The Pharma Innovation Journal 2019; 8(2): 169-173

www.ThePharmaJournal.com

The Pharma Innovation

ISSN (E): 2277- 7695
ISSN (P): 2349-8242
NAAS Rating: 5.03
TPI 2019; 8(2): 169-173

www.thepharmajournal.com
Received: 14-12-2018
Accepted: 18-01-2019

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A review on 3d printing in pharmaceutical

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Abstract
3Dimensional Printing is a fast prototyping or improver manufacturing is a fresh advanced skill that making 3D shapes in a layer by layer method straight by computer aided drug design technology. 3D printing has a high-class chance for the grounding of personalized medication to patient wants. In 3D printing sequential layers of material are shaped under computer control to create an object. It is consuming high degree of elasticity over controls over the release of drug which is formulated as in different layers of tablets. This review highlight with advantages, disadvantages, types, principle, steps involved, challenges and applications of 3D printing in Pharmaceutical.

Keywords: 3d printing, additive manufacturing, personalized medicine

Introduction

Today, three-dimensional printing is one of the firmest emerging divisions of technology, art and science, and quiet develops the applications. The term three-dimensional printing was clear by International Standard Organization as: fabrication of objects through the deposition material using a print head, nozzle, or another printer technology [1].

The overview and application of 3D printing (DP) have promoted huge innovations in many various fields, including aerospace industry, architecture tissue engineer, biomedical research and pharmacy. 3DP is gaining growing attention in pharmaceutical formulation development as an effective scheme to overcome some challenges of conventional pharmaceutical unit operations. For example, the conventional manufacturing unit operation involving milling, mixing, granulation and compression can result in disparate qualities of the final products with respect to drug loading, drug release, drug stability and pharmaceutical dosage form stability [2].

3D printing technology has allowed unprecedented flexibility in the design and manufacturing of complex objects, which can be used in personalized and programmable medicine [2]. 3D printing can play an important role in multiple active ingredient dosage forms, where the formulation can beas a single blend or multi-layer printed tablets with sustained release properties. This decreases the frequency and number of dosage form units consumed by the patient on a regular routine. 3D printing technology has high potential in individualized dosage form concept called the polyp ill concept. This carries about the possibility of all the drugs required for the therapy into a single dosage form unit.

Three dimensional printing technologies is a new rapid prototyping method in which solid objects are built by depositing numerous layers in structure. The rapid prototyping includes the building of physical models using computer-aided design in three dimensions. It is similarly known as additive manufacturing and solid free form fabrication. 3D printing technology has permitted unique flexibility in the design and manufacturing of complex objects, which can be utilized in personalized and programmable medicine [3].

The manufacture of solid objects by adding them layer by layer is called additive manufacturing. This term was promoted in the early 2000s and changed to a more popular one called “3D printing” [4]. All 3DP technologies are based on the principle of structure 20 objects by adding materials layer by layer [6].

In literature, the terms additive manufacturing, rapid prototyping, layered manufacturing, solid freeform fabrication, 3D fibbing, and 3D printing are used more or less synonymously. While “additive manufacturing” is favoured by most engineers, the term “3D printing” is far more common principally in the popular media. In this work, the terms “additive manufacturing” and 3D printing are both used to describe the same general manufacturing principle [7].

In 3D printing succeeding layers of material are formed under computer control to create an object1. 3D printing was used as a novel medicine formulation technique for production of

viable tablets capable of satisfying regulatory tests and matching the release of standard commercial tablets 2 [8].

3D printing is exclusive technology that was principal described by Charles Hull in 1986 [12]. Three-dimensional printing is powerful major innovations in a broad range of areas, including energy, biotechnology, medical devices, and many more [14]. Three-dimensional printing technology relies on computer aided designs to achieve unmatched flexibility, time-saving, and exceptional manufacturing capability of pharmaceutical drug products [15].

Advantages of 3d printing

Advantages of 3D Printed Drug Delivery are as follows:

