IOSR Journal Of Pharmacy
(e)-ISSN: 2250-3013, (p)-ISSN: 2319-4219
Volume 13, Issue 7 Series. I (July 2023), PP. 20-34
www.iosrphr.org

Recent Advances in 3d Printing: Application in Drug Delivery

Priyanka Sinha*, Safiya Aaliya M G[1], Vasanthi Ranganayagi J[1], Sapna M Jain[1]
C.L Baid Metha College of PharmacyChennai
Received 29 July 2023; Accepted 18 August 2023

I. INTRODUCTION

The technology sector has undergone a significant industrial revolution as a result of the scientific understanding and practical application of artificial intelligence and (3D) printing, which were previously unimaginable. Applications can be found in a variety of field, including aerospace, architecture industry, automobile industry, engineering, chemical industry, military, fashion industry, dental and in healthcare. Particularly in the pharmaceutical industry, the 3DP approach has so far proven to be one of the most inventive technologies [1]. The International Standard Organisation (ISO) defines 3DP as "fabrication of objects through the deposition of a material using a print head, nozzle, or other printer technology." Three-dimensional printing is one of the methods for fabricating additive layers [3]. The internal 3D printing procedure entails two steps: (i) Direct software data transfer to printed structures; and (ii) Repetition of print head placement in all three spatial dimensions to print the complete product layer by layer [5].

Using computer-aided drawing methods and programming, a 3D object is initially formed on a surface by successively layering each one after another. Alternately, utilising imaging methods like magnetic resonance imaging (MRI), objects can be made from 3D digital files. In this case, the material that will ultimately serve as the object's base is initially released from a printer head on an x-y plane. Then, when the printer advances along the z-axis, a liquid binder is extruded to a particular thickness at the base of the material. The object can be built layer by layer by repeating this method and following the computer-aided draught directions. The 3D object is created once the unbound substrate has completely been eliminated through treatment [1].

In 1980s Charles hull was the first person who initially introduced The concept of 3D printing for a commercial use .The design and fabrication of sophisticated materials that may be employed in personalised and programmed medicine were are all made possible by the remarkable versatility and diversity that is offered by 3D printing technology.it is a great tactic for conquering some of the difficulties in running a drug unit on a regular basis [1] and With the use of 3D printing, the manufacture of pharmaceutical items might be sped up from days to just a few hours. A quicker release of the drug products onto the market may result from accelerating the production process.

Additionally, the capacity of 3D printing to rapidly produce a medicinal product result in a significant cost decrease in the production process, which is very advantageous to the pharmaceutical industry. Additionally, it encourages invention, creation, and customisation [2].

A. The idea of PERSONALIZED MEDICATION has now been prioritized over the ONE- SIZE-FITS-ALL concept:

The US Precisions Medicine Initiative was established in 2015 with the goal of gaining an understanding of how a patient's genetic makeup, environment, and lifestyle might influence the most effective course of action for illness prevention or treatment [4]. The UK's healthcare policy has similarly prioritised individualised medicine. In 2016, the NHS released a report titled "Improving outcomes through personalised medicine," and more recently, the UK government released the "UK Genome Strategy 2020" and the "Life Sciences Vision 2021," both of which prioritise the use of personalised medicine in the provision of healthcare services. These attempts describe how to transition from a "one size fits all" approach to personalization, which calls for medication to be personalized to each patient while taking into account characteristics like physiology, disease state , drug response, concurrent therapy, genetic makeup, and further factors like sex, age, weight, and Improved medication adherence, fewer adverse drug responses, and better therapeutic results are only a few of the benefits of customising medications to a patient's needs through personalising treatments like mixing multiple medications into one tablet or choosing the right dosages [6].

When it comes to 3dp in pharmaceutical sector, let’s say that Pharmaceuticals and clinical pharmacy

practise are undergoing a paradigmatic change as a result of three-dimensional (3D) printing, moving away from the old mass manufacture of drugs and toward customised medication products that are unique to each person that is basically the personalized medication we could say. The idea has the potential to help patients, pharmacists, and the pharmaceutical industry by making it possible to create and produce flexible formulations with customised doses, sizes, forms, drug release, and multidrug combinations on demand. This is a pivotal moment in the history of 3D printing technology in the pharmaceutical industry, necessitating the involvement and cooperation of healthcare professionals, including, nurses, doctors, pharmacists, and pharmacy technicians, among others, to enable the widespread adoption of the technology in clinical practice [6].
In light of all of the significant points raised above, this review aims to highlight recent advancements in the use of 3D printing technology in the pharmaceutical industry, as well as their benefits over conventional methods [1].

EVOLUTION & PIVOTAL MOMENTS OF 3DP ERA

Hideo Kodama of the Nagoya Municipal Industrial Research Institute produced a 3D plastic model utilising photo hardening polymer, which is when 3D printing technology first became widely known. But in 1984, Charles Hull, who would later co-found 3D Systems, created stereolithography, which was a significant breakthrough [9].

From the early 1970s of the 20th century, the concept of 3DP has the application of powdered material and subsequent solidification of each layer by the use of a high intensity beam were described by Pierre A. L. Ciraud. Theoretically, meltable materials like metals or plastics might be employed in this situation to prepare the objects. Ross Housholder presented the concept of sand binding by various materials in an early 1980s patent entitled "BA moulding process for creating a three-dimensional product in layers," and Carl Deckard created a technique for solidifying powdery bed by laser beam known as "selective laser sintering" (SLS) [3]. Since those early times, the term "3D printing" has expanded to include a number of distinct technologies, the most popular of which are fused deposition modelling (FDM), stereolithography (SLA), and selective laser sintering (SLS). Each of these inventions, together with its subsequent patenting and trademarking, marks the beginning of the 3D printing era.

1980-1990s: Stereolithography was Chuck Hull's first commercially successful invention (SLA), it is widely used technique followed by vat photo polymerization technology and Followed by Fused deposition modelling (FDM) was first described by Scott Crump in a patent application towards the end of the 1980s and this method follows material extrusion process [3].

1990-2000s: Now is the moment when most people first became aware of 3D printing. Three-dimensional printing techniques were invented in the 1990s by Emanuel Sachs, an MIT scientist, and his colleagues. The most popular technique for 3D printing nowadays is inkjet printing. The first 3D printing method in pharmaceutics was accomplished using an inkjet printer [3]. followed by LOM first commercialized in 1991 [11]. In 1994 – DOS, colour jet printing was invented and using this 1997-3DP first placebo tab (DOS method) were made.

2000-2010s: In 2000s the advent of the RepRap project (2005) marked the largest development in 3DP. A British university was the origin of the RepRap project They created a 3D printer that could print all of its parts affordably [11]. In 2001, the market made yet another significant advancement as Objet released the first desktop 3D printer that was commercially accessible [5]. Then back in 2002 significant advancements in medical 3D printing laboratories throughout the globe when researchers successfully 3D printed a human kidney [11]. Afterwards First self-replicating printer to print its own components, Organovo printed first 3 d printed blood vessel in 2009 [4,11]

2010-2020s: All three of the primary 3D printing technologies SLA, SLS, FDM are now open source and available for testing and development after many patents pf additive manufacturing technique expired in this decade. Despite extensive testing that began in the 2010s by (FDA) approved Spritam in 2015.This tablet Spitram, a high dose oro-dispersible formulation created by Aprecia utilising the 3DP ZipDose technology, disintegrates when taken with fluids at an almost imperceptibly quick rate was created using 3D printing technology to cure epileptic seizures. This was the first and only 3Dprinted tablet that has received approval. The manufacturing process made use of a technique known as ZipDose. It was given FDA approval and was made available to consumers in the summer of 2016 by Aprecia Pharmaceuticals [10]

