Pharmaceutical Sciences & Analytical Research Journal
ISSN: 2640-6659

Academic Strive
Researcher's perception is our reality

Review Article *Volume 7 Issue 1*

Technological Advancement in Pharmaceutical Field for Different Formulation by 3D Printing Method

Bhatt D, Jasani V and Patel P*

Department of Pharmaceutical sciences, Saurashtra University, India

***Corresponding author:** Priya Patel, Department of Pharmaceutical Sciences, Saurashtra University, Rajkot-360005, India, Email: patelpriyav@gmail.com

Received Date: January 02, 2025; **Published Date:** February 06, 2025

Abstract

Advancements in 3D printing technologies have revolutionized drug delivery systems, enabling personalized and efficient therapeutic solutions. Oral dispersible films ensure rapid disintegration and enhanced dissolution, ideal for paediatric and geriatric patients. Transdermal systems, including microneedles and patches, provide precise drug administration for vaccines, pain management, and chronic diseases. Drug-eluting implants offer extended release for conditions like cancer and infections. Innovations such as hydrogels, nanofibers, and nanocapsules improve drug solubility, bioavailability, and controlled release. FDA-approved tablets and customizable capsules enhance compliance and enable targeted, on-demand therapies. These advancements highlight the potential of 3D printing to deliver patient-specific, efficient, and scalable pharmaceutical solutions.

Keywords: 3D Printing; Formulations; Novel Approaches; Nanoparticles; Recent Innovation

Abbreviations

FDM: Fused Deposition Modelling; SLS: Selective Laser Sintering; SLA: Stereolithography; ISO: International Standards Organization; APIs: Active Pharmaceutical Ingredients; PLA: Polylactic Acid; DIW: Direct Ink Writing; PVA: Polyvinyl Alcohol; PDMS: Polydimethylsiloxane; PCL: Polycaprolactone; EC: Ethyl Cellulose; HPMC: Hydroxypropyl Methyl Cellulose; PCL: Poly-ε-Caprolactone; PLGA: Polylactic/Glycolic Acid; nHAP: Nanohydroxyapatite; LAP: Laponite; CNC: Cellulose Nanocrystals; G/A: Gelatin and Alginate; CAD: Computer-Aided Design; LBL: Layer-By-Layer; μSL: Micro Stereolithography; IND: Investigational New Drug; PAH: Pulmonary Arterial Hypertension; MED&MIM: Melt extrusion Deposition Plus Micro-Injection Molding; AI: Artificial Intelligence.

Introduction

Three-dimensional (3D) printing, an innovative additive manufacturing technology, has emerged as a game-changer across various industries, including pharmaceuticals. Unlike traditional manufacturing methods such as compacting, milling, and molding, 3D printing fabricates objects layer by layer, enabling unprecedented precision, customization, and versatility. Initially developed over 30 years ago for rapid prototyping, the technology has advanced into a state-of-the-art tool that allows for the creation of complex structures

and personalized solutions. This shift has positioned 3D printing as a key driver of innovation in the pharmaceutical sector, addressing the industry's long-standing reliance on standardized manufacturing processes [1].

The pharmaceutical industry is witnessing a paradigm shift as 3D printing enables the development of tailored drug dosage forms. These can be customized to meet individual patient needs, considering factors like age, weight, organ function, and disease severity. This personalization is achieved by adjusting drug combinations, concentrations, and geometries. Furthermore, 3D printing facilitates rapid prototyping, enabling researchers to evaluate multiple formulations efficiently, thereby accelerating the path to innovative therapies [2].

A ground-breaking milestone in this field was achieved in 2015 when Aprecia Pharmaceuticals introduced **Spritam®** (Levetiracetam), the first FDA-approved 3D-printed drug, manufactured using patented ZipDose® technology. This marked the feasibility of 3D printing for large-scale pharmaceutical production and spurred significant interest in the technology. Healthcare professionals' growing inclination—over 60%—toward prescribing 3D-printed tablets underscores the potential of this innovation.

Beyond tablets, 3D printing has found applications in diverse areas such as bone tissue regeneration, cancer treatment, buccal implants, and transdermal patches. The technology's versatility has expanded its role in biomedicine, including tissue engineering, surgical models, implants, and bioprinting of living tissues. These advancements reflect a paradigm shift, bridging engineering and biological sciences to tackle complex healthcare challenges [3] (Figure 1).

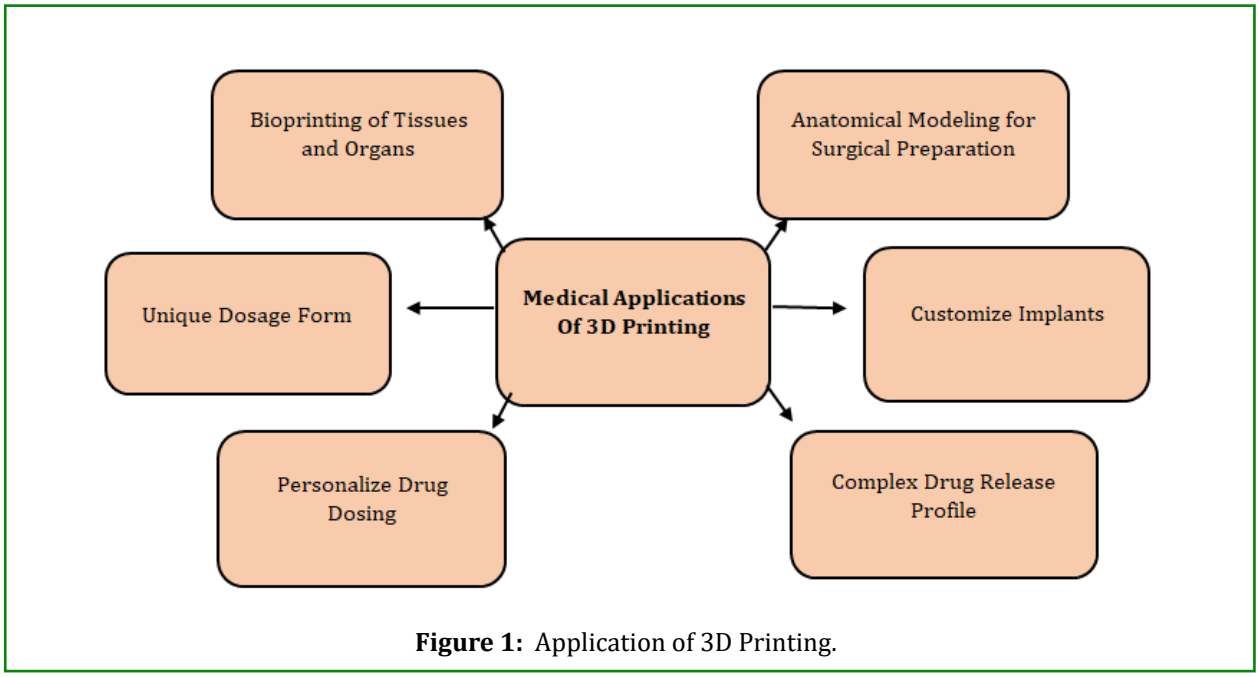

Figure 1: Application of 3D Printing.

