International Journal of Scientific Research in Engineering and Management (IJSREM)
Volume: 08 Issue: 03 | March - 2024 SJIF Rating: 8.176 ISSN: 2582-3930

Application and Development of 3D Printing Technology in Pharmaceutical and Health Industry

Prashanth Kumar Alay[1]

[1]Department of Health Management and Informatics, MU, School of Medicine.

Abstract - 3DP technique is one of the most ingenious technologies, especially in the pharmaceutical field since its first discovery in the early 1980s. 3D printing technology enables unprecedented versatility in the design and production of complex materials that can be used in customized and programmable medicine. The discussion and analysis revealed that several 3D printing technologies based on varying principles have been developed. Although 3DP is still in its growing stage, this technology has made the fabrication of extremely sophisticated and intricated dosage forms feasible. Conclusion: Despite numerous advantages and benefits in pharmaceutical and health care systems, there are several technical and regulatory challenges obstructing its extensive utilization. With the increasing investments and research in this direction, it has the potential to overcome the regulatory and technical limitations in the days to come.

***Key Words*:** 3D Printing; Three-dimensional printing; Personalized medicines; Stereolithography; Rapid prototyping; Additive manufacturing; Solid free-form fabrication.

1.INTRODUCTION

The technology sector has seen a major industrial revolution with the understanding and practical application of artificial intelligence and three-dimensional (3D) printing which were once imagination. Three-dimensional printing (3DP) has found its diverse application in sectors like engineering, chemical industry, military, fashion industry, architecture, and medical field. 3DP technique has so far proved to be one of the most ingenious technologies, especially in the pharmaceutical field. A dramatic and a significant increase has been observed in the research involving 3D printing technologies only in the last decade after its availability since the late 1980s. Three-dimensional printing is a novel technology for the rapid construction of 3D objects by the deposition or fusion of several successive layers in a sequence. International Standard Organization (ISO) defined 3DP as “fabrication of objects through the deposition of a material using a print head, nozzle, or another printer technology”, 3D printing technology enables unprecedented versatility in the design and production of complex materials that can be used in customized and programmable medicine. This is an excellent strategy to subjugate some of the challenges of routine drug unit operation. It was Charles Hull who first described 3D printing technology for a commercial purpose. In its simplest setup, a 3D object is produced onto a substrate by sequential layering one after the other with the aid of computer-aided drafting techniques and programming. The material is first ejected on an x-y plane from a printer head and forms the base of the object. The printer then moves with the z-axis, and a liquid binder is expelled to a certain thickness at the base of the material. This process is repeated by following the computer-aided draft instructions until the object is created layer by layer. After treatment for complete removal of the unbound substrate, the 3D object is formed. This printing technique is also known as additive manufacturing, solid freeform fabrication, or rapid prototyping technique. Basically, structures can be built from a 3D digital file using imaging techniques (such as magnetic resonance imaging (MRI)) or computer-aided design (CAD) software to instantly produce customized objects. Various 3DP technologies have been developed to create novel solid drug delivery systems, making them one of the most popular and unique products today. Direct printing of microscopic scaffolds of the desired shape and other properties can be created using 3D printers. Their biodegradable nature, site specificity and potential for drug delivery have made them favorable for bone-tissue engineering. 3D bioprinters provide the ability to create highly complex 3D structures with living cells. This sophisticated technology has become popular and applicable in the treatment of cancer. The 3DP technique offers many innovative approaches and strategies for the NDDS and hence a growing interest can be seen in the pharmaceutical industry Considering all such salient points mentioned above, this review has been prepared to highlight the developments in the pharmaceutical application of 3D printing technology including their positive prospects over conventional approaches. This review is expected to provide an insight into the 3DP approaches and probable challenges of such strategies.

