certain complex shapes exceed the capability of the printing process, limiting design flexibility[71].

Directional Dependency:

Layered manufacturing processes are inherently direction-dependent[72]. The mechanical strength and load-bearing ability of the printed object vary with the orientation of the deposited layers. Since filament extrusion is typically linear, print orientation can significantly influence the final product's performance.

Printer Quality:

Choosing an appropriate printer is critical for pharmaceutical applications. Parameters such as dosage size, drug concentration, and precision requirements must be matched with the printer's tolerance levels. Variations in machine accuracy may affect the uniformity and reproducibility of drug-loaded products.

Risk of Contamination:

Reusing drug formulation materials during printing poses contamination risks, as previously used inks or formulations may compromise quality. Printer components, such as brass nozzles containing lead in FDM printers, can also introduce contaminants[73]. Replacing them with medical-grade stainless steel components is essential to meet safety requirements.

Material-Related Challenges

Raw Material Considerations:

The choice of APIs and excipients is governed by their physicochemical stability and compatibility with the printing method. Key factors affecting printability include rheological properties, mechanical strength, particle size distribution (for powders), filament diameter tolerance (for solid filaments), and viscosity/viscoelasticity (for liquids)[74]. Additionally, polymers must meet standards regarding glass transition temperature, purity, moisture content, and molecular weight to ensure successful processing.

Mechanical Properties:

3D printing relies on stacking layers of materials, often leading to rough surfaces and reduced mechanical robustness[75]. The mechanical properties of dosage forms—such as hardness, friability, and uniformity—are influenced by factors like adhesive viscosity, nozzle size, and surface tension. Optimizing process parameters, refining nozzle design, and enhancing control software can significantly improve mechanical performance and reproducibility.

Cost-Related Constraints

3D printing remains an expensive approach due to the high costs of computer-aided modeling, segmentation software, specialized medical-grade printers, and skilled labor. This economic barrier limits widespread adoption in routine pharmaceutical manufacturing.

Structural and Microstructural Issues

Anisotropy:

Additive manufacturing results in microstructural variations between layers and interfaces, creating anisotropic mechanical properties. In heat-based processes like Selective Laser Sintering (SLS) or Selective Laser Melting

(SLM), reheating of previous layers causes microstructural changes due to thermal gradients, further contributing to non-uniformity[76].

Regulatory and Legal Challenges

***Liability Concerns*:**

Since multiple stakeholders are involved in designing, manufacturing, and distributing 3D-printed products, assigning responsibility in the event of product failure is challenging. Establishing a clear legal and regulatory framework is crucial to define accountability.

Lack of Standardized Guidelines:

Currently, there are limited standards specifically addressing 3D printing in pharmaceuticals and medical devices. Efforts are underway to develop and harmonize regulations to facilitate compliance and encourage broader adoption of this technology[77].

Design-to-Production Gap:

Computer-Aided Design (CAD) models are the foundation for 3D printing, but converting CAD data into physical objects often introduces errors—particularly in complex or curved geometries[78]. Optimizing layer slicing, support structure generation, and part orientation is essential to minimize deviations from the intended design.

Data Interoperability:

Since 3D printing workflows rely heavily on digital data, interoperability between software platforms used for modeling, simulation, and printing must be ensured to avoid errors and streamline production[79].

Regulatory Landscape

The absence of universally accepted quality control standards makes regulatory oversight challenging[80]. The FDA's 2017 guidance on 3D-printed medical devices was a significant step forward, but additional frameworks are required for pharmaceutical products, including methods for in vitro/in vivo testing, critical parameter identification, and consistency evaluation. Clear regulatory policies will be key to transitioning 3D printing from experimental research into mainstream drug manufacturing.

Transition to Personalized Medicine

Some 3D printing techniques alter the physical state of APIs, impacting their content uniformity and dissolution properties. Polymer filaments may undergo dimensional changes due to heat, resulting in inconsistent dosing or printer malfunction. Careful selection of printing parameters, lubrication, and nozzle size can help overcome these issues[81]. In addition, drug degradation at higher printing temperatures remains a challenge for thermolabile compounds.

Environmental Considerations

Additive manufacturing requires highly specialized raw materials and additional processing steps, which may increase the environmental burden compared to conventional manufacturing. Furthermore, the recovery and recycling of waste materials from AM processes remain insufficiently explored. Energy consumption, especially during material preparation and laser-based printing, also contributes to its overall environmental footprint[82].