Technological advancements have categorized 3D printing into various types, including material extrusion, binder jetting, powder bed fusion, vat photopolymerization, and material jetting. Each method offers unique advantages and applications in drug design. For instance, fused deposition modelling (FDM), selective laser sintering (SLS), and stereolithography (SLA) are extensively studied for creating modified-release dosage forms with precise drug release profiles. This flexibility allows the production of customized drug delivery systems that can be tailored for specific therapeutic needs.

3D printing's additive approach contrasts with traditional subtractive manufacturing, enabling the rapid and cost-effective production of individualized and complex structures. The International Standards Organization (ISO) defines 3D printing as the fabrication of objects through material deposition using a print head, nozzle, or similar technology. This process reduces prototyping time, lowers production costs, and enhances the flexibility of drug development.

The adoption of 3D printing in the pharmaceutical industry remains in its early stages, with start-ups like FabRx leading the charge alongside smaller innovative firms. However, its potential to revolutionize drug manufacturing is immense, offering solutions to unmet clinical needs, reducing development timelines, and improving patient outcomes.

This review delves into the recent advancements and challenges in 3D printing for pharmaceutical and biomedical

applications. It explores its role in developing personalized medicines, modified-release drug delivery systems, and regulatory considerations. By examining the evolution and current state of this technology, the article highlights its transformative impact on drug design, manufacturing processes, and healthcare innovation [4].

Different Formulation prepare by 3D Printing Method for Advancement of Drug Delivery

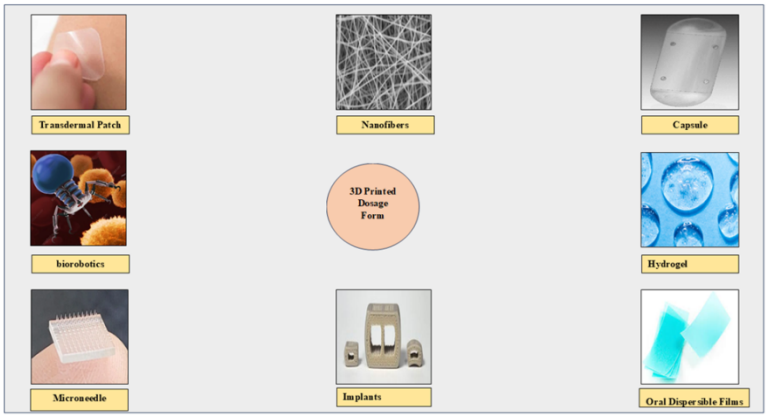

Figure 2: various dosage forms fabricated by 3DP.

Tablet: The first 3D-printed tablet was introduced in 1996, where solid samples were created using a desktop printer with PCL and PEO polymers mixed with blue and yellow dyes. This work demonstrated how complex drug delivery systems could be designed, such as the simultaneous release of multiple drugs or the multiphasic release of a single drug. Various construction techniques were explored to control drug release profiles [5].

Early research in 3D printing for drug delivery involved droplet binding techniques, where the binder was often not a polymer, but other materials like Eudragit® or mannitol. These studies highlighted that oral dosage forms with erosion or diffusion release mechanisms could be created [6]. In the beginning, researchers focused on the type of additive manufacturing process, printing parameters, and release profiles, including immediate or delayed release and first- or zero-order kinetic profiles [7].

Gbureck utilized a unique process combining 3D bioceramic powder printing with antibiotic adsorption to create drug delivery systems. Yu DG, et al. [8,9] produced acetaminophen-containing matrix tablets using desktop 3D printing, experimenting with different printing orientations to achieve varied dissolution mechanisms [8,9].

Other studies showed advancements like the creation of controlled-release bilayer tablets with extrusion-based 3D printing, and the FDA's approval of Spritam® in 2015, the first 3D-printed drug delivery system for treating epileptic seizures, utilizing ZipDose Technology [10,11].

Further work by Goyanes, et al. in 2015 examined FDM 3D printing using PVA filament for drug-loaded tablets, finding that release profiles depended on infill percentages and API types. Other researchers explored multi-compartment polypills and drug systems incorporating multiple APIs for controlled release [12].

More recent developments included the use of advanced techniques like inkjet printing and biocompatible photocurable bioinks for creating hydrophilic API tablets, and extrusion-based methods to print tablets containing various active pharmaceutical ingredients (APIs) [13]. Additionally, research in pediatric drug formulations, gastroretentive floating tablets, and the development of multi-layered and polypill systems highlighted the versatility of 3D printing in personalized medicine [14,15].

From 2017 to present, significant advancements were seen in the use of SLA technology for producing multi-layered tablets with varied API contents, as well as the introduction of custom tablets in different shapes and flavors to improve patient compliance [16,17]. New techniques were also explored for producing tablets with precise release profiles, such as the use of semi-solid extrusion and photoabsorbers for enhancing the SLS printability of tablets [18,19]. The amount of research on 3D-printed tablets has grown significantly, with studies focusing on the development of customizable drug delivery systems, improved dissolution behaviors, and

innovative drug formulations. These advancements show the potential of 3D printing in the future of pharmaceutical manufacturing [20].

Fast-Releasing Tablets: The fused deposition modeling (FDM) 3D printing technique holds significant promise for creating patient-specific dosage forms. One innovative approach involves designing caplets with perforated channels to enhance drug release from 3D-printed tablets. This method facilitates the production of immediate-release tablets, enabling on-demand customization of dosage forms. FDM operates by extruding a filament composed of thermoplastic polymers through a heated nozzle, where the temperature exceeds the polymer's glass transition temperature (Tg).

Despite its advantages, a major drawback of FDM is its limited suitability for manufacturing immediate-release tablets, which account for approximately 70% of all oral dosage forms. To address this limitation, Alhan's group developed immediate-release tablets using positively charged methacrylic polymers. Additionally, they investigated drug release profiles for Theophylline and Dipyridamole using polyvinylpyrrolidone polymers, achieving a complete release of the active ingredients within 70 minutes [21].

Commercialized Fast-Releasing Tablets

Spritam®: This is a 3D-printed fast-dissolving tablet formulation of levetiracetam, approved by the FDA in 2015. It utilizes ZipDose® technology, which allows for rapid oral disintegration due to its highly porous structure, providing a quick onset of action for epilepsy management.

3D-Printed Paracetamol Tablets: Various studies have demonstrated the ability to fabricate paracetamol tablets with different geometries (mesh, ring, and solid) using extrusion-based 3D printing. These tablets can achieve tuneable drug release profiles, from immediate to sustained release, depending on their design.

Capsule: The first 3D-printed capsular devices were produced in 2015 by Melocchi et al. They created hydroxypropyl cellulose-based filaments using hot-melt extrusion, which were then 3D printed. The resulting samples were designed as swellable, erodible capsules intended for oral pulsatile drug release.

