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REVIEW ON 3D PRINTING TECHNOLOGY

N.Jhansi[1], T.Balakrishna[1], A. Lakshmana Rao[1], T. Sravani, M.Sivasravani[1], A.Indira[2]

[1] Department of Pharmaceutics, V. V. Institute of Pharmaceutical Sciences, Seshadri Rao Knowledge village, Gudlavalleru- 521356.AP .India.

[2]Department of Chemistry, V V Giri government kalasala, Dumpagadapa, West Godavari district-534235

Abstract:

An innovative strategy for delivering drugs is three-dimensional printing technology. It has now been revealed that the drugs can be customised and made to fit the patient's needs. Additionally, it has been quickly modernising and developing the healthcare system. Since it was first patented in 1986, this method has not been widely used in research. However, in recent years, its value has grown, especially in the fields of bio printing, pharmaceutics, prosthetics, and medical 3D printing. Computer-aided design (CAD) software and programming are the basis of 3D printing. The successive layers of medicine have been deposited and create a three-dimensional structure in this additive layer manufacturing technology. According to the patient's unique needs, which may involve loading numerous medications, the drug material is incorporated. With the aid of a computer-aided design module, these drug substances are configured in three dimensions before being converted into a machine-readable form, which suggests the exterior appearance of a three-dimensional dosage form. The surface is then divided into several different printable coats and fed with these layers to the machine.

In this current review of 3D printing technology, we briefly discuss the history, basic steps involved, drug delivery devices, different pros, cons and as well as applications of this technology.

Keywords:

3D printing, patients unique needs,customization,fabrication,prosthetics,bioprinting,pharmaceutials, Computer aided design software.

Corresponding author:

Dr. Balakrishna Talamanchi,
Associate Professor & Head,
Department of Pharmaceutics,
Vallabhaneni Venkatadri Institute of Pharmaceutical sciences,
Seshadri Rao Knowledge village, Gudlavalleru-521356
Ph: +91-9494466340
Email ID:balakrishnathalamanchi@gmail.com

QR code

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1. INTRODUCTION:

3D printing technology has multiple ranges of applications in the printing and creating of organs and tissues, in diagnostic purposes, manufacturing of biomedical devices and in the designing of drug delivery systems[1,2]. 3D drug delivery is the technology in which the formulation is prepared in order to transport the therapeutically active substituents in the body to produce the therapeutic efficacy in safe and controlled pattern. The safety and efficacy of a compound can be achieved by modulation of drug release in a rate-controlled manner, which also interlinks with the pharmacokinetics. By taking into account the patient's unique genetic profile, age, race, gender, epigenetics, and environmental factors. 3D printing primarily aims to personalise medicine to meet their needs. The patients' health treatment is likely to improve as a result of this. Additionally, this technology may optimise dosage, appearance, flavour, dosage form, and release profiles while also lowers the administration frequency and dosing, significantly reducing on material waste, saving money, and preventing unnecessary side effects[3,4]. The additive method is used in the building of 3D printed objects[5], which creates an object by layering various elements, such as live cells, wood, alloys, thermoplastics, metals, etc., until the full object is attained. Rapid prototyping, layered manufacturing, additive manufacturing, computer automatic manufacturing, and solid free-form fabrication are the other terms for this technique[6].The final model is sliced into tens of thousands of horizontal levels by the software. One 3D object is produced as the object is built up layer by layer by the printer. New drug delivery systems, such as oral controlled release systems, microchips, implants, pills, instant release tablets, and multiple phase release dosage forms, have emerged in recent trends[7].

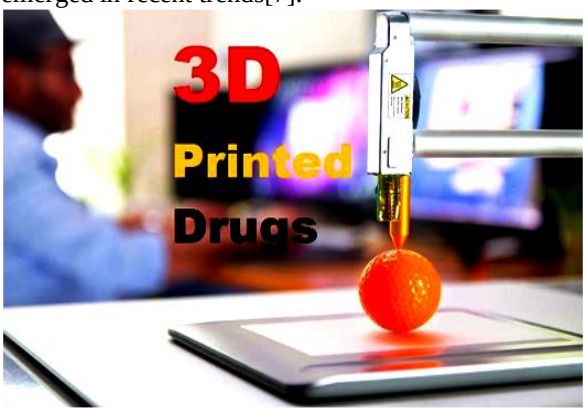

Figure 1.3D Printed Drugs.

2. BACKGROUND

In 1990, MIT (Massachusetts Institute of Technology, Cambridge, Massachusetts, USA) pioneered the use of 3D printing for rapid prototyping using inkjet printing, which was then regarded as personalised medicine. The final structure was created by repeatedly introducing a binder solution over the powdery bed, binding them together. Sachs et al. patented this process under the name "three-dimensional printing technique"[5]. The FDA's Center for Device and Radiological Health (CDRH) has amended and approved 3D printing medical devices, which is a significant accomplishment[8] . Scott Crump later applied for a patent on this technique using fused deposition modelling in 1989[9,10]. Many pharmaceutical companies, which tends to produce potential medications, has recently used 3D printing technology. The Spritam tablets [Levetiracetam], which were produced by Aprecia Pharmaceuticals as the first 3D-printed oral medication, were given FDA (Food and Drug Administration) approval in 2006 for use in treating epileptic seizures[9].

3. SOME IMPORTANT EVENTS IN 3D PRINTING

- The first RP technology patent was submitted in 1980 by Dr. Hideo Kodama.
- Charles Hull, who created the stereo lithography equipment (SLA) in 1984,
- Carl Deckard created equipment for selective sintering of pieces in 1986.
- Carl Deckard received a patent for SLA in 1989.
- In 1990, fused deposition modelling (FDM) was developed.
- The first SLA machine was created in 1992 using a 3D system.
- In 1993, E.M. Sachs received a patent for 3D printing.
- The first therapeutic use of biomaterials for tissue regeneration occurred in 1996.
- In the year 1999, Luke Massella became the first person to receive a 3D-printed bladder that was made of a combination of his own cells and 3D-printed biomaterials.
- SLM technology was introduced in 2000 by MCP Technologies.

- In 2002, a working miniature kidney was created.
- The term "Organ printing" was created in 2003.
- In 2004, Dr. Bowyer created the open-source, self-replicating 3D printer RepRap.
- The information on the first fully bioprinted blood arteries was published by Organovo in 2009.
- In 2011, silver and gold were used in 3D printing applications. The first artificial aircraft and 3D-printed vehicles were unveiled.
- In 2012, an artificial liver was created using extrusion-based bioprinting, and a 3D-printed artificial jaw was implanted.
- Solid Concepts created a metal cannon that was 3D printed in 2013.
- Multi-arm bioprinter implementation in 2014 will combine tissue creation with printed vascular structures.
- In 2015, the US FDA authorised the first 3D-printed pill. Data on the first totally bioprinted kidney was made public by Organovo[18].

