**Advancement in manufacturing technique: A review**

Review by-BHAVESH SONI

Guided by- proff Dr Praveen tahilani

Dean-Dr jitendra banweer

Sagar institute of research & technology-pharmacy Bhopal

# ABSTRACT

In the last decades many different additive manufacturing (AM) technologies for metal, plastic or ceramic processing raise from research to commercialization. As a result AM, grows into different business areas and transforms structures and processes. Hence, the contribution tends to show the change in added values through the availability of different additive manufacturing technologies based on a technology screening and market research. Its use has grown significantly in the last 10 years, with the pharmaceutical sector playing a significant role in this growth. Researchers from all around the world are working hard to create innovative pharmaceutical dosage forms, particularly customized ones that may meet each patient’s unique requirements. These dosage forms aim to meet the following needs: customized drugs, on-demand production, improved dose, size, and geometry, and higher bioavailability of the medicinal active ingredient. The application of additive manufacturing (AM) technologies is considered essential for the fabrication of oral dosage forms and polypills, as precision medicine has become more prevalent in healthcare. This opens up new avenues for the administration of customized drug formulations and combinations. While the widespread use and commercialization of AM methods may cause a disturbance to the existing healthcare supply chain, there is a chance that it may reduce the amount of waste generated by unused and expired pharmaceuticals. The purpose of this article is to highlight the innovative trends in 3D printing pharmaceutical dosage forms and to provide an overview of additive manufacturing techniques that are of great interest to the pharmaceutical industry. Additionally, the article will discuss the advantages, limitations, and future prospects of additive manufacturing in the field of research and development. The article also provides a number of references to research articles that demonstrate the practicality of different 3D printing methods and how they have been effectively used to produce novel pharmaceutical formulations.

#  INTRODUCTION

Manufacturing is a process in which raw materials are transformed into finished goods. Additive manufacturing (AM) or 3D Printing (3DP) has become one of the most innovative technologies in the pharmaceutical sector with the last decade witnessing a significant expansion in the manufacture of drug delivery models.

Additive manufacturing technology that can make anything. It eliminates many constraints imposed by conventional manufacturing. It leads to more market opportunities. It increased application such as 3D faxing sender scans a 3D object in cross sections and send out the digital image in layers and then recipient receives the layer image and uses an AM machine to fabricate the 3D object.

The AM facilitates the creation of pharmaceutical dosage forms by means of computer aided designing (CAD), which in turn generates a computer designed model that fabricates the desired product using layer upon layer feed disposition. AM also provides an innovative platform to overcome the limitations attributed to the conventional ‘ one size fits all’ concept.

3DP or AM technologies include a plethora of processes in which a solid object is created in a layer by layer process. The most commonly used 3DP technologies employed in pharmaceutical companies include electron beam melting (EBM), Extrusion based 3D printing, inkjet printing, multi jet fusion (MJF), powder bed deposition, Selective laser melting, selective laser sintering (SLS), and direct metal laser sintering (SLM/DMLS), and stereo lithography (SLA).

# Functional Principle

* The system starts by applying a thin layer of the powder material to the building platform.
* A powerful laser beam then fuses the powder at exactly the points defined by the computer generated component design data.
* Platform is then lowered and another layer of powder is applied.
* Once again he material is fused so as to bond with the layer below at the predefined points.

**METHODS**

# Fused disposition modelling (FDM) or Fused filament fabrication (FFF)

One of the most popular and effective methods for producing pharmaceuticals in the

Pharmaceutical industry since its launch in 2014 is fused deposition modeling, or FDM, 3DP of Fused Filament Fabrication, or FFF) 3DP. This method uses a filament, which is typically made by hot melt extrusion (HME) from a thermoplastic polymer. Pharmaceuticalgrade polymers, such as cellulose derivatives, polylactic acid (PLA),polymethacrylates, polyurethanes, polyvinylAlcohol (PVA), and polyvinyl pyrrolidine (PVP), are often used in the FDM 3DP.

This makes it easier to fabricate 3D geometries or tablets layer by layer by plasticizing and Extruding thermoplastic feedstock materials—which often include drugs—through a tiny nozzle and depositing them on the 3DP build platform. Recently, FDM technology has been expanded to produce, among other things, drug-eluting implants, functioning medical devices, and different kinds of tablets with different compartments and configurable release kinetic profiles. First off, HME must be used in the process of making the drugloaded filaments due to FDM.

# Stereolithographic (SLA)

Stereolithography/Stereolithography Apparatus – SL/SLA is the oldest method of additive manufacturing. A photosensitive resin / photopolymer layer is deposited on the work table. The Rapid Prototyping (RP) technology has a brief history dating not more than 30 years. This technology was a giant breakthrough in the manufacturing sector, due to the latter being the predecessor to the generation of 3D objects, by adding materials rather than fabricating a part by removing the material. Therefore, this is the ultimate reason that these techniques are referred to as additive manufacturing (AM) processes. Stereo lithography (SLA), a subset of liquid material based RP techniques invented and patented by Charles W. Hull in 1986, was the first RP method to be introduced.