Following the beginning of the 21st century, 3D printing equipment sold out quickly, and its cost progressively decreased [4]. Due of the numerous other 3D printing techniques that have been created. The topics highlighted above were a portion of the most significant 3D printing-related events in history, which contributed to the development of this technology. Although there have been many noteworthy developments in recent years, it's crucial to keep in mind that many of them are still in the early phases of development. They still have a long way to go before realising their full potential, so we may expect a lot more amazing technical

developments in the future

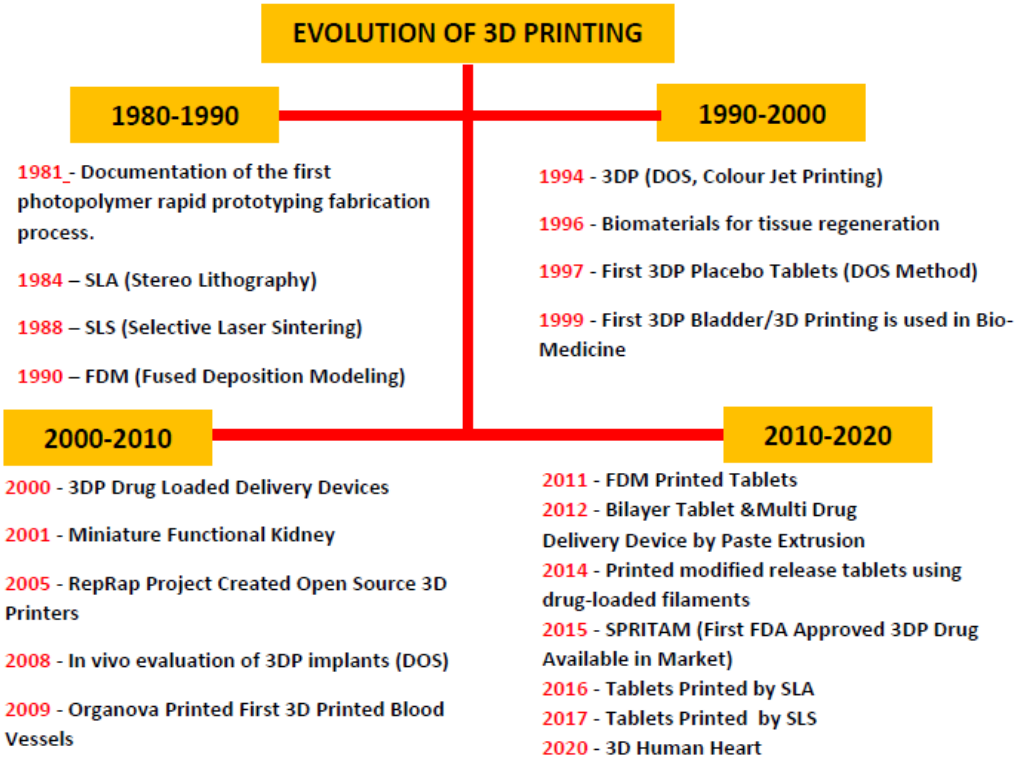

Fig 1: Evolution of 3D printing technique [1,3,11,20,21].

ADVANTAGES

3D printing is faster than traditional methodologies, and that has the additional benefit of higher precision and accuracy. This technology is specifically used for creating materials like implants, surgical instruments and prosthetics. This approach can produce accurate dosage of a potent drug as well as high drug loading. One of the most notable benefits of this technology is the ability to manufacture personalized drugs and medical equipment. Three-dimensional printers conserve time, which simplifies product development design cycles. 3DP can remove the need for tool fabrication, thus leads to low cost, time, and labour. The beginning of 3D printing technology into the pharmaceutical industry has enabled the development of novel complex drug products as well as multiple active drug pharmaceutical ingredients. Treatment can be tailored to improve patient adherence in the case of multi-drug therapy with multiple dosing regimens. Because of the flexible design, immediate and controlled release layers can be embedded in dosage forms. Small batch production is achievable, and the process can be performed in a single run [1,2,4,7].

DISADVANTAGES

The printing material must continue to flow even when the printer head pauses and resumes during the manufacture of successive layers. Improved mechanical resistance, notably resistance to friability in 3DP, is required, particularly for powdered particles. Imperfections on the surface of the completed product are caused by layer stacking, drying rate, and procedures, which are likely to result in surface flaws. The rapid rise of this technology diminishes the demand for labor in the manufacturing and production sectors, resulting in unemployment. When compared to traditional manufacturing methods, this method offers less options for raw materials, colors, and finishing materials [1,4,7].

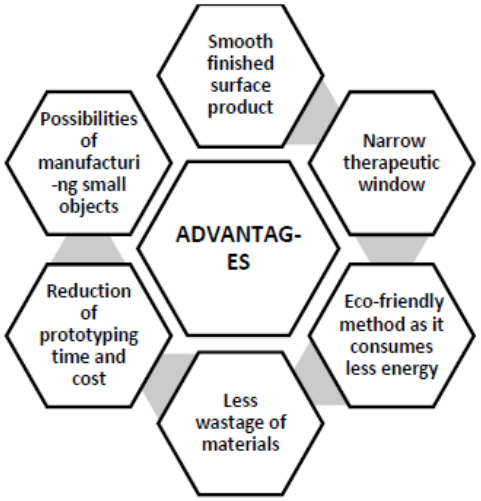

Fig 2: Advantages of 3D printing [4].

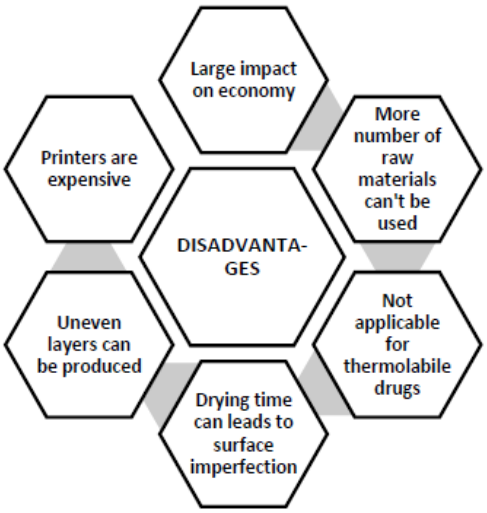

Fig 3: Disadvantages of 3D printing [4,8].

II. METHODS OF 3D PRINTING TECHNOLOGY

By altering the energy source, material source, and other mechanical parameters, many 3DP approaches have been developed [13]. Based on the additive technique employed, the American Society for Testing and Materials (ASTM) has divided 3D printing technology into seven basic groups. The methods include Vat Photopolymerization, Material Extrusion, Sheet Lamination, Directed Energy Deposition, Material Jetting, Binder Jetting, and Powder Bed Fusion. Every technique has benefits and drawbacks as well as its own specific area, but the variation is caused by the numerous additives used to satisfy consumer expectations. These technologies are capable of printing things from nanoscale to industrial-size materials, depending on the requirements [1].

1. Material jetting

Material jetting is a process that involves the selective deposition of droplets made of additives or building materials in layers to develop a product. This method is quite similar to that utilized in inkjet printers. The key distinction is that these processes employ building materials or additives rather than using ink or paper which get deposited directly and solidified on the surface of a construction platform then adjustment of the platform's height and angles takes place to obtain the desired product. Highly attractive polymers like acrylic-based photopolymers, elastomeric photopolymers, and wax-like materials were used since they were associated with long molecule chains and they were utilized as liquid substrates in this process. Products formed by material jetting have a high degree of dimensional accuracy and an extremely smooth surface finish. [1,14].

2. Binder Jetting

Traditional ink-jet printing technology serves as the groundwork for the binder jet printing method [19]. Through the printing device's nozzle, a liquid binder solution is sprayed to the powder base during the binder jetting process. After being moist, the particles of powder are subsequently bonded to create the layer. The plunger is lowered to the depth of the subsequent layer after printing the first layer onto the platform being constructed, and thereafter, more layers are printed and fused together. Up till the 3D product develops, the process is repeated [17]. This method also can be called as Drop on Solid (DoS) method, Zip dose method, M-printing, S-printing, etc [1,15]. Utilising this 3DP technology, Spritam, an oral solid dosage form, was developed, and it is the sole 3DP drug currently available for purchase. The benefits of the binder jetting process include that room temperature printing is possible and the powder bed's physical support allows for the building of highly complex dosage forms. The primary issue of the binder jetting process is the extremely fragilenature of the dosage forms that are produced [15].