4. 3D PRINTING TECHNIQUE VS CONVENTIONAL MANUFACTURING

The conventional dosage forms(tablets and capsules) traditionally produced by mass fabrication involve multiple processes of blending, mixing, milling, and then compression of tablets. They are considered to be large-scale mass production with only one dose fit approach, which means they cannot be considered as individual medication. This traditional

- In 2005, Z Corp unveiled the first colour 3D printer.
- Selective layer personalization and on-demand production of industrial parts in 2007.

medication is a time-consuming process, requiring skilled personnel and costly[11,12].The 3D printing technology is revolutionised, customized, innovative, creative technique and is different from the traditional conventional dosage forms. It is less time consuming, controlled release and drugs rapidly released into the market this causes a sustainable cost reduction favourable for the pharmaceutical industries[13,14].Majorly, the wastage is low and the used material can be explored further. The fabrication steps are clean, which increases patient compliance and accessibility. Recently, the samiei Beni-Suef university journal of basic and applied sciences(2020)9:12 page 2-12 is growing, which increases the market for 3D technology[15].Sometimes the drug release products such as matrix embedment, multiple compartment systems, and core-coat ones have a drawback of burst release which causes toxicity and adverse events to be happened. In this regard, different manufacturing routes are developed for advanced drug delivery with flexibility and complex geometry. It leads to potentially personalised medicine[16].It is already known that these are produced by means of CAD, which increases the stability. Therefore, 3DP must meet the same quality standards as conventional dosage forms with GMP guidelines[15,17].Although this technology has not been developed much due to its limitations.

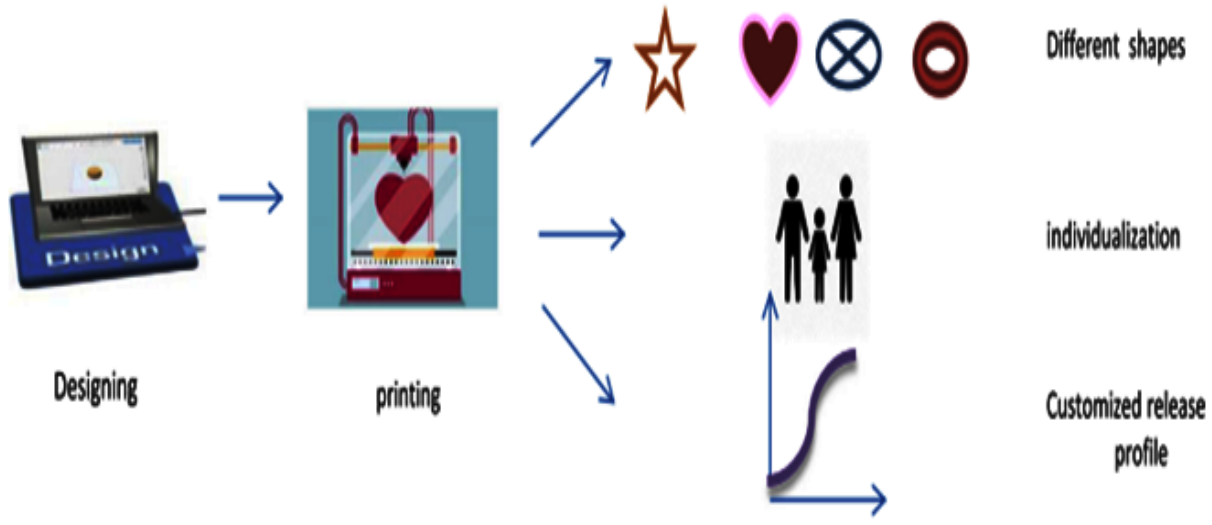

Figure 2. Representing the general view of 3D printing.

5. ADVANTAGES

- Drug loading capacity is high compared to conventional dosage forms.
- Only a negligible amount of dosage is required.
- Accurate and precise medication is possible.
- The medication is formulated on the basis of genetic variations, ethic differences, gender, age, and environment.
- In the case of multiple drug therapy with multiple dosing regimens, treatment can be customised to improve patient adherence.
- Low cost of production due to less material wastage.
- Suitable for drugs which are poorly water soluble, have a narrow therapeutic window, and are difficult to formulate the API.
- Flexible design.
- Rapid prototyping.
- Printing on demand.
- Strong and lightweight parts.
- Sustainable drug release.

6. DISADVANTAGES

- 3D printing is limited currently due to size constraints.
- The cost of the printers is high and also requires various types of printers for different objects.
- As with all new technologies, the job of manufacturing decreases. This leads to a larger impact on the economy of third-world countries, especially China, which depends on a large number of low-skilled jobs.
- It requires high energy.
- A scarcity of raw materials.
- Harmful emissions occur in low-space areas.
- Printers' capacity to work could be slow at times.
- Copyright issues can be seen .

7. BENEFITS

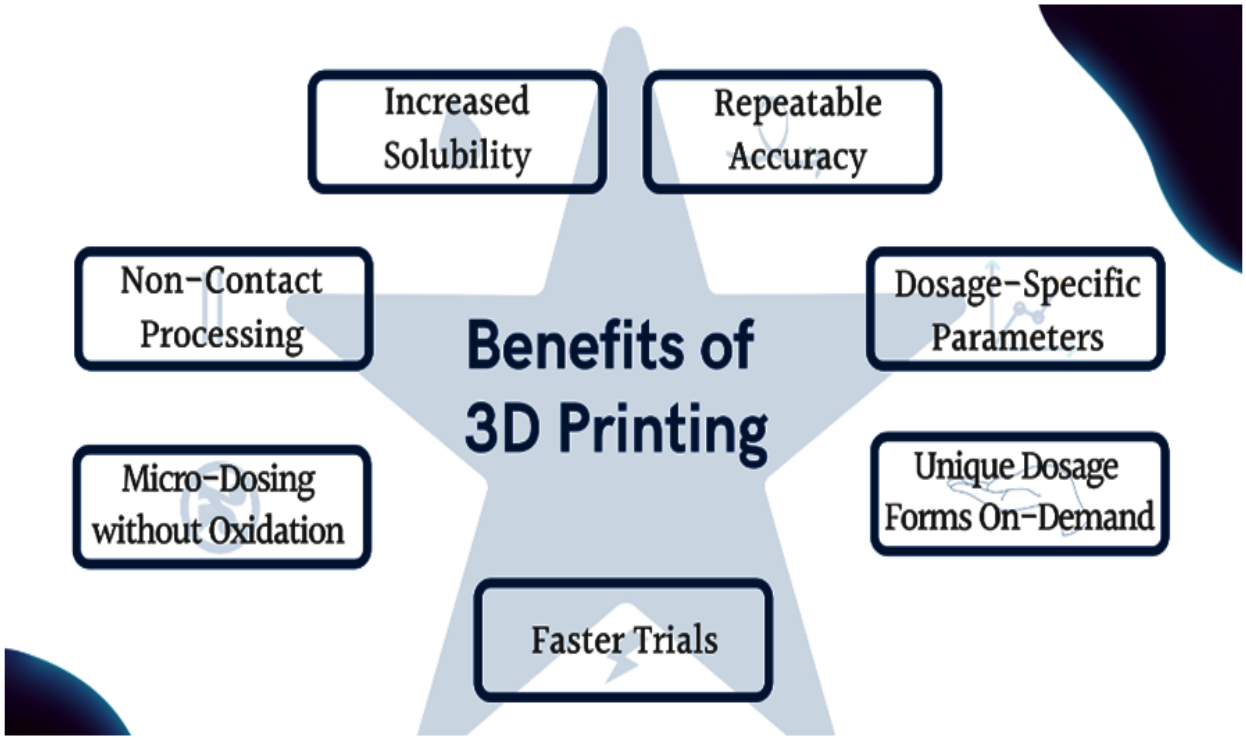

Figure 3. Benefits of 3D printing technology.

