NaSTech
Journal of Natural Sciences and Technologies
2024, 3(2), pp. 323-326, DOI: 10.5281/zenodo.14542537

3D PRINTING TECHNOLOGIES IN PHARMACEUTICALS: OPPORTUNITIES AND PROSPECTS

Bohdan Misan[1], Igor Nevliudov[1], Olena Ruban[2]
[1]Kharkiv National University of Radioelectronics, Ukraine
[2]National Pharmaceutical University, Ukraine
bohdan.misan@nure.ua, igor.nevliudov@nure.ua, Ruban_elen@ukr.net

ABSTRACT

In recent years, additive manufacturing, commonly known as 3D printing, has become an increasingly critical tool in the medical field due to its ability to produce unique, patient-specific devices. This technology enhances treatment efficacy by allowing for the customization of medical solutions tailored to individual patient needs. Additionally, 3D printing significantly reduces the time and cost associated with the production of medical devices and components. Specifically, it plays a key role in the development of implants, prosthetics, and personalized medical instruments, thereby positively impacting the personalization of healthcare. With the advancement of novel biocompatible materials, 3D printing enables the fabrication of products possessing the necessary mechanical properties for a diverse range of medical applications.

Keywords: 3D Printing Technologies, Additive Manufacturing, Medical Field Applications, Patient-Specific Devices, Customization, Implants, Prosthetics, Personalized Medical Instruments**.**

1. THE AIM OF THE STUDY

The study aims to investigate the innovative potential of 3D printing technology within the medical field, specifically its capacity to foster new treatment methodologies, develop individualized medical devices, and fabricate pharmaceutical dosage forms. By enabling adaptation to the specific anatomical and physiological characteristics of patients, 3D printing presents a promising avenue for advancing medical research and practice.

2. MATERIALS AND RESEARCH RESULTS

The history of the development of 3D printing begins in the 1980s, when the first prototypes for the rapid fabrication of objects through layer-by-layer printing were created. Gradually, the technology improved, finding applications in various fields, including medicine. A particularly rapid advancement of 3D printing in medicine started after the FDA approved the first drug created using 3D printing technology—Spritam (levetiracetam) in 2015. This milestone was significant because the drug had high porosity, which ensured rapid dissolution. This was made possible only due to the unique capabilities of 3D printing, allowing the creation of structures with specific properties that are difficult to achieve with traditional methods [1].