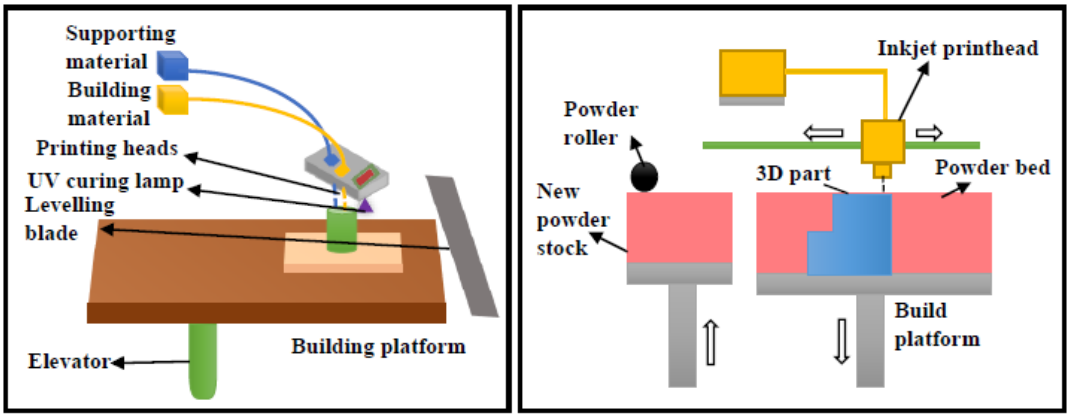

Fig 4: Material Jetting (i) and Binder Jetting (ii) [1].

3. Directed Energy Deposition (DED)

It is a method of melting the laser-focused materials that uses directed thermal energy or a laser beam for melting and that lead towards the nozzle and construction platform for producing 3D printed products. The mechanism is similar to that of material extrusion however here motion- controlled nozzle is used which can spin over multiple axes. This technique is mostly utilized for compounds that cannot be extruded. Metals and metalloids like aluminium, copper, nickel, cobalt, titanium, and stainless steel are chosen for this type of printing over polymers and ceramics.

Generally, this complex technique is employed to fix or add extra materials to existing elements. Notable examples of DED technology are Laser Engineered Net Shaping (LENS), Arc Melting, Laser Deposition (LD), and Electron Beam Plasma [1,7,14].

4. Sheet Lamination

The fundamental idea behind sheet lamination technology is the bonding of sheets of materials to form an object. Notable 3D printing techniques which utilize this method are LOM (Laminated Object Manufacturing) and UC/UAM (Ultrasound consolidation/ Ultrasound Additive Manufacturing). The LOM process involves, during the construction cycle, a glue-backed or adhesive-covered sheet of building material being moved onto the building platform. Then, as the platform moves, a previously planned and created structure is cut into a sheet using a laser. This cycle is repeated until the design is complete. UAM is a new process of joining layers of metal using sound and the metal is derived from featureless foil stock. Sheet lamination technology has benefits including full-colour printing capability, ease of handling, affordability, and recycling of excess materials [1,14].

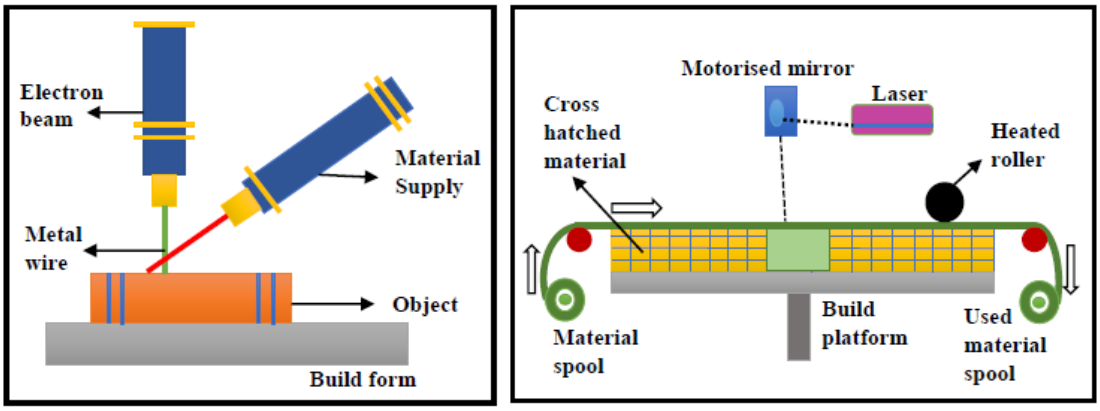

Fig 5: Directed Energy Deposition (i) and Sheet Lamination (ii) [1].

5. Vat Photopolymerization

Vat photopolymerization refers to the solidification and curing of liquid photoreactive polymers in a vat using a UV light source or a laser beam. Digital Light Projection (DLP), Continuous Light Interface Production (CLIP), Stereolithography (SLA), Lithography-based Ceramic Manufacturing (LCM) and Two-Photon Polymerization (2PP) are the 3D printing techniques that use vat photopolymerization technology. Most often employed techniques include SLA and DLP [1].

a. Stereolithography (SLA)

The Stereolithography method makes use of UV laser for curing liquid photoreactive polymers like acrylate or resin. By exposing the photo-polymerizable resin to UV light, the material is polymerized and solidified during the course of the process. When solidification of the resin occurs to a certain depth each time, the platform is lowered vertically to recoat the formed layer with resin. The self-adhesive feature of the material leads each subsequent layer to connect to the prior one, resulting in a 3D product that is completely built. SLA can make extremely precise and intricate polymer components [4,19]. It also reduces heating during printing, making it ideal for use with thermolabile drugs. Though SLA is frequently utilized in tissue engineering, its poor drug loading significantly affects its pharmaceutical applications [13].

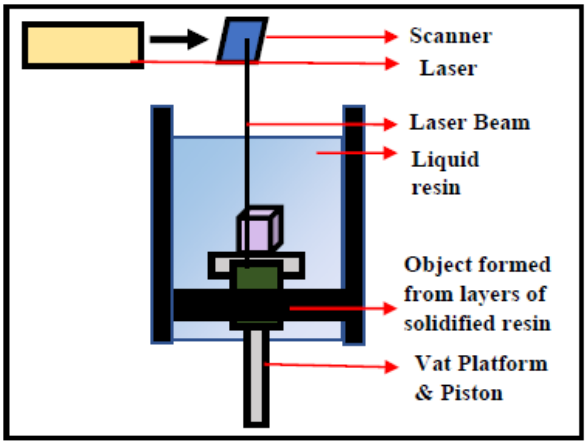

Fig 6: Stereolithography [12].

b. Digital Light Projection (DLP)

DLP process is similar to SLA but the variation relies on the use of a digital projector screen to display a picture of the print layer onto the resin container, and the curing of the entire layer of the 3D-printed design onto the construction plate occurs at once. This is done under the control of a digital mirror device. In comparison to SLA, it is a process with outstanding resolution and quick action. The other benefits of this process are that the layer thickness can be easily adjusted as well asminimal waste is produced [7,13,15].

c. Continuous Light Interface Production (CLIP)

CLIP was created to boost the printing speed and oxygen is the primary factor used for enhancing the pace at which photo-polymerization occurs. The process involves a digital light projector that uses UV radiation to project an image onto the surface. As the oxygen is permeable, a dead zone develops immediately below the surface. It thus presents the same impression to the building platform. This method acts in a way like material jetting and solidifies rapidly [7].