7.1 Dosage-specific parameters
Site-specific colon targeted medications are finally a reality thanks to Zip Dose technology, which combines the implant and drug delivery worlds. The anti-cancer drug fluorouracil has also been administered as a drop-on powder. To obtain precisely the proper dosages using fused deposition modelling FMD, researchers have explored a variety of polymer solutions. This study established the ability of optimised powder-based printing to generate

7.2 Micro dosing without oxidation
Ingredients in tablet fragmentation may oxidise. Accurate dosages are nearly impossible to achieve when drugs must be quartered. Unique dosage forms that give micro-doses without the risk of oxidation may be available through 3D printing.

7.3 Increased solubility
When you can use the technology to print active chemicals in a way that increases efficacy, why to restrict 3D printing to metal and plastic? Miconazole, a drug with a notoriously low solubility in aqueous conditions, has been produced via thermal inject printing (TIJ). Coated microneedles are used in TIJ micromolding as coatings for drug delivery. Microchips and polymeric nanoparticles, two examples of 3D-printed drug delivery systems, have become widely accessible and reasonably priced. Similar to vat photopolymerization, which uses light-activated polymerization for special drug delivery applications. Zip Dosing achieves a fast disintegrating formulation, raising the bar for solubility to whole new heights. Currently, scientists are examining how modifications in drug shape and hot-melt extrusion will affect drug release.

7.4 Faster trails
Vat photo polymerization and other 3D technologies have been employed by medical engineers to develop pre-clinical drugs for testing. More quickly than it has ever been feasible, this procedure. Innovation in pharmaceuticals is accelerating along with testing. become a significant equaliser in the pharmaceutical industry. The final consumer price should reflect the elimination of unnecessary resources. Even better, complicated drug release profiles provide for a greater

excipients devoid of thermal processing, enabling the production of thermo-sensitive medications in precise dosages. Binder volumes, jet dispenser speeds, and the number of shots fired were some of the printing characteristics covered in the study. Temperatures throughout production were kept at 50 degrees Celsius. In the end, homogeneous coatings created using drop-on-demand processes only needed the proper carrier particles.

Pharmacists are instantly altering drug design from a CAD file. As needed, new salt forms, doses, and excipients can be created thanks to this last link in the supply chain.

7.5 Unique dosage form on demand
Authorized blueprints can be used to create unique dosage formulations. As a result, the supply chain can be shortened by pharmacists. In this approach, logistics and distribution expenses can be cut, and doctors can treat multiple ailments with a single tablet.

7.6 No contact processing
Through a nanometer nozzle, inkjet printing can process up to 100 pl droplets into 3D objects. The liquid may be subjected to voltage or heated to boiling point. While contamination and heat damage can be reduced in this way, inkjet technology is capable of much more than merely creating layers. Additionally, it can be used to print additional biological components, such as pure protein arrays and magnetic nanoparticles. Consistency, filtration, and pH levels can all be used to tightly regulate drug release characteristics. Prednisolone solid dosage forms have been produced using this technology with the aid of heat and additional polymorphs.

7.7 Repeatable accuracy
Even for small-scale production lines, 3D printed technologies provide higher resolution, accuracy, and repeatability. The ability of small enterprises to develop complex goods on a limited budget will

degree of control over dosage form administration. Some drugs' effectiveness may even be enhanced by this[19].

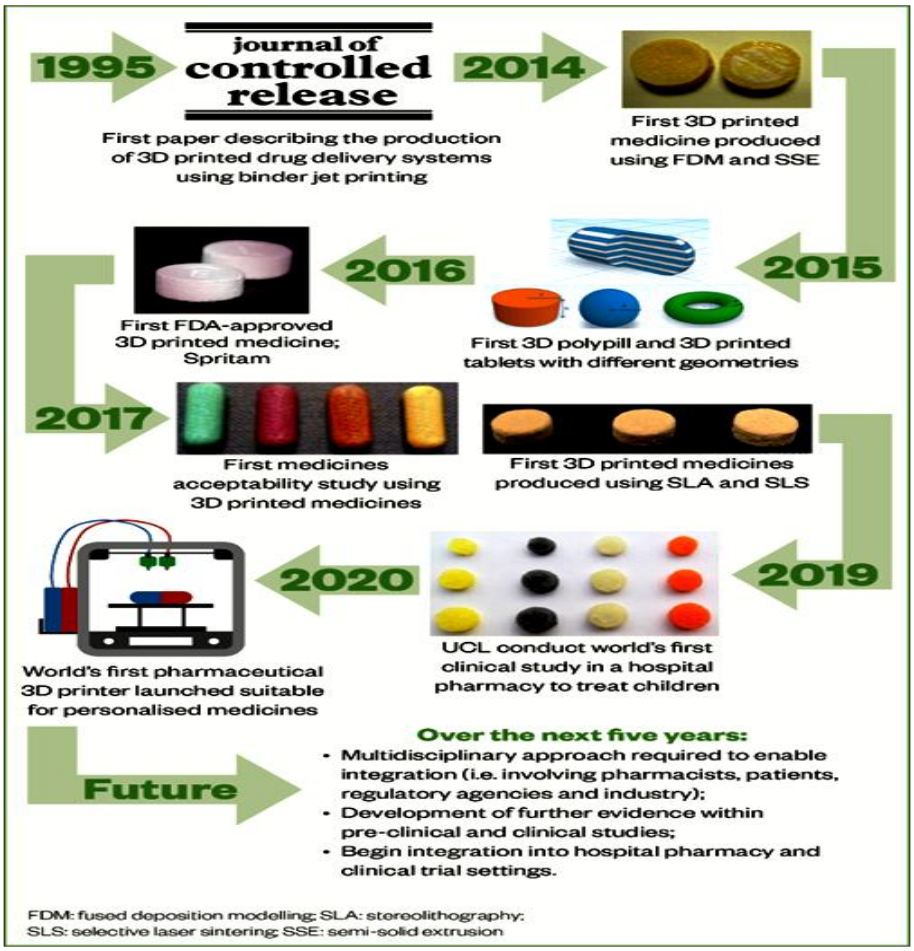

Figure 4. Representing the sequential development of the 3D printing technology

8. Procedure for 3D Printing

The most popular method used by researchers nowadays is the prototyping method. The 3D printer used by the companies can easily build the prototypes for testing and quality assurance requirements. Although there are numerous methods for developing Modelling is an initial aspect to be considered before the construction of software. This 3D printing is therefore linked with computer-aided software (CAD). After designing the object models, they are saved as stereolithography (STL) or an Additive Manufacturing File (AMF) format.