1.1 Background

Throughout history, the world has been subject to three major industrial revolutions related to production and manufacturing. We are now on the brink of the next Industrial Revolution. With significant technological advances of the twenty-first century, production is now being digitized. Since the introduction of 3D printing nearly three decades ago, this technology has transformed production into an unparalleled number of applications. Many people are not aware that 3D printing technology is not a recent or completely innovation. As a matter of fact, the first patent for 3D printing was successfully released in 1986. The history of 3DP dates to 1981 with the patent application for Dr Hideo Kodama's Rapid prototyping device that unfortunately could not complete the process before the one-year deadline due to financial constraints. Nevertheless, the idea of "rapid prototyping device" continued to develop. Jean-Claude Andre, Oliver de Witte and Alain Le Mahath applied for the patent in 1984, but without proper funding, they were forced to abandon the project. Later that same year, Charles Hull, a furniture manufacturer, who had been frustrated with the long and slow process of making small, ordinary parts, worked in the same direction turning the company's UV lamp for a different purpose (curing photosensitive resin layer after layer, to create an object at the end) and applied for the patent, naming his technology stereolithography, for which he was granted a patent in 1986. That same year he started his own company ‘3D Systems’ in Valencia, California and introduced SLA-1, their first product in 1988 for a commercial purpose.

Scott Crump in 1989 filed an application for a patent on another 3DP technology i.e., fused deposition modelling. In the early '90s, Emanuel Sachs of Massachuset Institute Technology (MIT) with his team invented and patented 3DP technique. This phase of the '90s has witnessed a surge in the number of companies competing for rapid prototyping technique. The most important breakthrough of 3D printing in the pharmaceutical field has been presented.

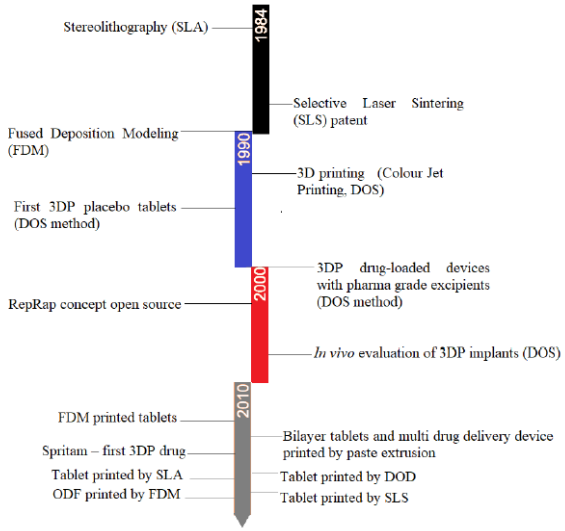

Figure 1 Breakthrough of 3DP technology in the pharmaceutical field over the years

2. ADVANTAGES OF 3DP IN PHARMACEUTICAL SECTOR:

I. Improved productivity: 3D printing works faster than traditional methods, especially when fabricating materials such as implants and prosthetics with the added advantage of better precision and accuracy, repeatability and reliability.

II. Customized and Personalized medicines: One of the prominent advantages of this technology is the flexibility to create customized medical equipment and products. Personalized implants, surgical instruments, prosthetics, can be a great blessing to both patients and physicians. Accurate dosing of a potent drug, high drug loading can be achieved with this technique.

III. Cost-effective: Products made with 3D printing are less expensive due to less wastage of materials.

IV. Sustainable/eco-friendly: 3 DP technology being a novel and innovative technique is eco-friendly as it uses less energy and better-quality material, ultimately producing minimum waste.

V. Timesaving: Three-dimensional printers are time efficient which shortens the product development design cycles.

VI. Tool-less: 3DP can eliminate the need for tool production and therefore, reduced cost, time and labour associated with it. Requirements of tools during production is not essential in 3DP, thereby reducing cost, time, and labour.

3. TYPES OF 3D PRINTING TECHNOLOGY:

According to ASTM (American Society for Testing and Materials), 3D printing technology can be divided into seven basic types based on the involved additive process. They are material jetting, binder jetting, directed energy deposition, sheet lamination, vat photopolymerization, powder bed fusion, and material extrusion. Each process has its advantages and disadvantages along with their specific field of application. The diversity comes from various additives used to fulfil the needs of consumers. Based on the requirements these technologies can print objects from nano to industrial scale materials.

