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3D Printing is Emergency Technology for Pharmaceutical and Medical Field

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Abstract

3D printing, or additive manufacturing, is a transformative technology revolutionizing various industries by enabling the creation of complex threedimensional objects from digital models. This process builds objects layer by layer using materials such as plastics, metals, and composites. The technology is gaining traction in sectors like healthcare, aerospace, automotive, and consumer goods due to its ability to expedite prototyping, customization, and production processes. In the pharmaceutical industry, 3D printing holds significant promise for personalized medicine, allowing for the precise tailoring of drug doses and combinations to individual patient needs. Recent advancements in 3D printing have led to the development of innovative products and applications, such as bio printing human tissues and organs, which could potentially revolutionize organ transplantation. The technology's ability to create intricate designs with high precision, reduce material waste, and enhance production efficiency underscores its growing importance. This review aims to highlight the latest developments and potential future directions of 3D printing, emphasizing its impact on manufacturing, healthcare, education, and food production. The democratization of design and enhanced collaboration facilitated by 3D printing are poised to drive further innovation and adoption across various fields.

Keywords: 3D printing, Additive manufacturing, Stereo lithography (SLA)

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1. Introduction

3D printing technology are unique technology which use CAD software and create 3D product layer by layer material (Ursan *et al.*, 2013). 3D printing, also known as additive manufacturing, is a revolutionary technology that has transformed the way we manufacture products. This technology enables the creation of three-dimensional objects from a digital model by layering materials such as plastics, metals, and composites, one

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layer at a time. 3D printing is becoming increasingly popular in manufacturing, prototyping, and designing industries as it allows for much faster prototyping and customization of products. This technology is also used in various industries, including healthcare, aerospace, automotive, and consumer goods, among others. As 3D printing continues to advance, it is essential to review the latest developments and advancements in the field to keep up with the latest trends and gain an understanding of its potential implications on the future of manufacturing (Perrot, 2019). 3D printing is a revolutionary technology that has the potential to transform many industries. This includes manufacturing, healthcare, education, and even food production. 3D printing allows for the creation of complex and intricate designs with a high level of precision, which is not possible with traditional manufacturing methods (Basit and Gaisford, 2018).

3D printing is technique for creating objects involves adding layers of material to form a 3D shape, rather than removing material as in traditional manufacturing. with 3DP, a wide range of shapes and sizes can be produced with exceptional accuracy, enabling businesses to create innovative products that were once impossible to make. Furthermore, this technology allows for a high degree of customization, ensuring that each product meets the specific needs of the user. Compared to traditional manufacturing methods, 3DP is faster, more efficient, and more cost-effective (Ursan et al., 2013). Table 1 Shows comparison between conventional technique and 3D printing techniques in pharma industry. Medicinal and pharmaceutical 3D printing applications are growing quickly and are expected to develop the health care industry (Ventola, 2014). Examples of personalized drugs, including dose, dose combination, or even actively tailored to the patient's genetics, are not yet fully understood (Kalaskar, 2017; Kamali et al., 2016). 3D printing is all about digital drawing and fabrication of article layer-by-layer (Norman et al., 2017). In realistic terms, this means that users can create practically anything that can be designed in a digital platform using computer-aided design (CAD) software (Souto et al., 2019; Izdebska and Thoma, 2016). Virtual must be created as stereo lithography (.stl) or object (.obj) files for use as templates in commercially available object printers. Democratization of design and production, enhanced collaboration, reduced time, customized geometrically complex objects in small quantities have helped reduce material use (Ursan et al., 2013). The term 3D printing refers to a series of additive mechanized processes, which construct products straight from digital design by creating layers of plastics, metals, or other materials. Due to the all-embracing research being done in this vicinity and all the investigational drug delivery systems intended and described in numerous papers over the past few years, pharmaceutical company like Aprecia® launched its ûrst approved 3DP manufactured product. 3D printing is built-up technique in which objects fabricate by depositing material like, plastic, metal, resin, powder, liquid, etc. to construct 3D object. 3D printers are like the traditional inkjet printers though, the ending creation differs within that a 3D printed object is produced (Peterson et al., 2014). Today, 3D printing is used in many industries for various applications. In the manufacturing industry, 3D printing is used for prototyping, tooling, and even end-use parts production. In healthcare, 3D printing is used for creating personalized prosthetics, implants, and surgical models (Liaw and Guvendiren, 2017). In education,

Table 1: Comparison Between Conventional Technology and 3D Printing Technology		
Conventional Technology	3D Printing Technology	
Subtractive manufacturing which involves the removal of material until the desired shape is formed.	Layer by layer construction of an object by adding thermoplastic or other materials.	
Requires skilled labor to operate and maintain machinery.	Offers the ability to produce complex and intricate geometries that are difficult to manufacture with traditional methods.	
Proven methods with years of expertise.	Prototyping and producing small volumes of products rapidly.	
Efficient for mass production to produce identical parts of high quality.	3D printing only uses the amount of material needed to print an object.	
Relatively high scrap rate due to cutting and shaping processes.	3D printing technology enables the creation of unique and custom parts on demand.	

