3D Printing in Manufacturing Sections of Pharmaceuticals and prosthetics: An overview

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ABSTARCT

In 2020 to 2021 the new research in the pharmacy and biotechnology field increases rapidly. The research of artificial intelligence (AI) in medical science also opened a new platform after the covid pandemic. Many companies are also investing huge amounts of money to newer vaccine and New Drug Delivery Systems (NDDS) associated with artificial intelligence. Computed tomography (CT) scan and magnetic resonance imaging (MRI) are two important tools for prosthetics preparations. Newer engineering has the capability for the preparation of novel dosage forms as target delivery system. However, the formulation of NDDS at commercial scale is limited to quite a bit and the factories are still producing the oral drug delivery system, mainly with controlled-release tablets. The application of AI and 3D printing technology in the pharma industry has brought into being a new purview in the delving of manufacturing for replacing and repairing the defected organs like kidneys, heart, eyes, lungs, etc. In this article, we are deliberating the perspective role of AI and 3D printing in the manufacturing of pharmaceuticals.

Keywords: 3D printing; Artificial intelligence; Prosthetics; Dosage form

1. INTRODUCTION

3D printing technology can design and carve any sculpture. Groundworks are going in the field of aeronautical design, carving of machines and buildings, warfare design, fashionable dress tailoring, API manufacturing, and biomedical engineering. Three-Dimensional Printing has a broad spectrum of utilization as tissue engineering [1-3]. organ printing, disease prediction, production of biomedical devices, and the design of new drug moiety and formulation developments in the biological field [4,5].

From the data originated by various techniques like computerized tomographic (CT) scan and magnetic resonance imaging (MRI), determining the complex anatomical and histological structures according to the need of patient can be fabricated. Supplanting and redressing the non-functioning organs like kidney, heart etc. that imitate the same functions as that of original are some additional uses of this technology. wearable cloths, spectacles, parts of motor vehicle can also be manufactured. Computerised programmable software is used here and hence is called layered manufacturing [2].

2. 3D PRINTING PROCEDURE

A virtual 3D design of an object is prepared by using digital design software like Onshape, Solidworks, Creo parametric, Autocad, Autodesk etc. is created.

↓

This digital model is then turns into stereolithography or (.STL) format

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Then the stereolithography file is converted into G file. It is done by cutting and separating the design into a series of 2D cross-sections by a software which is installed in the 3D printer

↓

The material will deposit 3 dimensionally to form the object [7]

↓

Projection micro stereolithography based 3D printing and its applications

↓

Maximum numbers of 3D printing technologies are compatible with (.STL) file format. If any software is not compatible with .STL then it is done by using software like Magics may be used during conversion. Some other type of software like additive manufacturing file format (AMF) and 3D manufacturing format (3MF) are used because .STL cannot handle the material for manufacturing, adding color, sharpness like features [8].

Now a days the 3D printing technology is used in API and pill formulation, tablet formulation like nifedipine, implant like rifampicin sodium, levofloxacin hemihydrate, caplet, oral film, facial mask manufacturing [6].

2.1. Types of 3D printing technology

2.1.1. Fused deposition modelling (FDM)

Here in this technique the polymer is liquified and passed through a heated nozzle. After layer formation the proper shape of the figure is formed. The nozzle rotates against three axis and deposits to form the figure.

2.1.2. Thermal inkjet (TIJ) printing

It works by heating and forming of bubble vapour thus the bubble nucleates and causes expansion

2.1.3. Inkjet printing

Here the powder material is used as the substrate. After spraying by the nozzle, the powder get solidifies to form solid mass.

2.1.4. Zip dose

This is applicable for manufacturing of highly porous material having high dissolution and disintegration [7].

2.1.5. Vat photopolymerization

Vat Polymerization is a process in 3D printing technology in which 3D printing can be done by using photopolymer synthesis. Digital polymer gets solidifies while exposed to digital light. It is light-induced polymerization where materials like photopolymers, radiation-curable resins, and liquid are collected in vats, which are successively cured into layers, one layer at a time by irradiating with a light source, thereby providing a 2D patterned layer. Here the process involves are stereolithography (SLA), digital light processing (DLP), and continuous direct light processing (CDLP) [16]. The vat is lowered from the top of the resin. UV light solidifies the resin layer by layer. The vat moves downwards and layers are built one by one. Some machines use a saw which moves between layers in order to provide a smooth resin base to build the next layer on. After finishing, the vat is drained of resin and the object removed. Depending on the orientation of light source and the surface where polymerization of the photoactive resin occurs.

