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Recent Advancement of 3D Printing Application in Pharmaceutical Industries

Sadia Parveen[1], Roshan Yadav[2], Shivangi Sangal[3], Himmat Singh Chawra[4], Gulshan Rathore[5]

[1,2,3,4,5]NIMS Institute of Pharmacy, Jaipur, Rajasthan- 303121

Abstract:

The process of digital fabrication, commonly known as 3D printing or additive manufacturing, involves gradually adding materials to a geometric representation to produce actual items. Technology for 3D printing is one that is rapidly developing. The various 3D printing processes are covered in the paper, along with their benefits and drawbacks. Each sort of 3D printing procedure is described together with a detailed overview of the many materials that work with it. The many application fields for each type of procedure are also presented in the study. The pharmaceutical manufacturing and formulation processes will change as a result of this technology. Here, we provide a summary of three-dimensional printing's advancements in the development of novel drug dosage forms and applications in pharmaceutical and biomedical research.

Keywords: Material for 3D printing; Additive manufacturing in the polymers; Applications Manufacturing; Challenges.

1.1 Introduction:

A new term for the process of creating three-dimensional objects layer by layer using a digital design platform is three-dimensional printing (3DP). Initially created for industrial use, 3D printing has steadily matured into a promising technology over the past few years. Due to the advent of 3D printing, the manufacturing of pharmaceutical items has undergone significant changes, and previously non-digitalized medical products can now be converted into digital 3D content. [1].

These days, pharmaceutical 3D printing is attracting a lot of attention as a promising technology that could improve efficacy, precision, and individualization while cutting costs associated with waste. Additionally, new oral dosage forms and medical devices can now be made thanks to the new technology, which is otherwise difficult to perform with current production techniques. A technique capable of replacing all or the majority of the current traditional fabrication method used to create medical devices is the ambitious goal of intensive research into 3D printing. This disruptive technology has the potential to significantly innovate several drug development methods. [2]. Early in the 1990s, at MIT (Massachusetts Institute of Technology, Cambridge, MA, USA), Sachs et al. developed and patented a rapid prototyping technique known as "three-dimensional printing techniques," which marked the beginning of a significant shift toward the development of 3D printing technology in the pharmaceutical industry.

The first commercial 3D tablet, called Spiratam® (levetiracetam), was approved by the US Food and Drug Administration (FDA) in August 2015 and put on the market despite the new technology's slow uptake and growth. [3].

1.2 History:

Hideo Kodama of Nagoya Municipal Industrial Research developed additive manufacturing fabrication techniques for 3D plastic models using photo hardening polymer. Here, the UV exposure area is managed by an institute a fibre transmitter that scans, or a mask pattern [4]. Check Hull of 3D Systems Corporation created a prototype for a system based on the stereolithography method in 1984. In the decade of the 2000s, the umbrella phrase additive manufacturing gained increased currency [5]. An inkjet printer was used to print a binder solution onto a powder bed, binding the particles together as a result with the help of the semi-liquid binder solution. This was the first 3D printing method employed in the pharmaceutical industry. Up until the required final structure was attained, the process was repeatedly repeated. This first occurred at MIT in the early 1990s (Massachuset Institute Technology). Spritam was the first 3D-printed medication to receive FDA approval and was made available to consumers in the summer of 2016 by Aprecia Pharmaceuticals. Today, the most popular 3D printing technique is inkjet printing. Scott Crump applied for a patent on a different 3D printing process in the previous decade, in 1989 [6] .

1.3 Different materials used in various 3D printing technology:

The next question that occurs to us after going over the different types of 3D printing is, "What are some of the materials that are used in these processes? What are the viability of those materials? What kind of properties do they provide? For what processes and applications do we use them?" After going through the different types that are incorporated into 3D printing, this is the next question that comes to mind. Accordingly, particular material features for each 3D printing method have been expounded upon based on these parameters in the following sections [7] .

Table A.1. Materials, Character and applications in SL (stereolithography) technique.

Materials	**Character**	**Applications**	**Reference**
Polycarbonate	Has a high tensile strength and modulus.	Stiffness and strength need for parts with high temperature resistance	[15,21]
ABS	Good dimensional stability and high strength.	The material is black in colour and commonly used in packaging, automotive parts	[16,17]
Polypropylene	Propylene providing excellent resolution and fine detail.	It's potential application including medical devices.	[18]

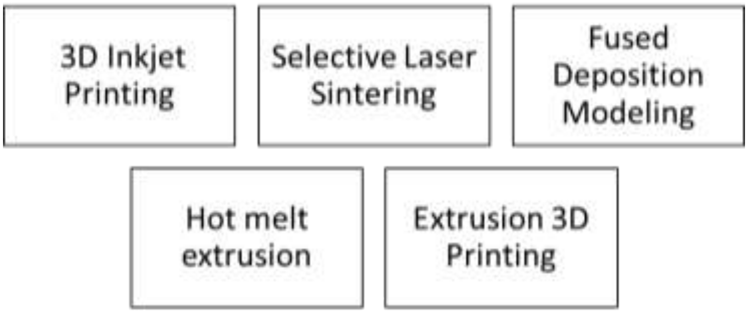
Table A.2. Materials, properties, and applications in FDM method.