During this procedure, there is a model file in which the errors are evaluated by the manufacturing companies. Most of these CAD systems detect errors that, if ignored, could cause defects in the printed object. Generally, some causes of errors could be holes, self-intersections, manifolds, errors, and faces.

Step 2

Printing: Building the object with a 3D printer

the 3D printing process, in general, all types have three basic steps.

Step 1

Modelling: Designing the object model in a CAD package.

The next step is the printing, building of an object if and so there are no any types of errors in the STL (or) AMF file, the company of manufacturing will be subject to the printer where and how to deposit the material.

3D printers may use different types of materials, such as thermoplastic, which is the most commonly used. Thermoplastic pellets (or) heads are extended out of the printer head, at which point they fall onto the bed where they form the printed object. This process is achieved by a layer-by-layer process in which first deposits the bottom layer and next highest layer, likewise the object is deposited on the bed.

Step 3

Finishing:Final touch.

The final step is the finishing step, which involves final touches to the object. For example, solvents are added in order to remove any superficial imperfections and also to create a smooth surface. Meanwhile, if any supporting materials are used to make objects, those materials would be removed during this step[20].

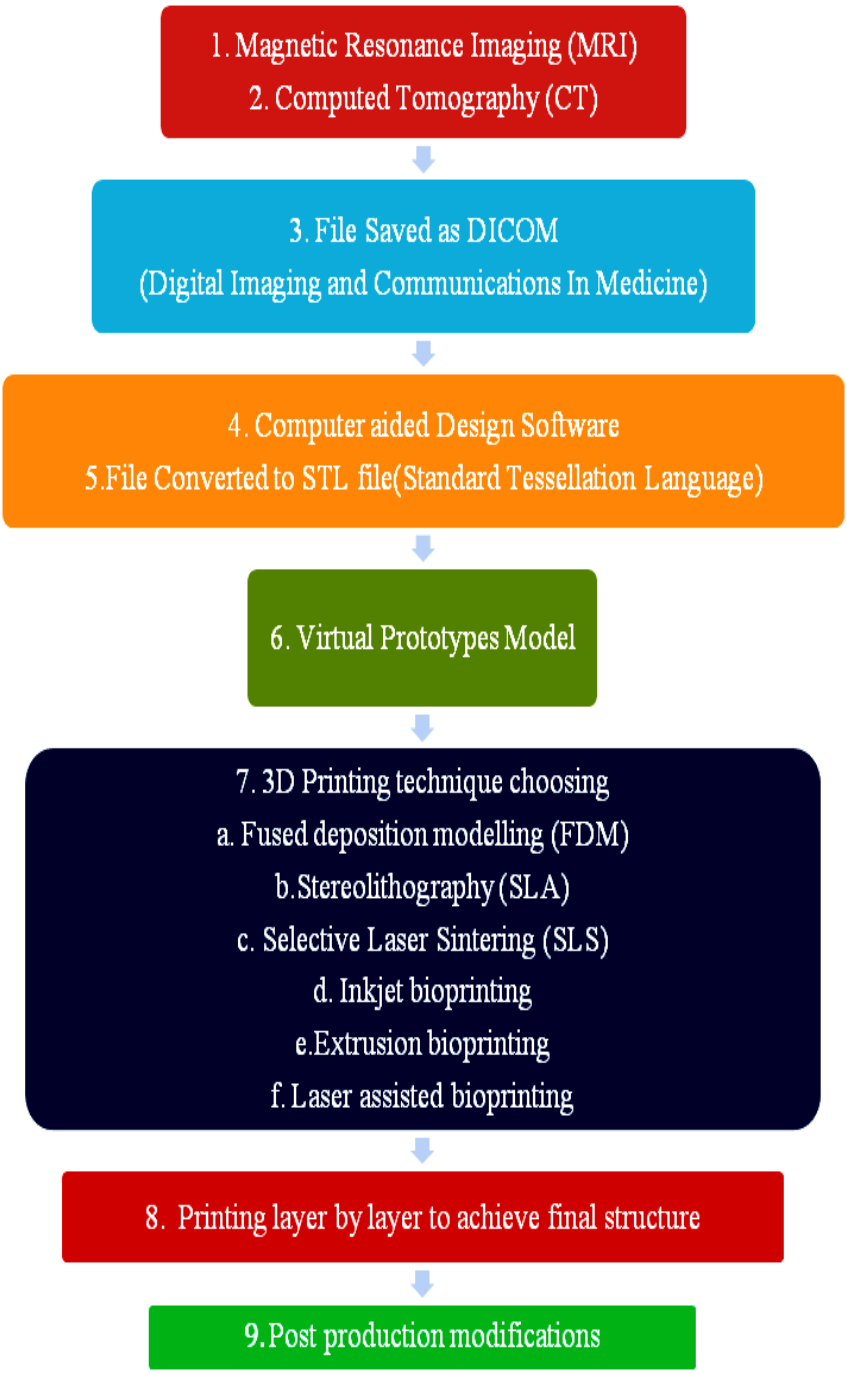

Figure 5. The flow chart representing the general 3D printing process.

9. 3D PRINTING TECHNIQUES

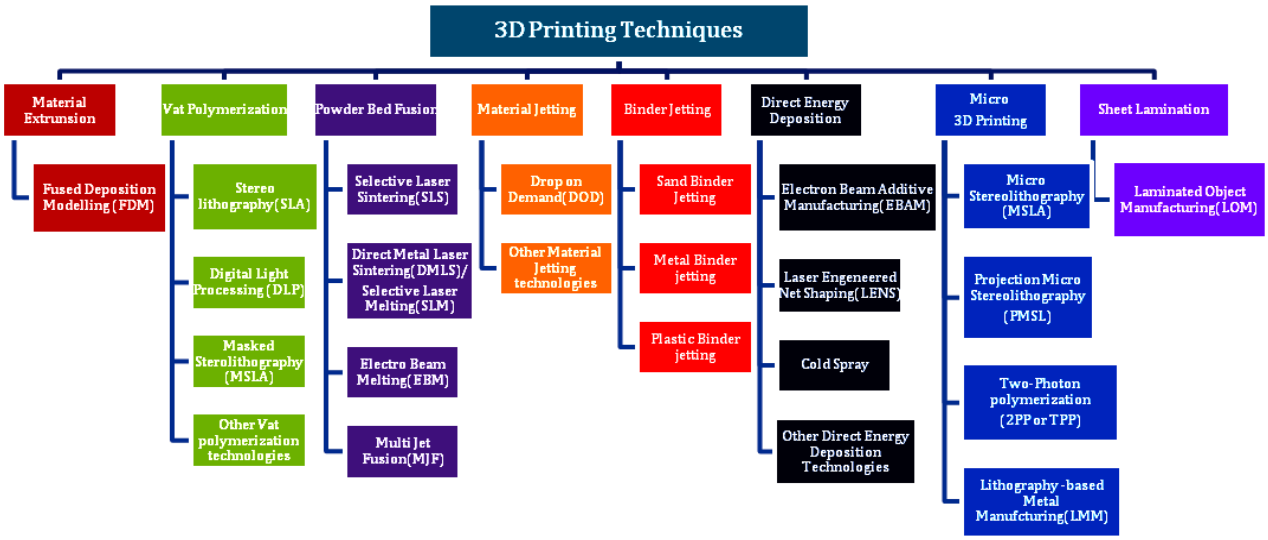

Figure 6. Representations of 3D Printing Technologies**.**

The terminology used in 3D printing already adheres to conventions. The "ISO/ASTM 52900 Standard Terminology for Additive Manufacturing-General Principles-Terminology" specification, which replaced "ASTM 52900:2015 Standard Terminology for Additive Manufacturing Technologies" in March 2020, is the most crucial one. This led to the categorization of 3D printing technology into several categories.