Currently, several different 3D printing technologies are used in medicine, each with unique advantages and specialized methods. PolyJet and MultiJet Printing (MJP) provide high accuracy and allow for the creation of objects with great detail. PolyJet stands out for its ability to use multiple materials simultaneously, making it suitable for complex anatomical models and personalized prostheses. MJP is similar to PolyJet but uses a thermal jet method, where the material is heated before application and polymerized using ultraviolet light. MJP is often used in dentistry and orthopedics due to its high precision. Binder Jetting employs layer-by-layer deposition of powder and a binding agent, allowing for the production of items with porosity necessary for certain medical applications, such as creating bioactive implants. Binder Jetting provides control over the material's structure, enabling the fabrication of objects with complex shapes, including drug delivery systems or scaffolds for tissue regeneration[2,3]. Vat photopolymerization, which includes stereolithography (SLA), digital light processing (DLP), and CLIP technology, is based on the curing of photopolymers under the influence of light. SLA uses a laser to gradually solidify the liquid material, DLP uses a digital projector to cure layers, and CLIP allows for continuous printing at high speeds. The high accuracy of these methods makes them suitable for creating medical products with complex shapes, such as models for preoperative planning[4]. Selective Laser Sintering (SLS) and Selective Laser Melting (SLM) use a laser to sinter or melt powders into a solid object. These methods are particularly useful for creating strong, complex metal or polymer products. SLS is a popular technology in orthopedics, while SLM is used in manufacturing durable metal implants[5]. Fused Deposition Modeling (FDM) uses a thermoplastic material that is melted and applied in layers to form an object. This is one of the most popular and accessible technologies, often used to create orthopedic prostheses and other medical devices that do not require extremely high levels of detail. Direct Ink Writing (DIW) employs viscous materials ("inks") to create porous structures, including biomaterials that can incorporate living cells. This technology enables the fabrication of structures for tissue engineering, such as scaffolds for cell growth or the creation of porous implants, and is promising in regenerative medicine. In addition to researching 3D printing methods, significant attention is devoted to the biocompatibility of materials used in the medical field. Studies focus on exploring and improving materials for 3D printing to ensure their safety, effectiveness, and stability in medical conditions. Polymers used in 3D printing can be categorized into biocompatible polymers, metals and alloys, and ceramics. Biocompatible polymers are materials that do not cause negative reactions in the body, making them ideal for medical applications[6,7,8]. They can integrate with tissues without causing irritation or rejection, which is crucial for use in implantology, prosthetics manufacturing, and medical devices. Some biocompatible polymers are also biodegradable, meaning they break down in the body into non-toxic products like water and carbon dioxide. This makes them suitable for temporary implants that can dissolve over time without requiring additional surgical removal. Biocompatible polymers are also widely used in regenerative medicine. They are utilized to create scaffolds that serve as a foundation for the growth of new cells and tissues. These scaffolds maintain the form and structure necessary for regeneration and decompose over time, leaving newly formed tissues fully integrated into the body. Metals and alloys are among the strongest materials used for medical 3D printing, especially in orthopedics and implant manufacturing. The most commonly used are titanium, cobalt-chromium alloys, and stainless steel. Titanium offers high strength and lightness, making it ideal for creating orthopedic implants such as hip and knee prostheses. Metals also demonstrate high biocompatibility, especially after special surface treatments that enhance integration with bone tissues. Metal alloys provide high wear resistance and durability, which is critically important for implants that withstand heavy loads. For example, cobalt-based alloys are often used in implants for knee and hip joints because they are resistant to corrosion and can withstand pressure well. Ceramic materials have both advantages and disadvantages for use in medicine. Their main advantages are biocompatibility and excellent mechanical properties, such as hardness and wear resistance, making them particularly useful in surgery and dentistry. For example, ceramics are often used for dental implants due to their similarity in properties to natural bone tissue. Additionally, some types of ceramics can stimulate bone tissue growth, which is beneficial for implantology. However, ceramics are brittle materials and can be prone to cracking or even breaking under high loads. Because of this, they are not always suitable for applications where high bending or tensile strength is required. Therefore, ceramic materials are usually used in cases where hardness and wear resistance are critically important, rather than flexibility. Among the polymers actively used in the medical field are materials like MED610, Clear RGD810, and Vero PureWhite RGD837, each possessing unique properties and advantages for specific medical applications. MED610 is distinguished by its high biocompatibility, allowing it to be used for products that come into contact with human tissues. This material is often employed in creating temporary implants and prostheses, as it meets safety standards and demonstrates good tolerability in the body. Research indicates that MED610 has a low risk of causing allergic reactions or cytotoxic effects, making it one of the most promising materials for medical products. Clear RGD810 is a material with high transparency and good mechanical strength, making it ideal for creating anatomical models needed during surgical preparation or for educational purposes. It is also used to produce accurate, transparent models of organs and tissues, enabling physicians to better assess the complexity of a case. Due to its transparency and resistance to mechanical wear, Clear RGD810 meets the requirements for use in complex medical conditions. Vero PureWhite RGD837 has high rigidity and is also biocompatible, making it suitable for manufacturing medical devices and instruments that come into contact with the patient's body. This material is widely used in orthopedic and dental products due to its strength and stability, as well as positive results in tests for biological inertness, confirming its safety in medical applications[10].