3D printing is used to teach STEM subjects and for creating educational models. In the food industry, 3D printing is used for creating fun and creative food designs. The popularity of 3D printing has also led to the development of 3D printing services, where individuals and businesses can send their designs to be printed by a third party. This has made 3D printing more accessible to those who cannot afford to buy their printers or those who need large-scale production (Hull, 1986). The future of 3D printing looks promising, with several potential applications being explored. One such application is in the field of construction, where 3D printing is in the field of medicine, where bio printing can be used to create functional human tissues and even organs. This could revolutionize the field of organ transplantation and help address the shortage of organ donors (Bradbury *et al.*, 2004).

In this review article, we will discuss the history of 3D printing, working procedures of 3D printing, types of 3D printing, application of 3D printing, and future trends.

2. History of 3D Printing

The history of 3D printing dates back to the 1980s, when Chuck Hull, the co-founder and former president of 3D Systems, invented a process called stereo lithography (SLA). This process uses a UV laser to cure a liquid photopolymer layer by layer, creating a solid 3D object. In 1988, Hull released the first commercial product, SLA-1 on market. In 1988, at the University of Texas, Carl Deckard a patent for the SLS 3D printing technique in which powder grains are fused together locally by a laser. In 1992, EOS GmbH was patented for Fused Deposition Modelling. MIT professors are credited first using the term 3D printer with their invention of a layering technique using standard inkjet print head to deposit "ink" or a binder solution into the powder bed to bind powder, again repeating this process layer-by-layer to produce the desired geometry. Throughout 2000, 3D printing technologies became more accessible and affordable, allowing for widespread adoption in industries such as manufacturing, healthcare, and aerospace. In 2001, the first 3D desktop printer was prepared by solid immersion. In 2002, first 3D printed kidney could filter blood and produce diluted urine in animals. In 2006, first SLS machine was developed. In 2009, the FDM patents fell into the public domain and this year the first 3D bio printed blood vessel was developed by Organovo. In 2010, MakerBot launched its first affordable desktop 3D printer, making the technology more accessible to consumers and small businesses. In 2012 Daniel Kelly's lab create first 3D printing bone. In 2015, first 3D printed drug (Spitram) manufactured by Aprecia pharmaceutical was approved by USFDA. In recent years, there have been advancements in 3D printing materials including metals, composites, and even organic substances like human tissue. Additionally, the development of 3D scanning technologies has also allowed for the creation of highly accurate and detailed 3D models of real-world objects (Anciaux et al., 2016; Vinogradov, 2019; Gross et al., 2014).

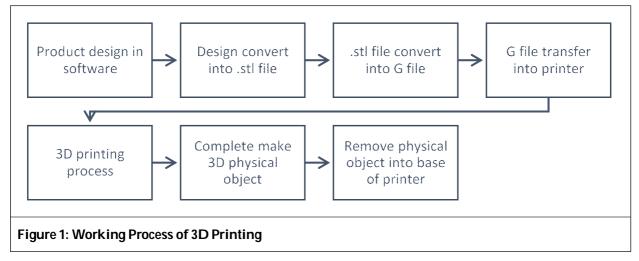
Today, 3D printing is being used in a variety of fields including prototyping, manufacturing, medicine, and even food production. As technology continues to advance, it is likely that we will see even more innovative uses of 3D printing in the future.

3. Working Mechanism of 3D Printing

In these 3D printing main 3 step involve for build upto final product. Major three step including

- **A. Designing a Digital Model:** A digital 3D model is created using specialized software or through 3D scanning. This model is the basis of the physical object to be printed.
- **B. Preparing the Printer:** Once the 3D model is developed, it needs to be loaded into the 3D printer software. The software then slices the model into layers and generates instructions for the printer to create each layer.
- **C. Printing a Physical Object:** The 3D printer starts printing the object by depositing material layer by layer according to the instructions generated by the software. The printer typically uses one of several 3D printing technologies, such as Fused Deposition Modelling (FDM), Stereo lithography (SLA), or Selective Laser Sintering (SLS).