Material's	Properties	Applications	Reference
TPU (Thermoplastic polyurethane) PEEK(Poly-ether-ketone)	Very high elasticity Has high mechanical performance	Sheet applications power tools and sporting goods. Applications are manufacturing of out of earth, metal implants.	[17,19] [18,19]
PET(Polyethylene terephthalate) PPSU(Polyphenylsulphone)	Smooth surface finish and good durability. Very high gamma radiation, impact resistance.	Its attractive applications for liquid container, graphic displays and food storage. Applications for smart devices, energy storage and healthcare.	[20,21,22] [23,25]

Table A.4. Materials, properties and applications in EBM method.

Materials	Properties	Applications	Reference
Nickel alloy	Nickel alloy are high strength and toughness, and no ferrous metals.	Is used to print parts in automotive, aerospace industries and biomedical.	[25,26]
Copper	Copper Printed on DMLS Machines	The ideal application for printing in copper include heat exchanger and electrical wiring. .	[26,27]

1.4. Types of 3D Printing:



1.4.1. 3D Inkjet Printing:

The same computer-operated inkjet printing method is the basis for this personalised treatment strategy By switching out the ink for pharmaceutical solutions carrying medications and the regular paper for edible sheets known as substrates, it was modified for use in the pharmaceutical industry. Changes to dose are made by adjusting the number of layers printed in a specific location or by altering the area that will be printed.

Designing the medicine and excipients in a ratio that allows it to potentially print as microdots onto an edible substrate. Thermal inkjet printers and piezoelectric inkjet printers are the two primary inkjet printing technologies used today. [8] . There are two types of printing-based inkjet systems: using Drop-on-demand and continuous inkjet printing

When printing inkjet continuously, the liquid An aperture with a diameter of 50 to 80 m is used to direct ink.making the ink flow continuously. It is made to flow the liquid.and split into drops at a particular rate and size at a piezoelectric crystal is used to generate periodicities. These parameters are managed via electrostatic discharge field. The droplets are therefore charged and separated by"droplets of guard" to reduce electrostatic attraction involving them. The generated electrostatic field guides the substrate with charged droplets [9,10].

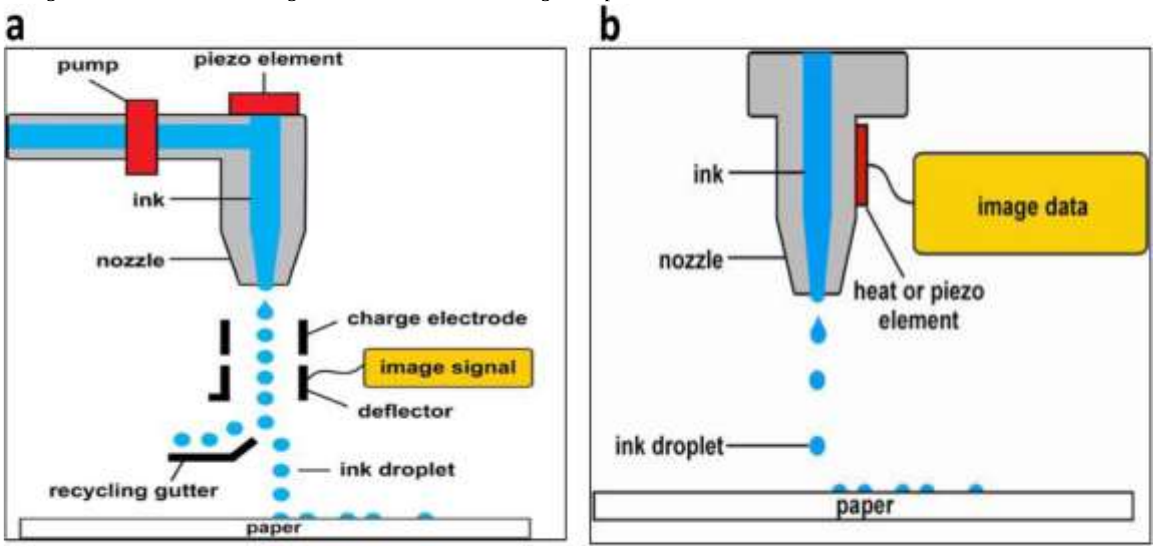


Fig1. (a) Continuous (CIJ), (b) Drop on Demand Inject Printing (http://www.imagepermanenceinstitute.org)