Capsules were fabricated using Fused Deposition Modeling (FDM) and inkjet printing, employing various polymer formulations. The capsules consisted of three parts: two hollow sections with a cylindrical closed end and a rounded open end, and a middle part serving as a joint and partition. These hollow parts varied in geometry and wall thickness. After being filled with model active pharmaceutical ingredients (APIs), the capsules successfully released the APIs in pulses within 2 hours.

One group of researchers combined the flexibility of 3D printing with the controlled geometry of nanocellulose hydrogel to regulate drug release properties. The capsules were filled with a dispersion of model drugs and anionic cellulose nanofiber hydrogel. This approach allowed for modulation of drug release by adjusting the inner geometry of the polylactic acid (PLA) capsule, and since the API did not undergo heating, a wide range of APIs, including proteins and liposomes, could be used.

Capsules made via 3D printing are being investigated by several research groups, though only hard-shell capsules can be produced. One of the key advantages of 3D-printed capsules, similar to personalized drug delivery tablets, is the ability to create flexible, on-demand doses, potentially leading to better health outcomes. However, challenges remain, such as ensuring API stability and the limited availability of pharmaceutical-grade polymeric carriers [20].

Benefits of capsules for thermo-labile drugs:
The use of capsules for thermo-labile drugs, particularly those manufactured through 3D printing, presents several advantages. Thermo-labile drugs are sensitive to temperature variations, which can compromise their stability and efficacy. Here's an exploration of the benefits of using capsules for these types of active pharmaceutical ingredients (APIs), along with specific examples and relevant diseases.

Enhanced Stability: Capsules can provide a protective barrier against environmental factors such as moisture and temperature fluctuations. This is particularly beneficial for thermo-labile drugs that require strict temperature control (typically between 2°C and 8°C) to maintain their stability and effectiveness.

Controlled Release: 3D printing technology allows for the design of capsules with tailored release profiles. This means that the drug can be released at a controlled rate, which is crucial for maintaining therapeutic levels in the bloodstream over extended periods. For example, using 3D printing, researchers have developed capsules that can release APIs like adalimumab in a sustained manner, improving patient adherence and outcomes.

Customization: The ability to customize capsule formulations through 3D printing enables the incorporation of various excipients that can stabilize thermo-labile drugs. This customization can also be adjusted based on individual patient needs, allowing for personalized medicine approaches.

Improved Patient Compliance: Capsules are generally easier to swallow than traditional tablets, making them more suitable for patients who have difficulty with oral medications, such as children or the elderly. Fast-dissolving capsules can enhance patient adherence to treatment regimens.

Examples of Thermo-Labile Drugs

Adalimumab (Humira): Adalimumab is an injectable monoclonal antibody used in treating autoimmune diseases like rheumatoid arthritis and Crohn's disease. It requires refrigeration to maintain its stability. Utilizing 3D-printed capsules can facilitate better delivery mechanisms while ensuring the drug remains effective.

Erythropoietin: Used primarily in treating anemia associated with chronic kidney disease, erythropoietin is another thermo-labile drug that must be stored under specific temperature conditions. Formulating it into a capsule via 3D printing could potentially enhance its stability during transport and administration [22].

Buccal Formulations: The 3D printing of oral formulations has gained significant attention in recent years, with buccal drug delivery emerging as a promising alternative to conventional methods. This approach offers distinct advantages for drugs that are susceptible to degradation by the liver's first-pass metabolism or the harsh conditions of the gastrointestinal tract. The buccal mucosa, characterized by its rich vasculature, enables direct systemic drug delivery, making it an effective route for both systemic and localized drug administration. Within the oral cavity, the buccal and sublingual mucosa are recognized as the most viable sites for drug absorption. Thin-film drug delivery systems, including mucoadhesive and dispersible thin films, have shown exceptional potential for facilitating this delivery method.

Traditional manufacturing techniques, such as solvent casting and hot-melt extrusion, have been widely used to produce oro-mucosal films and patches. However, these methods present notable limitations. Solvent casting requires extended processing times for solvent evaporation and is unsuitable for APIs prone to hydrolysis. On the other hand, hot-melt extrusion, while beneficial for enhancing drug solubility, is not ideal for thermo-labile drugs. Additionally, these techniques offer limited flexibility in personalizing dosages or integrating multiple functional materials to achieve varied drug release profiles.

In contrast, 3D printing has emerged as a transformative technology for designing buccal dosage forms, providing unprecedented customization and functionality. The technology allows for the production of personalized doses, the incorporation of multiple drugs in a single formulation, and the development of films with robust mechanical properties and controlled drug release characteristics. Various 3D printing methods have been investigated for manufacturing oral mucosal films, including fused deposition modeling (FDM), inkjet printing, flexographic printing, and direct ink writing (DIW) [21].

Mucoadhesive buccal films are a particularly promising development due to their enhanced retention and permeability properties. These films are typically composed of mucoadhesive agents, permeation enhancers, and film-forming materials, which may be combined with backing layers to direct and control drug release. The spatial arrangement of these components is crucial for ensuring efficient adhesion, controlled drug release, and effective absorption across the buccal mucosa.

Recent studies have highlighted the potential of FDM in creating multi-layered mucoadhesive films. For instance, FDM has been used to produce Diclofenac Sodium films containing poly(vinyl alcohol) and chitosan as mucoadhesive agents, paired with ethyl cellulose or wafer-based backing layers. These films exhibited excellent mechanical properties, with flexible, durable formulations that could endure over 300 folds without breaking. In vitro studies demonstrated consistent unidirectional drug release within 15 minutes and superior mucoadhesive strength (approximately 52%) in chitosan-containing films. These formulations also achieved a threefold increase in drug permeation across porcine buccal mucosa.

To address the limitations of FDM with temperature-sensitive drugs, researchers have combined FDM with inkjet printing. This dual approach has been used to create HPMC-based mucoadhesive films loaded with ketoprofen, with Lidocaine HCl and l-menthol deposited via inkjet printing to enhance permeation. The resulting films displayed consistent drug release and absorption across buccal epithelial cells. Analytical studies, including SEM and XRD, confirmed the presence of crystalline structures within the films, while DSC studies retained the material's integrity.

Another innovative technique, direct ink writing (DIW), has been employed to fabricate saquinavir-loaded buccal patches. These patches utilized inks with tailored pH-modifying microenvironments, combining acidic saquinavir-loaded HPMC ink, alkaline sodium-carbonate ink, and a methylcellulose backing layer. The resulting mesh-structured patches demonstrated superior stretchability and mechanical strength, ensuring effective drug delivery.

In conclusion, advancements in 3D printing technologies have revolutionized the development of buccal drug delivery systems. By addressing the limitations of traditional

manufacturing methods, 3D printing enables the creation of complex, patient-specific formulations with enhanced therapeutic efficacy. These innovations hold significant promise for advancing personalized medicine and improving drug delivery across the buccal mucosa [21].

