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3d Printing in Personalised Medicines, Nano Medicines and Bio Pharmaceuticals - A Review

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ABSTRACT
3D printing technologies enable medicine customization adapted to patients' needs. Personalized medicines represent a new frontier for developing customizable therapeutic formulations that consider an individual's genetic composition, medical history, and physiology. 3D printing permits rapid manufacturing, design, and bioprinting.
Must adhere to regulatory norms before entering the marketplace. The integration of biopharmaceuticals and nanotechnology-based drugs with 3D printing ("Nano printing") brings personalized Nano medicines into focus for the coming years. 3D printing allows th precise production of customized drug dosage form, implants and anatomical models tailored to individual patient needs. This technology enhances treatment efficacy, improves patient compliance, reduce adverse effect and supports precision medicine through individualized dosing and targeted drug delivery. 3D bioprinting has opened new possibilities in tissue engineering and regenerative medicines by creating biological functional tissue for research and therapeutic application. This review highlights the principles, technologies, applications and future prospects of 3D printing in personalized medicine.

Keywords: Personalized medicines, 3D Printing, Drug Delivery, Nanomedicines, Stereolithography, Fused Deposition Modeling

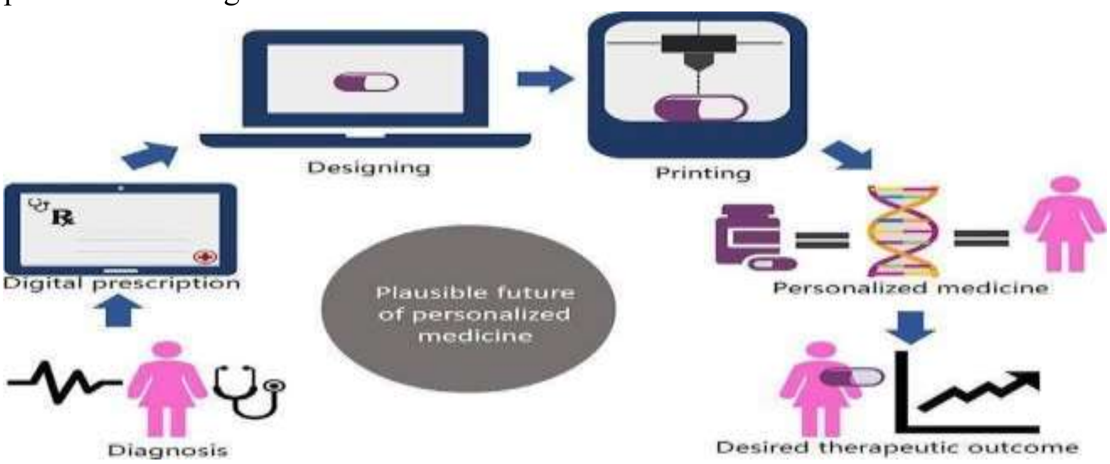

Figure 1: Graphical abstract of personalized 3D-printed medicine, from diagnosis and digital prescription to design, printing, and therapeutic outcome

INTRODUCTION

Drug delivery technique. Standard batch production generally requires complex optimization of numerous excipients, which is time consuming and resource-intensive. Additive manufacturing helps overcome these limitations, offering multiple advantages beyond traditional [1]

Personalized Medicine

Personalized medicine is a medical model that uses characterization of individuals' phenotypes and genotypes—such as lifestyle data, medical imaging, or molecular profiling—to tailor treatment at the right time, determine predisposition to disease, and deliver timely prevention [2]. According to the Research and Innovation Unit of the European Commission, personalized medicines address the challenges of conventional medicines that are often ineffective for many patients. This approach allows for custom made prevention and treatment strategies optimized for individuals or groups, reducing wasted resources on trial and-error treatments [2].

3D printing technologies have emerged as powerful tools for manufacturing personalized medicines, providing healthcare professionals with a wide range of techniques to fabricate custom-made formulations. Initially, these technologies were developed to produce solid dosage forms from simple formulations, containing required drugs and combinations of different release profiles adapted to patient needs.