9.1 Material extrusion

This method produces an object by printing layers of molten thermoplastic filaments on top of each other. A spool of filament is placed through a heated extrusion nozzle and melted. The printer rapidly deposits the melted filament at a particular location where it gets cooled and then turns into a solid state. The filament of solid thermoplastic materials such as polylactic acid (PLA), acrylonitrile butadiene styrene(ABS),polyetherimide (PEI), and polycarbonate(PC) were used. Extrusion is typically accomplished through fused deposition modelling (FDM) or hot melt extrusion (HME)[21,25].This technique is a solvent free method, making it an environmentally friendly method of production.

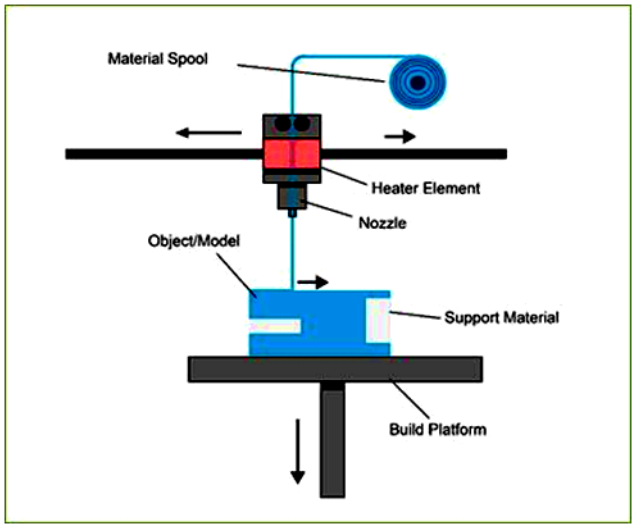

Figure 7. Material extrusion.

9.2 Vat polymerization

Vat photopolymerization is the collective name for a number of 3D printing techniques in which liquid photoreactive polymers are placed in a vat, solidified and cured using a laser beam or UV light source. Initially, photopolymers were a 1960s-era invention [26].Examples include stereolithography (SLA), Digital light processing(DLP),Masked stereo lithography(MSLA),and other vat polymerization technologies. The procedure includes [27]. A high-voltage on the surface of the liquid resin, a laser beam creates a cross-sectional portion. The platform of the elevator drops. The cross-sectional part is recoated with new building material after being scraped across by a blade that is packed with resin. Due to the need for supporting structures, it was next placed in a chemical bath.

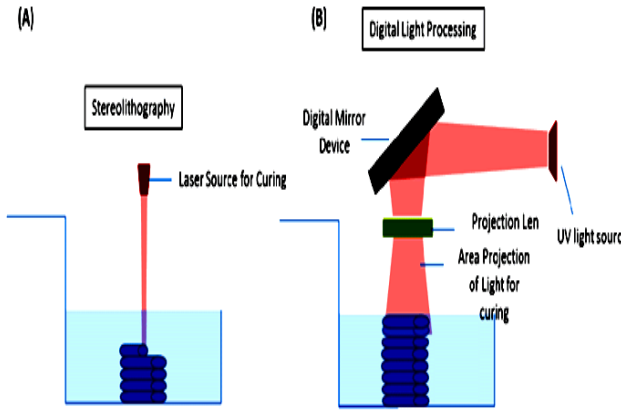

Figure 8. Vat polymerisation.

9.3 Powder bed fusion

It is a part of additive manufacturing technique that relies on the thermal energy-driven melting of powders to fuse them together. Carl Deckard made the well-known discovery of SLS in 1987. For this 3D printing technique, solid particles such as metals, polymers, and ceramics can be added as additives. New developments using quick lasers have been introduced to speed up the procedure[28,29,30].

Selective laser sintering (SLS), Direct metal laser sintering (DMLS), selective laser melting (SLM), Electron beam melting (EBM), and multi-jet fusion (MJF) are some of the general techniques used in this.The building process begins with the deposition of powder, continues with its solidification, and finishes with the reduction of the build platform by one layer thickness. These three steps are repeated until the final layer of the constructed object has been sintered[31,32,33,34,35].

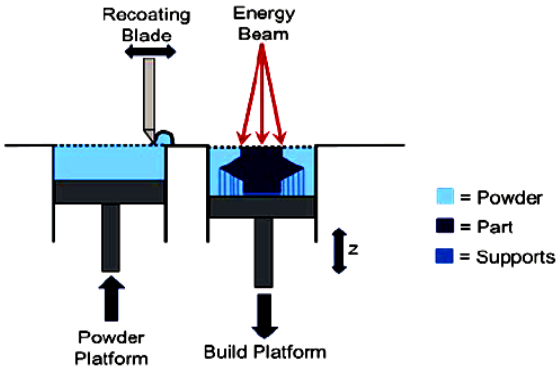

Figure 9. Powder bed fusion.

9.4 Material jetting

Material jetting is the selective layering down of construction of material or additive-containing droplets.Elastomeric photopolymers, acrylic-based photopolymers, and wax-like materials are utilised in this technique as liquid substrates.Due to their long molecular chains, these polymers are very attractive. By Optomec Company, the Aerosol Jet is another term used for material jetting[36,37,38,39]. The terms thermal inkjet printing and multijet printing are used to describe this process.Similar to inkjet printing, this technology sprays a liquid photopolymer onto a build tray before curing it with UV light. The process is known as thermal ink jet printing when heat is employed to create flow in the materials or to cross link them[32][35],[41][12][5][42][43].

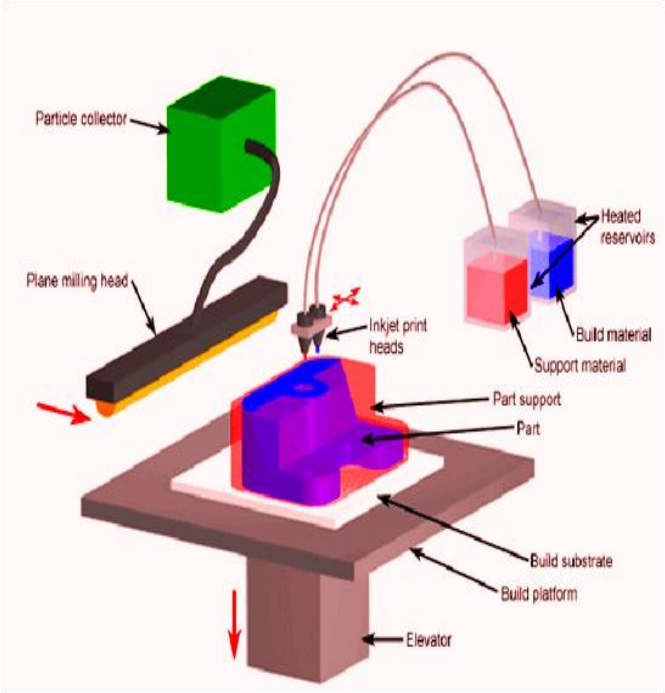

Figure 10. Material jetting.