3.1 Material jetting

In material jetting, droplets made of building material or additives are selectively deposited as layers to build up an object. This is a very similar process that is used in the Inkjet printers. The main difference is these process uses the additives or building material instead of ink and in the place of a paper, it directly deposited and solidify on the surface of a building. platform which changes its height and angles until the final product is achieved. In this process, elastomeric photopolymers, acrylic-based photopolymers, wax-like materials are used as substrates in liquid form. These polymers are highly attractive because of the long molecule chains associated with them. Material jetting process is also known as Aerosol Jet by Optomec Company, Ballistic Particle Manufacturing (BPM), Laser- Induced Forward Transfer (LIFT), Nano Metal Jetting (NMJ), Drop On Demand (DOD), NanoParticle Jetting (NPJ), Liquid Metal Jetting(LMJ), Polyjet by Stratasys Inc, Printoptical Technology by Luxexcel, Thermojet Printing, Multi-Jet Modelling(MJM) and Multi-Jet-Printing or MJP by 3D Systems Corporation.

3.2 Binder Jetting

It is a prototype process in 3D printing technology that uses a binding agent in liquid form to agglomerate powder as layers to get a solid 3D printed object. This technology was first invented at MIT in 1993 by Sachs et al. (1993). Ceramics like MgO doped alumina, metals like Cobalt, Copper, metal oxide like iron oxide, nickel oxide, cobalt oxide, polymers like polyglycolic acid (PGA), polylactic acid (PLA), polycaprolactone (PCL), polyethylene oxide (PEO), biomaterial like Poly L-Lactic acid, calcium phosphates, calcium silicate were generally used as binder material. An ideal binder should be of a low viscous material that can instant for droplets and easily falls off from the nozzle. Commonly, the binder is moderately dried out after each printed layer. This assists in improving the spreading of the following layer by eliminating surface dampness and can likewise decrease the immersion level. Binder jetting process can also be known as Zip dose, Theriform, M-printing, S-printing, etc

3.3 Direct Energy Deposition

DED or Direct energy deposition is a laser-focused material melting technique that utilizes focused thermal power or laser beam to melt material which is guided towards nozzle and a building platform of 3D printed object. Unlike other techniques, this process utilizes a motion-controlled nozzle that can rotate in multiple axes. Instead of polymers and ceramics metals and metalloids of stainless steel, copper, cobalt, nickel, aluminum, and titanium are preferred for DED printing. Laser deposition (LD), Laser Engineered Net

Shaping (LENS), Electron beam Plasma, Arc melting are a prominent example of DED technology.

3.4 Sheet Lamination

Sheets of materials are bonded together to build an object is the principle of sheet lamination technology. It is also known as laminated object manufacturing (LOM) which was first invented by a company called Helisys in 1991, later evaluated by Mcor-Technologies in 2012. With LOM, a sheet of building material (provided with a glue backing or covered with adhesive during the construct cycle) is progressed onto a building stage. A laser is then used to cut a formerly planned and designed structure into a sheet while the platform moves; the cycle is constantly rehashed until the culmination of the design. Other than metals, polymers and ceramics can also be used for this purpose. Ultrasound consolidation/ Ultrasound Additive Manufacturing (UC/UAM) is an example of this this technology.

3.5 Vat Photopolymerization

Vat photopolymerization is an overall term given to several 3D printing technologies where a vat contain liquid photoreactive polymers is solidified and cured with a laser beam or UV light source. Photopolymers were first introduced in the 1960s and so the process. stereolithography (SLA), continuous light interface production (CLIP), digital light projection (DLP), two-photon polymerization (2PP), and lithography-based ceramic manufacturing (LCM) are the example of vat photopolymerization technology, where stereolithography (SLA) and digital light projection (DLP) are mostly used techniques. Although same technologies, DLP and SLA differed in the light sources. SLA, the first vat photopolymerization technique uses a UV light source where DLP utilizes a conventional light source or arc lamp. The liquid polymer radiation-curable resins, when treated with a light source it will harden with good details and may bring out a premium product. Part accuracy and surface finish is the advantage of this technique.