6. Powder Bed Fusion

This method of additive manufacturing relies on the melting of particles using heat energy to fuse them. For this 3D printing method, solid particles such as metals, polymers, and ceramics are employed as additives. New advancements utilizing quick lasers are demonstrated to speed up the process. Various powder bed fusion techniques include Selective Laser Sintering (SLS), Selective Heat Sintering (SHS), Electron Beam Melting (EBM), and Direct Metal Laser Sintering (DMLS), with SLS being the most prevalent [1].

a. Selective Laser Sintering (SLS)

SLS employs a high-energy laser beam and the process involves layer-by-layer sintering of particles of the powder in a spreading platform. The powder placed in the powder bed gets distributed, and the surface is levelled by a rollerblade. The powder layer is then selectively scanned by the laser beam using predetermined CAD models, melting and curing the powder layer in particular places to create fusion. The next layer is then applied and fused after which the powder bed is depressed. Up till the 3DP product is complete, the process is continued [15]. SLS has benefits including speed, chemical resistance, accuracy, high resolution, no need for supporting structures, and highly configurable interior microstructures [13,16]. The main limitation is the drug degradation brought on by the powerful CO2 lasers operating in the Infrared (IR) portion of the spectrum, though this was tackled recently by using lower-intensity diode lasers which are employed in formulating novel drug products [19].

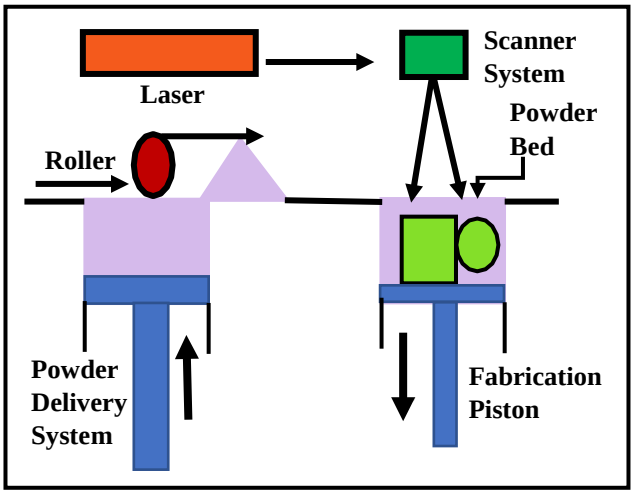

Fig 7: Selective Laser Sintering [12].

Direct Metal Laser Sintering (DMLS) resembles the SLS technique. However, SLS is used to create materials like polymers, metals, and ceramics, whereas DMLS is used for metal alloys [13].

b. Electron Beam Melting (EBM)

EBM can be known as a metal printing technique that is quite comparable to the laser sintering method. The only significant difference between EBM and laser sintering is the heat source. Here, an electron beam is the source of the heat, not a laser and this technique is performed under vacuum conditions. Compared to SLS, higher throughput and a more uniform thermal field distribution are offered by the EBM method but it has inferior accuracy and surface quality [7,13].

7. Material Extrusion

Material extrusion, as the name implies, here the material is extruded or forced to flow through an automated nozzle onto the substrate to transform it into the desired form and there is no need for any higher support material for this process [1,12]. Two distinct extrusion-based 3DP methods can be recognized, based on the material being used and the demand for a melting phase for easy extrusion through the nozzle. One is Fused Deposition Modeling (FDM) – which requires a melting phase and the other is Pressure-Assisted Microsyringe (PAM) – do not require a melting phase [15].

a. Fused Deposition Modeling (FDM)

Fused deposition modeling method involves the extrusion of a molten thermoplastic polymer filament through the nozzle which is deposited onto the building platform in layers with immediate solidification [13]. The most widely utilized polymers in FDM printing are polylactic acid (PLA), poly (methyl methacrylate) (PMMA), ethylene vinyl and polyvinyl alcohol (PVA), acetate (EVA), polycaprolactone (PCL), and acrylonitrile butadiene styrene (ABS) [16]. FDM is known to be a low- cost prototyping technique that has some benefits, including the ability to produce highly complex drugs, good mechanical strength, higher resolution as well as provide options to alter drug release profiles [7,13,18]. Additionally, the method necessitates high temperatures, which may cause thermolabile drugs to degrade. A polymer with a comparable melting temperature can be used in combination with the drug to bypass this restriction [15].

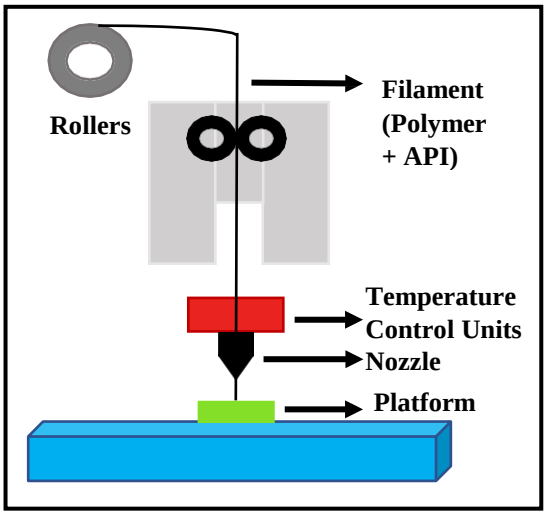

Fig 8: Fused Deposition Modeling [12].

Hot melt extrusion (HME)

A step before FDM is this. The process involves melting the polymer and the API with raised temperature and pressure. This process can be said as a continuous manufacturing process that performs several tasks, including heating, mixing, feeding, and shaping. This technique indeed boosted the factors like solubility and bioavailability of poorly soluble drugs [7].

b. Pressure-Assisted Microsyringe (PAM)

The PAM method involves, with the aid of a pressurised air piston and a microsyringe, viscous and semi-liquid materials are extruded and deposited layer by layer in accordance with the desired shape [13,18]. To ease the extrusion from the microsyringe and avoid occlusion, the paste needs to be uniform, smooth, and have appropriate rheological properties [15]. PAM can be carried out in a continuous flow at room temperature and is also used to develop complex drug delivery systems. Yet, the use of solvents throughout the production and drying processes may result in problems with stability and safety [13]. This method is employed for printing soft tissues [7].

c. Semi-solid Extrusion (SSE)

In this method, the semi-solid product is extruded using a syringe in a layer-by-layer fashion [7]. The semi-solid, which can be gel or paste, is a blend of polymer and solvent in a proportion that makes it appropriate for printing [8]. Here, the process uses low temperatures, which is appropriate for thermolabile active substances. This method is capable to produce a variety of dosage forms, including controlled-release tablets, paediatric gum formulations, solid lipid tablets, gastro-floating tablets, and immediate-release tablets. SSE has some drawbacks to be noted like it prints products at low resolution in contrast to FDM. And also, the starting material's physical properties have an impact on the drying process, i.e., in the case of insufficient hardness, it causes shrinking, deformity, or collapse of the product [17].

RISK ASSESSMENT

Risk identification is a vital step in preventing a breach of quality control measures such as appearance, content consistency, assay, and so on. Identifying risk entails analysing the process and process parameters to guarantee that a high-quality product is generated.

If a particular printer is unable to print a specific design, software controls should be used. Clogging of print heads may be avoided by ensuring particle size dispersion and monitoring inkjet flow.

Variations in binder viscosity or surface tension can cause due to inconsistent agglomeration or binding. Uneven layers can occur due to environmental condition and it can be controlled with temperature and humidity of the manufactured area. Thickness of the layer can be managed by using the real time layer thickness monitor. Positioning should be accurate while printing so monitor, print head height and print head speed to avoid errors [8].

PHARMACEUTICAL APPLICATIONS OF 3D PRINTING3DP TABLETS

The most widespread form of pharmaceuticals is oral dosage forms. The 3DP tablet is just as effective as a regular tablet, but they have huge benefits providing quicker onset of action. The 3DP also enables the production of tablets with various release patterns. Following, wide variety of 3D printed tablets used for multiple purposes are discussed [13,15].

POLYPILLS

Polypill (or multi-API tablet) is a combination of many drugs in a single tablet. The elderly population will greatly benefit from this idea, since patients of this age group are susceptible to various illnesses, necessitating multiple therapies [8]. A polypill with three API—captopril, glipizide and nifedipine, was produced by Khaled et al. employing an extrusion-based 3D printing approach. Here, captopril is contained in an osmotic pump compartment whereas glipizide and nifedipine are contained in a sustained-release compartment. This polypill useful for diabetes patients who are suffering from hypertension. Martinez et al. employed SLA technique, produced a polypill having 6 APIs such as chloramphenicol, prednisolone, paracetamol, caffeine, aspirin and naproxen. Moreover, a work by Goh et al. documented the drug release profile of a four-in-one 3D-printed polypill. Three vitamin B analogues, like vitamin B1, B3, and B6, and caffeine were present in this polypill. Vitamins B1, B2, and B6 were found to be rapidly released within 30 minutes after the two stage USP based in-vitro dissolution test, whereas caffeine displayed a 4-hour delayed release rate [15,23].