SLA demonstrates several desirable and salient features over other RP methods, such as the capability to produce finalized samples relatively quickly. Moreover, the fabricated models have significant resistances and are strong enough to be tested for friability. Furthermore, these procedures could be utilized to produce small batch quantities as a cost effective alternative to injection molding. Moreover, SLA may also be employed in the manufacturing of investment casting patterns for any type of material or polymer.

# Laminated object modeling/laminated object manufacturing (LOM)

This process is carried out using a foil onto which the laminate (heat-activated glue) has been applied. The foil is applied to the work table and then a heated roller binds/welds the foil to the work table. The laser cuts the correct shape of the layer (contour), then the rest of the foil (outer part of the contour) the laser cuts into small squares to easily remove unnecessary material after the process. The work table lowers and the next layer of foil is applied. The cycle is repeated many times, and part is produced layer by layer until the process is completed .

The Laminated Object Modeling or Laminated Object Manufacturing (LOM) technology, developed by fey gin and Pak in 1988 is a hybrid of additive and subtractive manufacturing techniques. It is a technique that feeds the adhesive coated thin film material, followed by the integration of the cutting and laminating processes to render the final product.

LOM processes find substantial utility, as they do not require a heating step during production that ensures the adhesive bonding of the sheets. In comparison to its shortcomings that arise in other techniques like FDM, the impact of this step on the non uniformities in the manufactured part is minimal. However, a drawback of the LOM is that the materials that could be utilized in the procedure are limited by their capacity to be shaped into sheets and then further merged with adhesive. Additionally, the LOM process poses sheet bonding problems that cause weak bonding, process failure, and problematic disengagement between the supporting frame and the Part.

# Hot melt extrusion (HME)

Over the last 12 years, the interest in the pharmaceutical applications of the hot melt extrusion (HME) techniques has grown tremendously. In the mid nineteenth century, HME was introduced in the plastics industry to manufacture polymeric insulation that was used in wire cover and then later used in the production of all plastic bags, pipes, and sheets. HME has long served as a popular method for the plastics and polymers industry but has proven to be a feasible way for the manufacture of a multitude of pharmaceutical dosage forms and drug transporting systems. HME Fabricated dosage forms are formed by intricate combinations of APIs, excipients, and other processing aids. HME also proves to be of great importance over conventional pharmaceutical processing procedures, including fewer processing stages, continuous operations, and lack of solvents, increased bioavailability, and the ability to generate solid dispersions. The HME is regarded as a continuous procedure that consists of the pumping of several polymeric substances at temperatures exceeding their glass transition temperature (Tg), and at times even exceeding their melting temperatures (TM), with a rotating screw that facilitates the admixing of active Compounds (Polymers, thermoplastic binders or both), at a molecular level.

# Direct powder extrusion (DPE)

Direct powder extrusion (DPE) is a relatively new, revolutionary, and innovative 3D printing method used for preparing amorphous print lets/tablets. It is a novel technology that consists of just a single step, which not only aids in ease of operations but also overcomes one of the major drawbacks of fused deposition modeling (FDM). In FDM, since the preparation of filaments using hot melt extrusion (HME) is necessary, the drugs undergo thermal stress which could possibly result in discoloration and sometimes even degradation via oxidation. After the filament is manufactured, the drug is fed into the 3D printer and heated once again. However, the most significant drawback is the limited availability of options of excipients and drugs to make filaments with the appropriate physical and mechanical properties for 3D printing. In a study conducted by Duranovic et al., paracetamol loaded filaments were processed using poly ether oxide (PEO) and poly (ecaprolactone) (PCL) polymers, and printed at 130 °C.

# Inkjet printing

Inkjet printing is a scalable method that has been employed for the preparation of pharmaceutical agents. The process involves the selective settling of liquid droplets onto a substrate followed by their solidification. This process is deemed responsible for the placement and digital control of the formation of small liquid droplets and also the beginning of the processing of »1−100 pl Liquid droplets into the 2D or 3D structures. The drops are generally created by either heating the liquid to a temperature greater than its boiling temperature or by passing a voltage to a piezoelectric transducer which further causes the vibrational movement of the material. This technology is classified on the basis of the physical properties by which droplets are prepared; into either continuous inkjet printing (CIJ) or drop on demand (DoD) printing. The CIJ employs a continuous stream of water, ejected from a nozzle, which accelerates its breaking up into a stream of drops due to surface tension forces. This breakdown can be enhanced by using a piezoelectric transducer behind the nozzle, which optimizes flow, at desired frequencies, and is effective only when individual drops are guided to a specific landing site to produce a printing pattern.

# CONCLUSION

Nowadays there are methods of additive manufacturing of materials from each group of engineering materials (polymers, metals, ceramics, composites). Some of these methods have been known for several decades. However, their development caused an increase in the dimensional accuracy of manufactured parts while increasing productivity. The process of joining materials to make objects from three- dimensional (3D) model data, usually layer by layer. AM is on the verge of shifting from a pure rapid prototyping technology.