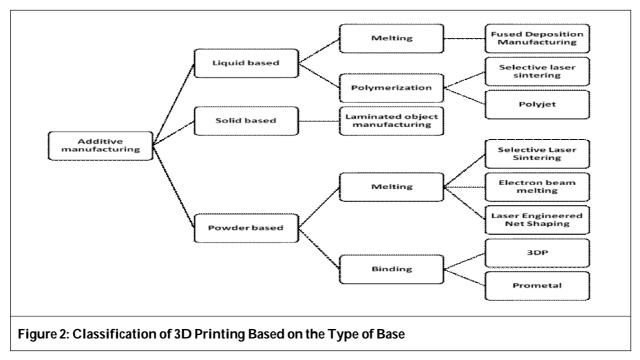
Figure 1 shows the working process of 3D printing. In FDM, the printer melts and extrudes a plastic filament layer by layer to build up the object. In SLA, the printer uses UV light to cure a liquid resin layer by



layer, solidifying it into the desired shape. In SLS, the printer uses a laser to fuse a powder material layer by layer, solidifying it into a solid object. Once the printing process is complete, any support structures used during the printing process are removed, and the finished object is cleaned and post-processed as needed. The result is a physical object that matches the 3D model created in the first step (Kaufui and Aldo, 2012; Schubert *et al.*, 2014). The many 3D printing technology can read (.STL) files. A programme like Magics (Materialise) may be used to solve any conversion problems that can arise while converting the 3D model to a.STL digital file. AMF and 3D manufacturing file formats, which are utilised as file types instead of .STL, are examples. .STL file does not have information regarding the type of material, its colour, texture, properties, and other features (Wong and Hernandez, 2012).

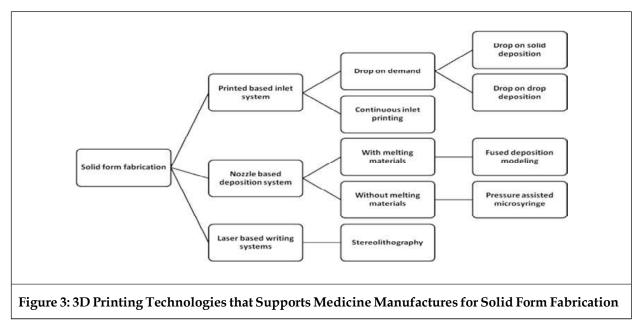
4. Type of 3D Printing Technologies

In the last 15 years, a large variety of 3D printing techniques has been introduced into the Rapid prototype (RP) industry. 3D printing is also known as the additive manufacturing (AM) process. Although other highly competitive processes, such as laser-based writing systems or nozzle-based deposition systems, have been extensively developed, printing-based inkjet systems is a frequently used procedure in three-dimensional method (Dimitrov *et al.*, 2006). It can furthermore be classified, Figure 2, into 3-D printing systems. 3D printing processes may also be related to (1) Solid method, (2) Liquid method, and (3) Powder methods. Melting is used in the fused deposition production method, followed by liquid-based printing. A laser is used to photo



polymerize a resin in stereo lithographic printing. Stereo lithography is used to create complicated nano composites by converting liquid polymers into solid layers using photo-curing UV blue light. Polyjet printing is a relatively new method of producing fast printing. Sachs *et al.* received a US patent for the technology in 1994. It creates physical model groups using inkjet technology. Laminated Object Manufacturing is great for producing huge quantities of items. The layers are bound together by applying pressure and temperature, as well as a heat adhesive film. The powder is sintered or fused using carbon dioxide laser beams in the selective laser sintering process. Electron beam melting is mostly used to create complicated polymer prototypes, which are already well established. As a process building material, laser engineered net shaping (LENS) employs virgin metal powder as the user's option. A liquid binder is deposited on a powder media utilising inkjets for printing using computer-aided design (CAD) data in MIT-licensed methods, 3DP and prometal (Murr *et al.*, 2012).

The pharmaceutical industry uses 3D printing techniques based on solid form fabrication that are further classified into printed based inlet system, nozzle-based deposition system and laser-based writing systems (Figure 3).



4.1. Printed Based Inlet System

Inkjet printing is overall term to describe a system that can digitally control formation and placement of small liquid drops onto substrate using a pattern generation device. There are basically two types of printing-based inkjet system 1) Continues inkjet printing system 2) Drop-on- demand (DOD) printing system. Inkjet printing is also called as mask less or tool-less approach because the formation of desired structure mainly depends upon the movement of inkjet nozzle or movement of the substrate for accurate and reproducible formation. Inkjet printing is based on Lord Raley's instability theory, developed in 1878, which explains the breaking of a liquid stream or jet into droplets (Gross *et al.*, 2014).

4.2. Continues Inkjet Printing System

The drops are formed by transducer or a droplets loading apparatus producing a continuous stream of droplet then the droplet is directed to electrically charged element to obtain the desired charge finally the formed droplet reach onto substrate and great the 3D product (Derby, 2010).