3.6 Powder bed fusion

As the name suggested, this additive manufacturing technique is based on the fusion of powders by melting them with the help of thermal energy. Selective Laser Sintering (SLS), Electron Beam Melting (EBM), Direct Metal Laser Sintering (DMLS), Selective Heat Sintering (SHS) are the different powder bed fusion techniques, where SLS is prominent and was discovered by Carl Deckard in 1987. Solid particles like metals, polymers, ceramics can be used as an additive for this 3D printing technique. To increase the speed of the process, new improvements using fast lasers are presented.

3.7 Material Extrusion

It is a 3D printing process in which material is forced to flow through a nozzle to convert it into the desired shape. Different techniques are available for different raw materials. Fused Deposition Modeling (FDM) or Fused Filament Fabrication (FFF) or Fused Layer Modelling (FLM), Semisolid extrusion is the known process utilizes material extrusion mechanism. Among them, Fused deposition Modelling is utilized widely for its low cost. It was first developed in 1990 and commercialized in late 1991. FDM utilizes polymers as additive material, mainly thermoplastic polymers are used It builds parts layer-by-layer from bottom to top by heating and extruding thermoplastic filament. The semisolid extrusion also employs. a nozzle system which extrudes a Gel or Pastes on the building plate in a layer-by-layer approach. Just Like FDM, the extruded material then solidifies after the solvent is evaporated. Upon melting of polymers or gel materials they can be feed into an FDM 3D printing system

4. 3D PRINTING PROCEDURE

4.1. Material jetting

The basic process involved in material jetting is as follows:

I. The printer head is placed above the build platform.
II. Build material is deposited from a horizontally movable nozzle across the build platform.
III. Build material forming layers are then cured and solidified using ultraviolet light (UV).
IV. Droplets of the build material harden and make the first layer.
V. Build Platform descends.
VI. Products obtained with good accurateness and surface finish.

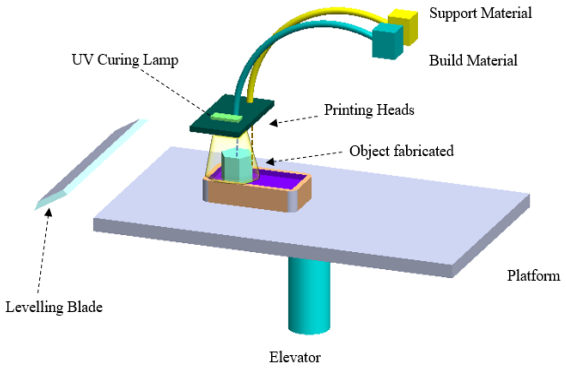

Figure 2: Basic diagram of Material jetting equipment

4.2 Binder Jetting

The basic process involved in the binder jetting method are as follows:

I. First, binder material is jetted from an inkjet print head.
II. Then, on top of the existing layer, the roller is used to spread a new layer of powder.
III. Subsequent layers are then printed and are tacked to the previous layer by the jetted binder.
IV. Finally, the residual powder in the bed ropes overhanging structures.

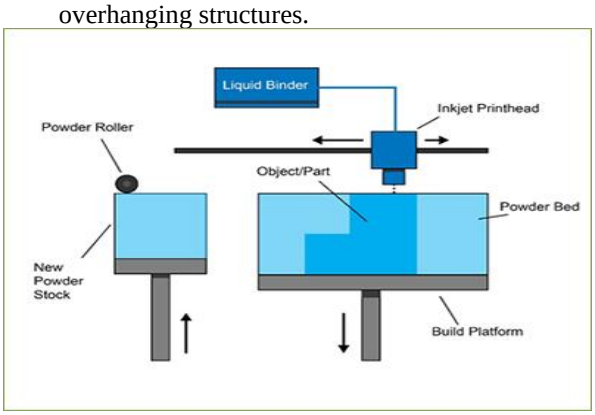

Figure 3: Basic diagram of Binder Jetting equipment

4.3 Direct energy deposition

The basic process involved in the direct energy deposition technique are as follows:

I. A four or five-axis arm with a nozzle moves around a static object.
II. Building material is deposited over the surface of the object from the nozzle.
III. Building material is either provided in powder or wire form and it is melted with a laser, electron beam, or plasma arc upon deposition.
IV. Further material is added and solidifies layer by layer and produce the final object.