Future Aspects

Personalized Medicine

3D printing holds immense promise for advancing the concept of patient-specific therapeutics. It enables the production of medicines tailored to individual requirements based on age, genetics, medical history, and disease profile. This level of customization is particularly valuable for managing complex conditions such as cancer, cardiovascular disorders, and pediatric diseases, where precise dosing is essential. In the near future, 3D-

printed pharmaceuticals are expected to play a central role in personalized treatment regimens, improving therapeutic outcomes and patient compliance[83].

Development of Advanced Biocompatible Materials

The next generation of 3D printing in healthcare will focus on developing a wider range of biocompatible materials, including biodegradable polymers, stimuli-responsive "smart" materials, and hybrid composites. These innovations will allow the creation of highly functional implants, drug delivery systems, and scaffolds for regenerative medicine. Such materials will enhance the integration of medical devices with biological systems, paving the way for tissue engineering and organ regeneration applications.

On-Demand Drug Manufacturing

One of the most disruptive potentials of 3D printing lies in its ability to decentralize pharmaceutical production. Medications can be manufactured on-site at hospitals, clinics, or pharmacies, eliminating the need for large-scale supply chains and long storage durations. This approach is especially valuable during public health crises, such as pandemics, or in geographically remote areas with limited access to centralized production facilities.

Integration with Nanotechnology

Combining nanotechnology with 3D printing offers the possibility of developing highly targeted drug delivery platforms. Such systems could release therapeutic agents with exceptional precision, minimizing systemic side effects and maximizing efficacy—especially for oncology treatments, where targeted delivery is critical[23]. Nanostructured drug carriers produced via 3D printing may allow spatiotemporal control over drug release, ushering in a new era of precision medicine.

Sustainable and Cost-Effective Manufacturing

3D printing inherently reduces material waste and energy consumption compared to conventional manufacturing techniques. As the technology matures, it is expected to become a more sustainable option, making small-scale, cost-effective production feasible. This will be particularly advantageous for orphan drugs and rare-disease medications, where demand is too low to justify mass production using traditional methods.

Regulatory and Quality Control Innovations

As the adoption of 3D printing in pharmaceuticals grows, regulatory frameworks will evolve to accommodate its unique characteristics. Agencies such as the FDA are already working on refining approval protocols to ensure that 3D-printed dosage forms meet stringent safety, quality, and efficacy requirements. Improved regulatory clarity will accelerate the translation of research into clinical practice and facilitate market approval for 3D-printed medicines and medical devices[84].

Conclusion

3D printing technology has emerged as a transformative tool in pharmaceutical science, enabling the fabrication of complex, precisely engineered dosage forms and drug delivery systems. By allowing control over microstructure, shape, and drug release characteristics, this technology paves the way for personalized, patient-centered treatment strategies. The ability to produce medicines on demand offers additional advantages, including enhanced patient adherence, reduced wastage, and improved management of drugs with short shelf lives.

Despite these promising opportunities, challenges remain—such as the limited availability of suitable biocompatible materials, high production costs, void formation between layers, and the need for robust regulatory guidelines. Overcoming these barriers will be essential for translating 3D printing from a laboratory innovation to a commercially viable, large-scale pharmaceutical manufacturing approach.

Overall, 3D printing represents not just a technological advancement but a paradigm shift in how medicines and medical devices are designed, developed, and delivered. With continued research, material innovation, and regulatory alignment, 3D printing has the potential to revolutionize conventional pharmaceutical manufacturing and usher in a new era of patient-specific healthcare.

Acknowledgements

I sincerely express my heartfelt gratitude to Dr. Ujwala Desai, Ph.D., for her valuable guidance, constant support, and critical review of this manuscript. Her expertise in drug delivery systems and 3D printing greatly contributed to improving the quality of this work. I also thank my friend Mr. Shivam Yadav, M.Pharm, for his kind support and help in manuscript preparation and data compilation

Author contributions

All authors contributed equally to this work. The authors have contributed significantly in the conception, writing, and revision of the manuscript.

Disclosure statement

No potential conflict of interest was reported by the authors.

Funding

The authors reported there is no funding associated with the work featured in the article.

Data availability statement

As this article is a review no new data is available.

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