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Review Article

3D PRINTING TECHNIQUE: A REVIEW ON THE APPLICATIONS IN PHARMACEUTICAL MANUFACTURING

ABHISHEK YADAV*, MANISH YADAV, ASHISH KUMAR YADAV, SHWETA MISHRA, JITENDRA JENA, JITENDRA KUMAR RAI

Pharmacy College Azamgarh, Itaura, Chandeshwar, Azamgarh-276128, Uttar Pradesh, India

*Corresponding author: Ashish Kumar Yadav; Email: ashish979323@gmail.com

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ABSTRACT

In the realm of pharmaceutical manufacturing, 3D printing technology stands on the brink of a transformable revolution. This article passionately explores the boundless potential of 3D printing in shaping the future of pharmaceuticals, aiming to inspire researchers. It delves into crucial aspects: an overview of 3D printings in drug development, its advantages in drug production, and the pivotal role of personalized medicine. The article also discusses the creation of patient-specific medical devices, novel drug delivery systems, and the anticipated challenges in adopting 3D printing. Real-world case studies showcase successful applications while addressing the regulatory challenges associated with 3D-printed pharmaceuticals. By bridging existing knowledge gaps, this comprehensive article acts as a guiding light for those dedicated to advancing pharmaceutical research. It empowers researchers with profound insights into this disruptive technology, fostering innovation and collaboration within the community. The untapped potential of 3D printing in pharmaceuticals is vast and promising. Together, researchers can pioneer the future of pharmaceutical manufacturing, benefiting patients globally and propelling scientific advancement. Join us in this exhilarating journey of exploration and discovery as we harness the full capabilities of 3D printing for the betterment of healthcare and the progress of science.

Keywords: 3D Printing, Personalized medicine, Drug delivery

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INTRODUCTION

3D(three-dimensional) printing is an "additive manufacturing" technology, as opposed to the traditional manufacturing methods of "subtractive manufacturing," where a model is built using computer-aided design software, sliced, and transmitted to a printer, and the 3D printed object is then assembled. Then, a product is built utilising the layered manufacturing approach, layer by layer [1, 2]. Numerous new 3D printing technologies have developed as a result of research and development in the field. The American Society for Testing and Materials divided 3D printing technologies into seven categories based on their technical principles [3, 4], including material extrusion, binder jetting, powder bed fusion, vat photopolymerization, material jetting, directed energy deposition, and sheet lamination. Each 3D printing technology uses a different material, deposition technique, layering manufacturing mechanisms, and final product characteristics.

The usage of three-dimensional printing technology is widespread in a variety of industries, including the automotive, building, aerospace, and medical ones. Global interest in 3D printing research is now on the rise in the pharmaceutical industry [5, 6]. To meet a variety of clinical needs, precise control of drug release, a high degree of flexibility and creativity to customise pharmaceuticals, and a significant reduction in preparation development time, 3D printing offers advantages over conventional preparation technologies. These advantages include flexibility in the design of complex 3D structures within drugs, the adjustment of drug doses and combinations, and rapid manufacturing and prototyping [7-9]. Several pharmaceutical items, including immediate-release tablets, controlled-release tablets, dispersible films, microneedles, implants, and transdermal patches, have been manufactured using three-dimensional printing technology [10]. Binding jet 3D printing (BJ-3DP), Fused Deposition Modelling (FDM), Semisolid extrusion (SSE), and Melt extrusion deposition (MED) in material extrusion, as well as Stereolithographic (SLA), are the primary 3D printing technologies utilised in the pharmaceutical industry. At each stage of the drug development process, these technologies are described in table 1 along with their qualities, benefits, and drawbacks [11].

MATERIALS AND METHODS

The search was performed on PubMed/MEDLINE/Research Gate, and studies were selected according to their relevance and the objectives of this review. The following term was used in combination within the search string: ”3D(three-dimensional)”; “Personalized Medicine”; ”3D printing techniques”; “NDDS”;. The search was restricted to English and experimental studies.