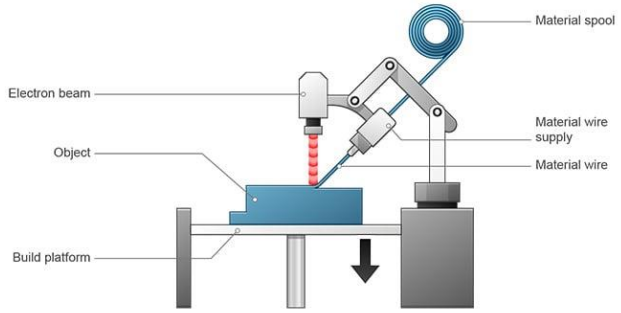

Figure 4: Basic diagram of Direct energy deposition equipment

4.4 Sheet Lamination

The basic process involved in the Sheet Lamination technique are as follows:

I. The building material or sheet is positioned in place on the cutting tray.
II. The building material is bonded with the previous layer, using the adhesives.
III. The required shape is then cut from the placed layer, by laser or scrapper.
IV. The next layer is added, and the same process runs.

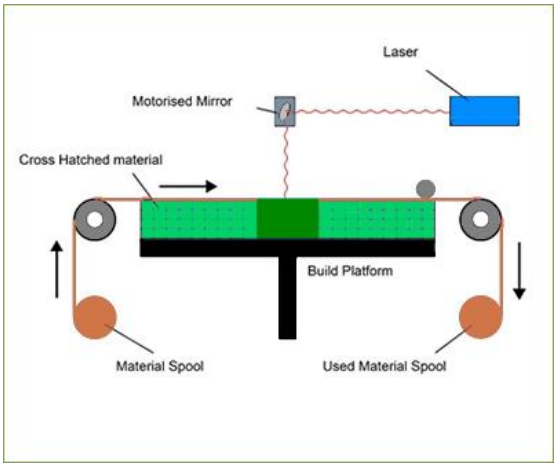

Figure 5: Basic diagram of Sheet Lamination equipment

4.5 Vat Photopolymerization

The basic process involved in Vat Photopolymerization are as follows:

I. A high voltage Laser beam traces a cross-sectional part on the surface of the liquid resin.
II. The elevator platform descends.
III. A resin-filled blade scraps down across the cross-sectional part and further re-coats it with fresh building material.
IV. Then it immersed in a chemical bath because this requires the use of supporting structures.

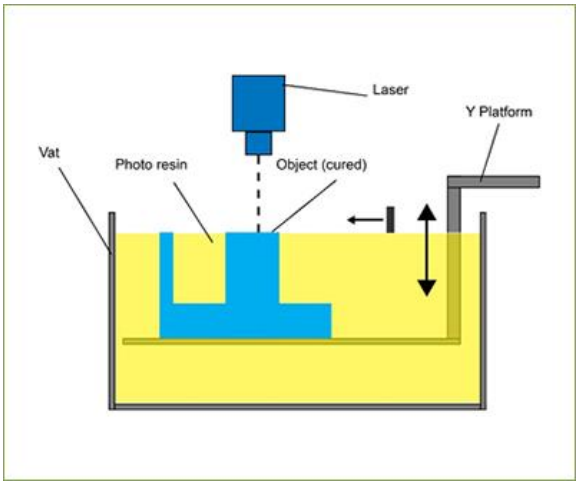

Figure. 6: Basic diagram of Vat Photopolymerization equipment.

4.6 Powder bed fusion

The basic process involved in Powder bed fusion are as follows:

I. Firstly, building material (powder) is spread over the build platform to form a layer, having a thickness of 0.1 mm.
II. The SLS (Selective Laser Sintering) machine warm up the powder material in the powder bed.
III. A laser beam is used to fuse the first layer.
IV. Another new layer of powder is spread over the first layer.
V. Subsequent layers with cross-sections are fused and added.
VI. This flow of process repeats till the final object is created.