2.2. Advantages of 3D printing in the pharmaceutical manufacturing field

It is more accurate, reliable, speedy and can be used in the moulding of items like implants, prosthetics etc. fabrication of medical devices, surgical tools, prosthetics, fixtures can be done by the technique. Patient specific prosthetics, medical device can be manufactured based on the size. The process can be implemented on the small-scale production, complex designing also can be done and the production cost is also low. It can be implemented on complex drug release profiles

2.3. Disadvantages of 3D printing in the pharmaceutical manufacturing field

In inkjet printing, there should be a proper flow of the ink for printing otherwise printing will not be done properly and ink formulation material should have the property of self-binding but should not bind to other printer elements. There may be issues with hardness as the resulting product is printed and drug release profiles can be hampered as the printing material can react with other binding materials.

2.4. Use of 3D printing

The main challenge of modern medical science is organ failure due to any disease, trauma due to burnt skin. Until the last century, the only one solution of the problem is the organ and tissue transplant from a donor or from a dead body. But there is a problem with the transplant and that is the shortage of fresh dead bodies and donors. So some people get treatment and others die due to shortage. The treatment is also needed a huge amount of money and long-term drug therapy as there may be the chance of rejection. In the conventional method of tissue engineering from a small tissue sample, stem cells are separated treated with growth factor, and then cultured in the incubator. Then the cell proliferation and differentiation occur and converted into a complete tissue. Among all type of polymer, hydrogels are considered to be the most suitable for building artificial tissues. In recent discovery artificial ear, liver, bones, cartilage, skin is prepared by help of hydrogel.

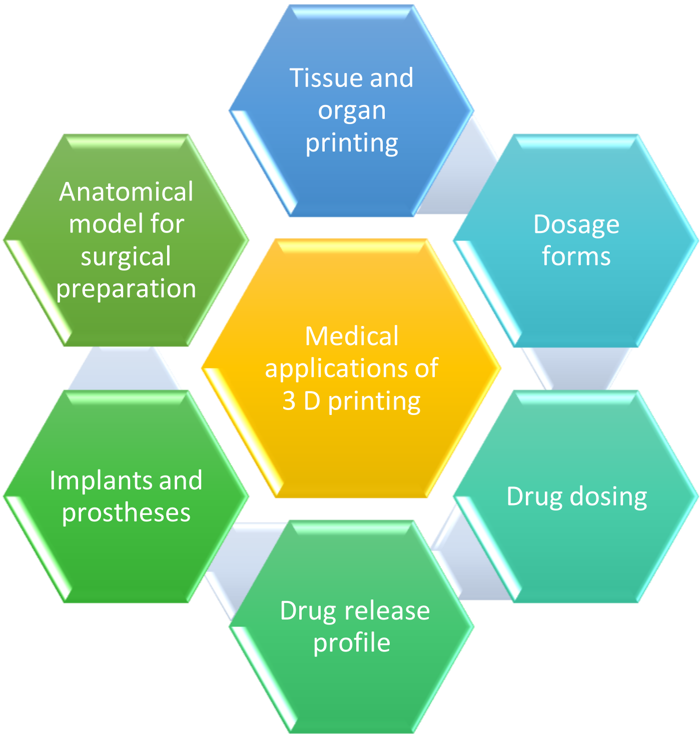

Figure 1. Applications of 3D printing technology

Several types of formulations can be manufactured using 3D printing. In pharmaceutical and biotechnological industries, the Inkjet-based 3D printing and inkjet powder-based 3D printing are used mainly. Microcapsules, antibiotics, and Nano suspensions are formulated by using 3D printing technology. The list of active and inactive ingredients used in 3D printing is mentioned in table 1.

Table 1: List of active and inactive ingredients used in 3D printing

Active pharmaceutical ingredients	**Inactive pharmaceutical ingredients**
Vancomycin	Glycerin
Ofloxacin	Methanol
Folic acid	Acetone
Dexamethasone	Surfactants (like Tween 20)
Theophylline	Kollidon SR
Acetaminophen	Ethanol-dimethyl sulfoxide
Paclitaxel	Propylene glycol
Tetracycline	Cellulose

2.5. Personalized drug dosing

Increasing the efficiency of dosage forms and as well as reducing the chances of adverse effects of the API, personalized medication should be promoted by 3 D printing. Drugs with narrow therapeutic index can easily be prepared using 3D printing; and, by knowing the patient's pharmacogenetic and genomic profile, the optimum dose can be given to the patient. New tablets can be prepared by the technique where multilayer can be done with multiple components that are not readily available in the market. [8]

2.6. Complex drug release dosing

3D printing has also been used to print antibiotic micropatterns on paper, which have been used as drug implants to treat Staphylococcus epidermidis. One example is the printing of a multilayered bone implant with a distinct drug release profile alternating between rifampicin and isoniazid in a pulse release mechanism.

2.7. Customized implants and prostheses

By using the x-ray and CT scan or MRI the measurement of the implantable tooth or bone can be determined and after that, with the help of 3D printing, the prosthesis can be prepared. Standard marketed, as well as complex surgical implants and prosthetic limbs, can be made with speed. Spinal dental and hip implants have been fabricated so far but their validation is a time-consuming process. Previously, in order to achieve a desired shape and size that fits perfectly, surgeons had to craft metal or plastic pieces and perform bone grafting and drill machines to modify the standard implants. This kind of problem will be very problematic in cases of fracture correction, especially in maxillofacial and neurosurgery due to the irregular shape of the skull and mandible whose fitting is a complex procedure. In this type of case, the 3D printing is very helpful [9].