3D Printing in pharmaceuticals

Additive manufacturing, sometimes referred to as 3D printing, describes several procedures used to create three-dimensional objects. To produce an object using 3D printing, successive layers of material are generated under computer control [2]. One of the fields of technology, art, and science that is now advancing freest is three-dimensional printing, which continues to expand its applications. According to ISO, 3D printing involves employing a print head, nozzle, or other printer technology to deposit material to create things. In this procedure, pieces are prepared using 3D models before being assembled layer by layer [3]. 3D printing is employed in innovative medicine delivery systems to produce functional tablets. These tablets are created in a way that they can pass regulatory examinations and meet the requirements for commercial tablets [4]. A cutting-edge method for quick prototyping, three-dimensional printing technology creates solid things by sequentially depositing several layers. The development and use of 3D printing have greatly accelerated innovation across a wide range of industries, including the aerospace industry, architecture, tissue engineering, biomedical research, and pharmaceuticals. Based on its adaptability and diversity, 3D printing technology appears to be the new method of the next industrial revolution.

As science and technology advance, 3D printing technology becomes sufficiently developed that anybody may use it using open-source software at a relatively reduced material cost [5]. The design and production of complex products have never been more flexible thanks to 3D printing technology, which may be used in personalized and programmed medicine [6]. It offers several benefits over the manufacture of conventional pharmaceutical products, including.

- High drug loading can be achieved with accuracy and precision, especially when a powerful drug is given in a small dose.
- Low production costs and the ability to use a wide range of pharmaceutical active ingredients, including those that are poorly water-soluble, peptides, and proteins, as well as medications with constrained therapeutic windows, can ultimately reduce material waste [7].

Three-dimensional printing technology has been used to create a variety of drug delivery systems, including oral controlled release systems, micro pills, microchips, drug implants, quick-dissolving tablets, and multiphase release dosage forms [8]. A layer-by-layer procedure called 3D printing may create 3D medicinal items from digital files. The 3D printing technology is unmatched in its flexibility, speed, and ability to manufacture pharmaceutical items of the necessary quality [9].

Table 1: Types of 3D printing techniques

Types of 3D printing technology	Technical characteristics			Advantages	Disadvantages	References
	Preprocessing	Print processing	Post processing			
BJ-3DP	Prefabricated powder bed or ink containing drug	Room temperatur e/heating	Removal and recovery of powder, drying of preparations	Wide range of available accipients	Lack of flexibility in product design	
				High drug loading capacity	Complex post-processing	
				No support material Required	High requirement for packing and transport	[11]
				Suitable for immediate release preparation	Large equipment	
FDM	Prefabricated powder bed or ink containing drugs	Heating	Removal of support material none	Simple and inexpensive equipment	Required to prefabricate drug-containing filaments with suitable mechanical property	
				Ability to create a variety of 3D structured preparations	Fewer material options available	
					High printing temperature	
					Low drug loading capacity	
SSE	Prefabricated semi-solid materials containing drug	Room temperatur e/heating	Drying/none	Simple and inexpensive equipment	Prefabricated semisolid materials with suitable properties	
				Can be printed at room temperature	Often requires post-processing	[11]
				Use of disposable syringes for easy change of material	Low printing accuracy	
MED	None	25-250 °C	None	High precision	The process of material mixing and melting	
				Wide range of available printing materials	The properties of the materials used need to be well understood in order to set the right parameters	
				Complete industrial production line available		
SLA	Prefabricated polymer monomers containing drug	Photopoly merization	Separation from untreated polymer monomers and re-curing	High printing accuracy and can be used to prepare microneedles	Few print materials available	
					Long preprocessing process	
				Can be printed at room temperature	Postprocessing process available	

Advantages of 3D printing in pharmaceuticals manufacturing

Personalized dosage (Customization for patients)

With 3D printing, pharmaceuticals can be customized to meet individual patient needs. This is achieved by precisely controlling the composition and dosage within each printed pill or tablet. For instance, a child may require a smaller, unique dosage, which can be accurately manufactured, ensuring effective treatment without unnecessary side effects [10].