Basic Procedure of 3D Printing

Several techniques are available, including:

- 3D inkjet printing
- 3D powder bed printing
- Selective laser sintering differences, the fundamental workflow remains the same:

1. Product design using computer-aided design (CAD) software.
2. Conversion into a printer-compatible file format (commonly STL).
3. Preparation of selected materials.
4. Printing: raw materials are deposited or fused layer by layer.
5. Post-processing: drying, polishing, or other finishing steps.
6. Recycling: unused materials can be collected and reused [3,4].

Figure 2: Basic procedure of 3D printing, from CAD design to post-processing3D Printing of Medicines

3D printing involves the accumulation of a series of two-dimensional (2D) layers that together [9, 10].
3D Printing Techniques Used in Pharmaceutical Manufacturing r form a three-dimensional
(3D) object. The versatility of 3D printing techniques, along with the lower cost of the required equipment, has made these technologies increasingly popular. In pharmaceutical applications, 3D printing allows medicines to be personalized in a precise and individualized manner according to each patient's needs.
3D printing offers endless possibilities for manufacturing medicines in various dosage forms, including topical, oral, and parenteral formulations. It also enables the development of personalized implants that are customized to the dimensions of a patient's tissues or body cavity [5, 6, 7, 8]. These implants are commonly fabricated from 3D-printed hydrogels, which possess high water content while remaining biodegradable. The implant designs are created using computerized medical imaging techniques such as MRI. Furthermore, 4D printing, where time acts as the fourth dimension, is under research to develop implants that can adapt after being integrated into the patient's body
Research on the application of 3D printing in the pharmaceutical field has demonstrated its significant potential for manufacturing a wide range of medicinal products. These studies have shown that 3D printing can be used to develop rapidly dissolving or dispersible formulations, Controlled-release systems, Gastro retentive tablets, Suppositories, Minitablets [11, 12].

1. Inkjet Printing Method

Inkjet printing is a technique that uses pattern-generating devices to digitally control and deposit tiny liquid droplets onto a substrate. It is a digital printing method that sprays microscopic liquid ink droplets onto a surface such as paper or fabric [13].

(a) Continuous Inkjet Printer (CIJ)

Continuous Inkjet (CIJ) printing continuously ejects a stream of liquid droplets onto a substrate.
Droplets that are not required for printing are recycled.
In this process, pressure waves are introduced into the ink stream, causing it to break into uniformly sized droplets
Through nozzle vibrations. These droplets are then expelled from the nozzle. This technique provides rapid and
Continuous droplet generation while reducing the likelihood of nozzle clogging [13].

b) Drop-on-Demand Inkjet Printer (DOD)

These printers generally contain multiple nozzles, ranging from 100 to 1000. Unlike continuous inkjet systems, droplet ejection is driven by external pressure [14]. This technique is relatively simple, cost effective, and capable of high precision. It enables accurate placement of small droplets with controlled sizes while significantly reducing drug wastage [15, 16].

2. Thermal Inkjet Printer (TIJ)

Thermal Inkjet Printing uses thermal energy to eject droplets from the nozzle. The printhead contains embedded resistors that are in direct contact with the ink. When an electric current is applied, the resistors rapidly generate heat, producing a vapor bubble within the volatile fluid. The expanding vapor bubble forces a small volume of ink out of the nozzle as a droplet [17].

Piezoelectric Inkjet Printer (PIJ)

This technology composed of a piezoelectric element or actuator which that changes its shape in response to an electric voltage. This generates the pressure which heads to the fluid being ejected out of the nossle. After the element gets back to its actual shape, the nozzle is reloaded with the fluid and is ready to be activated again [18, 19].

THERMAL INJECT PRINTER

Thermal inject printer, also known as the Drop-on-Powder method, is an application of inkjet printing.
The printhead of a binder jet printer may be either thermal or piezoelectric. The process consists of a powder bed that is built layer by layer. A printer nozzle containing a liquid binder moves along the X-Y axis and deposits the binder onto the loose powder bed.
The powder is wetted by the binder droplets, resulting in hardening and solidification of the printed layer. Solidification occurs through the formation of binder bridges or by recrystallization of particles.
The fabrication platform gradually moves downward along the Z-axis, while the powder delivery platform moves upward. A roller spreads a fresh layer of powder over the previously printed layer. This process is repeated until the complete three-dimensional object is formed [19].