1. Production of small batch is viable and the process can be completed in a single run.
2. 3D printers inhabit minimal space and are affordable.
3. Avoids batch-to-batch variations seen in bulk manufacturing of conventional dosage forms
4. As instant and controlled release layers can be combined due to the flexible design and manufacture of this dosage form, it helps in selecting the best therapeutic regime for an individual
5. In case of multi drug therapy with multiple dosing regimen, treatment can be customized to improve patient devotion.
6. High drug filling ability when compared to predictable dosage forms
7. Accurate and precise dosing of potent drugs which are administered at small doses
8. Decreases cost of production due to lesser material wastage.
9. Appropriate drug delivery for difficult to formulate active ingredients like poor water solubility, drugs with.
10. Fine therapeutic window.
11. Medicine can be tailored to a patient in particular based on genetic variations, ethnic differences, age, gender and environment.[3]
12. One of the most important profits of 3D printing is facilitating dose personalisation.
13. 3D printing could be suitable for use in hospitals, mobile military facilities and for low stability drugs.
14. 3DP can prove pretty useful in preparing dosage forms for clinical trials.
15. Dissolution of poorly soluble APIs is upgraded.
16. Disintegration and dissolution rates can be enlarged either by printing hollowed or highly porous structures, thus increasing the contact surface area, either using 3DP extrusion methods resulting in amorphous dispersions or even filling inner cavities with loose powders.
17. Tremendously low quantities of API can be printed, even as low as 3ng of API.
18. When considering smaller batches, 3D printing is less luxurious than traditional industrial manufacturing.
19. Slight stability APIs could be printed for immediate administration, while different research proposes associating simple API synthesis with 3DP [5].

Drawback of 3d printing

Process Challenges

1. Raw material selection: printability, physicochemical characteristics, thermal conductivity, Print fluid characteristics and viscoelastic stuff has to be sensibly inspected along with safety of the raw materials for human use.
2. Powder based 3D printing: narrowed or special area is required to perform the printing as powder spillage is critical and can pose as an occupational hazard.
3. Mechanical resistance: friability is higher in 3D dosage forms particularly in powder based technique. Production technology is important for good dosage form strength.
4. Certain manufacturing process may not be appropriate for thermo labile drugs when printing at high temperatures.
5. The material choices, colours, and surface finishes currently available for 3D printing are relatively limited when compared to conventional tablet compression processes.
6. Nozzle mechanism: throughout 3D printing, nozzle mechanism is used to form the layers of the dosage form. As the printer head stops and pick up during the sequenced layer formation, consistent flow of the printing material is necessary [3].
7. Appropriate materials are still limited for drug 3D printing.
8. Post processing including drying using hot air, microwaves or infrared sources may be needed in some instances, when residual solvents need to be removed from the final product.
9. When considering polypills, boundaries occur especially when taking into account the number of APIs used and the size of the final product.

Principle of 3d Printing

The Principle behindhand a 3D printer can be expected to be parallel to a regular printer. 3D printer consists of an extruder that moves horizontally on an axis which is held on top of two axes that allow it to move back and forward in x-y plane to create the base of the object. These two axes are involved to the sides of the printer. The only alteration is the 3D printer has a base that moves vertically along the z axis to create the layers over the object. Whereas printing the first layer the extruder remains at the top and moves only in 2D. The base that holds the substrate will decrease in height so that next layer could be built upon it. The process is repeated following the computer-aided drafting instructions until the object is built layer by layer.

This procedure is denoted to as additive manufacturing, rapid prototyping (RP), or solid freeform technology. 3D printers are used to print various porous scaffolds with controlled chemistry, interconnected porosity and special shapes. These prints are biodegradable and proved to be ideal for drug delivery abilities. Some of the highly complex structures incorporating living cells can be created by this technique and has gained popularity and applicability in cancer management.

Dissimilar types of drug delivery systems such as oral controlled release systems, micro pills, microchip, drug implants, fast dissolving tablets and multiphase release dosage forms have been developed using 3DP technology [10].

Steps involved in a 3d printed dosage form

Three-dimensional printing involves three major steps.

a. Modelling
b. Printing
c. Finishing

(a) Modelling: Virtual blue print from computer aided design.

(b) Printing: 3D printer read the design and lay down successive layer of materials.

(c) Finishing: After printing the support are removed or dissolved to get the final product [9].

1. Pharmaceutical product is designed in three dimension with computer aided design.
2. Design is converted to a machine readable format which describes the external surface of the 3D dosage form.
3. The computer program then slices this surface into several distinct printable layers and transfers that layer by-layer to the machine [3].

Classification of 3d printing

1. Inkjet printing method
2. Fused deposition method
3. Direct inkjet writing method
4. Zip dose method
5. Thermal inkjet printing method
6. Binder deposition method
7. Material jetting method
8. Extrusion method
9. Powder bed fusion method
10. Photo polymerisation method
11. Pen based 3DP method
12. Direct energy deposition method
13. Sheet lamination method [10, 11, 12].

Type of 3d printing technology

Examples of current 3DP technologies in pharmaceutical drug delivery.

Inkjet Printing

In the method, different mixtures of active ingredients and excipients (ink) are exactly sprayed in small droplets in changing sizes layer by layer into a non-powder substrate. The technique includes powder-based 3D printing that uses a powder foundation for the sprayed ink where it solidifies into a solid dosage form.