Complex drug delivery systems (Precision medicine)

3D printing allows the creation of highly complex drug delivery systems that are otherwise challenging or impossible to produce using traditional methods. These systems can include multi-compartmental tablets or implants that release drugs at specific rates or locations in the body. Such precision is particularly valuable for diseases where targeted drug delivery is critical [11].

Improved solubility (Enhanced drug formulations)

Poor solubility often limits the effectiveness of certain drugs. 3D printing addresses this challenge by selecting polymers and printing techniques that enhance drug solubility. This means that drugs that were once difficult to dissolve can now be formulated in ways that improve their bioavailability and therapeutic impact [12].

Reduced waste (Sustainability)

Traditional pharmaceutical manufacturing can produce significant waste through processes like milling and compression. 3D printing, on the other hand, is an additive manufacturing process which minimizes material waste. This is not only environmentally friendly but also cost-effective, as it reduces the amount of material required for production [13].

Rapid prototyping (Accelerated drug development)

3D printing enables rapid prototyping of new drug formulations. Researchers can swiftly test various drug combinations and formulations, saving time and resources in the drug development process. This agility in testing can lead to quicker identification of effective treatments, ultimately benefiting patients and pharmaceutical companies alike [14].

Personalized medicine (PM)

Personalized medicine, also known as precision medicine, is a groundbreaking approach that has transformed the landscape of healthcare and pharmaceuticals. At its core, it recognizes that everyone is unique, and their genetic makeup, environment, and lifestyle play pivotal roles in determining their health and response to treatments. This paradigm shift from one-size-fits-all to tailored medical care has the potential to significantly enhance patient outcomes and reduce the burden of adverse effects [15].

The foundation of personalized medicine lies in the analysis of an individual's genetic information. Advances in genomics, exemplified by the Human Genome Project's completion in 2003, have provided a comprehensive reference for human genetic information. By examining a person's DNA, healthcare providers can uncover genetic variants, mutations, and predispositions to specific diseases. Pharmaceutical companies are leveraging this genetic information to develop targeted therapies. These drugs are designed to precisely target the genes or proteins associated with a particular disease, maximizing treatment efficacy while minimizing side effects. For instance, Herceptin (trastuzumab) is a targeted therapy used in breast cancer treatment, specifically for patients with the HER2 gene mutation [16]. Diagnostic tools, such as genetic tests, are integral to personalized medicine. They enable healthcare professionals to identify the most suitable treatment options for individual patients. Companion diagnostics, like the BRAF mutation test used alongside vemurafenib in melanoma treatment, exemplify the synergy between diagnostics and tailored therapeutics [17].

In practice, personalized medicine empowers physicians to create treatment plans tailored to a patient's genetic profile. This approach minimizes the "trial and error" often associated with conventional treatments and can lead to more successful outcomes. Research articles and clinical trials in fields like oncology have demonstrated the real-world applications of personalized treatment plans [18].

The benefits of personalized medicine extend beyond clinical outcomes. It offers patients the promise of treatments that are not only more effective but also potentially associated with fewer adverse reactions. However, it is important to consider the ethical and regulatory aspects, as personalized medicine involves sensitive genetic data. Ethical guidelines and regulatory frameworks provided by organizations like the FDA and EMA help ensure patient privacy, informed consent, and safety in the implementation of personalized medicine [19].

In conclusion, personalized medicine represents a monumental shift in healthcare, harnessing the power of genetic information to provide tailored treatment solutions. It improves patient outcomes, minimizes adverse effects, and offers a glimpse into the future of healthcare-a future where medicine is as unique as the individual it treats [20].

Role of 3D printing in personalized medicines

3D printing technology has revolutionized the field of personalized medicine by enabling the creation of patient-specific medical devices, implants, and drug delivery systems. Its key contributions include:

Custom implants

3D printing allows for the fabrication of personalized implants tailored to a patient's anatomy. This is particularly valuable in orthopedic and craniofacial surgeries, where precise fit and function are essential.

Anatomical models

Medical professionals use 3D-printed anatomical models for preoperative planning and surgical training. These models replicate a patient's unique anatomy, enhancing surgical precision and reducing complications.