The pharmaceutical business has been significantly influenced by recent breakthroughs in Additive manufacturing (AM) methods, which have allowed for the production of intricate, customized pharmaceuticals and improved drug formulation capabilities. 3D printing technologies have facilitated improvements in medication solubility, bioavailability, and controlled release.

# REFERENCE

1. Barakh Ali SF, Mohamed EM, Ozkan T, Kuttolamadom MA, Khan MA, Asadi A, et al. the effects of formulation and process variables on the printlets quality Manufactured by selective laser sintering 3D printing. Int J Pharmaceut [Internet] 2019 Oct;570:118651 Available from. Doi: 10.1016/j. ijpharm.2019.118651.

1. Alhnan MA, Okwuosa TC, Sadia M, Wan K−W, Ahmed W, Arafat B. Emergence of 3D Printed dosage forms: opportunities and challenges. Pharmaceut Re [Inter- net] 2016 May 18;33(8):1817–32 Available from. Doi: 10.1007/s11095−016−1933−1.

1. Allen Jr L V. Basics of compounding: standardization of compounded medica- tions. Int J Pharm Compd 2019;23(1):35–44

1. Water JJ, Bohr A, Boetker J, Aho J, Sandler N, Nielsen HM, et al. Three−dimen- sional Printing of drug−eluting implants: preparation of an antimicrobial poly- lactide feedstock Material. J Pharmaceut Sci [Internet] 2015 Mar;104(3):1099– 107 Available from. Doi: 10.1002/jps.24305

1. Melocchi A, Uboldi M, Cerea M, Foppoli A, Maroni A, Moutaharrik S, et al. A graphical Review on the escalation of fused deposition modeling (fdm) 3d print- ing

in the Pharmaceutical field. J Pharmaceut Sci [Internet] 2020 Oct;109 (10):2943–57 Available From. Doi: 10.1016/j.xphs.2020.07.011.

1. Tahaineh LM, Gharaibeh SF. Tablet splitting and weight uniformity of half−tab- lets of 4 Medications in pharmacy practice. J Pharm Pract [Internet] 2012 Apr 27;25(4):471– 6 Available from. Doi: 10.1177/0897190012442716.

1. Shah VP, Yamamoto LA, Schuirman D, Elkins J, Skelly JP. Analysis of in vitro dissolution of whole vs. half controlled−release theophylline tablets. Pharm Res 1987;4(5):416–9 Available from. Doi: 10.1023/a:1016442514205.

1. Mathew E, Pitzanti G, Larran~eta E, Lamprou DA. 3D printing of pharmaceuticals and drug delivery devices. Pharmaceutics [Internet]. MDPI AG; 2020 Mar 15;12 (3):266. Available from. Doi: 10.3390/pharmaceutics12030266.

1. Azad MA, Olawuni D, Kimbell G, Badruddoza AZM, Hossain MS, Sultana T. Poly-mers for extrusion−based 3D printing of pharmaceuticals: a holistic materials process perspective. Pharmaceutics [Internet]. MDPI AG; 2020 Feb 3;12 (2):124. Available from. Doi: 10.3390/pharmaceutics12020124.

1. Zhu X, Li H, Huang L, Zhang M, Fan W, Cui L. 3D printing promotes the develop- ment of drugs. Biomed Pharmacother [Internet] 2020 Nov;131:110644 Available from. Doi: 10.1016/j.biopha.2020.110644.

1. Li H, Fan W, Zhu X, Three Li H, printing F. The potential technology widely used in medical fields. J Biomed Mater Res Part A [Internet] 2020 Jun 20;108 (11):2217–29 Available from. Doi: 10.1002/jbm.a.36979.

1. Goyanes A, Buanz ABM, Basit AW, Gaisford S. Fused−filament 3D printing (3DP) for fabrication of tablets. International Journal of Pharmaceutics [Internet] 2014 Dec;476(1−2):88–92 Available from. Doi: 10.1016/j.ijpharm.2014.09.044.

1. Annaji M, Ramesh S, Poudel I, Govindarajulu M, Arnold RD, Dhanasekaran M, et al. application of extrusion−based 3D printed dosage forms in the treatment of chronic diseases. J Pharmaceut Sci [Internet] 2020 Dec;109(12):3551–68 Available from. Doi: 10.1016/j.xphs.2020.09.042.

1. Habib WA, Alanizi AS, Abdelhamid MM, Alanizi FK. Accuracy of tablet splitting:

Comparison study between hand splitting and tablet cutter. Saudi Pharmaceut J

[Internet] 2014 Nov; 22(5):454–9 Available from. Doi: 10.1016/j. jsps.2013.12.014.

1. Konta A., García-Pin~a M., Serrano D. Personalised 3D printed medicines: which techniques and polymers are more successful? Bioengineering [Internet]. MDPI AG; 2017 Sep 22; 4(4):79. Available from: [http://doi.org/10.3390/b](http://doi.org/10.3390/)ioengineering4040079