9.5 Binder jetting

Powder-binding technology and colour-jet printing are other terms for binder jetting. Material jetting is a technique that is related to this. A powder layer is deposited, a liquid binding agent is dispensed, and then the construction platform is lowered to enable printing of the following layer. Pressurized air is then used to remove any leftover powder. No support structures are required because the surrounding powder sustains the unconnected parts as the prototype is constructed. Starch, plastic cement, poly (lactide-co-glycoside), and PCL metallic ceramic powder are only a few of the powders are employed. The binder solutions can either be aqueous or non-aqueous dispersions of inorganic materials like silica, aluminium nitrate, silver nitrate, or polymer solutions and dispersions that, when dried, form films and securely connect to the particles, binding them together[32,33,34,35],[41]. It consists of plastic binder jetting, metal binder jetting, and sand binder jetting (PBJ).

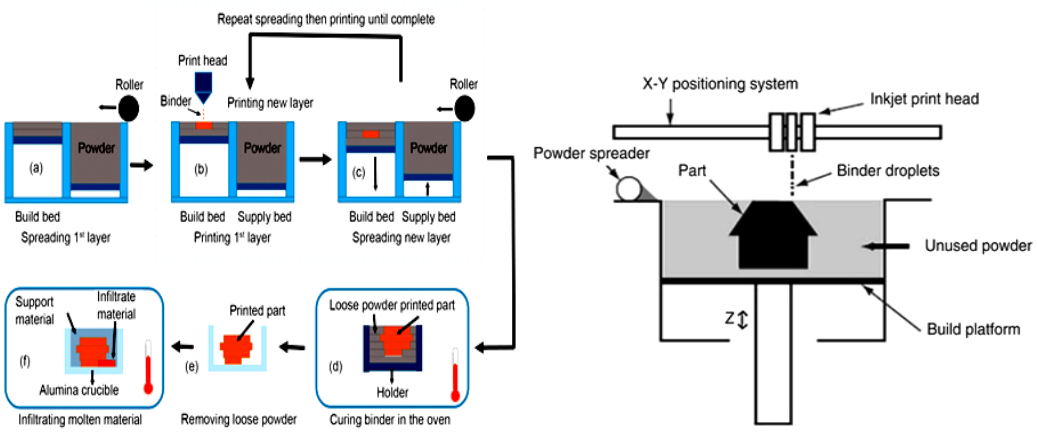

Figure 11. Diagram of binder jetting process.

9.6 Direct energy deposition

Intense heat energy is used in the additive manufacturing process of direct energy deposition to create three-dimensional objects. High energy sources include lasers, plasma welding torches, and electron beams, among others. Energy is used to fuse things like metal or powder by melting and stacking[33][44]. This method uses direct energy deposition technologies such as cold spray, laser-enhanced net shaping, electron beam additive manufacturing, and electron beam additive manufacturing (EBAM).

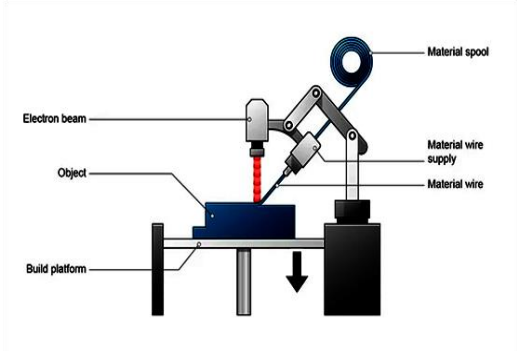

Figure 12. Direct energy deposition.

9.7 Micro 3D printing

Using additive manufacturing (AM) methods that are based on layer-by-layer manufacture, it is possible to create actual 3Dmicroproducts. Within the past ten years, AM technologies have been widely used to create complex 3D components. By implementing certain necessary changes and upgrades to create the ideal conditions for microfabrication, several specialised AM technologies can be used to fabricate 3D microparts and structure[45,46,47,48,49,50]. This technology includes Micro stereolithography(μSLA), Projection Micro Stereolithography (PμSLA), 2photon polymerization(2PP or TPP), and lithography-based metal manufacturing (LMM).

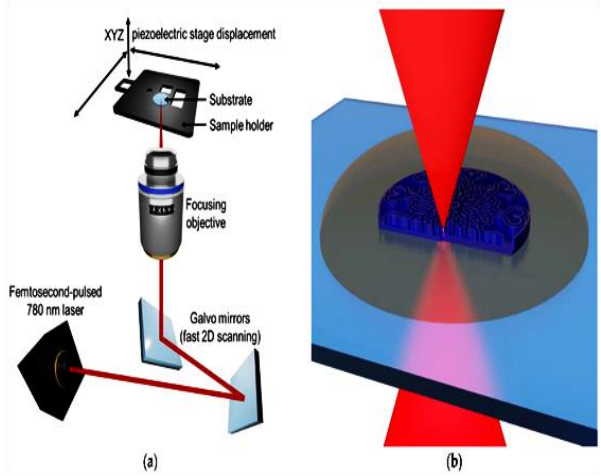

Figure 13. Micro 3D printing.

9.8 Sheet lamination

The laminated object manufacturing (LOM) process involves stacking, slicing, and pasting thin sheets of paper, plastic, or metal together to produce 3D objects. LOM is a hybrid manufacturing technique that combines additive manufacturing with subtractive processing. The first stage involves feeding adhesive-coated sheets to the constructing platform, where they are laminated with the aid of a hot roller. In the subsequent stage, the sheet is cut utilising the contour provided by the 3D CAD data. A carbon dioxide laser or knives attached to the print head are used for contouring. Fresh sheets are provided by the rollers,

and the process is repeated until the entire structure is built. On the construction platform or on the roller, heat is used in the LOM process to fuse the sheets together. The materials utilised are laminates made of metal, plastic, or Polyvinyl Caprolactam (PVC).[51,52,53][33].

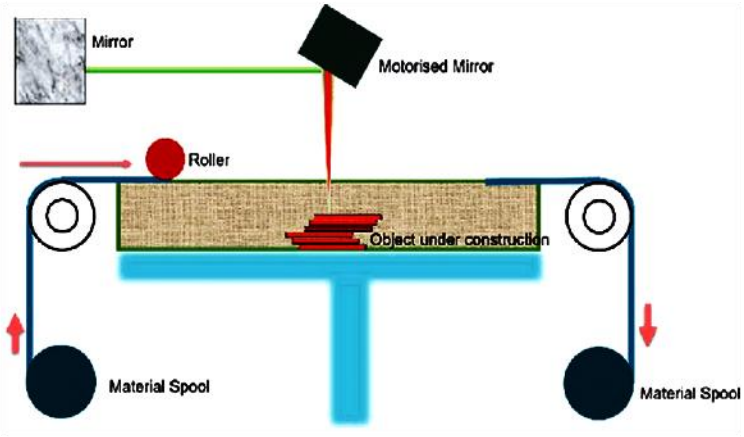

Figure 14. Sheet lamination.