4.3. Drop-On-Demand (DOD) Printing System

DOD inkjet printers fabricate individual drops when considered necessary and are therefore more economical with ink delivery than Continues inkjet printing systems. Drop printing system the pharmaceutical based ink is convert to a droplet form ink is convert to a droplet form by applying a voltage to a piezoelectric crystal transducer to vibrates the materials or heating the formulation to the temperature higher than the boiling

temperature there by creating droplet. Then dots of solution are driven from orifice to the printer head's nozzle and solidified drop wise. Drop on demand (DOD) inkjet printer generate individuals drops when required and thus more economical with ink delivery than are continues inkjet printer system. DOD are classified into two types: (1) Drop on solid deposition (DOS), (2) Drop on Drop deposition (DOD). DOD print head usually contains multiple nozzles (100-1000) (Konta *et al.*, 2017).

DOD technology can largely be split into technology utilising heat (thermal inkjet printer) and those utilising piezoelectricity (piezoelectric inkjet printer). Table 2 shows list of drugs prepared by thermal and piezoelectric inkjet printer. These are both (thermal and piezoelectric inkjet) characterized by presence printer head and the need control both drop formation velocity and liquid viscosity.

Table	Table 2: List of Drugs Prepared by Thermal and Piezoelectric Inkjet Printer			
S. No.	Drug/API	Dosage Form	Application	References
1	Salburamol sulphate	Oral film tablet	Anti-Asthmatic	(Choi <i>et al.,</i> 2015)
2	Prednisolone	Tablet	TabletAnti-inflammatory, Immunosuppressant(Asma et al.,	
3	Felodipine	Solid dispersion Antihypertensive (Meléndez et al., 2		(Meléndez <i>et al.,</i> 2008)
4	Carbamazepine	Co crystals Antiepileptic drug (Nikola		(Nikolaos <i>et al.,</i> 2011)
5	Terbutaline sulphate	Solution Bronchodilator ((Van Arnum, 2013)
6	Folic acid	Nano suspension	Anaemia	(Sharma <i>et al.,</i> 2013)
7	Felodipine	CR tablet	Antihypertensive	(Takala <i>et al.,</i> 2012)
8	Piroxicam	Solid dispersion NSAIDs (Pardeike <i>et al.</i> , 20		(Pardeike <i>et al.,</i> 2011)
9	Miconazole	Micro needle	Anti-fungal	(Scoutaris <i>et al.,</i> 2011)
10	Paclitaxel	Micro particles	Anticancer	(Raijada <i>et al.,</i> 2013)

4.4. Drop-on-Solid Deposition

Drop on solid deposition (powder bed fusion) to spread thin layer of powder and simultaneously applying liquid binder drop with the help of inkjet printer. The link (binder + API or binder solution) is sprinkled over a powder bed in 2D fusion to make the final product in layer-by-layer fusion. DOD technologies are easier in the pharmaceutical industry than other technologies (Boehm *et al.*, 2014). The stability of the final product is often achieved by thermal sintering, which permits the elimination of residual volatile solvents. The binder may cause the particles of the ink to stick, or the powder bed may play a role after its own solidification. These techniques are prejudiced by two powder characteristics: powder topology and the response of materials with binder. Table 3 shows the list of drugs prepared by drop on solid deposition technique.

Table 3:	Table 3: List of Drugs Prepared by Drop on Solid Deposition Technique			
S. No.	Drug/API	Dosage Form	Application	References
1	Acetaminophen	Tablet ER	Antipyretic	(El Aita <i>et al.,</i> 2018)
2	Pseudoephedrine HCl	Tablet ER	Nasal congestion	(Yu et al., 2007)
3	Acetaminophen	ODT	Antipyretic	(Bhusnure <i>et al.,</i> 2016)
4	Levetiracetam	ODT	Anti-epileptic	(Yu et al., 2009)
5	Levofloxacine	Implant CR	Bacterial infection	(Duppala <i>et al.,</i> 2016)
6	Warfarin	ODT	Anticoagulant	(Gross et al., 2014)

The first 3D printed pill, an anti-epilepsy drug called Spritam, was recently approved by the FDA. Created by Ohio-based Aprecia Pharmaceuticals, Spritam is made with Aprecia's proprietary 3D printing technology, Zip Dose. Zip Dose creates pills that instantly dissolve on the tongue with a sip of liquid, a potential boon to those who have trouble swallowing traditional medications (Boehm *et al.*, 2014).

4.5. Drop-on-Drop Deposition

In drop-on-drop deposition, the printer head ejects the droplets onto each other to produce a solid layer, resulting in a high-resolution 3D structure. This direct writing IJ-printing method is capable of fabricating microscopic drug delivery systems having diverse geometries, where droplet size is about 100 µm in diameter and layer thicknesses are smaller than the droplet size, maybe due to surface wetting, solvent evaporation, or shrinkage. The entire formulation in printable fluid should be suitable for jetting and rapid solidification. The droplets produced are characterized by the volume of some picoliters, which corresponds to the normal range of 18-50 µm. The major negative aspect of the process is that the three-dimensional structures are very fragile and irregular, deficient hardness, unconvinced resolution finish, and low drug loadings. The physical properties of the printable fluid, such as viscosity and volatility, are also important to prevent the coffee ring effect, fluid leaking and nozzle clogging (Cooley *et al.*, 2002). Advantage of these techniques, the use of heat post-treatment of a three-dimensional manufactured product is essential for removing the solvents used during the process, as printed drugs are beneficial for avoiding impurities and solvent residues in the inside.