1.4.2. Selective Laser Sintering (SLS):

Generally used for rapid prototyping, selective laser sintering is a quick manufacturing method based on the utilisation of powder coated metal additives. As a heating source, a continuous laser beam is utilised to scan and align particles in the layers according to preset sizes and shapes. The geometry of the scanned layers matches different portions of the computer-aided design models or files created through stereolithography[11,12]. This technology employs a high power laser to combine tiny granules of plastic, metal, ceramic, or glass into a mass that has the desired three-dimensional shapes analysing the 3D cross section or layers modelling software for a powder bed's surface, laser the powdered material was only partially bonded, resulting in The layer thickness of the powder bed is reduced.the top is then covered with a fresh layer of material, and The procedure is carried out once more till the goal is achieved[12].

1.4.3. Fused Deposition Modelling:

Compared to Selective Laser Sintering printers, Fused Deposition Modeling printers are far more accessible and less expensive. An inkjet-like print head is utilised by fused deposition modelling printers**.** [13]. Instead of ink, heated plastic beads are discharged from the print head as it travels, constructing the object in minute layers. The procedure is continuously done in order to shape each layer. meticulous management of each's quantity and position Ever before the The material is heated to either bind or fuse with the layers beneath. [14]. Each layer of plastic hardens as it cools, gradually forming the solid item as more layers are added. A Fused Deposition Modeling printer may have improved features like numerous Print heads, depending on how complicated and expensive it is. A number of plastics can be utilised in fused deposition modelling printers. In actuality, the thermoplastics used in conventional injection moulding and 3D Fused Deposition Modeling printed products are frequently the same. [15].

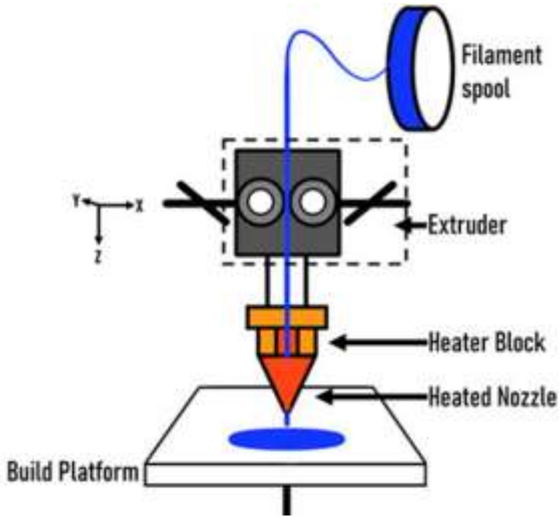


Fig 2. Fused depositiomn modelling

1.4.4. Hot Melt Extrusion: :

In this method polymers are melting & drug at high temp and the pressure is applied in the apparatus incessantly for blending [16]. It is an ongoing manufacturing process that encompasses a number of steps, including feeding, heating, mixing, and shaping [17]. In recent years, it has been clear that Hot Melt Extrusion can increase the solubility and bioavailability of medications that aren't very soluble. [18] .

1.4.5. Extrusion 3D Printing:

This method eliminates the need for additional support material by extruding the material directly from the automated nozzle onto the substrate. It is only employed in the production of expectorant tablets containing guaifenesin.Molten polymers, suspensions, semisolids, and pastes are among the materials that can be extruded. [19,20].

2.1 3D printing Applications:

Dental implants and personalised prosthetics were the first items made using 3D printing in the field of medicine. The current applications of 3D printing in medicine can be divided into several major categories, including the manufacture of tissues and organs, the development of prosthetics, implants, and anatomical models, and pharmaceutical research on drug discovery, delivery, and dosage forms [21,22,23].

2.1.1 Bio Printing Tissues and Organs:

By layer-by-layer producing cells, biomaterials, and cell-laden biomaterials using 3D printing technology, organ printing can directly manufacture 3D tissue-like structures [24]. A knee meniscus, heart valve, spinal disc, as well as other kinds of cartilage and bone, as well as an artificial ear, have all been produced by researchers using 3D printers [25,26,27].

2.1.2 Customized Implants and Prostheses :

X-ray, MRI, and CT images can be converted into digital 3D print data, allowing for the creation of implants and prostheses in almost any shape possible. This method has been applied to the creation of hip, spinal, and dental implants. [28].