Table 1. Represents the Basic principles, Materials, Advantages, Disadvantages of 3D printing technology

CATEGORY	BASIC PRINCIPLE	EXAMPLE TECHNOLOGY	ADVANTAGES	DISADVANTAGES	MATERIALS
Binder jetting	A liquid bonding agent is selectively deposited to join powder materials.	✓ 3D inkjet technology	Free of support. Design freedom. Large build volume. High print speed. Relatively low cost.	Fragile parts with limited mechanical properties. Many requires post processing.	Polymers. Ceramics. Composites. Metals. Hybrids.
Direct energy deposition.	Focused thermal energy is used to fuse materials by melting as they are being deposited.	Laser deposition. Electron beam. Plasma arc melting.	High degree control of grain structure. High quality parts. Excellent for repair applications.	Conflicts in surface quality and printing speed.	Metals. Hybrids.
Material extrusion.	Material is selectively dispensed through a nozzle or orifice.	Fused deposition modelling(FDM), Fused Filament Fabrication.(FFF)	Wide spread use. Inexpensive. Scalable. Fully functional. large range of material options.	Vertical anisotropy. Step-structured surface.	Polymers. Hybrids. Metals. Composites.
Material jetting.	Droplets of build materials are selectively deposited.	3D inkjet technology. Direct ink writing.	High accuracy. Low waste. High compatibility.	Support material is often required. Conflicts in speed and resolution.	Polymers. Ceramics. Composites. Hybrids. Biologicals.
Powder bed fusion.	Thermal energy selectively fuses regions of the powder bed.	Electron Beam Melting(EBM). Selective Laser Sintering(SLS).	Relatively inexpensive. Small footprint. Large range of material options.	Conflicts in speed and quality. High power required. Powder residue.	Metals. Ceramics. Polymers. Composites. Hybrids.

Sheet lamination.	Sheets of materials are bonded to form a part	Laminated object manufacturing. Ultrasound consolidation(UC).	High speed. Low cost.	Vertical quality depends on adhesive used. Limited materials used.	Polymers. Metals. Ceramics. Hybrids.
Vat polymerization	Liquid photopolymer in a vat is selectively cured by light activated polymerization.	Stereolithography (SLA). Digital light processing.	Excellent resolution and surface quality.	Limited materials. Relatively expensive.	Polymers. Ceramics. Biologicals.

CATEGORY	BASIC PRINCIPLE	EXAMPLE TECHNOLOGY	ADVANTAGES	DISADVANTAGES	MATERIALS
BJ	A liquid bonding agent is selectively deposited to join powder materials	• 3D inkjet technology	• Free of support • Design freedom • Large build volume • High print speed • Relatively low cost	• Fragile parts with limited mechanical properties • May require post-processing	• Polymers • Ceramics • Composites • Metals • Hybrid
DED	Focused thermal energy is used to fuse materials by melting as they are being deposited	• Laser deposition • Electron beam • Plasma arc melting	• High degree control of grain structure • High-quality parts • Excellent for repair applications	• Conflicts in surface quality and printing speed	• Metals • Hybrid
ME	Material is selectively dispensed through a nozzle or orifice	• Fused deposition modelling (FDM)/Fused Filament Fabrication (FFF)	• Widespread use • Inexpensive • Scalable • Fully functional • Large range of material options	• Vertical anisotropy • Step-structured surface	• Polymers • Hybrid • Metals • Composites
MJ	Droplets of build material are selectively deposited	• 3D inkjet technology • Direct ink writing	• High accuracy • Low waste • High compatibility	• Support material is often required • Conflicts in speed and resolution	• Polymers • Ceramics • Campsites • Hybrid • Biologicals
PBF	Thermal energy selectively fuses regions of a powder bed	• Electron beam melting (EBM) • Select Laser Sintering (SLS)	• Relatively inexpensive • Small footprint • Large range of material options	• Conflicts in speed and quality • High power required • Powder residue	• Metals Ceramics • Polymers • Composites • Hybrid
SL	Sheets of material are bonded to form a part	• Laminated Object Manufacturing • Ultrasound consolidation (UC)	• High speed • Low cost	• Vertical quality depends on adhesive used • Limited material use	• Polymers • Metals • Ceramics • Hybrids
VP	Liquid photopolymer in a vat is selectively cured by light-activated polymerization	• Stereo Lithography (SLA) • Digital Light Processing	• Excellent resolution and surface quality	• Limited materials • Relatively expensive	• Polymers • Ceramics • Biologicals

Table 1: Basic principles, materials, advantages, disadvantages, typical build volumes and tool manufacturers of seven ASTM categories of Additive Manufacturing (AM)

Table 2. Techniques, dosage forms and generally used active ingredients and polymers in 3D printing technology.

Types of 3D process/technique.	**Dosage form**	**Active ingredient/polymer.**
Stereolithography(SLA).	Hydrogel	Ibuprofen, riboflavin, polyethylene glycol, diacrylate.
FDM 3D printing	Tablet	Felodipine, PEG, PEO, Tween 80,Eudragit EPO
UV inkjet 3D printed.	Tablet	Ropinirole, cross linked poly(ethylene glycol diacrylate) (PEGDA)
Semi solid extrusion 3D printing technique in combination with UV-LED crosslinking	Tablet	Prednisolone, polydimethylsiloxane(PDMS)
FDM AND SLA	Model of a nose adapted to the morphology of an individual	FPLA-salicy;ic acid and PCL-salicylic acid
FDM	Tablet	Haloperidol
Thermal inkjet(TI) printing.	Solid dosage forms	Rasagiline mesylate
FDM and Hot Melt Extrusion(HME).	Tablet	Domperiodone, hydroxy propyl cellulose(HPC)
FDM	Nanocapsules	Deflazacort, poly caprolactone(PCL)
FDM and HME	Compartmentalized shells.	Rifampicin (RIF) and isoniazide(ISO)
FDM	Tablet	Hydrochlorthiazide
3D PRINTED	Biodegradable patch	Poly(lactide-co-glycolide),polycaprolactone and 5-flurouracil
FDM and HME	Subcutaneous rods	Indomethacin, ethylene vinyl acetate(EVA),copolymers.
FDM and HME	Three-compartment hallow cylinder	Polymer vinyl alcohol(PVA),mannitol and Hydrochlothiazide(HCTZ),polylactic acid(PLA).
FDM	Tablet	Nitrofurantoin, polylactic acid and hydroxy propyl methylcellulose
FDM and HME	T-shaped prototype of intrauterine system(IUS)	Indomethacine, poly caprolactone
HME with 3D Printing(3DP)	3D printed- cube, pyramid, cylinder, sphere and torus	Paracetamol loaded filament of polyvinyl alcohol.