Personalized drug formulations

3D printing enables the creation of patient-specific drug formulations with precise dosages and release profiles. This is especially beneficial in oncology and pharmacology for optimizing treatment outcomes.

Prosthetics and orthotics

Individuals with limb differences benefit from 3D-printed prosthetics and orthotics designed to fit their specific needs and preferences.

Dental applications

In dentistry, 3D printing is utilized for creating customized dental implants, crowns, and orthodontic devices, improving patient comfort and treatment outcomes.

Drug testing and development

Researchers use 3D-printed tissue models to study drug responses and disease mechanisms, facilitating the development of personalized medicine approaches.

The versatility of 3D printing empowers healthcare providers to deliver more precise and patient-centric care, ultimately improving treatment effectiveness and patient quality of life [21].

Advantages of personalized medicines

Tailored treatments

Personalized medicine customizes healthcare based on an individual's unique genetic, molecular, and clinical characteristics. This precision approach ensures treatments are most effective for each patient.

Improved outcomes

By targeting specific disease mechanisms or genetic factors, personalized medicine often leads to better treatment outcomes, reduced side effects, and higher patient satisfaction.

Early detection

Personalized medicine enables early disease detection through genetic screening and biomarker analysis, allowing for proactive interventions and improved prognosis.

Optimized drug selection

Pharmacogenomics identifies how a patient's genetic influence drug response, guiding the selection of medications with the highest likelihood of success.

Reduced healthcare costs

Targeted treatments and reduced adverse effects can lead to cost savings in healthcare by minimizing the need for trial-and-error treatments and hospitalizations.

Patient empowerment

Patients actively participate in their healthcare decisions, leading to a greater sense of control and engage in their treatment plans[22].

3D printing for patient-specific medical devices

3D printing has revolutionized the fabrication of patient-specific medical devices, such as implants and prosthetics, by enabling a tailored approach to healthcare. Here is a brief explanation of how 3D printing is used for this purpose:

Patient-specific design

In the realm of personalized medicine devices, 3D printing plays a pivotal role in creating patient-specific designs. Medical imaging data, such as CT scans or MRIs, can be converted into precise 3D models of the anatomical region in question [23]. These 3D models serve as the foundation for designing implants and prosthetics that perfectly match the patient's unique anatomy [24].

Tailored implants

Patient-specific implants are meticulously designed to match the exact dimensions and contours of the patient's body, ensuring a tight fit and optimal functionality [25]. This tailored approach significantly reduces the risk of complications, such as implant loosening or discomfort, leading to improved patient outcomes [26].

Rapid prototyping

3D printing enables rapid prototyping of medical devices, allowing for quick iterations and. Improvements in design and function [27]. Healthcare professionals and manufacturers can create multiple prototypes, test them, and refine the design before producing the final personalized device [28].

Material selection

3D printing offers a wide range of material options, including biocompatible polymers and metals, which can be chosen based on the specific requirements of the medical device [29]. Materials are carefully selected to ensure they are safe for implantation and can integrate seamlessly with the patient's body [30].

Prosthetics and orthotics

Beyond implants, 3D printing is instrumental in creating customized prosthetic limbs and orthotic devices [31]. These devices are tailored not only to the patient's anatomy but also to their lifestyle, ensuring comfort and improved functionality [32].

Minimized surgery time

Patient-specific 3D-printed implants lead to shorter surgery times as they are designed to fit precisely, reducing the need for extensive adjustments during surgery [33]. This can translate into quicker recovery for patients and reduced healthcare costs [34].

Cost-effectiveness

While the initial cost of 3D printing can be higher than traditional manufacturing methods, it often leads to long-term cost savings. Reduced revision surgeries, shorter hospital stays, and improved patient outcomes contribute to the cost-effectiveness of patient-specific 3D-printed medical devices [34].

3D printing in NDDS (Noval Drug Delivery System)

3D printing technology has emerged as a game-changer in pharmaceutical manufacturing, particularly in the development of novel drug delivery systems such as implants and transdermal patches. This cutting-edge approach offers a range of advantages that revolutionize drug delivery, ultimately benefiting patient care and treatment outcomes.