Oral Dispersible Films: Oral dispersible films are thin polymer-based systems designed to dissolve rapidly in the oral cavity. These films disintegrate in the presence of saliva, releasing active drug compounds that are either absorbed through the oral mucosa or ingested with saliva into the gastrointestinal tract.

Fused deposition modeling (FDM) has been utilized to fabricate dispersible films containing Aripiprazole and polyvinyl alcohol (PVA) as a base material. The physical and mechanical properties of these 3D-printed films were compared with those of films prepared using the solvent casting technique. Thermal and crystallographic analyses, including DSC and XRD studies, indicated that the 3D printing process transformed the crystalline nature of Aripiprazole into an amorphous form. This transition resulted in a notable enhancement in the dissolution rate, with 3D-printed films achieving 95% drug release within 15 minutes, compared to 75% drug release within the same time frame for films prepared by solvent casting [21].

Transdermal Drug Delivery: 3D printing has emerged as an effective method for fabricating pharmaceutical dosage forms with various geometries tailored for transdermal drug delivery. Depending on therapeutic needs, 3D printing has been successfully employed to develop systems such as microneedles, patches, and implants for both systemic and localized drug delivery.

In one study, a piezoelectric inkjet printing process was utilized to fabricate vaccine-loaded dissolvable microneedles. This process involved dispensing liquid formulations using a drop-on-drop deposition technique onto Polydimethylsiloxane (PDMS) microneedle molds. It was observed that the precision of the piezoelectric dispensing system depended significantly on the formulation's viscosity, wettability, and actuation settings. A 1% PVA-based formulation with a viscosity between 4–8 cP demonstrated optimal wetting of PDMS molds (contact angle <100°) and stable drop formation. Biological integrity testing of the vaccine revealed that maintaining integrity was feasible only at low voltage settings (30 V). These findings validated the use of piezoelectric inkjet 3D printing for creating vaccine-loaded microneedle systems.

Another study employed the inkjet printing technique to coat 3D microneedle arrays with three anticancer agents: curcumin, cisplatin, and 5-fluorouracil. The piezoelectric dispensing method achieved uniform and reproducible drug coatings on the microneedles.

Additionally, utilized stereolithography produce 3D-printed microneedle arrays made from biocompatible resin for transdermal insulin delivery. The printing process yielded microneedles with improved penetration efficiency using minimal forces (2–5 N). Pharmacokinetic studies demonstrated rapid insulin action, achieving effective hypoglycemic effects within 60 minutes [21].

3D Printable Implants: The emergence of 3D printing technologies has significantly transformed the development of drug-eluting implants, offering innovative solutions for personalized medicine. These implants utilize diverse printing techniques and biocompatible materials to enable precise drug delivery for various medical conditions, including cancer, infections, and chronic diseases. Unlike traditional manufacturing methods, 3D printing allows for the customization of drug release profiles, providing site-specific and sustained therapeutic outcomes.

In oncology, 3D-printed implants have demonstrated considerable potential. Nanogel-based implants have been developed to target residual glioblastoma cells after surgery. Designed to fit within tumor cavities, these implants release DNA nanocomplexes, effectively delaying tumor progression and recurrence in preclinical models. Microsphere-eluting polymeric implants have shown efficacy in treating hepatocellular neoplasia, while implantable microdevices capable of delivering multiple chemotherapeutic agents have been used to manage non-small cell lung carcinoma. These advancements underscore the versatility of 3D printing in addressing the complexities of cancer treatment [21].

Beyond oncology, 3D-printed implants play a crucial role in managing infections. Antibiotic-loaded implants, such as those containing ciprofloxacin and tobramycin, have been developed for treating bone infections like osteomyelitis.

For tuberculosis, multi-layered cylindrical implants with rifampicin and isoniazid enable controlled drug release, ensuring therapeutic concentrations over extended periods. These innovations demonstrate the ability of 3D printing to enhance the treatment of infectious diseases through precise and sustained drug delivery.

Long-acting drug delivery systems have also benefited from 3D printing. Implants designed to release dexamethasone continuously for over four months highlight the potential for managing chronic conditions. Similarly, ethylene vinyl acetate-based intrauterine devices and subcutaneous rods have shown sustained drug release for up to 30 days, reducing the need for frequent medical interventions.

The choice of materials used in 3D-printed implants significantly impacts their drug release profiles. Polymers such as polycaprolactone (PCL), polylactic acid (PLA), and ethyl cellulose (EC) have been utilized to tailor dissolution rates. For example, PCL provides rapid drug release, while EC enables slower, sustained delivery. These material innovations allow for the optimization of therapeutic outcomes, adapting to the specific needs of patients and conditions.

The ability to create patient-specific implants is a transformative advancement in personalized medicine. In hernia treatment, 3D-printed meshes with customizable pore sizes and thread thicknesses, loaded with ciprofloxacin, have demonstrated improved wound healing and infection prevention. Similarly, implants for orthopedic applications, such as screws and bone plates infused with drugs like gentamicin and methotrexate, provide localized treatment for infections and osteosarcoma. These personalized solutions account for individual anatomical and physiological differences, enhancing treatment efficacy.

Complex drug release patterns have been achieved through 3D printing, as seen in levofloxacin-loaded PLA implants that exhibit a biphasic release over 100 days. Implants containing multiple anticancer drugs have enabled simultaneous and sustained chemotherapy, reducing the need for repeated interventions. These advanced release profiles improve patient compliance, particularly in conditions requiring long-term therapy.

While the potential of 3D-printed drug-eluting implants is immense, their clinical adoption faces challenges such as regulatory approval, scalability, and long-term safety data. Current commercially available implants often lack the customization required to address individual patient factors like age, gender, and disease progression. However, advancements in digital manufacturing and materials science are expected to overcome these barriers, paving the way for broader clinical implementation.

In summary, 3D-printed drug-eluting implants represent a groundbreaking innovation in medicine, enabling tailored and site-specific drug delivery. These implants have the potential to significantly improve therapeutic outcomes in cancer, infections, and chronic diseases. As research and technology progress, 3D printing is poised to become an integral component of future healthcare strategy [20].

Biorobotics: Bio-inspired hybrid devices capable of mimicking various biological functions have recently garnered significant attention. These biorobots consist of artificial scaffolds made from polymer elastomers or hydrogels that support soft biological components such as proteins, living cells, or tissues. Compared to traditional robots, biorobots exhibit greater flexibility, allowing them to perform various movements like walking or swimming and interact effectively with their environment. Rotary machines, often associated with the conversion of chemical energy from ATP hydrolysis into mechanical work, are among the most innovative developments in this field. Cell-based actuators are typically cultured on thin, flexible substrates, where cell contraction induces film deflection and actuation, as demonstrated using mammalian cardiac and skeletal muscle cells.

Leveraging the advantages of 3D bioprinting for tissues and organs, biorobots hold great promise as small mechanical devices for tissue regeneration and drug delivery. They also serve as valuable models for understanding the locomotive mechanisms of microorganisms. For instance, Williams and colleagues developed a flagellar swimmer composed of a polydimethylsiloxane (PDMS) filament with a long tail and short head, cultured with cardiomyocytes. Their study suggested that the technique could be extended to other homotypic cell types, such as optogenetic muscle cells, or heterotypic combinations, such as turtle cardiomyocytes with fibroblasts or neurons with muscle cells, for sensing-based intelligent swimming.