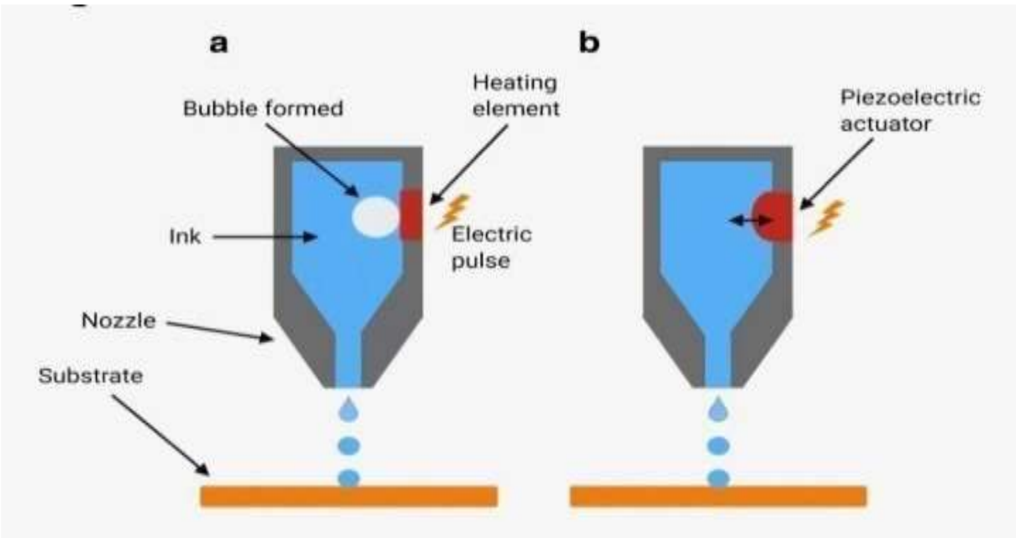

Figure 3: Schematic of (a) thermal inkjet and (b) piezoelectric inkjet printing mechanism

3. Implementation of 3D printing in Personalized Solid, Topical, parenteral Dosage FORM

Powder Binder Jetting is the only 3D printing technology that has reached industrial-scale commercialization for pharmaceutical manufacturing. Aprecia Laboratories implemented this technology to manufacture pritam, a 1000 mg levetiracetam oral dispersible tablet.