ORODISPERSIBLE TABLETS

Orally disintegrating tablets (ODTs) that provide disintegration over three minutes, as per the European Pharmacopoeia (EP), but the FDA refers to them as oral dosage forms that can dissolve in the mouth within thirty seconds. ODTs will be very appealing for the individuals with dysphagia.

Allahham et al. utilised SLS technique to develop ODTs containing the anti-emetic medication ondansetron in cyclodextrin complexes and the formulation also included mannitol as a taste masker [15]. The first three-dimensional printed commercial drug, Spritam® (levetiracetam) is an orodispersible tablet which is an antiepileptic drug approved by FDA, made by Zipdose technology (binder jetting). This 3DP tablet has a very porous structure that enables quick disintegration in the patient's mouth with just minimal water, even at high doses of 1000 mg of the API [19].

TABLETS FOR SPECIAL POPULATON

For Geriatric, Polypills are quite useful which is discussed above as the geriatric people would be going through polypharmacy. Even ODTs are fruitful for them as they may suffer from dysphagia.

For Paediatric, Researchers have developed minitablets, chewable dosage forms to ease administration. For instance, Scoutaris et al. made candy-like SODFs (solid oral dosage forms) that contained indomethacin using FDM technique. Different shaped dosage forms, such as heart, lion, and bottle shaped have been produced successfully. The formulations were successful in minimising the harsh taste of indomethacin and ensuring its rapid release. Another example such as, using SSE method, chewable isoleucine printlets in four different dosages and six distinct flavours and colours were produced, and researchers assessed each formulation's acceptability and isoleucine blood levels [6,15].

For visually impaired, A study utilised SLA technique, made orally dispersible tablets which have prints of Moon and Braille patterns on the surface, in order to help patients in identify the medication after it is removed from the main packaging [23].

COMPLEX DRUG-RELEASE PROFILES

Frequently explored or investigated application of this breakthrough technology is the developing of drugs containing complex drug release properties. Many researchers by altering tablet shape, tablet filling density, polymer type and quantity, they have created tablets that offer various release profiles such as **immediate, delayed or sustained release.** Paediatric formulations, orodispersible tablets comes under immediate release category. Khaled et al. using an extrusion-based 3D printing method developed a two-layered guaifenesin tablet incorporating sustained release (SR) and immediate release (IR) layers. By producing an early explosive release and keeping therapeutic drug delivery levels with time, they hoped to mirror the drug delivery profile of a marketed guaifenesin bilayer tablet. Sodium starch glycolate and microcrystalline cellulose as disintegrants and HPMC 2910 (hydroxy propyl methyl cellulose) as binder were utilised to produce the IR layer. The hydrophilic matrix for the sustained release (SR) layer was composed of poly (acrylic acid) and four varying concentrations of HPMC 2208 (6%, 8%, 10%, and 14% w/w) [17,19].

A new kind of tablet called **gastro floating tablets** which prolongs the gastric retention time of the drug to increase its therapeutic efficacy were also successfully produced by 3D printing. For particular, the FDM technique has been used to develop Pregabalin-containing intra-gastric floating tablets with controlled release. It has been proven that pregabalin is primarily absorbed in the stomach and upper gastrointestinal tract; as a result, reducing the frequency of administration by enhancing gastric retention of the formulation [15,17].

3DP CAPSULES

Unlike traditional capsules, 3DP capsules promote the personalized medication with the adjustment of the dosage and the loaded drugs [1]. Melocchi et al. were the first to look into 3DP's potential for use in capsule

production. A swellable/erodible capsular device constructed with HPC (hydroxy propyl cellulose) was prepared for oral pulsatile release using FDM technique. Before the medicine was released quickly, the device displayed a lag time. When in contact with water, the 3DP device exhibits analogous morphological changes and a similar release pattern to ChronoCap, a prior capsular device made by IM (injection moulding) by the exact research team. The modern encapsulation of several APIs in one dosage form or through various doses and/or formulations of one API was made possible by multi-compartment capsular devices, which were also successfully 3D printed. For instance, Maroni et al. produced multi-compartment capsular devices using FDM and IM methods for two-pulse delivery [15].

3DP IMPLANTS

In comparison with conventional implants, 3DP based implants offer effective local delivery, high performance and controlled drug release for prolonged duration. Multi API loaded 3DP implants tend to have additional therapeutic effect, for example, levofloxacin, rifampicin with lactic acid polymeric matrix produced by powder bed fusion technique. Other 3DP implants include those with levofloxacin and tobramycin packed implants for osteomyelitis treatment and an antimicrobial implant containing nitrofurantoin with hydroxyapatite (HA) mixed polylactide feedstock by FDM [1,13]. 3DP implants have been used in several surgical specialties, including tracheobronchial, dentofacial, cardiovascular, orthopaedic, and spine surgery, thanks to their excellent mechanical properties and biocompatibility [22]. Even a new kind of 3DP implant developed that focuses on prolonged drug release for chronic diseases called patch-like implant [13].

MICRONEEDLE

Microneedles, comes under transdermal drug delivery system, comprises clusters of microscopic needles onto the outer layer of a matrix to improve the entry of biologically active compounds into the skin [13]. Earlier, microneedles were made using micro-electro-mechanical system (MEMS) technology, but currently, 3DP technology has advanced in regards to resolution and accuracy, so 3DP can develop microneedles of appropriate sizes [19]. Ochoa et al. (2015) combined 3DP with hydrogel casting/shrinking processes to create a new fabrication method for polymeric microneedles with complicated shapes. The 3DP resolution limit was successfully raised using this method, and sharper microneedles with 9.6 µm radius-of-curvature tips were created that might be used to administer vaccines [13]. Researchers made 25 microneedle arrays with dacarbazine-loaded poly (propylene fumarate)/diethyl fumarate to treat skin cancer, and they also developed microneedle arrays with trehalose, mannitol, and xylitol as carriers to enable transdermal insulin delivery. Both of these products were produced using SLA technique [1].

NANOMEDICINES

Nanomedicine is the use of nanotechnology to create nanomaterials for a variety of therapeutic purposes, such as the diagnosis, treatment, observation, and control of diseases. Ma et al. employing extrusion-based 3D printing process, made cellulose nanocrystal hydrogels with viscoelastic characteristics. Beck et al. using nanotechnology, first created drug delivery devices in order to provide deflazacort in the format of 3D printed tablets filled with nanocapsules made by FDM technique. Lee et al. successfully achieved nanotopology and sustained delivery of a bioactive substance by incorporating core shell nanoparticles onto the nerve scaffolds using SLA technique forpromoting nerve regeneration in peripheral nerve injuries [27].

OTHER APPLICATIONS BIOPRINTING TISSUES AND ORGANS

Organ failure, caused by factors like age, disease or accident, the treatment mostly relies on organ transplantation but there are two main problems to deal with is shortage of human organs and tissue rejection. Regenerative medicine and tissue engineering-based therapies are being explored as a potential remedy. However, 3D bioprinting in place of traditional tissue engineering provides various benefits such as cell concentration, resolution, highly precise cell placement and high digital control of speed, diameter of printed cells and drop volume. Though 3D bioprinting methods can be laser, inkjet, or extrusion-based, the most used type is inkjet bioprinting. Heart valve, knee meniscus, spinal disc, various kinds of cartilage and bone, as well as an artificial ear, have all been produced by researchers using 3d printing technology. For instance, Wang et al developed an artificial liver by depositing various cells into different biocompatible hydrogels using 3D bioprinting [24].