Implants

3D printing enables the precise fabrication of drug implants with intricate designs. Unlike traditional manufacturing methods, which can be limited in terms of customization, 3D printing allows pharmaceutical researchers to tailor implants to specific patient needs. This customization extends beyond the physical shape and size of the implant; it includes the ability to control drug release rates. By precisely engineering the structure of the implant, drug release can be modulated to match the required therapeutic regimen. This level of control is invaluable for long-term therapies where sustained drug release is necessary. Moreover, 3D printing facilitates the incorporation of multiple drugs into a single implant. This is particularly advantageous in cases where combination therapy is essential. With traditional manufacturing, producing such complex implants would be challenging, if not impossible. 3D printing, however, provides the precision needed to create multi-drug implants, enhancing treatment efficacy and patient convenience [35].

Transdermal patches

In the realm of transdermal patches, 3D printing offers innovations that improve drug delivery. By utilizing microstructures and precise design, 3D-printed patches can control drug release rates more effectively. These patches adhere to the skin better, ensuring consistent drug delivery while minimizing the risk of skin irritation. Furthermore, 3D printing customization capabilities extend to transdermal patches, allowing for patient-specific designs that account for unique skin characteristics. Another remarkable aspect of 3D printing for transdermal patches is the ability to create complex designs that incorporate multiple drugs. This opens doors to versatile treatment options, where a single patch can deliver multiple therapeutic agents simultaneously. Such versatility enhances the potential of transdermal patches in various medical applications.

In conclusion, 3D printing has significantly advanced the development of novel drug delivery systems, particularly in the domains of implants and transdermal patches. The ability to customize implant structures, control drug release profiles, and incorporate multiple drugs into a single device has tremendous implications for pharmaceutical manufacturing. These innovations not only improve patient care by tailoring treatments to individual needs but also enhance the efficiency and convenience of drug delivery, marking a transformative era in pharmaceutical research and development [36].

Case study and success story

Aprecia pharmaceuticals and spritam

Aprecia Pharmaceuticals is a pioneering pharmaceutical company that utilized 3D printing to develop SPRITAM, an epilepsy medication. This marked the first FDA-approved 3D-printed prescription drug.

Success story

Aprecia's use of 3D printing technology allowed them to create a highly porous, rapidly disintegrating tablet that dissolves with a sip of water. This innovation addressed a significant challenge in epilepsy treatment, where patients often struggle to swallow conventional pills. SPRITAM received FDA approval in 2015, demonstrating that 3D printing can be a game-changer for medication delivery and patient compliance [37].

FabRx's printlets"

FabRx, a UK-based pharmaceutical company, specializes in 3D printing personalized medicines. Their Print lets technology combines 3D printing with pharmaceutical science to create tailored drug formulations.

Success story

FabRx's Printlets have been used to customize medications for pediatric patients, the elderly, and individuals with specific dosing requirements. By 3D printing drugs with precise dosages and release profiles, they enhance therapeutic outcomes and patient adherence. This approach exemplifies how 3D printing can revolutionize drug development, ensuring that each patient receives the right medicine in the right form [38].

Glaxo Smith Kline (GSK) and ventolin evohaler

GlaxoSmithKline, a leading pharmaceutical company, utilized 3D printing technology to improve the design and production of the Ventolin Evohaler, a widely used inhaler for asthma patients.

Success story

By employing 3D printing, GSK was able to create a more efficient and precise inhaler device with optimized airflow and drug delivery. This innovation not only improved patient compliance through easier use but also ensured accurate dosing and enhanced therapeutic outcomes for asthma sufferers [39].

University of glasgow's 3D-printed microneedles

Researchers at the University of Glasgow developed 3D-printed microneedles for drug delivery through the skin. These microneedles can be tailored for specific medications and patient needs.

Success story

The 3D-printed microneedles offer a minimally invasive and painless way to administer drugs, especially for individuals who are averse to traditional injections. This innovation holds promise for various applications, including vaccine delivery and personalized medicine.