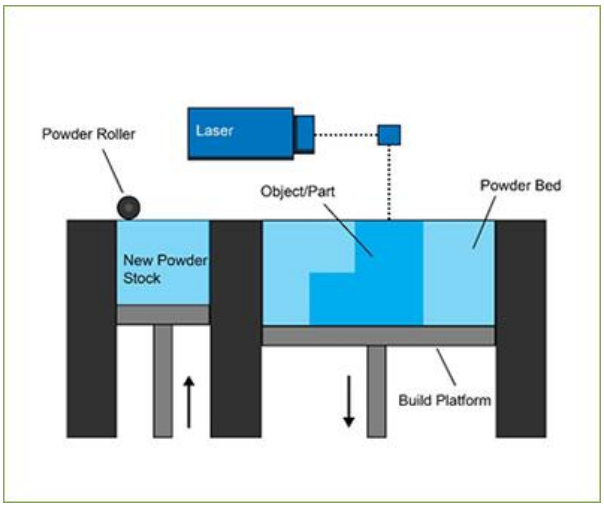

Figure 7: Basic diagram of Powder bed fusion equipment

4.7 Material Extrusion/ Fuse deposition modelling (FDM)

The basic process involved in Material extrusion or Fuse deposition modeling (FDM) are as follows:

I. Building material is preheated and drawn by a nozzle and deposited layer by layer.
II. To build the First layer, the nozzle deposits material was required in the cross-sectional area.
III. Further layers are added onto the top point of the past layers.
IV. At a melted state, the layers are deposited to form an object.

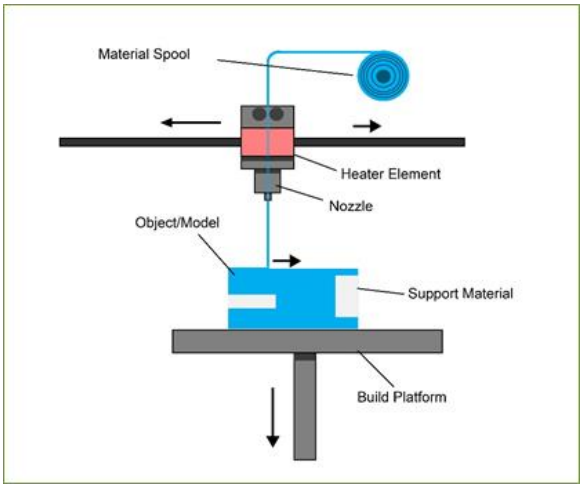

Figure 8: Basic diagram of Material Extrusion equipment.

5. APPLICATION OF 3DP TECHNOLOGY TO PHARMACEUTICAL DOSAGE FORMS

The applications of 3D printing to manufacture different pharmaceutical dosage forms and delivery systems are wide. Over the last 20 years, this technique is used to produce many unique implants, Tablets, capsules, transdermal drug delivery patches, Self-emulsifying drug delivery systems with a one-directional target of producing a personalized medicine. Since the revolution of precision medicine in the USA in 2015, more tailoring therapies have been conducted and so the implementation of 3D printing. In 2017, FDA published a guideline for additive manufacturing techniques, As far as the regulatory bodies are aware of this technique, 3D printing can now officially accelerate this process by producing tailored formulation in small batches for more precise use.

5.1. 3D Printed Implants

An implant is a drug delivery structure containing one or more than one APIs loaded for continuous delivery to the targeted tissue, giving advantages to patients who need long-term treatment of medications. While the conventional methodology for implant advancement was mainly targeted on expanded and delayed drug release, late 3DP-based inserts are intended to have a complex matrix and large-scale structures in a solitary device, for multi APIs stacking and accomplishing more advanced drug discharge characteristics. Scientists have successfully developed 3D printed implants utilizing different technologies like Rifampicin, levofloxacin implants based on the lactic acid polymeric matrix made by powder bed fusion technology, Nitrofurantoin antimicrobial implant with hydroxyapatite (HA) mixed polylactide feedstock by Fused deposition modelling, 5-Fluorouracil implants with Poly-lactic-co-glycolic acid scaffolds by Electro-hydrodynamic jet (E-jet) technology for orthotopic breast cancer, Levofloxacin and tobramycin loaded implants for osteomyelitis therapy by a customized 3D printing technology. With adequate performance and controlled drug release, targeted local delivery, 3D Printing based inserts seem to be a promising dosage form for chronic diseases and extend the drug utilization for personalized medicine development.