ANATOMICAL AND PHARMACOLOGICAL MODELS

Studies of disease mechanisms, efficacy of preclinical therapy, drug pharmacology testing, and the structural organisation of complex organs all greatly benefit from the use of 3D printed tissue models. A skin tissue model was developed using skin-derived extracellular matrix (SdECM) bioink using 3D bioprinting by Byoung Soo Kim et al (Kim B. S. et al., 2018). Adipose-derived stem cells (ASCs) and endothelial progenitor cells (EPCs) integrated into the skin tissue model, which boosted wound healing, particularly in neovascularization and re-epithelialization [22].

ORGAN-ON-CHIP

Organs-on-chips (OoCs) are microfluidic devices that can replicate the vital structures and functions of living organisms by containing bioengineered tissues or portions of biological tissues or organs. A human glioblastoma-on-a-chip was bioprinted in 2019 by H.G. Yi et al. to detect possible individualised responses to chemotherapy. To mimic the core hypoxia of the cancerous tissue, an oxygen gradient was created on the chip using a combination of permeable and impermeable materials. S. Elezoglou et al. implanted lung cancer cells in an organ-on-chip platform in 2022 for the purpose of studying lung cancer migration using laser-induced forward transfer as bioprinting technique [25].

SENSING TECHNOLOGY

A sensor is a device that detects events or variations in the environment and transmits the associated actual data to a computer. There are two ways to create 3D-printed sensors: either a sensor can be inserted into printed structures or the full sensor can be created by 3D printer [26]. Rogenes et al. produced a disposable, transportable electrochemical sensor using stereolithography technique.

This sensor was quickly utilised to measure the enzymatic activity in tissue and cells and to identify the biomarker alkaline phosphatase [23].

3DP USES DURING COVID-19

As 3D printing offer digital adaptability, quick prototyping and easy customization of complex designs, it turns to be an effective response to emergencies like during pandemic situation.

PPE (personal protective equipment), testing and visualisation aids, medical devices, emergency dwellings and personal safety devices are just a few of the many applications for 3DP used to combatCOVID-19 [28].

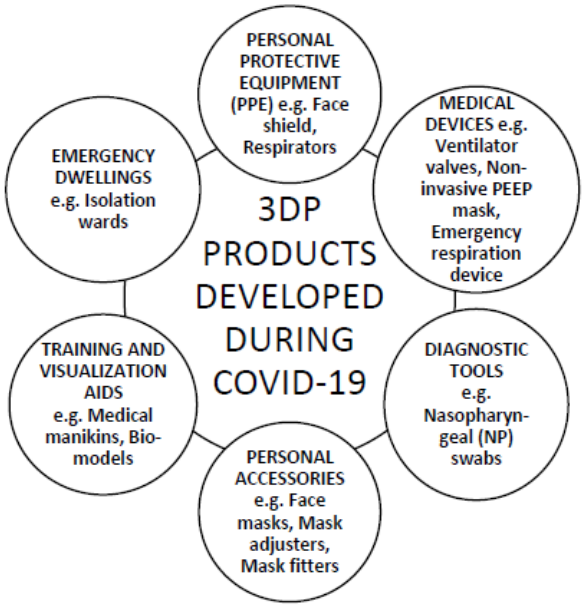

Fig 9: Products developed during COVID-19 using 3D printing technique [29].

AN EVOLUTION: 4D PRINTING

4D printing is a subclass of 3D printing. "4D printing" refers to the employment of intelligent and functional materials in the 3D printing process which can respond to external stimuli like heat, pH changes, and so forth. Tissue engineering, organ printing, and self-assembling human scale biomaterials are just a few examples of how 4D printing technology is fundamentally altering the healthcare sector. As a result, biomedical splints, stents, bioprinting, and orthodontic devices are developed in accordance with human growth. For biomedical applications, different materials have been produced using 4D printing, including lipids, biopolymers, and hydrogels. Stimulus-responsive hydrogels, both synthetic and natural, are one of the most useful materials in the 4D printing process. The potential applications of this technology are enormous and could have an impact on every industry, including healthcare, manufacturing, and education [30,31].

FACTORS TO CONSIDER IN 3DP

I. Pre-processing factors
II. In-processing factors
III. Post-processing factors

1) PRE-PROCESSING FACTORS

a. PRINTER ACCURACY: Printing devices must be first evaluated for the printer's accuracy. While buying a printer, one should take into account the picture quality, size, speed, convenience of handling, and other parameters. Dimensional and spatial precision might be challenging to get when utilizing a 3D printer. Picking a reference print and comparing the results of your printer's dimensional correctness with CAD drawings are ideal place to start [32].

b. MATERIAL AND METHOD SELECTION: Materials used must be durable and reinforce able commonly materials that are used for 3d printing are plastic like - Acrylonitrile butadiene styrene (ABS), Polycarbonate (PC), Polyvinyl alcohol plastic (PVA, Polylactic acid (PLA), powder like - Polyamide (Nylon) Alumide, resigns - Paintable resign, High details reigns, Transparent resigns. Also used other materials like nitinol papers, metals, graphite, carbon fiber, and graphene. Commonly used methods are Digital Light Process (DLP), Selective Laser Sintering (SLS), Stereo lithography (SLA), Fused Deposition Modeling (FDM), Digital Light Process (DLP)and other methods are involved as well [34].

c. PRE-FORMULATION STUDIES: The current study aims to evaluate the application of a customized preformulation methodology incorporating physicochemical analyses, including the rheological profiles of the materials, to direct the creation of medications via 3D printing. Yet material incompatibilities might affect a substance's chemical, thermal, and rheological properties. Preformulation studies can help with the selection of compatible components and the search for optimal processing conditions to produce pharmaceutical goods. This is accomplished by optimizing the 3D printing process [42].

d. THERMOSENSITIVE DRUGS: Concerns about the feasibility of the techniques for printing thermolabile medications are raised by the heating required in some 3D printing technologies since these drugs require precise temperature control throughout processing to ensure their safety and efficacy. According to studies, the most often used printing method for producing thermosensitive pharmaceuticals is semi-solid extrusion (SSE). As they don't employ heating components, binder jetting, stereo lithography, and digital light processing (DLP), among others, can also be used to create thermosensitive pharmaceuticals. For the manufacturing of thermosensitive materials, processes such as fused deposition modelling (FDM) in conjunction with filling procedures providing protection against heat deterioration might be utilized alone or in combination with other techniques [40].

2) IN-PROCESSING FACTORS

a. NOZZLE SIZE: The nozzle size is a crucial factor in selecting the best nozzle for your appliance. As it is often installed as standard equipment and provides an excellent mix between resolution, accuracy, and printing speed and flow rate, the 0.4 mm nozzle has become the industry standard for most 3D printers. The quality of the final print can besignificantly impacted by the nozzle size of a 3D printer [35].

b. PRINTING SPEED: The most important level setting for 3D printing technology is print speed. Print speed, as the name suggests, refers to how rapidly the printer's motors move. It consists of the extruder motor as well as the electric X- and Y-axis control motors. The print is less exact as the extrusion speed increases. In order to calculate the ideal travel speed, which can reduce print time by a large amount without causing layer shifting, ringing, or motion blur errors, or even print failure, If the print quality is good, keep increasing the speed;if not, slow it down [33,35].

c. LAYER HEIGHT AND THICKNESS:

Shortened printing duration -> Poor layer resolution= Low strength Long print time -> High layer resolution = High strength.

The layer's height must match the nozzle's diameter for the extruded filament to have a precisely circular form. The extruded filament flattens as the layer height lowers as a result of the nozzle's constant diameter, resulting in a greater area of contact with the following layer. Also, in order to attain the same dimensions for the printed product, the height of the layers must be decreased but their number must be increased. It is believed that a reduction in layer height would result in a rise in resistance. altering the layer height on a 3D printer is one of the most popular causes. A print's resolution and quality will often decline when layer height is increased. For each print, layer height may be adjusted to achieve the quickest print time while retaining a certain level of quality [33]. The object loses its delicate look because printing on a bigger layer result in the layers being more apparent (lower quality resolution). Although printing thicker layers takes longer, the part's resolution improves as a result [37].

d. TEMPERATURE: The most crucial factor influencing the 3 printing was found to be temperature. An appropriate temperature for 3D printing can be chosen from a temperature profile created using thermomechanical analysis. It demonstrates how temperature profiles may be created using thermal and thermomechanical analysis to choose temperature-related3D printing settings [38].