Another example involves cardiomyocyte seeding on a PDMS membrane to create a micro-spherical heart pump capable of controlling microchannel flow through the diaphragm's pulsatile motion.

Biorobots are inherently self-sufficient in energy and nutrients, as their cells can generate power for motion and absorb essential components for maintaining life processes. However, challenges like cell viability and motility control remain. Strategies to address these issues include enhancing cell contraction force through anisotropic alignment, applying electrical stimulation to regulate contraction rates, and creating stimuli-responsive robots by incorporating light-sensitive cells.

The use of 3D bioprinting in biorobot manufacturing paves the way for developing robust, tailor-made medical devices with specialized architectures and functionalities [23].

Controlled Release System: A controlled-release drug delivery system is designed to release active pharmaceutical ingredients (APIs) gradually over an extended period. This approach enhances the safety and effectiveness of drugs and ensures better patient compliance by reducing the need for frequent dosing. Such systems are intended to maintain a stable drug level in the plasma, which is key to improving treatment outcomes. Various drug delivery systems, including controlled and targeted delivery, fast-dissolving systems, pulsed release, and time-controlled release systems,

have been developed using nanotechnology, aiming to create precision medicines. Additionally, 3D printing is being explored to advance the design of nanomedicines.

Thakkar utilized 3D printing technology to develop a tablet based on the concept of fill density. The tablets were fabricated by incorporating pharmaceutically active agents into hydroxypropyl methylcellulose (HPMC) acetate succinate, using a combination of hot-melt extrusion and fused deposition modeling (FDM) techniques. The impact of fill density on drug release was studied, and the results indicated that higher fill densities (up to 80%) allowed for controlled release in various pH environments, showcasing the potential of 3D printing in controlled-release drug delivery.

Algahtani MS, et al. [18] developed a 3D printed shell for an immediate-release tablet using extrusion-assisted 3D printing. The shell was made of cellulose acetate and designed to modulate the release of propranolol hydrochloride from immediate to sustained release. The shell, containing cellulose acetate and D-mannitol, created pores during the dissolution process. The resulting release behavior followed Korsmeyer–Peppas kinetics, demonstrating the potential of 3D printed shells for sustained drug release and better patient adherence.

Zhang J, et al. [17] produced strontium-incorporated mesoporous bioactive glass scaffolds using 3D printing. These scaffolds exhibited superior mechanical properties and porosity compared to traditional scaffolds. Additionally, the controlled dissolution of strontium ions enhanced bone regeneration, demonstrating the application of 3D printing in producing drug-eluting scaffolds for tissue regeneration.

Li Q, et al. [14] investigated the use of 3D printing technology to design a controlled-release system for glipizide using polyvinyl alcohol (PVA) filaments. By employing a dual-nozzle 3D printer, they were able to control the drug release pattern, which followed the Korsmeyer-Peppas model. The study confirmed that varying the concentration and distribution of the drug within the filaments allowed for a controlled release of the drug.

Gioumouxouzis and colleagues developed an oral device for controlled release of hydrochlorothiazide using dual extrusion–FDM 3D printing. The device was made with mannitol and PVA, and the characterization of the device confirmed the incorporation of hydrochlorothiazide in an amorphous form. Drug release tests in different pH conditions demonstrated zero-order release behavior, supporting the use of 3D printing for controlled-release drug delivery.
In another study, a controlled-release capsule containing budesonide was designed using FDM-based 3D printing. The release of the drug was observed in the mid-small intestine, with sustained release behavior in the distal intestine and colon, indicating that 3D printing is a promising tool for designing controlled-release formulations tailored for specific regions of the gastrointestinal tract.

Zhang J et al. [17] aimed to achieve zero-order release of acetaminophen by dispersing it in hydroxypropyl methyl cellulose (HPMC) and producing tablets with various geometries using 3D printing. By adjusting the fill density of the core and the thickness of the external shell, they were able to ensure a steady, constant drug release rate, demonstrating the potential of 3D printing in achieving controlled drug delivery.

Kyobula and colleagues used solvent-free inkjet 3D printing to create fenofibrate-loaded tablets with a honeycomb structure, using FDA-approved beeswax. This approach allowed for optimized wettability and cell size, which could be tailored to design personalized medicines and medical devices.

These studies highlight the continuous development of 3D printing technologies in conjunction with nanotechnology to design controlled-release drug delivery systems. The advances in this field are contributing to the creation of precision medicines with enhanced efficacy and patient compliance [23].

Nanofibers: Nanofibers are a class of materials consisting of fibers with diameters in the nanometer range, offering high porosity and a large surface-to-volume ratio. These fibers are made from various polymers, including chitosan, cellulose, poly-ε-caprolactone (PCL), PLA, and copolymers of polylactic/glycolic acid (PLGA). The first ultrafine fibers were developed and patented by Formhals in 1934. Since their invention, nanofibers have found a wide range of applications, including tissue engineering, wound healing, drug delivery, nanocomposites, filters, and separator membranes.

One of the most common methods for fabricating nanofibers is three-dimensional printing, which involves layer-by-layer construction using electrospun nanofibers. This process utilizes a printer with multiple nozzles to push polymeric fluid through tiny fibers, with an electric field used to draw the fluid out. In tissue engineering, 3D-printed nanofiber scaffolds are crucial as they provide a porous structure that allows cell penetration and creates a suitable microenvironment for the synthesis of proteins that aid in tissue repair.

Yu DG, et al. [8,9] developed a 3D-printed bone tissue engineering scaffold by infusing PCL/gelatin-dispersed nanofibers into a PCL printing scaffold. The scaffold's

porous structure plays a significant role in promoting cellular responses. Huang WD, et al. [8] created a dual-scale 3D-printed scaffold for bone tissue repair using PCL nanofibers.

Ambrus and colleagues explored the effects of drug-loaded nanofibers on enhancing the low solubility of the drug loratadine. They used electrospinning to create amorphous nanofibers, which exhibited a remarkable 26-fold increase in solubility and dissolution. Compared to the pure drug, these nanofibers released 60% of the drug, whereas the pure drug released only 4%.

De Araujo fabricated PCL nanofilaments containing bioactive ceramics, including nanohydroxyapatite (nHAP) and Laponite (Lap), using an extrusion process with a 3D pen. Nanohydroxyapatite aids in osteogenesis, and Lap is synthetic clay that promotes bone formation, cell proliferation, and attachment. The results showed that the nanofilaments were non-toxic and exhibited good dispersion of nHAP and Lap within the polymeric matrices, indicating their potential for bone tissue regeneration [24].