Zip Dose

Provides modified dose in adding to the delivery of a high drug-load with high disintegration and dissolution levels by manufacturing highly porous material.

Fused deposition modelling

The procedure can be practical to multiple dosage forms that apply polymers as part of the framework such as implants, zero-order release tablets, multi-layered tablets and fast-dissolving devices. In the procedure the polymer of interest is melted and extruded concluded a movable heated nozzle. The layer by layer ejection of the polymer is frequent along x-y-z stage, followed by solidification to create a shape previously defined by the computer aided design models.

Thermal inkjet (TIJ) printing

TIJ system contains of a micro-resistor that heats a thin film of ink fluid (located in the ink reservoir) founding a vapour bubble that nucleates and expands to push the ink drop out of a nozzle. TIJ affords the opportunity of dispensing extemporaneous preparation/solution of drug onto 3D scaffolds [13, 14].

Direct-write

Usages a computer-controlled translational stage that moves a pattern-generating device in order to achieve, layer-by-layer, 3D microstructure [15].

General 3d printing methods, technologies and materials

Table 1: General 3D printing methods, technologies and materials [5].

3DP Method	Traditional materials	Technologies
Binder Jetting	Polymer powders, sand, ceramic and metal powders	Binder Jetting
Photo polymerisation	Liquid photopolymers	DLP: Direct/Digital Light Processing. CLIP: Continuous Liquid Interface Production. SLA: Stereo lithography
Powder Bed Fusion	Metal powders	EBM: Electron Beam Melting SLM: Selective Laser Melting DMLS: Direct Metal Laser Sintering
Material Jetting	Liquid (photo)polymers, waxy polymers	DoD: Drop on Demand / Drop on Drop.
Extrusion	Thermoplastic polymer filament	FDM: or FFF: Fused Deposition Modelling or Fused Filament Fabrication

Role of 3d printing in medical field

Here are some of the ways in which 3D printer is being already used in healthcare industry.

1. Prosthesis development
2. Tissue engineering
3. Skin for Burn Victims
4. Drug Development
5. Social change
6. 3D Model libraries [9].

Recent innovations

The FDA displays the first 3D printed pill to help to stop epileptic seizures. The 3D printed LEVETIRACETAM pill was permitted for use by US FDA this past august by the trade name of SPRITAM® and expected to be offered soon in 2016. SPRITAM utilizes Apraxia's proprietary Zip Dose® Technology platform, a ground breaking advance that uses three-dimensional printing to produce a porous formulation that rapidly disintegrates with a sip of liquid. Whereas 3DP has been used previously to manufacture medical devices, this approval marks the first time a drug product manufactured with this technology has been approved by the FDA. Zip dose creates pills that instantly dissolve on the tongue with a sip of liquid a potential born to those who have trouble swallowing traditional medication.

Personalized medication

The dream behind 3D printing is that medication will be tailored to individual in way that makes it safer and more effective. The size, dose, appearance and rate of delivery of a drug can be designed to suit an individual. 3D printing has enabled the creation of high dose rapid dissipation pills, affording doctor reliable customization and complete control over the speed and strength of delivered dosage. The word "personalized medicine" is regularly described as providing "the right patient with the right drug at the right dose at the right time [8].

Current 3dp technologies and pharmaceutical formulations for drug delivery

Table 2: Current 3DP technologies and pharmaceutical formulations for drug delivery [2].

Type of 3D process/technique	Active ingredient/polymer	Dosage form
3D printed	Poly (lactide-coglycolide),	Biodegradable patch
FDM	Hydrochlorothiazide	Tablet
Stereo lithography (SLA)	Ibuprofen, Riboflavin, Polyethylene	Hydrogel
UV inkjet 3D printed	Ropinirole, Cross-Linked Poly(Ethylene Glycol Acrylate)	Tablet
FDM and SLA	FPLA-salicylic acid and PCL salicylicilic acid.	Model of a nose adapted to the morphology of individual.
FDM and Hot Melt extrusion	Domperidone, Hydroxypropyle Cellulose	Tablet
FDM 3D printing	Felodipine, PEG, PEO, Tween 80, Eudragit.	Tablet
Thermal Inkjet (TIJ) Printing	Rasagiline Mesy late	Solid dosage forms
FDM	Poly (E-Caprolactone) (PCL)	Nano capsules

Challenges in 3d printing technology

1. The challenges comprise optimization of the development, improving presentation of device for versatile use, selections of appropriate excipients, post treatment method, etc.,
2. To complete quality 3DP products, many important parameters need to be optimized like printing rate, printing passes, line velocity of the print head, interval time between two printing layer, distance between the nozzles and the powder layer, etc [12].