3) POST-PROCESSING FACTORS

a. PRICING: 3D printing is affordable, and because it only has to be used in one step of the manufacturing process, it eliminates the need for extra equipment, saving both time and money. Installing 3D printers and allowing them to operate without continual supervision isanother possibility [41].

b. DEFECTS: Printing mistakes Minor and large flaws may arise when a physical part is printed because the material flow may occasionally be blocked by unique problems. Also, the 3D printing process should be fully understood, and precautions should be made to prevent these sorts of flaws. Otherwise, a typo results in a loss of resources like time and money. The printing flaws can be categorised using the criteria below: i. Misaligned print platform; misaligned nozzle; clogged nozzle; depleted supply of printing material; or obstructed material flow ii. Vibration or stress (from the printer or another cause); iii. Inaccurate changes to printer settings; Lack of adherence to the print platform; Loss of adhesion to the print platform [36].

c. STABILITY: Due to the high temperatures used during manufacture, one of the difficulties in creating three-dimensionally printed pharmaceuticals is connected to their stability. Exhibited distinct symptoms of heat instability and chemical disintegration in addition to physical alterations. Setting up processes that imitate processing and storage circumstances is essential for producing stable pharmaceutical dosage forms utilising three-dimensional printing technology [39].

REGULATORY CONCERNS FOR 3DP

Regulatory approval is necessary for 3D printed drugs, medical equipment, and biological products. It specifies particular requirements for the manufacture of high-quality products, the maintenance of product efficacy and safety standards, and the removal of hazardous production materials. On the contrary, there are no specified standards for manufacture and administration of 3D printed products, making it difficult for regulatory agencies to handle this issue. It is critical to distinguish between compounding and manufacturing a 3D printed item. A catastrophic occurrence at the New England Compounding Center (NECC) in 2012, as well as other safety issues, have recently surfaced, underscoring the pharmaceutical industry's safety concerns. Despite the fact that 3D printing has changed the form and flexibility of pharmaceutical items, regulatory issues persist. The FDA has published 3D printing rules in the medical device guidance agenda. Aprecia Pharmaceutical received the first FDA permission for making antiepileptic tablets needed to treat epilepsy, leveraging a novel approach to build the customized drug in system; pharmaceutical manufacturers have always been a part of the 3D printing discourse. Aprecia is a world leader in pharmaceutical production, having created the globe's initial and only FDA-validated commercial 3D printing technique. Nonetheless, manufacturers face considerable challenges in bringing such technology to pharmacies, physicians, and hospitals via 3D printers, resulting in patient-specific drugs.[18]

III. CONCLUSION AND FUTURE PERSPECTIVE

The rapid development of 3D-printed formulations employing a range of techniques, such as inkjet printing, fused deposition modelling, material extrusion, and stereolithography, has attracted interest from the healthcare industry. Recently, researchers used 3D printing to provide several dosages with negligible material loss. It is possible to swiftly and securely make poly-pills and pharmacological devices. Individualised 3D printing lessens market rivalry, boosting pharmaceutical companies' profitability. The potential for spatially customised devices and formulations to treat diseases ranging from infection to cancer may open up new directions for medical and pharmaceutical research.

Because of this, the creation of customised drugs and medical transport systems, which would lead to substantial breakthroughs in both healthcare and medicine, has the potential to be a crucial component of 3D printing. Alternately, 3D printing might be used to create custom on demand dose forms that are adapted to the needs of difficult-to-treat patient populations, such small children and the elderly, whose dosing requirements are very different from those of adults. Utilising cutting-edge techniques like 4D printing in the pharmaceutical industry is useful, particularly for the development of controlled drug delivery. For example, using 4D printing to construct intricate, high-resolution structures may increase the process' efficiency in terms of time and money while also enabling the creation of customised treatments. The best use of this approach in pharmaceutics is the creation of specialised drug delivery systems for targeted therapy.

A digital health revolution might be sparked by the adoption of 3D printing in clinical settings, changing how drugs are created and prescribed to patients. However, the healthcare industry is renowned for being difficult to change because of the existence of regulatory regulations and clinical standards, both of which provide technological and quality control challenges. Indeed, as the evidence for 3D printing accumulates, it is evident that action is required to translate the theoretical advantages of 3D printing into actual advantages for patients. To improve pharmaceutical uptake, different 3D printing geometries might be used. In a recent world-first clinical research study, a 3D printer was integrated into a hospital pharmacy for the individualised treatment of kids with a rare metabolic disorder. Such advancements point to the transformative potential of 3D

printing, but more study is required to take this technology beyond the realm of academia and towards benefits for patients in thereal world [43].

REFERENCES

[1]. Islam R, Sadhukhan P. An insight of 3D printing technology in pharmaceutical development and application: an updated review. Current Trends in Pharmaceutical Research. 2020;7(2):55-80.

[2]. Samiei N. Recent trends on applications of 3D printing technology on the design and manufacture of pharmaceutical oral formulation: a mini review. Beni-Suef University Journal of Basic and Applied Sciences. 2020;9(12):1-12. https://doi.org/10.1186/s43088-020-00040- 4.

[3]. Jamroz W, Szafraniec J, Kurek M, Jachowicz R. 3D Printing in Pharmaceutical and Medical Applications – Recent Achievements and Challenges. Pharmaceutical research. 2018;35(176):1-22. https://doi.org/10.1007/s11095-018-2454-x.

[4]. Gujrati A, Sharma A, Mahajan SC. Review on Applications of 3D Printing in Pharmaceuticals. International Journal of Pharmaceutical Sciences Review and Research.2019; 59(1):148-154.

[5]. Ramya A, Vanapalli SL. 3D printing technologies in various applications. International Journal of Mechanical Engineering and Technology (IJMET). 2016;7(3):396–409.

[6]. Basit AW, Trenfield SJ. 3D printing of pharmaceuticals and the role of pharmacy. The Pharmaceutical Journal (PJ). 30 March 2022; 308(7959):1-30. https://pharmaceutical- journal.com/article/research/3d-printing-of-pharmaceuticals-and-the-role-of-pharmacy.

[7]. Anand N, Singh D, Singh G, Kaur L, Dhawan RK, Kaur N. 3D Printing Technology in Pharmaceutical Delivery System: Recent Advancement in Innovative Approach. Journal of Pharmaceutical Sciences. 2020;45(3):253-268.

[8]. Preethy Ani Jose, Peter Christoper GV. 3D Printing of Pharmaceuticals – A Potential Technology in Developing Personalized Medicine. Asian Journal of Pharmaceutical Research and Development. 2018;6(3):46-54.

[9]. Bhandari S, Hasan S. 3D Printing: A Revolution in Pharmaceutical Industry. International Journal of Research Publication and Reviews. 2021;2(9):105-111.

[10]. Bacskay L, Ujhelyi Z, Feher P, Arany P. The Evolution of the 3D-Printed Drug Delivery Systems: A Review. Pharmaceutics. 2022;14(7): 1312. https://doi.org/10.3390/pharmaceutics14071312.

[11]. Alghamdi SS, John S, Choudhury NR, Dutta NK. Additive Manufacturing of Polymer Materials: Progress, Promise and Challenges. Polymers. 2021;13(5):753. https://doi.org/10.3390/polym13050753.

[12]. Ponni RT, Swamivelmanickam M, Sivakrishnan S. 3D Printing in Pharmaceutical Technology – A Review. International Journal of Pharmaceutical Investigation. 2020;10(1):8-12.

[13]. Park BJ, Choi HJ, Moon SJ, Kim SJ, Bajracharya R, Min JY, Han HK. Pharmaceutical applications of 3D printing technology: current understanding and future perspectives. Journal of Pharmaceutical Investigation. 2019;49: 575–585. https://doi.org/10.1007/s40005-018- 00414-y.