During the study, key indicators determining the suitability of samples for medical applications were considered: cytotoxicity, temperature resistance, and chemical stability. According to the research, the materials MED610, Clear RGD810, and Vero PureWhite RGD837 demonstrated low levels of cytotoxicity. This is crucial because contact with the human body requires that the material does not cause inflammation or allergic reactions. Tests using cell lines showed that after polymerization, these materials become inert and safe, but residual particles of uncured photopolymer require thorough removal. For instance, PolyJet technology necessitates special cleaning to eliminate cytotoxic residues. Medical devices are often subjected to thermal treatment for sterilization, making temperature resistance an important characteristic. Metallic materials such as titanium and cobalt-chromium alloys exhibit high thermal stability and can withstand the high temperatures required for autoclaving. Ceramics also endure high temperatures, rendering them suitable for sterilization[11]. Biocompatible polymers like MED610 may have limited temperature resistance, so alternative sterilization methods such as UV treatment or low-temperature sterilization are employed. In addition to resistance to thermal treatment, the chemical stability of materials is also critical, as devices may come into contact with biological fluids or pharmaceuticals[12]. Metals generally possess high chemical stability and are resistant to corrosion after special treatment, making them durable for long-term implants. Polymers can be less stable and may alter their properties under the influence of certain substances, but materials like Clear RGD810 demonstrate good chemical resistance under controlled conditions, maintaining transparency and integrity when in contact with biological fluids. Research findings also indicate that each 3D printing technology has its own advantages and limitations for medical applications, depending on the material, printing parameters, and potential side effects. Among the technologies studied, the following can be highlighted. **PolyJet** provides high resolution and the ability to use multiple materials simultaneously, making it ideal for personalized anatomical models and implants. However, the polymers used in PolyJet may sometimes exhibit cytotoxic properties in their uncured state, necessitating thorough cleaning to remove residual photopolymers. **Selective Laser Sintering (SLS)** and **Selective Laser Melting (SLM)** are ideal for producing strong, durable products, particularly in orthopedics. SLS utilizes polymers and metals to create complex shapes with high mechanical stability, while SLM offers even greater strength through complete melting of metals. The drawbacks include the high cost of equipment and the requirement for controlled conditions to prevent deformations and ensure material stability. **Binder Jetting** allows for the fabrication of porous structures, which can be beneficial in the biomedical field for creating implants and scaffolds that promote tissue regeneration. However, materials used in Binder Jetting require additional biocompatibility testing, as some binding agents may cause undesirable reactions. **Fused Deposition Modeling (FDM)** is an accessible and popular technology used for creating orthopedic and other prostheses. Nevertheless, due to the relatively low detail and strength of the products, this technology is more frequently applied to temporary medical devices. To meet medical standards, 3D-printed products must not only be effective but also safe for the patient. Evaluating biocompatibility, durability, and compliance with safety standards is crucial for the adaptation of 3D printing in the medical field. PolyJet technology is one of the most flexible in terms of personalization and high resolution, which is vital for medical implants and anatomical models. PolyJet complies with medical standards due to its precise processing capabilities and the use of biocompatible materials like MED610. SLS, with its high strength and ability to print complex structures, is also suitable for manufacturing medical devices, particularly orthopedic implants. Binder Jetting shows promise for producing porous medical products that can facilitate tissue growth but requires adaptation to medical standards. The use of binding agents in this technology demands additional testing to ensure biocompatibility. SLM, which enables the creation of durable metal implants, also meets medical standards due to the high strength of the products and the ability to sterilize them. This technology is widely used in orthopedics, as the manufactured products exhibit high stability and integrate well into the body. Overall, PolyJet and SLS are considered the best technologies for medical applications due to their biocompatible materials and compliance with safety and quality requirements. Binder Jetting and SLM also hold great potential but require additional adaptation and testing to fully meet all medical standards. The future prospects involve the development of new biocompatible materials. The further advancement of 3D printing in medicine requires the improvement of materials to enhance their biocompatibility and safety. One of the critical aspects is the development of non-toxic binding agents and biocompatible resins that can be used in binding technologies like Binder Jetting or in photopolymer methods such as PolyJet. Biocompatible resins and materials that decompose into non-toxic components are important for minimizing risks associated with immune reactions and cytotoxicity. As the requirements for medical materials become more stringent, the development of polymers and composites that combine mechanical strength with minimal biological reactivity will help expand the range of applications for 3D-printed implants and prostheses in medical practice. Automation and software optimization are also crucial. The integration of artificial intelligence (AI) and machine learning into 3D printing opens up possibilities for automation and increased process accuracy. AI can help automatically adjust printing parameters, taking into account the material, design, and desired properties of the final product, which will reduce human factors and optimize the printing process for various medical applications. Moreover, AI allows for the creation of systems for automatic defect detection at early stages of printing, which can significantly reduce waste and enhance the safety and effectiveness of medical products. Implementing such solutions will facilitate the adaptation of the technology to meet medical standards and make 3D printing more accessible for use in complex and personalized projects. Post-processing and surface enhancement of products are key stages in ensuring the safety and quality of medical products. For medical 3D-printed items, surface smoothness, wear resistance, and aesthetic appearance are particularly important. Further research into surface treatment methods such as grinding, polishing, painting, and galvanization aims to improve the functional and aesthetic properties of the products. For example, galvanization allows for the addition of metal coatings to the surface, which can enhance biocompatibility, corrosion resistance, and wear resistance. The development of coating methods will also enable the creation of antibacterial or anti-allergenic coatings, which is especially important for implants and instruments that come into contact with biological tissues. Post-processing and surface enhancement of products will help meet medical standards and improve comfort and safety for patients.