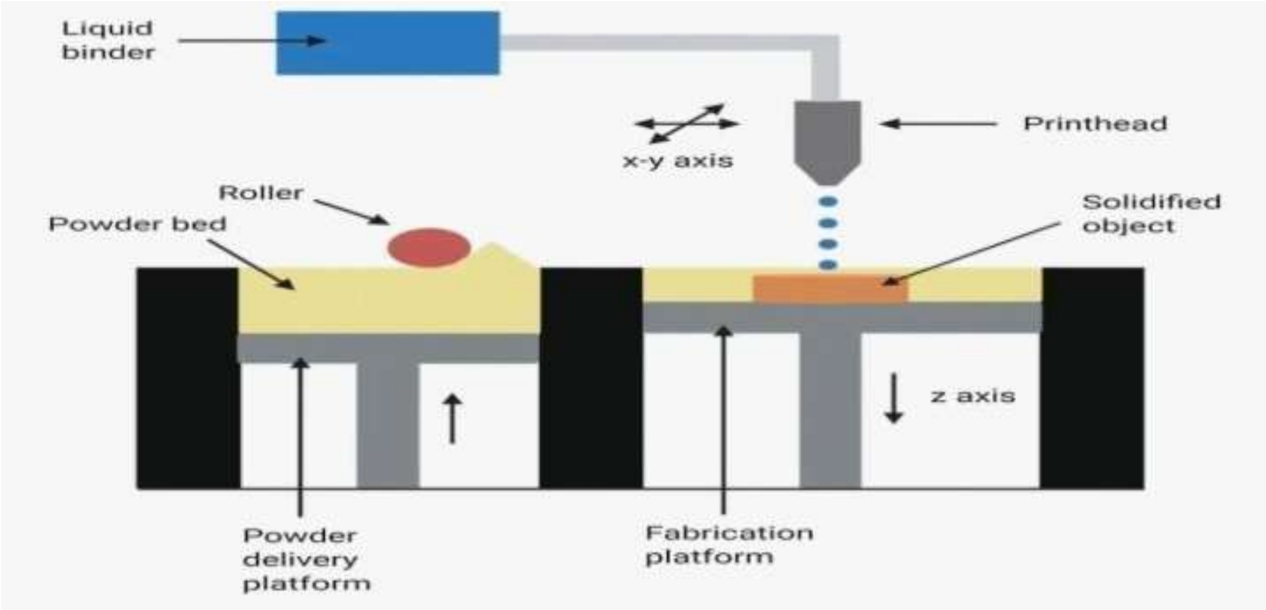

Figure 4: Schematic of the binder jet (powder bed) 3D printing process

BINDER JET PRINTER

This method does not require heat during tablet fabrication. Instead, it uses a powder bed and a liquid binder that joins each printed layer together.

The tablets are printed directly into blister packs, reducing the need to handle finished dosage forms or recycle unused powder.

The preformed or dispersible tablet shell and lid are assembled using an automated zip-dose assembly system.

The tablet disintegration time is less than one minute, facilitating easy swallowing and providing a rapid onset of action (21).

THE Rationale of Personalized Medicine

Personalized medicine (PM) involves tailoring therapies to participants' specific requirements, traits, and opinions [23]. Individualizing medications based on distinctive features is highly recommended in today's environment. However, it remains challenging to personalize therapies for a broader population with numerous variations.

Quality Control of Personalized Medicine

Quantifying the active pharmaceutical ingredient (API) and other constituents has both benefits and drawbacks. The choice of analytical methodology depends on the printed form [24].

Attenuated Total Reflectance Fourier Transform Infrared Spectroscopy (ATR-FTIR) has been utilized for quantitative evaluation of printed formulations.

Materials Used in 3D Printing Manufacturing

Three-dimensional (3D) printing is transforming pharmaceutical manufacturing and clinical pharmacy by enabling a shift from conventional large-scale production to the development of personalized, patient tailored dosage forms [25].

The selection of suitable excipients and materials for 3D printing drug products depends on several critical factors, including the intended drug release characteristics, the chosen printing technique [26, 27].