[14]. Shahrubudin N, Lee TC, Ramlan R. An Overview on 3D Printing Technology: Technological, Materials, and Applications. Procedia Manufacturing. 2019; 35: 1286–1296. https://doi.org/10.1016/j.promfg.2019.06.089.

[15]. Pitzanti G, Mathew E, Andrews GP, Jones DS, Lamprou DA. 3D Printing: an appealing technology for the manufacturing of solid oral dosage forms. Journal of Pharmacy and Pharmacology. 2022;74(10):1427–1449. https://doi.org/10.1093/jpp/rgab136.

[16]. Al-Gawhari FJ, Mohammed Ali A. Types of 3D Printers Applied in Industrial Pharmacy and Drug Delivery: Review Article. Technium BioChemMed. 2022;3(2):1-14.

[17]. Karalia D, Siamidi A, Karalis V, Vlachou M. 3D-Printed Oral Dosage Forms: Mechanical Properties, Computational Approaches and Applications. Pharmaceutics. 2021;13(9):1401. https://doi.org/10.3390/pharmaceutics13091401.

[18]. Warsi MH, Yusuf M, Al Robaian M, Khan M, Alsaab H, Muheem A, Khan S. 3D Printing Methods for Pharmaceutical Manufacturing: Opportunity and Challenges. Current Pharmaceutical Design. 2018;24: 1-8.

[19]. Jassim ZE. Application of 3D Printing In Innovated Drug Delivery: A Review. International Journal of Applied Pharmaceutics. 2021;13(4):77-86.

[20]. Shahbazi M, Jager H. Current Status in the Utilization of Biobased Polymers for 3D Printing Process: A Systematic Review of the Materials, Processes, and Challenges. ACS Appl. Bio Mater. 2021;4(1):325−369. https://doi.org/10.1021/acsabm.0c01379.

[21]. Lamichhane S, Bashyal S, Keum T, Noh G, Seo JE, Bastola R, Choi J, Sohn DH, Lee S. Complex formulations, simple techniques: Can 3D printing technology be the Midas touch in pharmaceutical industry?. Asian Journal of Pharmaceutical Sciences. 2019;14(5):465–479. https://doi.org/10.1016/j.ajps.2018.11.008.

[22]. Fan D, Li Y, Wang X, Zhu T, Wang Q, Cai H, Li W, Tian Y, Liu Z. Progressive 3D Printing Technology and Its Application in Medical Materials. Frontiers in Pharmacology. 2020;11: 122.
[23]. Varghese R, Sood P, Salvi S, Karsiya J, Kumar D. 3D printing in the pharmaceutical sector: Advances and evidences. Sensors International. 2022;3: 100177. https://doi.org/10.1016/j.sintl.2022.100177.
[24]. Ventola CL, MS. Medical Applications for 3D Printing: Current and Projected Uses. Pharmacy and Therapeutics (P&T). 2014;39(10):704-711.
[25]. Chliara MA, Elezoglou S, Zergioti I. Bioprinting on Organ-on-Chip: Development and Applications. Biosensors. 2022;12(12):1135. https://doi.org/10.3390/bios12121135.
[26]. Xu Y, Wu X, Guo X, Kong B, Zhang M, Qian X, Mi S, Sun W. The Boom in 3D-Printed Sensor Technology. Sensors. 2017;17(5):1166. https://doi.org/10.3390/s17051166.
[27]. Jain K, Shukla R, Yadav A, Ujjwal RR, Flora SJS. 3D Printing in Development of Nanomedicines. Nanomaterials. 2021;11(2): 420. https://doi.org/10.3390/nano11020420.
[28]. Wang Y, Ahmed A, Azam A, Bing D, Shan Z, Zhang Z, Tariq MK, Sultana J, Mushtaq RT, Mehboob A, Xiaohu C, Rehman M. Applications of additive manufacturing (AM) in sustainable energy generation and battle against COVID-19 pandemic: The knowledge evolution of 3D printing. Journal of Manufacturing Systems. 2021;60: 709–733. https://doi.org/10.1016/j.jmsy.2021.07.023.
[29]. Aydin A, Demirtas Z, Ok M, Erkus H, Cebi G, Uysal E, Gunduz O, Ustundag CB. 3D printing in the battle against COVID-19. Emergent Materials. 2021; 4:363–386. https://doi.org/10.1007/s42247-021-00164-y.
[30]. Eshkalak SK, Ghomi ER, Dai Y, Choudhury D, Ramakrishna S. The role of three- dimensional printing in healthcare and medicine. Materials and Design. 2020;194: 108940. https://doi.org/10.1016/j.matdes.2020.108940.
[31]. Javaid M, Haleem A. 4D printing applications in medical field: A brief review. Clinical Epidemiology and Global Health. 2019;7(3): 317–321. https://doi.org/10.1016/j.cegh.2018.09.007.
[32]. M. Hanon M, Zsidai L, Ma Q. Accuracy investigation of 3D printed PLA with various process parameters and different colors. Materials Today: Proceedings. 2021;42(5): 3089- 3096. https://doi.org/10.1016/j.matpr.2020.12.1246.
[33]. Miazio L. Impact Of Print Speed On Strength Of Samples Printed In FDM Technology. Agricultural Engineering. 2019;23(2): 33-38. https://doi.org/10.1515/agriceng-2019-0014.
[34]. Shinde AA, Patil R, Dandekar A, Dhawale N. 3D Printing Technology, Material Used For Printing and its Applications. International Journal of Scientific and Engineering Research.2020;11(7):105-108.
[35]. https://www.researchgate.net/publication/345763830_3D_Printing_Technology_Material_Us ed_For_Printing_and_its_Applications.
[36]. M. Prabhakar M, A.K. Saravanan, A. Lenin H, I. leno J, K. Mayandi, P. Ramalingam S. A short review on 3D printing methods, process parameters and materials. Materials Today: Proceedings. 2021;45(7): 6108-6114. https://doi.org/10.1016/j.matpr.2020.10.225.
[37]. Gunaydin K, Prof. Dr. Turkmen HS. Common FDM 3D Printing Defects. https://www.researchgate.net/publication/326146283_Common_FDM_3D_Printing_Defects.
[38]. Druga C, Serban L, Braun B, Tulica A. Analysis of the Influence of the Layer Height on the Strength of 3D Printed Structures. In: 11th International Conference on Information Science and Information Literacy, Sciendo. 2021;177-181. https://doi.org/10.2478/9788395815065- 019.
[39]. Lee D, Wu G-Y. Parameters Affecting the Mechanical Properties of Three-Dimensional (3D) Printed Carbon Fiber-Reinforced Polylactide Composites. Polymers. 2020;12(11):2456. https://doi.org/10.3390/polym12112456.
[40]. Silva IA, Lima AL, Gratieri T, Gelfuso GM, Sa-Barreto LL, Cunha-Filho M. Compatibility and stability studies involving polymers used in fused deposition modeling 3D printing of medicines. Journal of Pharmaceutical Analysis. 2022;12(3):424-435. https://doi.org/10.1016/j.jpha.2021.09.010.
[41]. Abdella S, Youssef SH, Afinjuomo F, Song Y, Fouladian P, Upton R, Garg S. 3D Printing of Thermo-Sensitive Drugs. Pharmaceutics. 2021;13(9):1524. https://doi.org/10.3390/pharmaceutics13091524.
[42]. Sun L, Hua G, T.C.E. Cheng, Wang Y. How to price 3D-printed products? Pricing strategy for 3D printing platforms. International Journal of Production Economics. 2020;226: 107600. https://doi.org/10.1016/j.ijpe.2019.107600.
[43]. Pinho LAG, Lima AL, Sa-Barreto LL, Gratieri T, Gelfuso GM, Marreto RN, Cunha-Filho M. Preformulation Studies to Guide the Production of Medicines by Fused Deposition Modeling 3D Printing. AAPS PharmSciTech. 2021;22: 263. https://doi.org/10.1208/s12249-021-02114-7.
[44]. Mahmood MA. 3D Printing in Drug Delivery and Biomedical Applications: A State-of-the-Art Review. Compounds. 2021;1(3):94–115. https://doi.org/10.3390/compounds1030009.