Hydrogel: Hydrogels are 3D networks that contain water, offering structural integrity with characteristics such as super absorbency, flexibility, high stretchability, and self-healing properties. These qualities have made hydrogels widely used across various scientific fields. They exist as colloidal systems with water as the continuous phase. However, current hydrogels are primarily designed for single applications, and ongoing research aims to develop hydrogels with multiple properties to broaden their range of uses.

Advancements in 3D printing technologies, including inkjet printing, microvalve-based printing, extrusion-based printing, laser-assisted forward transfer, and stereolithography (SLA), have significantly enhanced the utility of hydrogels. Among these, extrusion-based printing has been the most extensively researched in recent years.

In one study, Ma created hydrogels using cellulose nanocrystals (CNC) with viscoelastic properties through extrusion-based 3D printing. They tested various CNC concentrations (0.5–25 wt%) to evaluate the hydrogels' rheological properties and printability. CNC hydrogels at a concentration of 20 wt% achieved the best print resolution and fidelity, with a high degree of CNC alignment (72–73%) along the printing direction.

Abouzeid and colleagues developed aqueous hydrogels for 3D printing by combining PVA cellulose nanofibers with sodium alginate and hydroxyapatite (HAP), which showed promise for bone tissue engineering applications. Cheng fabricated semisolid theophylline tablets with drug loadings ranging from 75–125 mg using extrusion-based 3D printing with HPMC K4M or E4M hydrogels. The study found that hydrogels with higher excipient concentrations had increased yield stress, storage modulus, and hardness.

Extrusion-based hybrid hydrogels made from gelatine and alginate (G/A) were prepared in varying concentrations (3%, 5%, and 7%) and G/A ratios (1:2, 1:1, and 2:1). These hydrogels exhibited porous structures with potential for encapsulating and delivering bioactive compounds, such as enzymes, vitamins, antioxidants, and probiotics.

Zhang J, et al. [17] utilized electrostatic interactions and hydrogen bonding to physically crosslink poly(sulfobetaine-co-acrylic acid)/chitosan–citrate, forming a double-network hydrogel. This hydrogel exhibited high transparency, excellent self-healing properties (up to 95.4%), good electrical conductivity (0.11 S/m), and reasonable sensitivity [17].

Nanocapsule: Nanocapsules are spherical colloidal structures featuring a hollow core encased by a polymeric shell, capable of loading both hydrophilic and hydrophobic drugs. These nanocapsules typically range in size from 10 to 1000 nm and offer advantages over other drug delivery systems by serving as intelligent carriers that enhance bioavailability, efficacy, and safety. One of the first products to utilize nanocapsules was an anti-wrinkle lotion containing vitamin E nanocapsules.

3D printing is increasingly being used in the design of nanoformulations, including nanocapsules, to reduce manufacturing time, minimize waste, and improve automation through computer-aided design (CAD) software. Techniques such as stereolithography (SLA), fused deposition modeling (FDM), selective laser sintering, liquid inkjet printing, and pressure-assisted microsyringes have been employed in the 3D printing of these nanoformulations.

Beck R, et al. [13] first combined 3D printing with nanotechnology to develop drug delivery devices, using FDM to create 3D printed tablets loaded with nanocapsules containing deflazacort. They soaked the printed filaments in a suspension of deflazacort nanocapsules along with various polymers (PCL, Eudragit® RL100) and channeling agents like mannitol. The resulting nanocapsules had a positive zeta potential of +6.87 mV and sizes under 0.284 µm, with a narrow polydispersity index of 0.10. In vitro testing showed 65% drug release over 24 hours, with the release following Fickian diffusion and case-2 transport patterns.

Rupp developed small core-shell capsules through a dual-step 3D printing process using a CAD program. The top and bottom layers were tightly loaded with thermoplastic

polymer PCL and nanocapsules via FDM, while middle layers contained oils such as linalool and limonene, printed using an inkjet print head. These microsized capsules, ranging from 200–800 μm, exhibited thermal stability up to 80°C [24].

Nanoparticle: Stereolithography (SLA) is a laser-based 3D printing system that employs a layer-by-layer (LbL) assembly method to create aligned micro- and macro-sized 3D structures. However, it is not capable of achieving nanoscale architecture. Lee et al. integrated core-shell nanoparticles onto nerve scaffolds produced with SLA, successfully achieving nanotopology and enabling the sustained delivery of bioactive molecules to enhance nerve regeneration in peripheral nerve injuries.

3D printing is also used to fabricate biomaterials with customized scaffolds and pre-determined characteristics such as shape, porosity, pore size, and interconnectivity, ensuring high reproducibility. Nanoparticles are often incorporated to improve the surface and biological properties of these scaffolds.

Roh introduced magnesium oxide nanoparticles into PCL and hydroxyapatite (HAP) composites to enhance bone regeneration. Magnesium, a vital natural mineral for bone growth and a biodegradable metal, was found to promote osteoblast cell proliferation. The resulting PCL/HAP/magnesium oxide nanoparticle scaffolds with interconnected pores exhibited maximum bioactivity compared to other materials. In a separate study, Abdal-hay blended bioresorbable magnesium hydroxide nanoparticles with the biodegradable polymer PCL, using 3D printing technology to create composite scaffolds. These scaffolds promoted osteoblast metabolic activity, attachment, and proliferation, unlike those made from polymer alone.

From these studies, it can be concluded that 3D printing holds promising potential for designing precision medicine and nanomedicine, offering the flexibility to create scaffolds, devices, and systems tailored to individual needs [24].

Microneedle: In early research by Ovsianikov et al., a placebo microneedle was developed using femtosecond laser two-photon polymerization 3D printing technology. In 2013, they created an amphotericin B-loaded microneedle by combining visible light dynamic mask micro stereolithography, micro moulding, and piezoelectric inkjet printing. This process was found to be scalable and capable of incorporating pharmacological agents, even those with complex solubility profiles, into microneedles. The same researchers also produced miconazole-containing microneedles using a special polymer, Gantrez® AN 169 BF (poly(methyl vinyl ether-co-maleic anhydride)), for potential use in the transdermal treatment of cutaneous fungal infections.

A dacarbazine-containing drug delivery system was developed for localized skin cancer therapy using a special 3D printing technique called multi-material micro stereolithography (μSL). The microneedle array was first built, and then the active pharmaceutical ingredient (API) was added through blending, aided by the crosslinking effect of the polymer.

Ross et al. constructed insulin polymeric layers on metal microneedles. The dissolution profiles indicated rapid insulin release in the first 20 minutes, suggesting that solid-state insulin delivery via microneedles is feasible.

Lim used 3D printing to create a dual-function microneedle array on a personalized curved surface, designed for both drug delivery and splinting of the affected finger. The microneedle splint showed good penetration efficiency and biocompatibility, with significantly more diclofenac permeating the skin compared to intact skin. This approach could offer a new way to treat trigger finger while maintaining normal hand function.

Two research groups fabricated insulin-releasing microneedles using Dental SG material, employing inkjet printing and the SLA technique. Pere, et al. achieved rapid API release within 30 minutes, while Economidou, et al. achieved better glucose control and hypoglycaemia management.