5.2 3D printed Tablets

Tablets are the most examined and developed 3D printed dosage form. They can be divided into single API and multiple API tablets. For example, single API tablet includes prednisolone loaded poly(vinyl alcohol) (PVA) tablets, Guaifenesin immediate release bi-layer tablets with HPMC 2910 as a binder whereas sodium starch glycolate and microcrystalline cellulose as disintegrants were used for an immediate release feature printed using Fused Deposition Modelling (FDM), Pseudoephedrine HCl controlled-release tablets with hydroxypropyl methylcellulose (HPMC) and Kollidon as carriers were designed by Powder bed inkjet technology. Multiple API containing tablets are developed using fused deposition modelling (FDM) like Lisinopril, Indapamide, Rosuvastatin, Amlodipine loaded polypill with distilled water as a temporary plasticizer for the therapy of cardiovascular diseases. 4-aminosalicylic acid, 5-Aminosalicylic acid loaded tablets with polyvinyl alcohol filaments for Inflammatory Bowel Disease (IBD). Researchers have developed an osmotic pump-based tablet containing captopril, glipizide, nifedipine as APIs with 3D printing extrusion technology. As these methods can regulate the drug release profiles through the inner matrix system, it seems capable of making customized drug tablets for rare diseases and therapies.

5.3. 3D printed capsules

Researchers have developed ChronoCap® an erodible pulsatile release capsule made up of hydroxypropyl cellulose (HPC) that can be used for various drug formulations developed utilizing FDM 3D printing technology was successfully adjusted with varying size and thickness. It can be filled with various liquid and solid dosage forms such as solutions, dispersions, powders, pellets, and other formulations. Another recent research developed gastro-resistant multi-compartmental PVA capsules named Super-H and Can-capsule loaded with ascorbic acid and dronedarone hydrochloride powder capable of intestinal delivery of a drug, these were formulated using Fused deposition modeling technology. These oral dosage forms can further contribute towards personalized drug delivery by personalizing the dosage and the loaded drugs.

5.4. 3D printed transdermal delivery systems

Transdermal drug delivery systems are important because they bypass first pass or hepatic metabolism and produce local action from skin. 3D printing technology offers layer by layer printing of customized patches and microneedles loaded with personalized drug molecules for individual use. Researchers have developed, Decarbazine loaded poly (propylene fumarate)/ diethyl fumarate blended 25 microneedle arrays targeting skin cancer therapy, transdermal insulin delivery made possible by developing microneedle arrays trehalose, mannitol, and xylitol as carriers, both the product utilize stereolithographic 3D printing technology. Research has shown, Diclofenac loaded microneedle with personalized curved surfaces using the Direct Light Processing technique. Recently, the Institute of polymers, composites, and biomaterials, Italy has developed an ornamental transdermal

patch Named "Anura", having Anti-shock properties, which could be further utilized for drug delivery with moderate patient compliance.

Dosage Form	Printing Technology - API used
Controlled release Implant	Powder Bed Fusion -Rifampicin, Levofloxacin FDM - Nitrofurantoin Electro-hydrodynamic jet (E-jet) -Five-Fluorouracil (5-FU) Custom - Levofloxacin and tobramycin
Tablets	FDM - Lisinopril, Indapamide, Rosuvastatin, Amlodipine, Prednisolone (2–10 mg), 4-aminosalicylic acid, 5-Aminosalicylic acid Powder bed inkjet - Pseudoephedrine HCl Laser-assisted system - Paracetamol, 4-Aminosalicylic acid Material Extrusion - Captopril, nifedipine, and glipizide
Capsule	FDM - Dronedarone hydrochloride, ascorbic acid
Microneedle	Micro-Stereolithography - Dacarbazine Stereolithography - Insulin Digital Light Processing - Diclofenac
Self-micro emulsifying drug delivery system	Dropwise additive manufacturing system -Celecoxib
Suppository	FDM - Hollow