4.6. Nozzle Based Deposition System

Technologies are always evolving, and new technologies are continuously developed to overcome the limitations of previous ones. The nozzle-based deposition method consists of a combination of drugs and polymers and other solid materials prior to 3D printing. The nozzle based deposition system mixes the solid components with the binder prior to 3D printing and directly deposits the mixture through a nozzle to create a 3D object. Such systems can be divided into processes based on content melting and non- melting processes. There are two types of printing, depending on the kind of material use: fused deposition modeling, which uses dissolved components, and pressure-assisted micro syringes, which do not use dissolved materials (Khatri *et al.*, 2018).

4.7. Fused Deposition Modeling

Fused deposition modelling was developed by S.Scott crump in the late 1980 and was commercialized in 1990 by stratasys (Kaufui and Aldo, 2012). In the Fused deposition modelling process, the copy or part is usually produced by extruding slim 200-400 µm threads of polymer-based matter that alleviate immediately to structure a solid layer (Wong and Hernandez, 2012). Working process of fused deposition modelling a molten thermoplastic polymer filament is extruded by two rollers through a high temperature nozzle and there after solidified onto a build plate. Table 4 list of drugs prepared by FDM technique. The print head can move within the X and Y axes whereas the platform which can be thermostat can move vertically on the Z axis, creating a 3D structure layer by layer by fusing the layers together. The process has a limited of various shapes that can be fabricated.

Tabl	Table 4: List of Drugs Prepared by Fused Deposition Modeling Technique			
S. No.	Drug/API	Dosage Form	Applications	References
1	Acetaminophen, caffeine	Tablet (IR, MR)	Antipyretic	(Dumitrescu <i>et al.,</i> 2018)
2	Ciprofloxacine hydrochloride	CR	Bacterial infection	(Goyanes <i>et al.,</i> 2015)
3	Lisinopril, Amlodipine, Indapamide, Rosuvastatin calcium	Tablet	Antihypertensive and CHF	(Saviano <i>et al.,</i> 2019)
4	Carvedilol	ER	Antihypertensive	(Pereira <i>et al.,</i> 2019)

Table 4: List of Drugs Prepared by Fused Deposition Modeling Technique				
5	Guaifenesin	CR	Common cold	(Ilyés et al., 2019)
6	Glipizide	SR	SR Antidiabetic	
7	Carbamazepine	IR	IR Anti-epileptic	
8	Captropil, Nifedipine	Tablet SR	Antihypertensive and CHF	(Khaled <i>et al.,</i> 2015)
9	Prednisolone	Tablet (ER)	Immunosuppressive drug	(Conceição <i>et al.,</i> 2019)
10	Acetaminophen	Tablet (MR), capsule	Antipyretic	(Water <i>et al.,</i> 2015)
11	5-ASA and 4-ASA	Tablet (MR)	Antibiotics	(Skowyra <i>et al.,</i> 2015)
12	Fluorescein	Tablet	Corneal ulcer and Herpetic corneal infection	(Melocchi <i>et al.,</i> 2015)
13	Pravastatin	Tablet (IR, SR)	Lower bad cholesterol	(Khaled <i>et al.,</i> 2015)
14	Atenolol, Ramipril	Tablet (IR, SR)	Antihypertensive	(Khaled <i>et al.,</i> 2015)
15	Aspirin	Tablet (IR, SR)	NSAID	(Khaled <i>et al.,</i> 2015)
16	Hydrochlorothiazide	Tablet (IR, SR)	Anti-hypotensive	(Khaled <i>et al.,</i> 2015)
17	Dye	Implant CR	Excipient	(Masood, 2007)
18	Diclofenac sodium	Tablet (MR)	NSAID	(Zidan <i>et al.,</i> 2019)
19	Theophylline	Tablet (IR)	Anti-asthmatics	(Isreb <i>et al.,</i> 2019)
20	Domperidone	Tablet	Nausea, Vomiting	(Chai <i>et al.,</i> 2017)
21	Budesonide	Capsule	Ulcerative colitis	(Tochukwu et al., 2017)
22	Nitrofurantoin	Catheter, Implant	UTI	(Sandler <i>et al.</i> , 2014)
23	Hydroxyapatite	Implant	Carrier	(Yan <i>et al.,</i> 2018)
24	Ibuprofen	Tablet	NSAID	(Alvaro et al., 2015)
25	Aminosalicylate	Tablet	Antibiotic	(Christos <i>et al.,</i> 2018)
26	Metformin, Glimepiride	Tablet	Ant diabetic	(Muzna <i>et al.,</i> 2018)
27	Hydrochlorothiazide	Tablet	Diuretic	(Weisman <i>et al.,</i> 2015)
28	Enalapril maleate	Tablet	Antihypertensive	(Weisman <i>et al.,</i> 2015)
29	Captopril	Tablet IR	Hypertension, CHF	(Tochukwu et al., 2017)
30	Gentamicin sulphate, methotrexate	General Device	Antibiotic and Anticancer	(Melocchi <i>et al.,</i> 2015)