One of the major advantages of 3D printing is the ability to incorporate pharmacological agents with complex solubility profiles into microneedles tailored to patient needs. These microneedles provide accurate dosing while maintaining mechanical strength compared to traditional metal microneedles. Additionally, the nano-scale tips of 3D-printed microneedles allow for effective skin penetration and potentially targeted delivery to cells [20]. In Table 1 mentioned various 3D Printing applications in the different dosage form.

FDA-Approved Products or Patient Outcomes

Spritam® (Levetiracetam): Approved in 2015, Spritam became the first FDA-approved prescription drug product manufactured using 3D printing technology. It utilizes Aprecia Pharmaceuticals' proprietary ZipDose® technology, which allows for rapid disintegration in the mouth without the need for water. Studies have shown that Spritam can improve patient compliance, especially among those with swallowing difficulties, by providing a convenient dosage form 26.

Triastek's T22: Recently, Triastek received Investigational New Drug (IND) clearance from the FDA for its T22 3D printed gastric retention drug, aimed at treating pulmonary arterial hypertension (PAH). This product is notable for reducing the dosing frequency from three times a day to just once,

which may enhance adherence to treatment regimens. The T22 utilizes Triastek's Melt extrusion Deposition plus Micro-Injection Molding (MED&MIM) process and incorporates a unique microstructure for optimized drug delivery.

T19: Another product from Triastek, T19, is designed for rheumatoid arthritis and has also received IND approval. This highlights the growing portfolio of 3D printed drugs aimed at chronic conditions.

Formulation	Key Features	Applications	References
Fast-Releasing Tablets	FDM technique; patient-specific design; rapid drug release (complete within 70 minutes).	Immediate-release dosage forms.	[21]
Buccal Formulations	Direct systemic delivery; use of mucoadhesive films; customizable designs for controlled release.	Drugs bypassing first-pass metabolism.	[21]
Oral Dispersible Films	Dissolves in the oral cavity; enhanced dissolution rate (95% release in 15 minutes).	Pediatric and geriatric drug delivery.	[21]
Transdermal Systems	Microneedles and patches for localized/systemic delivery; precise and reproducible.	Vaccines, pain relief, chronic diseases.	[21]
3D-Printed Implants	Customizable; extended release over months; biocompatible materials.	Cancer, infections, orthopedic applications.	[20,21]
Controlled Release Systems	Zero-order drug release; material innovations like PVA and HPMC; tailored drug release profiles.	Chronotherapy, regional drug delivery.	[22]
Nanofibers	High surface area; biocompatibility; enhanced drug solubility and dissolution rates.	Tissue engineering, wound healing, drug delivery.	[23]
Hydrogels	Superabsorbent, flexible; used for encapsulating bioactive compounds like vitamins and enzymes.	Bone tissue engineering, drug delivery systems.	[23]
Nanocapsules	Intelligent carriers; dual drug loading capabilities; enhanced bioavailability and safety.	Controlled and sustained release formulations.	[23]
Microneedles	Nano-scale precision; effective skin penetration for localized/systemic therapy.	Transdermal drug delivery, localized therapies.	[20,23]
Biorobotics	Bio-inspired devices; energy self-sufficient; flexible for drug delivery and tissue regeneration.	Tissue regeneration, dynamic drug delivery.	[22]

Table 1: 3D Printing Applications.

Future Directions in 3D Printing Technologies

The landscape of 3D printing is rapidly evolving, particularly with advancements in technology, integration with artificial intelligence (AI), and the potential for mass customization. These developments promise to transform various industries, enhancing efficiency, sustainability, and product personalization.

Advancements in 3D Printing Technologies

Recent Trends Indicate Significant Strides in Several Areas of 3D Printing:

Large-Scale and Metal Printing: Innovations in large-scale 3D printing are facilitating applications in construction, such as the creation of homes and bridges. Additionally, advancements in metal 3D printing are expanding its use across aerospace, automotive, and healthcare sectors [25].

Material Innovations: The introduction of specialized materials is crucial for producing complex parts with varied mechanical properties. Multi-material and multi-color printing technologies enable the creation of functional prototypes that meet specific industry needs.

Sustainability Initiatives: There is a growing emphasis on sustainability within the 3D printing sector. This includes the development of eco-friendly filaments and recycling initiatives aimed at reducing waste and environmental impact.

Integration with AI

The integration of AI into 3D printing processes is revolutionizing how products are designed and manufactured:

Process Optimization: AI can optimize printing parameters, predict potential issues, and automatically generate complex designs. This integration enhances efficiency and reduces the likelihood of errors during production [26,27].

Real-Time Monitoring: Machine learning algorithms can monitor printing parameters in real-time, allowing for

immediate adjustments to improve quality and reduce defects. This capability is essential for maintaining high standards in mass production [28].

Automated Design Processes: Companies are developing AI-driven platforms that can autonomously create intricate structures based on design specifications. This shift towards automation is expected to streamline workflows and shorten production cycles [25].

Potential for Mass Customization

Mass customization through 3D printing offers unprecedented flexibility in product design:
Personalized Products: The ability to produce customized items on-demand allows consumers to tailor products to their specific needs. This trend is particularly beneficial in sectors like healthcare, where personalized medical devices can be created rapidly [25].

Decentralized Manufacturing: As 3D printing technology becomes more accessible, companies can decentralize their manufacturing processes. This approach enables localized production, reducing lead times and operational costs while increasing responsiveness to consumer demands.

Future Research Directions: Future research should focus on enhancing the accuracy and efficiency of 3D printing technologies, expanding their applications across various fields, including medical devices and sustainable manufacturing practices [26,27].

In summary, the future of 3D printing is marked by significant technological advancements, a strong integration with AI, and a robust potential for mass customization. These developments not only promise to enhance manufacturing processes but also to reshape consumer experiences across multiple industries.

The Role of 3D printing in Conjunction with Other Emerging Technologies like Nanotechnology

Enhanced Material Properties: Nanomaterials, such as carbon nanotubes and silver nanoparticles, are integrated into 3D printing processes to improve electrical conductivity and mechanical strength. This allows for the production of flexible and compact electronic devices, as well as advanced tissue engineering scaffolds that can better support cell growth and differentiation.

Applications in Electronics: The use of nanomaterials in 3D printed electronics enables the fabrication of multi-material circuits with improved performance characteristics. For instance, integrating nanomaterials allows for the creation of more efficient sensors and components that are essential for modern electronic devices.

Biomedical Applications: In tissue engineering, nanomaterials enhance the bioactivity and electroconductivity of scaffolds, which is crucial for applications such as cardiac tissue regeneration. The incorporation of nanostructures improves scaffold performance by providing physiochemical cues that guide cellular behaviour.

Conclusion

3D printing has emerged as a transformative technology in pharmaceutical sciences, offering unprecedented opportunities for designing innovative and personalized drug delivery systems. Its versatility enables the creation of diverse formulations, including oral dispersible films, transdermal patches, implants, hydrogels, nanofibers, and controlled-release systems, tailored to meet specific therapeutic requirements. The ability to achieve rapid drug release, as seen in oral films, or extended delivery over weeks to months, as demonstrated by implants and capsules, underscores the adaptability of 3D printing in addressing a wide range of clinical needs.