Pharmaceutical applications of 3d printing

1. 3D Pinting is presently used or below research for oral drugs, implantable drug delivery devices, tissue bio printing, strategies such as prosthesis and even food products.
2. When compared to traditional drug manufacturing, it was observed that 3DP is capable of producing reasonably priced, on-demand, patient tailored drugs and/or an increased product complexity.
3. Certain of the aims are minimising side effects, by achieving near-zero-order release by printing tropical, cylindrical or perforated oral formulations or by using radial gradients of erosion or diffusion-controlling excipients.
4. The aptitude to produce unique, individual or multi-drug and/or multi-dose formulations, can be the other important advantage of 3DP medicines, as demand for personalized medicine is increasing and becoming a megatrend, according to the FDA passes, line velocity of the print head, interval time between two printing layer, distance between the nozzles and the powder layer [5].

Medical and current applications

1. Wound Dressing
2. Implants and Prostheses
3. Models for Surgical Planning and Training, Phantoms
4. Bio printing and Organs-on-Chip
5. 5.4th Dimension of Printing
6. Bio robotics [1].

Conclusion

3D printing has developed a valuable and impending instrument for the pharmaceutical sector, primary to modified medicine focused on the patients' desires. 3D Printing technology is developing as a new prospect for innovative drug delivery with built-in flexibility that is well suited for tailored medication. 3D Printing technology will develop the pharmaceutical manufacturing style and formulation techniques.

Acknowledgements

The authors are thankful to Hazrat Maulana G.M. Vastanvi sahab, President of Jamia Islamia Ishaatul Uloom's Ali Allana College of Pharmacy Akkalkuwa Dist. Nandurbar for providing the research facilities.

References

1. Witold J, Joanna S, Mateusz K *et al*. 3D Printing in Pharmaceutical and Medical Applications – Recent Achievements and Challenges, Pharm Res. 2018; 35:176.
2. Diego JH. 3D Printing of Pharmaceutical Drug Delivery Systems, Arc Org Inorg Chem Sci. 2018; 1:2.
3. Preethy Ani Jose. 3d Printing of Pharmaceuticals-A potential technology in developing personalized medicine, Asian Journal of pharmaceutical research and development. 2018; 6(3):46-54.
4. Mammadov E. Three-Dimensional Printing in Medicine: Current Status and Future Perspectives. Cyprus J Med Sci. 2018; 3(3):186-8.
5. Ion-Bogdan D, Dumitru L, Cristina Manuela D *et al*. The Age of Pharmaceutical 3d Printing. Technological and therapeutical implications of Additive manufacturing. Pharmacia. 2018; 66:3.
6. Wen-Kai H, Barbara L, Herbert R. 3D printing of oral drugs: a new reality or hype? Expert opinion on drug delivery, 2017.
7. Samuel Clark Robert L, Jürgen S *et al*. Polymers for 3D printing and customized additive manufacturing, chemical reviews, ACS publication, 2017.
8. S Swati, N Jyothi, G Nirmala Jyothi, N Lakshmi Prasanthi, A Review On 3d Printed Tablets: A downloadable medicine, Asian journal of pharmaceutical technology & innovation. 2016; 04(20):34-39.
9. Sharma S, Goel SA. Three-dimensional printing and its future in medical world. Journal of Medical Research and Innovation. 2019; 3(1).
10. Monisha B, Varun S, Gurfateh SS *et al*. 3D Printing for the future of pharmaceuticals dosages forms, Int. J App Pharm. 2018; 10(3):1-7.
11. Bhusnure OG, Gholve SV, Dongre RC, *et al*. 3D printing & pharmaceutical manufacturing: opportunities and challenges. International Journal of Bioassays. 2016; 5(1):4723-4738.
12. Maulvi FA, Shah MJ, Solanki BS, Patel AS, Soni TG *et al*. Application of 3D Printing Technology in the Development of Novel Drug Delivery Systems. Int. J Drug Dev & Res. 2017; 9(1):44-49.
13. Shaban A Khaled, Morgan R Alexander, Derek J Irvine *et al*. Extrusion 3D Printing of Paracetamol Tablets from a Single Formulation with Tunable Release Profiles

Through Control of Tablet Geometry, AAPS Pharm Sci. Tech, 2018, 19(8).
14. Lei D, Ting C, Chao D *et al*. 3D printing using plant-derived cellulose and its derivatives: A review, Carbohydrate Polymers. 2019; 203:71-86.
15. Jassim-Jaboori AH, Oyewumi MO. 3D Printing Technology in Pharmaceutical Drug Delivery: Prospects and Challenges. J Biomol Res Ther, 2015, 4(4).