4.8. Pressure-Assisted Micro Syringes (PAM)

The PAM method is printing process developed by Vozzi *et al.* in 2002 as alternative printing technology for tissue engineering (Goole and Amighi, 2016). This technique uses a syringe extruder for oily and semi-liquid material deposition according to the geometry design. Viscosity, apparent elastic limit and viscoelasticity, are the root parameters that establish the fertility of this technology. The PAM printing method requires a viscous semi-solid system as a starting material. After preparation, the material is filled into a syringe and a piston, or plunger is placed on the top. The printing process is triggered and controlled by applying pressurized air. The extruded strands are printed onto a platform to create 3D objects. It has the potential to work continuously in an oven and at room temperature. Solvents used can be toxic to health and may cause stability problems in

Table 5: List of Drugs Prepared by Pressure-Assisted Micro Syringes Technique				
S. No.	Drug/API	Dosage Form	Applications	References
1	Guaifenesin	Tablet CR	Common cold	(Vozzi and Ahluwalia, 2007)
2	Glipizide	Tablet SR	Ant diabetic	(Khaled <i>et al.,</i> 2014)
3	Carbamazepine	Tablet IR	Anticonvulsant	(Khaled <i>et al.,</i> 2015)
4	Diclofenac sodium	Tablet MR	Analgesic	(Conceição <i>et al.,</i> 2019)
5	Levetiracetam	Tablet IR	Anticonvulsant	(Zidan <i>et al.,</i> 2019)

Table 5: List of Drugs Prepared by Pressure-Assisted Micro Syringes Technique

certain APIs. Table 5 shows a list of drugs prepared by PAM technique. Nozzle with different diameter can be fixed to the syringe. The choice of the suitable printing nozzle depends largely on the viscosity of the used printing formulation. Viscosity should be analyzed to avoid printing errors, which can be caused by clogged nozzle. The printing formulation are based on solvent and requires a suitable drying step. Because of this drying step, shrinkage of the printed object must be expected (Goole and Amighi, 2016).

4.9. Stereo Lithography

Stereo lithography (SLA) printing is early and widely used 3D printing technology. In the early 1980, Japanese researcher Hideo kodama first invented the modern layered approach to SLA by using ultra violate light to cure photosensitive polymer (Bradbury et al., 2004). 1984 just before Chuck Hull filed his own patent. Alain le mehaute, Olivier de witte and jean Claude Andre filed a patent for the stereo lithography process (Pamela, 2017). In stereo lithographic printing, a laser is used to photo polymerize a resin. Stereo lithography converts liquid polymer resins and composites into solid layers using photo curing UV blue light (Ventola, 2014). The focused UV laser is vector-scanned over the top of a bath of a photo polymerizable liquid polymer plastic resin. Polymerization may occur up to a few micrometers below the surface, leading to the solidification of the resin. When the first layer is formed, it is lowered into the bath to a depth equivalent to the thickness of the polymerized layer, which is recoated with liquid resin. A pattern is then cured in this second layer as the UV light exhibits a depth of penetration that exceeds the layer thickness. This cures the previously solidified material, which allows adhesion between the layer thicknesses. The process is repeated until a multiplicity of superimposed layers forming the desired part is obtained. Finally, the excess of unpolymerized resin is washed off. This technology produces high-quality components for biomedical applications or gears with integrated moving components and complex nano composites. Table 6 list of drugs prepared by stereo lithography technique.

Table 6	Table 6: List of Drugs Prepared by Stereo Lithography Technique			
S. No.	Drug/API	Dosage Form	Applications	References
1	Paracetamol	Tablet MR	Antipyretic	(Jie <i>et al.,</i> 2016)
2	4 ASA	Tablet MR	Antibiotic	(Jie <i>et al.,</i> 2016)
3	Salicylic acid	Ánti acne patch	Psoriasis	(Goyanes <i>et al.</i> , 2016)
4	Ibuprofen	Hydro gel	Anti-inflammatory and anti-pyretic	(Martinez <i>et al.,</i> 2017)

