Available online @ www.iaraindia.com
RESEARCH EXPLORER-A Blind Review & Refereed Quarterly International Journal
ISSN: 2250-1940 (P) 2349-1647 (O)
Impact Factor: 3.655 (CIF), 2.78 (IRJIF), 2.62 (NAAS)
Volume VIII, Issue 27
April – June 2020
Formally UGC Approved Journal (63185), © Author

A REVIEW ON: 3D PRINTING IN PHARMACEUTICAL TECHNOLOGY

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Abstract

The 3D PRINTING technology has paid attention towards medical devices industry and pharmaceutical industry due to its applications on various platforms in health care industry. 3D printing is using computer- aided design to plan fast prototyping. The technology allows easy process drug combinations that are required and tailored dosing. It becomes one of the most new and beneficial tools serving as a technology of good manufacturing of developed dosage forms, tissue engineering and disease modeling. It is a valuable strategy to overcome some challenges of conventional pharmaceutical processes The recent introduction of the first FDA approved 3D-printed drug has fulfilled interest in 3D printing technology, which is set for revolutionize the healthcare.

Keywords: Keywords: *3D printing, Novel drug delivery, personalized medicine.*

INTRODUCTION

3D printing plays an important role in multiple active ingredient dosage forms, where the formulation can be a single blend or a multi-layer printed tablets having a sustained release properties. This reduces the frequency and number of dosage form units consumed by the patient on a daily routine. 3D printing technology has a great potential in an individualized dosage form concept i.e the polypill concept. [1] This brings about the possibility of all the drugs required for the therapy into a single dosage form unit. Three-dimensional printing is a technology which uses computer aided drafting technology to produce three dimensional objects by layering material onto a substrate.

3DP can be used throughout the drug development process, starting from preclinical development and clinical trials, to the medical care. [2] When compared to the manufacturing process of conventional pharmaceutical product, it has a lot of advantages like high production rates due to its fast operating systems; ability to achieve high drug-loading with much desired precision and accuracy especially for potent drugs that are applied in small doses; reduction of

material wastage which can save in the cost of production and agreeable to broad types of pharmaceutical active ingredients that include poorly water-soluble, peptides and proteins, as well as drug with narrow therapeutic windows.[3]

STEPS INVOLVED IN A 3D PRINTED DOSAGE FORM

Pharmaceutical product is designed in three dimensions with computer aided design. Converting the Design into a machine readable format or a Data which describes the external surface of the 3D dosage form. The computer program then Divides this surface into several different printable layers and transfers those layer and layer to the machine. [4, 5]

Advantages Delivery of 3D Printed Drug

- High drug loading ability when compared to conventional dosage forms.
- Accurate and precise dosing of potent drugs which are administered at small doses.
- Due to lesser material cost of production reduces.
- Suitable drug delivery for difficult to formulate active ingredients like poor water solubility, drugs with narrow therapeutic window.
- Medication can be tailored to a patient in particular based on variation in genetics, differences in ethnic, age, gender and the environment.

3D PRINTING TECHNOLOGIES

3D printing or additive manufacturing is a highly pleasing or attractive technology that produces 3-dimensional objects by constructing layers of the used material under the control of computer software. It has established its ways in engineering and also in non-medical practices, and also in the automobile industries. [6,7]

Types of 3D printing

1. Polypill concept

The concept of "polypill" refers to a single tablet that involves the combination of many drugs. This concept is mainly beneficial for geriatric population, as patients of this age are categorized to multiple disorders and hence multiple therapy is being suggested. [8,9] This technology has been realized through the research in which five different active pharmaceutical ingredients with different release profiles have been formulated or made in a single 3D dosage form. Three drugs namely (pravastatin, atenolol, and ramipril) has to be printed in the extended release compartment. The drugs were physically separated by a permeable membrane of hydrophobic cellulose acetate. An immediate release compartment containing hydrochlorothiazide and aspirin were deposited on top of the extended release compartment.[10,11]

2. Inkjet Printing

In the inkjet printing an approach to a personalized medicine begins from the technique of computer-operated inkjet printing and includes use of inkjet printers. The practicing was done for pharmaceutical use by the replacing the ink with pharmaceutical solutions containing drugs and normal paper with edible sheets known as substrates. Dose changes are done by changing the number of layers printed in a given area or altering the area to be printed. The drug and excipients are designed in a ratio such that it has a potential or a power to print as microdots on an edible substrate. [12, 13]