6. LIMITATIONS AND CHALLENGES OF 3DP IN PHARMACEUTICAL FIELD

Although 3DP technology has shown propitious results in pharmaceutical applications, the technology is still in its evolving stage. The challenges that need to be addressed include: the choice of raw materials, printability, physical and chemical properties, thermal conductivity, fluid printing features and viscoelastic characteristics, should be carefully evaluated for the use and safety of human.

I. Nozzle mechanism: In 3DP, the layers of the dosage form or objects are created with the aid of the nozzle mechanism. Persistent flow of the printing material is mandatory even when the printer head stops and restarts in the course of the formation of successive layers. Nozzle clogging in the printer head, binder displacement, scraping, bleeding and improper powder feeding is the commonly encountered problems. For instance, the most frequently used Drop-on-demand (DoD) printer heads in 3DP technology manifest main issue of nozzle clogging.

II. Production involving powder-based 3DP technologies faces the challenge of a high degree of friability in 3D dosage forms. Polymers used in such techniques must be in the fine particulate form.

III. There is limited availability in the choices of raw materials, colours and the finishing material in comparison to the conventional method of production. 3DP techniques involving printing at high temperature is not suitable for thermolabile drugs.

IV. Expensive: The pricing of a 3D printer is very high. The requirement of different types of printers and materials for different processes make it more expensive for small manufacturers.

V. With the advancement in such technologies, jobs in the manufacturing and production sector will decrease drastically. This will have a huge impact on the economy.

To achieve standard 3D products, some important parameters need to be optimized such as line velocity of the print head, printing rate, time gap between two printing layers, space between the powder layer and the nozzles, etc. Special scrutiny of the post-process such as dry methods is also essential to obtain a better-quality output.

7. CONCLUSION

The versatility and the promising developments of 3DP technology since its first invention around 30 years ago as can be analyzed from the review exhibit that this technique will be a vital and a potential tool in the field of pharmacy and health care soon. Although the progress is in its infancy stage, 3DP technology has made the fabrication of extremely. sophisticated and intricated dosage forms feasible. Innovative 3DP has shown a promising way for novel drug delivery systems to efficiently achieve better patient compliance, optimum drug release profiles, better shelf life and stability, cheap and on-demand patient-specific dosage forms. The researchers and scientists believe that this technology has immense potential to revolutionize the pharma industry. Despite numerous advantages and benefits in pharmaceutical and health care systems, there are several technical and regulatory challenges obstructing its extensive utilization. The incessant innovation and progress of 3DP systems will address many challenges such as mechanical, scientific and even regulatory limitations and ultimately the rapidly evolving 3DP technologies will be more refined and appropriate for a wide range of dosage forms and even for on-demand personalized medicines at a nominal cost in days to come.

8. REFERENCES

1. Awad A, Fina F, Goyanes A, Gaisford S, Basit AW. 3D printing: Principles and pharmaceutical applications of selective laser sintering Int J Pharm. 2020 Aug 30;586:119594
2. Koçak E, Yıldız A, Acartürk F. Three dimensional bioprinting technology: Applications in pharmaceutical and biomedical area. Colloids Surfaces B Biointerfaces. 2020;197.
3. Ghadge S, Aloorkar N SS. A Decisive overview on Three Dimensional Printing in Pharmaceuticals. J Drug Deliv Ther. 2019;9(3):400–2.
4. Galante R, Figueiredo-Pina CG, Serro AP. Additive manufacturing of ceramics for dental applications: A review. Dent Mater. 2019 Jun;35(6):825–46.
5. Shahrubudin N, Lee TC, Ramlan R. An overview on 3D printing technology: Technological, materials, and applications. Procedia Manuf (August):1286–96.
6. Norman J, Madurawe RD, Moore CMV, Khan MA, Khairuzzaman A. A new chapter in pharmaceutical manufacturing: 3D-printed drug products.