5. Biological and Medical Application of 3D Printing

Additive manufacturing was used to design and manufacture lightweight machines for various purposes, like parts for rockets, planes, formula one car (Bletzinger and Ramm, 2001; Milewski, 2017). In the early 2000s, the expertise was first used to create dental implants and custom prosthetics. After that, medical applications of 3D printing have advanced extensively. Recently published reviews tell the use of 3D printing intended for skeleton, ears, exoskeleton, windpipes, stem cells, jawbones, spectacles, vascular network, cell culture, blood vessels, organs and tissues, novel dosage forms, and drug delivery devices Table 7 (Schubert *et al.*, 2014).

able 7: Biological Applications of 3D P	rinting (Souto <i>et al.,</i> 2019)
Tissue Engineering	The current treatment for organ failure is largely based on organtransplantation of live or else deceased donors. On the other hand, present is a stretched scarcity of human organs obtainable for transplantation. Researchers are working on methods to grow complete human organs, which can be used, for selection purposes at some stage in drug discovery. 3D bio printing have been doing well in produce knee meniscus, heart valves, artificial ears as well as the manufacture of custom-made barrier absorbable trachea, which has already been implanted in neonates with tracheobronchomalacia.
Customized Implants andProstheses	Planting and prosthesis can be made in almost any conceivable geometry by translating X-ray, MRI or CT scar digital.stl 3D print documents. 3D printing is productively used in health care, both standard and complex, used for surgical implant and prostheses, sometimes within 24 hour Used for fabricating dental, spinal, and hip implants.
Surgical Anatomical Models	3D Printed neuro anatomical providing can be especially helpful for neurosurgeons by introducing some of the most complex structures in the human body A real model, modeling the relationship between lesions with regular brain structure, can help determine the safes surgical corridors and may be useful for rehearsing challenging cases for neurosurgeons. Multipart spinal deformity can be better studied using a 3D model. Models for colonoscopy and liver transplant studies have been designed in the USA and Japan, respectively. Polypeptide chain models with secondary folds structures were designed with the inclusion of bond rotating barriers.
Aesthetic Surgery	In the future, using a three-dimensional printed model wil be able to print personalized breast implants to suit any patient's anatomy and personalneeds. Not only the shape but also the implant's design can be adjusted, giving the breast a more natural appearance and a natural experience
Hand Surgery	Recently, customized three-dimensionally printed prostheses have emerged, and various commercial companies offer personalized three-dimensionally printed finger, hand, and arm prosthetics. It is now doable to order 3D printed finger or arm prosthetic for only \$20 to \$50. Pri- biomimetic prosthetics combined with diverse neurons layers may probably make prosthetic limbs a entirely functional piece of the body.
Treatment of Burn Wounds	Researchers at the Wake Forrest Institute of Regeneration Medicine used this method to bio print amniotic fluid- derived stem cells and skin cells directly onto wounds and burn defects. The escalating speed and resolution of three- dimensional bio printers, this approach may develop into viable for the in vivo regeneration of tissues straight away after injury or during surgery.

In critical medical issues is the failure of organs and tissues as a result of accident, congenital defect, aging, etc., and the current resolution for this problem is organ transplant from dead or living donors. Organ transplants are more expensive that it is out of reach of common people and other problem with transplant surgery is that donors with tissue match are difficult to find. In 3D printing technology are bio printing organ and tissue using patient's own body cell and decrease risk of tissue or organ rejection (Gross *et al.*, 2014; Konta *et al.*, 2017). 3D printing technology to build various tissue and organ prototypes layer by layer. Living cell can be mixed with gel to produce a biopolymer that acts as a scaffold material. Sample of cell mixed with growth factors and multiplied in the laboratory. These cells are scaled up to create an organ with a working vascular system. Example is developing functional cardiac tissues particularly the heart valves by 3D bio printing technique. Trieaflet aortic valve was designed and develop by 3D bio printing technique using hybrid hydro gel. After 7 day of in vivo culture conditions the valve was well maintained, and the high visibility of cell was found with a high potential of remodelling. The development of heart and liver anatomy has been successfully by 3DP technology. Liver was first time prepared by Organovo by using 3D printing technology (Cui *et al.*, 2012).

5.1. Pharmaceutical Applications of 3D Printing

5.1.1. Personalised Medicine

In the pharmaceutical industry, drug development purpose is to increase efficacy and decrease adverse reactions. 3D printing is used to synthesize personalised medicine. Oral tablet is most used dosage form because of easy manufacturing, good patient compliance, pain avoidance, accurate dosing. The pharmaceutical industry has no method available to routinely use to make personalized solid dosage forms such as tablets. Oral tablets are prepared via a well-established process such as mixing, milling and dry and wet granulation of powder ingredients that form tablets by compression or molds (El Aita *et al.*, 2019). In manufacturing step, some problems observed, like drug degradation, form change, possibly leading to problems with formulation. This manufacturing method is unsuitable for creating personalized medicine. Personalized 3D-printing drugs particularly benefit patient who are known to have a pharmacogenetic polymorphism or who use medication with narrow therapeutic indices. Pharmacist can be analyze a patient pharmacogenetic profile such as age, race, gender to determine optimum therapeutic dose. A pharmacist could then print and dispense the personalized medication an automated 3D printing system. Personalized medication is fast dissolution than conventional medication (Mazhar and Tariq, 2019).