Type of 3D process/technique	Dosage form	Active ingredient/polymer
Stereolithography (SLA)	Hydrogel	ibuprofen, riboflavin, polyethylene glycol, diacrylate
FDM 3D printing	Tablet	felodipine, PEG, PEO, Tween 80, Eudragit EPO
UV inkjet 3D printed	Tablet	ropinirole, cross-linked poly(ethylene glycol diacrylate) (PEGDA)
semi-solid extrusion 3D printing technique in combination with UV-LED crosslinking	Tablet	prednisolone, polydimethylsiloxan (PDMS)
(FDM) and (SLA)	model of a nose adapted to the morphology of an individual	FPLA-salicylic acid and PCL-salicylic acid
FDM	Tablet	haloperidol
Thermal Inkjet (TIJ) Printing	Solid dosage forms	rasagiline mesylate
(FDM) and Hot Melt Extrusion (HME)	Tablet	domperidone, hydroxypropyl cellulose (HPC)
FDM	Nanocapsules	deflazacort, poly(ε-caprolactone) (PCL)
FDM and HME	Compartmentalized shells	rifampicin (RIF) and isoniazid (ISO)
FDM	Tablet	Hydrochlorothiazide
3D printed	Biodegradable patch	poly(lactide-co-glycolide), polycaprolactone, and 5-fluorouracil
FDM and HME	Subcutaneous rods	indomethacin, ethylene vinyl acetate (EVA) copolymers
FMD and HME	Three-compartment hollow cylinder	polymer polyvinyl alcohol (PVA), mannitol and hydrochlorothiazide (HCTZ), polylactic acid (PLA)
FDM	Tablet	nitrofurantoin, polylactic acid and hydroxypropyl methylcellulose
FDM and HME	T-shaped prototypes of intrauterine system (IUS)	indomethacin, poly(ε-caprolactone)
(HME) with 3D printing (3DP)	3D-printed—cube, pyramid, cylinder, sphere and torus	paracetamol loaded filaments of polyvinyl alcohol

Table 3. Some of the marketed formulations.

3DPrinting Technology	Dosage Forms	Active Ingredients.
Fused deposition modelling(FDM)	Tablets	5-aminosalicylic acid (5-ASA, mesalazine) and 4- aminosalicylic acid (4-ASA)
3DP extrusion-based printing	Tablet	Captopril with Nifedipine and Glipizide
3DP machine	Multi-drug implant	Rifampicin and Isoniazid
Desktop 3D printer	Tablet	Guaifenesin
3DP technology	Tablet	Acetaminophen
Inkjet 3DP	Nanosuspension	Folic Acid
Inkjet 3DP	Implant	Levofloxacin
Thermal Inkjet (TIJ) Printing	Solid dosage forms	Prednisolone
Thermal Inkjet (TIJ) Printing	Solution	Salbutamol sulphate
Inkjet 3DP	Nanoparticles	Rifampicin
FDM	Tablet	Hydrochlorothiazide
(FDM) and Hot Melt Extrusion (HME)	Tablet	Domperidone, hydroxypropyl cellulose (HPC)
FDM	Tablet	Nitrofurantoin, polylactic acid and hydroxypropyl methylcellulose
3D printed	Biodegradable patch	poly(lactide-co-glycolide), polycaprolactone, and 5-fluorouracil

10. APPLICATIONS OF 3D PRINTING

- ❖ Potential applications for process enhancement and performance modification in industrial design, aircraft, medical engineering, synthetic biology, architecture, and pharmaceuticals.
- ❖ It focuses primarily on two possible locations for advancing the development of pharmaceutical products into unexplored areas and producing complex delivery and personalised medicine systems.
- ❖ Manufacturing dental implants is a part of the healthcare industry.
- ❖ On creating a coordinated release multi-drug implant for the treatment of bone TB.
- ❖ It deals with cell-laden materials, biomaterials, and organ printing[54].
- ❖ In personalised drug dosingthe aim of drug development is to increase drug efficacy while simultaneously reducing the risks of an adverse reaction. This can be done by using 3D printing to develop customised treatments[55,56,57].
- ❖ In a multiple drug release profile, by facilitating the controlled release of drugs and having a multiple drug loading capacity, which is more beneficial to the patient.
- ❖ In the manufacturing of solid oral dosage forms,transdermal drug delivery, in the manufacturing of microneedles which produce very mild pain.
- ❖ This 3D printing is also employed in pulsatile drug delivery systems, which means a particular amount of drug is released rapidly after a predetermined off-release period. It targets the drug at an appropriate site of action within a short span of time[58,59,60].

11. CHALLENGES

- ✓ It demonstrates the positive outcomes of drug delivery systems. It must overcome numerous obstacles, including those related to the optimization process, enhancing device functionality for multiple uses, choosing suitable excipients, post-treatment techniques, etc.
- ✓ Some crucial parameters, such as printing rate, printing passes, line velocity of the print head, interval time between two printing layers, distance between the nozzles and the powder layer, etc., must be optimised in order to increase the performance of 3D printed products, to broaden their application range in novel drug delivery systems, and to achieve the quality of 3D products.
- ✓ Post-processing after prototyping, such as drying (hot air heat, microwaves, and infrared) procedures, is especially crucial since they have a significant impact on the quality of the final 3D-printed products.
- ✓ Uniaxial compression and suspension dispersed techniques are used to boost the drug loading capacity in 3D printed processed tablets, although this technique suffers from increased complexity and spray nozzle clogging[61,62,63].
- ✓

12. FUTURE PERSPECTIVES

In the future, many unique dosage forms will be created and manufactured using a 3D printing technique. Although it is still difficult to produce these novel dosage forms commercially, 3D printing technology will usher in a new era in the development of personalised medicine, allowing optimised drug release from dosage forms, compacting or avoiding drug-drug incompatibilities, protection of biomolecules during the manufacturing process, and the construction of multiple drug dosage forms and multiple drug release products, limiting degradation of biological molecules and supporting delivery systems. On-demand printing of drug products can be used as an alternative to conventional drug manufacturers for pharmaceuticals with a short shelf life or those prescribed specifically for a patient. Innovation in garage biology could result from it in the future. Due to the fact that the technology is so new, there are no regulations or security and safety concerns regarding 3D printing. Therefore, these problems could be resolved in the near future[64,65,66].

13. CONCLUSION:

With the fundamental goal of modifying medicine to be patient-centred, 3D printing has evolved into a significant and impending tool for the pharmaceutical industry. Technology for 3D printing is evolving as a new possibility for creative drug delivery with inherent flexibility that is ideally suited for individualised treatment. The pharmaceutical manufacturing and formulation processes will progress owing to 3D printing technology. Despite having many advantages and benefits for pharmaceutical and healthcare systems, there are a number of regulatory and technical obstacles preventing its massive usage. In the future, the rapidly developing 3DP technologies will be more refined and suitable for a variety of dosage forms, including on-

demand personalised medicines at an affordable price. This is due to the 3DP systems' constant innovation and progress, which will address many challenges like mechanical, scientific, and even regulatory limitations.

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