3. Fused Deposition Modelling (FDM)

Fused deposition modelling (FDM) is commonly used technique in 3D printing and also known as fused filament fabrication (FFF), in this the materials are soften or melted by heat to create objects during printing. FDM 3D printing helps in manufacturing of delayed release printlets without an

outer enteric coating, and also helps to provide personalised dose medicines. [14,15] FDM 3D printing however, indicates several drawbacks of the system such as lack of suitable polymers, slow and often incomplete drug release the reason is the drug remain trapped in the polymers and the miscibility of the drug and additives with the polymers used was not evaluated.[16]

4. Drop-on-powder deposition

Due to the mixture of powder (bed) and binder (ink) they make a solid structure in a layer-wise manner. They allow the elimination of remaining volatile solvents for the stability of the final product Powder particle sticks due to the ink binder and results for the solidification.[17,18] Powder topology and material reactivity by binder are the main two characteristics of powder in the drop on powder deposition.

5. Nozzle-based deposition systems

In Nozzle-based deposition systems mixing of drugs, polymers and other solid elements takes place prior to 3D printing. Direct writing is done, and computer-controlled manufacturing methods are used that place ink direct through a nozzle to create a 3D pattern layer-bilayer with controlled composition and designing.[19,20] Such systems may basically be divided into processes based on material melting and also on processes without material melting.

6. Hot melt extrusion

Hot melt extrusion is the process of melting polymer as well as drug at high temperature and the pressure is applied to the instrument continuously for the purpose of blending. It is a continuous manufacturing process that includes several operations such as feeding, heating, mixing as well as shaping. In recent years, it has been proved that Hot Melt Extrusion have an ability to improve the solubility and bioavailability of poorly soluble drugs.[21,22]

RISK ASSESSMENT DURING 3D PRINTING PROCESS

Risk identification is an important tool to prevent failure of quality control parameters like appearance, content uniformity, assay etc. Identification of risk involves through analysis of the process and process variables to assure that a quality product is being manufactured. Such a critical assessment was done by Norman et al. When a given printer is unable to print a given design, software control should be employed or used.

- Variability or changes in layer thickness has to be controlled by real – time layer thickness monitoring.
- Improper layering due to environmental conditions should be dealt with controlling the temperature and humidity of the manufacturing area.
- Inaccurate position during printing can be stopped by monitoring print head height and print head speed.
- Uneven layers can be avoided by checking powder water content and powder particle size distribution.

3D printing in pharmaceuticals

As per United States Government Accountability Office (GAO),3D printing makes 3D objectives from digital models, and its aim are to produce by layer by layer process.3D printing is gaining and increasing attention in pharmaceutical formulation as they produce different dosage from in various shapes, sizes & release various features.3D printing technology overcomes some challenges in conventional pharmaceutical preparation. Traditional pharmaceutical preparation involves milling, mixing, granulation, compression which may result in drug loading, drug release, drug stability and also in dosage form stability.

Application of 3D printed drug

Commercially available 3D printed drugs

Spritam is marked by Aprecia Pharmaceuticals using the Zip Dose technique based on powder bed fusion. Spritam made by the layer-by-layer production system. The pharmacological efficacy of Spritam was found to be equivalent to conventional tablets. The great improvement is the solubilization time of Spritam was significantly reduced due to its porous and soluble matrix composition.[23]

Personalized topical treatment devices

Nose-shaped masks, loaded with salicylic acid, used for anti-acne treatments, have been developed in a short and efficient manner. The face of the patient was scanned and the taken image was projected to the autocad program, through which the nose section was selected. FDM and SLA, to determine which one was more favourable in terms of engineering, the morphological characteristics of the object, drug release, and the stability during printing. SLA was the most accurate technology for mask manufacture.[24]

3D Printing for cancer treatment

Chemotherapy has widely applied in cancer treatment but chemotherapy can cause side effect. Chemotherapeutic drugs have poor solubility in aqueous media; thus, they are administering through a different route. Currently, the construction of patches loaded with 5-fluorouracil, poly (lactic-co-glycolic) acid, and PCL have been effectively printed and implanted directly into pancreatic cancer.[25,26]