5.1.2. Complex Drug Release Profile

A compressed dosage form made from a homogeneous mixture of active and inactive ingredients and frequently limited to a simple drug release profile (Ursan *et al.*, 2013). In 3D printing technology, complex drug release profile that allows fabrication of complex geometries that are porous and loaded with multiple drugs each other surrounded by a barrier layer that modulates release. One example, chlorpheniramine maleate was 3D printed onto a cellulose powder substrate in amounts as small as 10-12 moles to demonstrate that even a minute quantity of drug could be released at specified time. Chlorpheniramine maleate are improve accuracy for the release of very small drug doses compared with compressed dosage form. Other example is the printing of a multi-layered bone implant with a drug release profile alternating between rifampicin and isoniazid in pulse release mechanism (Gross *et al.*, 2014).

5.1.3. Unique Dosage Form

Inkjet-based 3D printing and inkjet powder-based printing are more used in pharmaceutical industry. Many novel dosages form are formulated using 3D printing like Microcapsule, Antibiotic printed micro patterns, Hydro gel, Nano suspension, mesoporous bioactive glass scaffolds and hyaluronan-based synthetic extracellular matrices are formulated using 3D printing. Active ingredients used in 3D printing are steroidal anti-inflammatory drugs, acetaminophen, Caffeine, Vancomycin, Ofloxacin, Theophylline, Tetracycline, Paclitaxel, folic acid. Inactive ingredients used in 3D printing are acetone, methanol, propylene glycol, cellulose, glycerin, surfactant, ethanol dimethyl sulfoxide (Gross *et al.*, 2014).

5.1.4. First FDA Approved Drug

First 3D drug Spritam (levetiracetam) manufactured by Aprecia pharmaceuticals was approved by FDA. This drug is used in the treatment of epilepsy. Spritam drugs are marketed by Aprecia Company using Zip dose technology. This technology is based on powder bed fusion by layer by layer produced without using compression force. In this technology, thin layers powder are repeatedly spread on top of one another, and liquid droplets are deposited into selected area of each powder layer. Zip dose technologies produce a highly porous structures with high loading dose result medication quickly disintegrates on contact with liquid by breaking the bonds created during the 3DP process.

5.1.5. Personalized Topical Treatment Device

Nose-shaped masks for acne treatment filled with salicylic acid have been developed efficiently. Here, facial scan of patient was exported to the program, after which the section was selected. The most promising technique was for mask manufacturing, allowing high drug loading for the significant conductivity of salicylic acid during 3D printing (Perrot, 2019).

5.1.6. 3D Printing of Transdermal Delivery Systems

To avoid first-pass metabolism and/or pH mediated degeneration or ease of administration for patients with chronic illnesses such as diabetes, transdermal delivery systems may be beneficial. Layer-by-layer 3D printing technology can with no trouble used for the foundation of multifaceted transdermal patches of films. 3D technology offers the unique advantage of printing drug-filled micro needles for transdermal delivery. Micro needles are usually less than 500 μ m in height and are meant to penetrate the stratum corneum (10-15 μ m) to deliver active agent. SL was used to produce micro needles of biodegradable polymer (methyl vinyl ether-alt-maleic anhydride). To coat a quantum dotted needle as a model active agent inkjet printing can be used (Prasad and Smyth, 2016).

6. Future Trends

3D printing plays an important role in personalized medicine, nutritional products, organs and drugs. Drug manufacturing and distribution are more cost effective. 3D printing technology in two or more tablets convert one polypill to reduce patient taken more tablet per day and increase the patient compliance. In future 3D printing approach utilized in fabricate and engineer various novel dosage form, achieve optimized drug release profiles, develop new excipients, supporting delivery, limit degradation of biological molecules. 3D printing is fabricating the complex organ and prosthetics for the individual patient. 3D printing technology has created a fully functional heart in less than 20 years. This technique is complex heterogeneous tissue, like kidney and liver tissues, will be fabricated successfully in the future. In future, is possible to print out patient tissue as a strip that can be used in test to determine what medication will be most effective. Advance in robotic bio printer and robot-assisted surgery may also development tissue and organs.

7. Conclusion

Our well-thought-out review summarizes the accessible literature on current techniques designed for pharmaceutical manufacturing and dosage form development. Useful individual/personalized drug delivery for the narrow therapeutic window drug in 3D printing technology printing in the picoliters and reduce the adverse effect or side effect of the API for pediatrics and geriatrics. 3D printed fabrication of the products with complex release profile and personalized delivery. The effect of formulation geometry on release rate was studied, which gave a way and idea to study other factors using printing technology to produce dosage forms.

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