Future prospects and challenges

Future prospects

Personalized medicine

The future of pharmaceuticals lies in personalization, and 3D printing is at the forefront of this revolution. It enables the creation of bespoke medications tailored to an individual's unique needs, from dosage to formulate. Patients can receive treatments that are more effective with fewer side effects, enhancing overall healthcare outcomes.

Complex drug delivery systems

3D printing allows for the fabrication of intricate drug delivery systems, such as multi-compartment tablets or devices with controlled release mechanisms. These advanced systems can improve patient compliance, reduce dosing frequency, and enhance the targeted delivery of medications.

Accelerated drug development

Rapid prototyping using 3D printing can significantly accelerate the drug development process. Researchers can quickly iterate and test various formulations, reducing time and costs. This acceleration could lead to faster drug discovery and more efficient development pipelines [40].

Supply chain efficiency

On-demand 3D printing of pharmaceuticals has the potential to disrupt traditional supply chains. It reduces the need for extensive warehousing and transportation. This efficiency can result in cost savings, reduced waste, and improved access to medications.

Research and education

3D printing serves as an invaluable tool for research and education in pharmaceutical sciences. It provides tangible models of drug formulations, dosage forms, and delivery systems for experimentation and learning. This hands-on approach can enhance the understanding of complex pharmaceutical concepts [41].

Challenges

Regulatory compliance

Meeting stringent regulatory standards is paramount. Ensuring that 3D-printed pharmaceuticals comply with safety, quality, and efficacy requirements is complex and resource-intensive. Regulatory agencies must establish clear guidelines for 3D printing in the pharmaceutical sector.

Material selection

Selecting suitable materials for 3D printing that meet pharmaceutical-grade standards is challenging. Material consistency, biocompatibility, and suitability for various dosage forms are critical considerations. Ongoing research is needed to expand the range of printable pharmaceutical materials.

Validation and standardization

Developing robust validation processes for 3D printing and establishing industry-wide standards is an ongoing challenge. Variability in 3D printing processes and equipment can make validation complex and requires collaboration across the industry.

Intellectualism property

Navigating intellectual property issues related to 3D-printed pharmaceuticals is complex. Patent disputes and protecting innovative designs pose legal challenges. Clearer regulations and guidelines on intellectual property in 3D printing are essential [42].

Cost and accessibility

Initial setup costs for 3D printing equipment and technology can be prohibitive for some organizations, limiting accessibility. Efforts are needed to reduce costs and make 3D printing more accessible, especially in developing countries.

Bioprinting and complex structures

Bioprinting of living tissues and organs for drug testing and transplantation is a promising but intricate area. Challenges include ensuring cell viability, functional integration, and regulatory approval for bioprinter pharmaceuticals.

Ethical and regulatory dilemmas

The ability to print drugs at home or in small-scale settings raises ethical and regulatory questions concerning drug diversion, misuse, and patient safety. Striking a balance between accessibility and control is a significant ethical challenge [43].

CONCLUSION

In the swiftly evolving landscape of pharmaceuticals, 3D printing emerges as a revolutionary force with the potential to redefine healthcare. It promises personalized medicines tailored to individual biology and cost-effective, on-demand production for broader accessibility. This transformative technology beckons us to step into a brighter future, urging researchers, Innovators, and visionaries to act. We possess the power to shape a world where healthcare is uniquely tailored, universally accessible, and profoundly transformative. With 3D printing as our catalyst, we embark on a journey toward a healthcare revolution that can enhance countless lives and advance pharmaceutical science. Researchers and pioneers must seize the opportunity to planer innovations and reshape the future of medicine. This article serves as a guiding light, illuminating the uncharted territories of 3D printing in pharmaceuticals, not only highlighting potential applications but also navigating the intricate regulatory landscape. As a beacon of knowledge, it fills the gaps in our understanding, offering a roadmap to explore this transformative field. By forging ahead into this uncharted territory, researchers have the chance to effect meaningful change in medicine and push the boundaries of what is possible.

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CONFLICT OF INTERESTS

Declared none

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