2.8. Anatomical models for surgical preparations

Sometimes, in the field of neurosurgery and maxillofacial abscission, it is very difficult to gather detailed information about the skull architecture, maxillary curvatures, cranial nerves, and blood vessels from radiographic 2D images only. Minute error in the operational procedure can be fatal. Here comes the role of 3D models, which are more realistic and provide in detail comparison and contrast between a normal brain structure and a brain with deformity or lesions, which suggest the surgeon's safer procedures to follow. For liver transplantation, Japan's Kobe University Hospital had used 3D printed models by using a replica of patients' own organs, to find out how to precisely craft a donor liver with the least tissue loss. [10]

3. CONCLUSION

3D printing is very useful for pharmaceutical manufacturing, leading to personalized medicine focused on the patients' needs. It offers numerous advantages, such as the manufacturing speed. 3D printing has revolutionized the way in which manufacturing is done. It improves the design manufacturing and reduces lead-time and tooling costs for new products. 3D printing is a very important and useful tool for pharmaceutical manufacturing. The cost efficiency and manufacturing speed will be increased. Although buying a 3D printer is much cheaper than setting up a factory, the cost per item you produce is higher, so the economics of 3D printing don't compete against mass production yet. It also can't match the smooth finish of industrial machines, nor offer the variety of materials or range of sizes available through industrial processes. However, like so many household technologies, the prices will come down and the capabilities of 3D printers are required to improve over time.

4. CONFLICT OF INTEREST

The authors express no conflict of interest

5. AUTHORS' CONTRIBUTIONS

All authors made substantial contributions to conception and design, acquisition of data; took part in drafting the article or revising it critically for important intellectual content; agreed to submit to the current journal; gave final approval of the version to be published; and agreed to be accountable for all aspects of the work.

REFERENCES

1. Paul D, Sanap G, Shenoy S, Kalyane D, Kalia K, Tekade RK. Artificial intelligence in drug discovery and development. Drug Discov Today 2021;26(1):80–93. https://doi.org/10.1016/j.drudis.2020.10.010
2. Do TD, Sutter R, Skornitzke S, Weber MA. CT and MRI Techniques for Imaging Around Orthopedic Hardware. Rofo. 2018;190(1):31-41. https://doi.org/10.1055/s-0043-118127.
3. Patra JK, Das G, Fraceto LF, Campos EVR, Rodriguez-Torres MDP, Acosta-Torres LS, Diaz-Torres LA, Grillo R, Swamy MK, Sharma S, Habtemariam S, Shin SH. Nano based drug delivery systems: recent developments and future prospects. J Nanobiotechnology. 2018;16:71. https://doi.org/10.1186/s12951-018-0392-8.
4. Bishop ES, Mostafa S, Pakvasa M, Luu HH, Lee MJ, Wolf JM, Ameer GA, He TC, Reid RR. 3-D bioprinting technologies in tissue engineering and regenerative medicine: Current and future trends. Genes and Disease. 2017;4:185-195. https://doi.org/10.1016/j.gendis.2017.10.002.

5. Chena FM, Liuc X. Advancing biomaterials of human origin for tissue engineering. Prog Polym Sci. 2016;53:86-168. https://doi.org/ 10.1016/j.progpolymsci.2015.02.004.
6. Mathew E, Pitzanti G, Larrañeta E, Lamprou DA. 3D Printing of Pharmaceuticals and Drug Delivery Devices. Pharmaceutics. 2020; 12(3): 266. https://doi.org/10.3390/pharmaceutics12030266.
7. Vaz VM, Kumar L. 3D Printing as a Promising Tool in Personalized Medicine. AAPS PharmSciTech. 2021 Jan; 22(1): 49. https://doi.org/10.1208/s12249-020-01905-8.
8. Tucker GT. Personalized Drug Dosage – Closing the Loop. Pharm Res. 2017; 34(8): 1539–1543. https://doi.org/10.1007/s11095-016-2076-0.
9. Honigmann P, Sharma N, Okolo B, Popp U, Msallem B, Thieringer FM. Patient-Specific Surgical Implants Made of 3D Printed PEEK: Material, Technology, and Scope of Surgical Application. Biomed Res Int. 2018;2018:4520636. https://doi.org/10.1155/2018/4520636.
10. Inserra A, Borro L, Spada M, Frediani S, Secinaro A. Advanced 3D "Modeling" and "Printing" for the Surgical Planning of a Successful Case of Thoraco-Omphalopagus Conjoined Twins Separation. Front Physiol. 2020; 11: 566766. https://doi.org/10.3389/fphys.2020.566766.