CHALLENGES IN 3D PRINTING TECHNOLOGY

3D printing technology showed promising and efficient results in drug delivery applications, the technology is still under the developing stage. Hence it undergoes and faces many challenges such as optimization process, improving performance of device for versatile use, selections of appropriate excipients, post treatment method, etc., to improve the performance of an 3D printed products and to expand the application range in novel drug delivery systems.[27,28] Apart from the cost of developing new formulations or re-designing existing formulations through 3DP, the built-in flexibility may be a major source of liability from safety point of view.

CONCLUSION

3D printing has become a useful for the pharmaceutical sector, leading to personalized medicine focuses on the patient's needs and effectiveness. 3D Printing technology is emerging as a new horizon for advanced drug delivery with built-in flexibility that is well suited for personalized/customized medication. 3D Printing technology will change or modify the pharmaceutical manufacturing style and formulation techniques.

However, to ensure that 3D printed medicines have the same efficacy, safety, and stability as the pharmaceuticals that are manufactured by the Pharmaceutical Industry there have been a significant barrier. Regarding the establishment of guidelines, laws, quality systems and safety as well as use and consumption of 3D printed medicines, it is a great challenge for the regulatory authorities entailing great obstacles, given the traditional requirements by the pharmaceutical sector.

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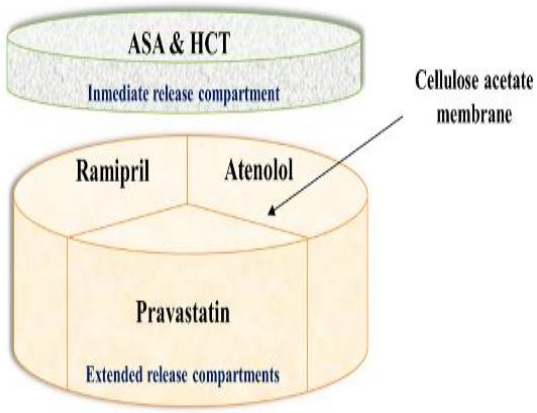

Fig1: 3D Printed polypill

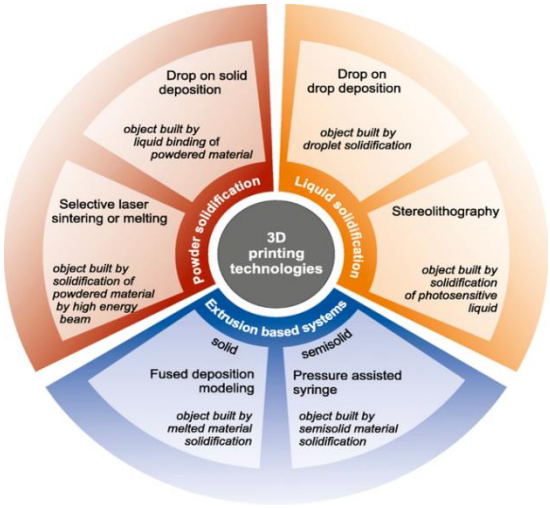

Fig 2: 3D Printing Technologies

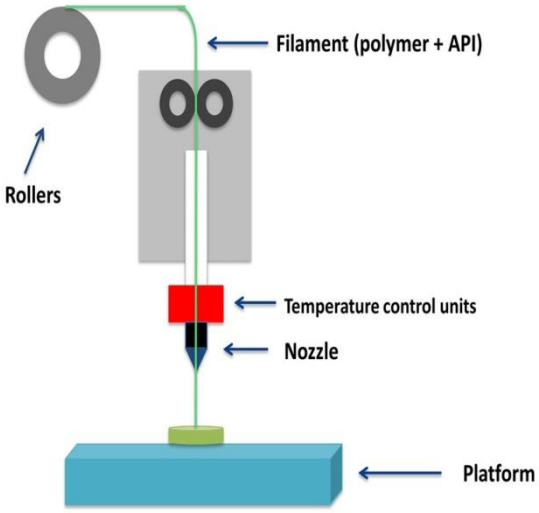

Fig 3: Fused Deposition Modelling (FDM) Printing Systems