2.1.3 Anatomical Models:

A representation of some of the most intricate human body structures may be found in 3D-printed neuro-anatomical models, which can be very beneficial for neurosurgeons [24].

2.1.4 3D-Printed Dosage Forms and Drug Delivery Devices And Personalized Medicine:

Since it allows for precise control of droplet size and dose, great reproducibility, and the production of dosage forms with intricate drug-release profiles, 3D printing has been used in the pharmaceutical industry alongside other techniques. [25]. The use of 3D printing can also be used to standardise complicated drug manufacturing processes, making them easier and more practical. The advancement of personalised medicine may also greatly benefit from the use of 3D printing technology[23].

2.1.5 Unique Dosage Forms :

Inkjet-based or inkjet powder-based 3D printing techniques are the main 3D printing technologies utilised in the production of pharmaceuticals. These technologies allow for the creation of countless dosage forms, which is expected to pose a problem for traditional medication manufacturing. Numerous innovative dosage forms have already been created using 3D printers, including nano suspensions, hyaluronan-based synthetic extracellular matrices, antibiotic-printed micropatterns, mesoporous bioactive glass scaffolds, and microcapsules[21,24].

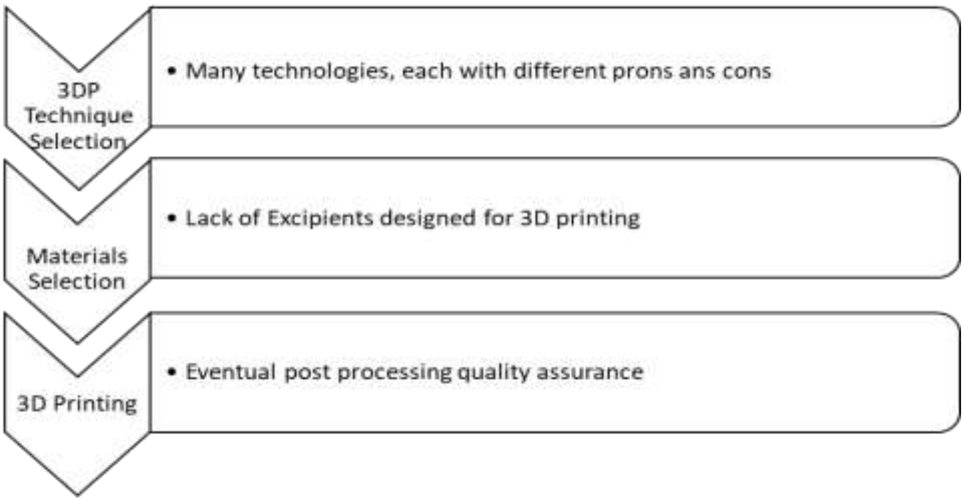
2.2 Challenges associated with different 3D printing techniques:

Applications for medicine delivery offer encouraging outcomes. Numerous obstacles must be overcome in order to enhance the functionality of 3D printed products and broaden their scope of use in novel drug delivery systems, including the optimization process, improving device performance for multiple uses, choosing suitable excipients, and post-treatment techniques[27]. A number of crucial parameters, including printing rate, printing passes, line velocity of the print head, interval time between printing layers, distance between nozzles and powder layer, etc. must be tuned in order to produce 3D objects of high quality[28,29]. Uniaxial compression and suspension dispersed techniques are used in 3D printed processed tablets to boost the medication loading capacity, yet this method is hampered by a clogged spray nozzle and additional complexity[30].

Table A.5.Main Factors Affecting 3D Printing Product:

Method	Factors	Reference
Size and Complexity	When bigger the size of an object the higher the amount of material you need to get done it indicates pay more amount and this factor affect the 3D printing price.	[11,12,15]
Pay attention to printer adjustment	It can involve completely different steps like improvement of the inside or lubricating after you optimize your printer it can involve completely different..	[23,26]
Filament adheres	For most common problems warping is one in every of the 3D printing for this reason don't adhere well to the print bed.	[23,24]

2.3. Stages in 3D Printing & Relative pharmaceutical chalenges :



3.1. Conclusion:

This brief review's examination of a few experimental investigations has demonstrated that 3D printing technology may be successfully applied on a small scale to create custom drug dosages and offers significant advantages when producing oral dosage forms. In terms of the future of 3D printing, the new technology is probably going to concentrate on manufacturing in pharmacies and hospitals for specific individuals or specialised populations. Additionally, 3D printing may present an alluring new potential for research and development to enhance medicine formulation and administration of already existing active pharmaceutical ingredients.

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