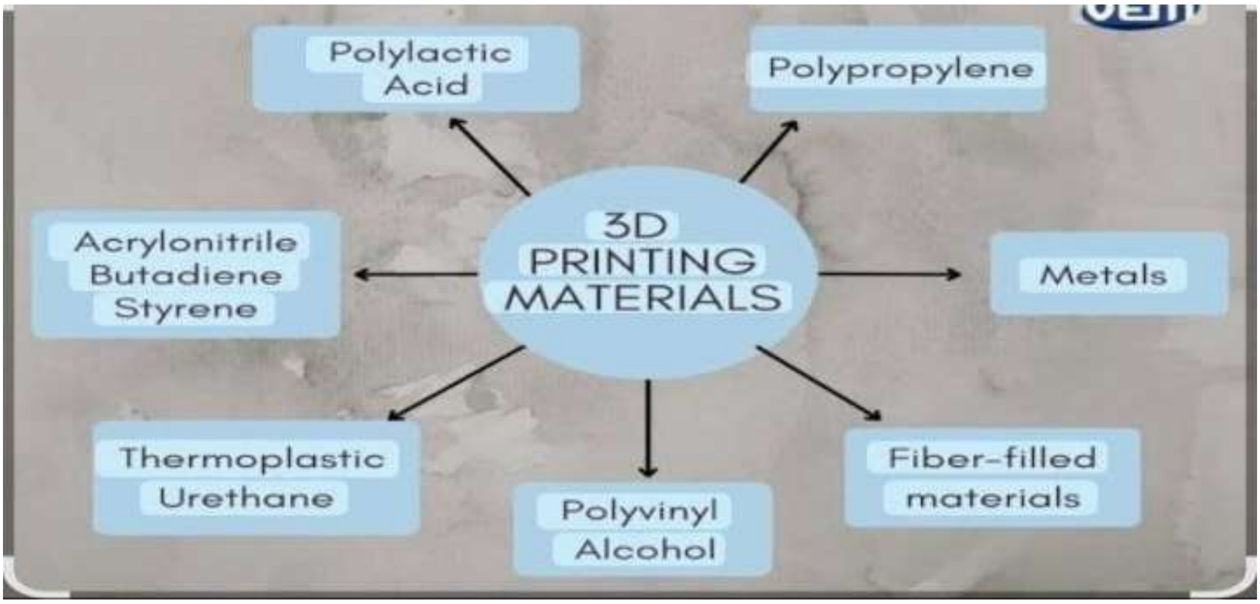

Figure 5: Overview of materials used in 3D printing

3. Materials for 3D printing

3.1 Polymers

The most often utilized components in this procedure are polymers. are a family of materials that include rubber, polymer blends, resin, and at least one cross-linked or chain-extended polymer that can be melted and shaped into various forms. Each of the several polymers used in 3D printing is selected for its unique properties and uses. This study examines and reviews the most popular polymers used in 3D printing [25].

An eco-friendly substitute for oil-based polymers, Polylactic Acid (PLA) is a biodegradable polymer made from renewable resources such maize starch, sugarcane, and tapioca roots [26]. Wallace Carothers created

PLA in the 1930s, and Cargill began producing it in the 1980s. Because of its biocompatibility and ease of processing, PLA is frequently used for 3D printing. It requires warping, denoted by a heated bed, and has a glass transition temperature between 190 and 230°C.

3.1.2. Polyvinyl Alcohol

Water-soluble, colorless, odorless, and extremely strong, Polyvinyl Alcohol (PVA) is a thermoplastic synthetic polymer. It is produced by hydrolyzing polyvinyl acetate, and the degree of hydrolysis determines its properties[27]. PVA's T_m ranges from 180°C (partially hydrolyzed) to 220°C (completely hydrolyzed), and its viscosity ranges from 3.4–52 m Pas to 4–60 m Pas.

3.1.3. Hydroxypropyl Methylcellulose

Hydroxypropyl Methylcellulose (HPMC) is known to be a biocompatible, non-toxic polymer that has been extensively used in the pharmaceutical setting for the 3D printing technology of controlled drug release. It creates a water-loving gel barrier, which controls drug transport in a slow manner[11]. HPMC forms a gel when plasticized, and softens rather than melts with the addition of plasticizers, permitting extrusion at low heat suitable for thermolabile drugs [28].

3.2. Bio-inks and gel-based materials

One of the most interesting developments occurring in pharmaceutical 3D printing, is that which involves use of soft materials (gels) and gel precursors, for example: hydrogels/bio-inks (Table 1) making it ideal with regard to patient centric formulations. Their potential to resemble living tissue and incorporate both hydrophilic and hydrophobic drugs makes them suitable for personalized, comfortable dosage and shape recovery occurs rapidly [30]. forms [29]. Polymeric hydrogels formulated with e.g., PEG, PVA, alginate, gelatin and collagen show shear-thinning behavior that facilitates smooth extrusion through a nozzle Using the realization that gel concentration or crosslinking degree can be varied to suit patient requirements, such as pediatric dosages or sustaining long term therapy.

Table 1: Common hydrogel/bio-ink materials used in pharmaceutical 3D printing

Material	Type / Origin	Key Property Relevant to 3D Printing	Role in Pharmaceutical Bio-inks
PEG (Polyethylene glycol)	Synthetic polymer	Shear-thinning behavior; tunable viscosity	Facilitates smooth extrusion through the printing nozzle
PVA (Polyvinyl alcohol)	Synthetic polymer	Water-soluble; biocompatible; tunable crosslinking	Adjustable gel strength for controlled drug release
Alginate	Natural polysaccharide	Rapid ionic crosslinking; rapid shape recovery	Patient-tailored gels for pediatric or long-term dosing
Gelatin	Natural protein	Biocompatible; thermoresponsive gelation	Loading of both hydrophilic and hydrophobic drugs
Collagen	Natural protein	Resembles native extracellular matrix	Supports tissue-mimicking, patient-centric bio-printed forms