The integration of advanced materials, such as polymers and bio composites, with sophisticated printing techniques, including fused deposition modeling and inkjet printing, allows for precise control over drug release profiles, enhanced bioavailability, and improved patient compliance. Furthermore, innovations like nanocapsules, microneedles, and bio-inspired robotic systems expand the scope of 3D printing to include intelligent drug delivery and dynamic therapeutic applications.

Despite these advancements, challenges remain, including regulatory hurdles, scalability for mass production, and the need for long-term safety and efficacy data. However, as digital manufacturing and material science continue to advance, 3D printing holds the promise of revolutionizing personalized medicine by providing patient-specific solutions that address anatomical, physiological, and therapeutic complexities.

In summary, 3D printing represents a paradigm shift in drug delivery, enabling the development of efficient, scalable, and patient-centric formulations. Its potential to overcome limitations of traditional manufacturing methods and cater to evolving medical needs makes it a cornerstone technology for the future of healthcare.

References

1. Wang S, Chen X, Han X, Hong X, Li X, et al. (2023) A Review of 3D Printing Technology in Pharmaceutics: Technology and Applications, Now and Future. . Pharmaceutics 15(2): 416.
2. Basit AW, Trenfield SJ (2022) 3D printing of pharmaceuticals and the role of pharmacy. Drug discovery and development.
3. Chakka LRJ, Chede S (2023) 3D printing of pharmaceuticals for disease treatment. Front Med Technol 4: 1040052.
4. Achala AM, Raksha LM (2020) A Review on 3D Printing Technologies in Pharmaceutical Science. Bull Env Pharmacol Life Sci 9(9): 126-134.
5. Wu BM, Borland SW, Giordano RA, Cima LG, Sachs EM, et al. (1996) Solid free-form fabrication of drug delivery devices. Journal of Controlled Release 40(1-2): 77-87.
6. Katstra W, Palazzolo R, Rowe C, Giritlioglu B, Teung P, et al. (2000) Oral dosage forms fabricated by Three Dimensional Printing™. Journal of controlled release 66(1): 1-9.
7. Wang CC, Tejwani MR, Roach WJ, Kay JL, Yoo J, et al. (2006) Development of near zero-order release dosage forms using three-dimensional printing (3-DP™) technology. Drug development and industrial pharmacy 32(3): 367-376.
8. Yu DG, Yang XL, Huang WD, Liu J, Wang YG, et al. (2007) Tablets with material gradients fabricated by three-dimensional printing. Journal of pharmaceutical sciences 96(9): 2446-2456.
9. Yu DG, Branford-White C, Ma ZH, Zhu LM, Li XY, et al. (2009) Novel drug delivery devices for providing linear release profiles fabricated by 3DP. International journal of pharmaceutics 370(1-2): 160-166.
10. Khaled SA, Burley JC, Alexander MR, Roberts CJ (2014) Desktop 3D printing of controlled release pharmaceutical bilayer tablets. International journal of pharmaceutics 461(1-2): 105-111.
11. Bhattacharya S, Singh S, Shrestha S, Baghel Y, Maity D, et al. (2019) Recent findings and development of 3D printing technology in pharmaceutical formulation development: an extensive review. Int J Drug Dev Res 11: 1-14.
12. Khaled SA, Burley JC, Alexander MR, Yang J, Roberts CJ (2015) 3D printing of tablets containing multiple drugs with defined release profiles. International journal of pharmaceutics 494(2): 643-650.
13. Beck R, Chaves P, Goyanes A, Vukosavljevic B, Buanz A, et al. (2017) 3D printed tablets loaded with polymeric nanocapsules: An innovative approach to produce customized drug delivery systems. International journal of pharmaceutics 528(1-2): 268-279.
14. Li Q, Guan X, Cui M, Zhu Z, Chen K, et al. (2018) Preparation and investigation of novel gastro-floating tablets with 3D extrusion-based printing. International journal of pharmaceutics 535(1-2): 325-332.
15. Scoutaris N, Ross SA, Douroumis D (2018) 3D printed "Starmix" drug loaded dosage forms for paediatric applications. Pharmaceutical research 35: 1-11.
16. Goyanes A, Madla CM, Umerji A, Pineiro GD, Montero JMG, et al. (2019) Automated therapy preparation of isoleucine formulations using 3D printing for the treatment of MSUD: First single-centre, prospective, crossover study in patients. International Journal of Pharmaceutics 567: 118497.
17. Oblom H, Zhang J, Pimparade M, Speer I, Preis M, et al. (2019) 3D-printed isoniazid tablets for the treatment and prevention of tuberculosis—personalized dosing and drug release. Aaps Pharmscitech 20: 1-13.
18. Algahtani MS, Mohammed AA, Ahmad J, Abdullah MM, Saleh E (2021) 3D printing of dapagliflozin containing self-nanoemulsifying tablets: Formulation design and in vitro characterization. Pharmaceutics 13(7): 993.
19. Yang Y, Xu Y, Wei S, Shan W (2021) Oral preparations with tunable dissolution behavior based on selective laser sintering technique. International Journal of Pharmaceutics 593: 120127.
20. Bacskay I, Ujhelyi Z, Feher P, Arany P (2022) The evolution of the 3D-printed drug delivery systems: a review. Pharmaceutics 14(7): 1312.
21. Abdella S, Youssef SH, Afinjuomo F, Song Y, Fouladian P, et al. (2021) 3D Printing of thermo-sensitive drugs. Pharmaceutics 13(9): 1524.
22. Jamroz W, Szafraniec J, Kurek M, Jachowicz R (2018) 3D printing in pharmaceutical and medical applications–recent achievements and challenges. Pharmaceutical research 35: 1-22.
23. Jain K, Shukla R, Yadav A, Ujjwal RR, Flora SJS (2021) 3D printing in development of nanomedicines. Nanomaterials 11(2): 420.

24. Lacroix R, Seifert RW, Timonina-Farkas A (2021) Benefiting from additive manufacturing for mass customization across the product life cycle. Operations Research Perspectives 8: 100201.

25. Goh GD, Sing SL, Yeong WY (2021) A review on machine learning in 3D printing: applications, potential, and challenges. Artificial Intelligence Review 54(1): 63-94.

26. Mohammed R, Shaik AS, Mohammed S, Bunga KK, Aggala C, et al. (2025) Advancements and Challenges in Additive Manufacturing: Future Directions and Implications for Sustainable Engineering. Advance Sustainable Science Engineering and Technology 7(1): 0250108.

27. Jagadeesh P, Puttegowda M, Rangappa SM, Alexey K, Gorbatyuk S, et al. (2022) A comprehensive review on 3D printing advancements in polymer composites: Technologies, materials, and applications. The International Journal of Advanced Manufacturing Technology 121(1): 127-169.