3. CONCLUSION

Research demonstrates that 3D printing technologies have great potential for application in the medical field due to their ability to provide high precision, adaptability, and the capability to create personalized medical products. A comparative analysis of different printing methods has shown that each technology has its advantages and limitations depending on specific medical applications. For example, PolyJet and SLS are suitable for high-precision anatomical models and orthopedic implants, while Binder Jetting is promising for creating porous structures that promote tissue regeneration. 3D printing technologies are already contributing to the development of personalized medicine, allowing for the creation of implants, prosthetics, and other devices that are maximally adapted to the anatomical features of individual patients. Moreover, they open up new opportunities in medical research and development by providing scientists and physicians with tools to create accurate models of organs and tissues, significantly simplifying the planning and preparation processes for complex medical interventions. However, further research is needed to improve the biocompatibility of materials and expand the capabilities of the technology. Specifically, the development of new polymers, biocompatible resins, and non-toxic binding agents will help minimize the risks of side reactions and enhance the long-term stability of products. Subsequent studies should also focus on expanding the range of materials, optimizing printing parameters, and improving post-processing methods to ensure compliance with strict medical standards and patient safety. Thus, 3D printing is a promising technology capable of revolutionizing the medical field, and its further development will allow for even greater precision, biocompatibility, and effectiveness in patient treatment.

REFERENCES

[1] Ngo, T.D.; Kashani, A.; Imbalzano, G.; Nguyen, K.T.; Hui, D. Additive manufacturing (3D printing): A review of materials, methods, applications and challenges. *Compos. Part B Eng.* **2018**, *143*, 172–196.

[2] Mohammed, A. A., Algahtani, M. S., Ahmad, M. Z., Ahmad, J., & Kotta, S. (2021). 3D Printing in medicine: Technology overview and drug delivery applications. *Department of Pharmaceutics, College of Pharmacy, Najran University, Najran 11001, Saudi Arabia; Department of Pharmaceutics, Faculty of Pharmacy, King Abdulaziz University, Jeddah 21589, Saudi Arabia.*

[3] Li HZ, et al. Dental ceramic prostheses by stereolithography-based additive manufacturing: potentials and challenges. *Adv Appl Ceram.* 2019;118(1–2):30–36. doi: 10.1080/17436753.2018.1447834.

[4] Gonzalez G, et al. Materials Testing for the development of biocompatible devices through Vat-polymerization 3D printing. *Nanomaterials (Basel)* 2020;10(9):1788. doi: 10.3390/nano10091788.

[5] Charoo, N. A., Barakh Ali, S. F., Mohamed, E. M., & co-authors. (2020). Selective laser sintering 3D printing– an overview of the technology and pharmaceutical applications. *Drug Development and Industrial Pharmacy*, 46(7), 1152-1162.

[6] Kristiawan, R. B., Imaduddin, F., & Ariawan, D. (2021). A review on the fused deposition modeling (FDM) 3D printing: Filament processing, materials, and printing parameters. *Open Engineering, 11*(1), 644-660.

[7] Rajan, K., Samykano, M., Kadirgama, K., & Others. (2022). Fused deposition modeling: process, materials, parameters, properties, and applications. *International Journal of Advanced Manufacturing Technology, 118*(5-6), 1781-1800.

[8] Shahzad, A., & Lazoglu, I. (2021). Direct ink writing (DIW) of structural and functional ceramics: Recent achievements and future challenges. *Composites Part B: Engineering, 215*, 108787.

[9] Wang, L., Ma, Q., & Ding, Y. (2021). Polylactic acid blends and composites: Processing, properties, and medical applications. *Materials Science and Engineering: C*, 128, 112333.

[10] Königshofer M, et al. Mechanical and dimensional investigation of additive manufactured multimaterial parts. *Front Phys.* 2021;9:635736. doi: 10.3389/fphy.2021.635736.

[11] Li, X., Wang, C. T., Zhang, W., Li, Y., & Li, B. (2020). Additive manufacturing of titanium alloys for biomedical applications: A review. *Journal of Materials Science & Technology*, 35(2), 285–305.

[12] Wang, X., Jiang, M., Zhou, Z., Gou, J., & Hui, D. (2017). 3D printing of polymer matrix composites: A review and prospective. *Composites Part B: Engineering*, 110, 442–458.