3.3. Drug-polymer compatibility

In 3D printing, compatibility of the drug with polymer is important for a uniform and effective formulation. Stable molecular interaction leads to strong bonds in drug distribution and predictable release. When compatible, the drug is dispersed uniformly through the polymer matrix, allowing for smooth extrusion and maintaining dosage uniformity. Yet, incompatibility can lead to crystallization, phase separation, or change in release profiles which will be detrimental to the safety and efficacy of a 3D printed drug product [33].

A drug compatibility is an essential factor in 3D printing process as a result of heat and mechanical actions. Polymers such as HPMC, Eudragit provide protection against thermal degradation of drugs and PVA may bring about decomposition of thermolabile compounds [34]. Choosing appropriate glass transition temperature, wettability, and thermal resistance of the polymers can guarantee high bioavailability with sustainable release.

FUTURE PROSPECTIVES

As three-dimensional (3D) printing for drug delivery continues to advance, its integration with emerging technologies such as artificial intelligence (AI), digital health platforms, and smart materials is anticipated to usher in a new generation of intelligent, patient-tailored therapeutics [28].

One of the most transformative innovations in this area is four-dimensional (4D) printing, in which printed structures undergo controlled changes over time or in response to external stimuli such as pH, temperature, or light [29]. Recent investigations into 4D printing have demonstrated the development of stimuli-responsive dosage forms, including Shape-memory polymer-based floating systems, Electro responsive printed devices These advances highlight the potential of smart adaptive platforms to enable on-demand drug delivery that extends beyond static 3D-printing constructs[30].

AI-driven strategies are increasingly being applied to optimize 3D-printed formulations and structural designs. Machine learning tools, including conditional generative adversarial networks (cGANs), have been used to predict printability, processing conditions, and drug release behavior.

Recent developments in fused deposition modeling (FDM) have enabled the generation of novel printable formulations, pointing toward a data-driven approach for designing future personalized dosage forms [31].

The integration of nanotechnology with 3D printing may result in smart drug delivery systems. These systems are expected to provide Improved bioavailability, Improved bioavailability, Targeted drug delivery, Enhanced therapeutic efficacy [32].

Despite challenges, technological advancements are anticipated to make 3D printing an essential component of future precision medicine and patient-centered healthcare systems. Overall, 3D printing technology is expected to significantly improve healthcare outcomes [33,34].

CONCLUSION

Three-dimensional (3D) printing has emerged as a promising technology in personalized medicine, offering innovative solutions for patient-specific healthcare. It enables the fabrication of customized drug formulations, implants, prostheses, medical devices, and tissue-engineering scaffolds tailored to individual patient requirements. Through precise control over dosage, shape, size, drug-release characteristics, and the incorporation of combination therapies, 3D printing can improve therapeutic efficacy, minimize adverse effects, and enhance patient adherence [39–41].35

In addition, 3D printing has important applications in surgical planning, regenerative medicine, and personalized drug-delivery systems. These applications can contribute to improved diagnostic accuracy and better treatment outcomes. The integration of bioprinting, advanced biomaterials, artificial intelligence, and digital healthcare is expected to further expand the scope of 3D-printing technologies in medicine .

Despite its considerable advantages, several challenges must be addressed before 3D printing can be widely implemented in clinical practice. These challenges include high production costs, the limited availability of suitable pharmaceutical-grade printable materials, quality assurance, regulatory approval, reproducibility, and scalability for large-scale manufacturing . Continued research and technological innovation, along with collaboration among healthcare professionals, researchers, industry stakeholders, and regulatory authorities, are essential for establishing clear standards and facilitating the successful adoption of this technology.

In conclusion, 3D printing has the potential to transform modern healthcare by making personalized medicine more precise, effective, and patient-centered. With continued advancements, it is expected to play an increasingly important role in disease management, improving patients' quality of life, and shaping the future of pharmaceutical and medical sciences.

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