OPEN ACCESS

Saudi Journal of Medical and Pharmaceutical Sciences
Abbreviated Key Title: Saudi J Med Pharm Sci
ISSN 2413-4929 (Print) |ISSN 2413-4910 (Online)
Scholars Middle East Publishers, Dubai, United Arab Emirates
Journal homepage: https://saudijournals.com

Review Article

3-Dimensional Printing – Challenges for An Extrapolation to Dosage forms

Reshma Thadipatri[1], Shakir Basha Shaik[3], Pavan Kumar Chintamaneni[2], Nawaz Mahammed[2*], Charitha Bandlapalli[2]

[1]Department of Pharmaceutical Quality Assurance, Raghavendra Institute of Pharmaceutical Education and Research (RIPER)-Autonomous, Ananthapuramu, Andhra Pradesh, India
[2]Department of Pharmaceutics, Raghavendra Institute of Pharmaceutical Education and Research (RIPER)-Autonomous, Ananthapuramu, Andhra Pradesh, India
[3]Department of Pharmaceutical Analysis, Raghavendra Institute of Pharmaceutical Education and Research (RIPER)-Autonomous, Ananthapuramu, Andhra Pradesh, India

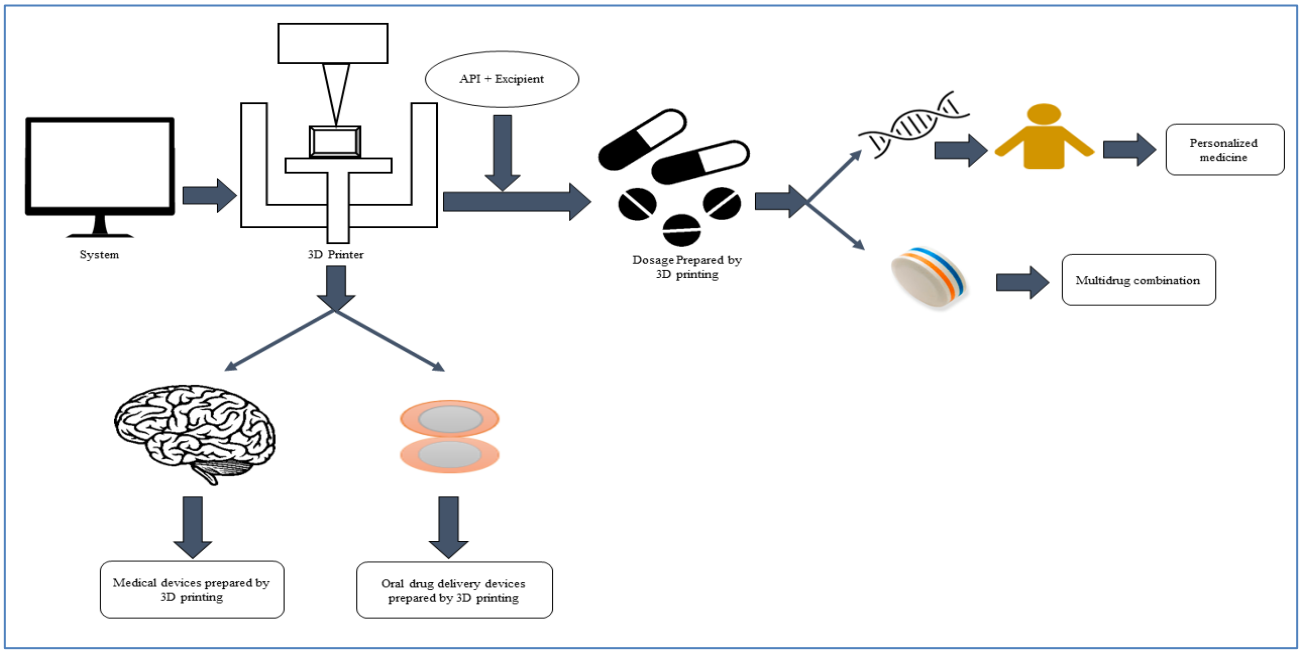
DOI: 10.36348/sjmps.2021.v07i08.005 | **Received:** 17.07.2021 | **Accepted:** 21.08.2021 | **Published:** 24.08.2021

***Corresponding author:** Nawaz Mahammed

Abstract

Background: Three-dimensional printing is a revolutionary technique with Computer-Aided Design software and Standard Triangle Language (STL). This software helps print tablet (object) by placing material on the substrate, 3-D printing is an additional process in the manufacturing technology, where a 3-D object forms sub-substrate, the successive material layers are deposited. ***Method:*** 3-D printing technology requires technologically operated instruments for the layer-by-layer formulation of Active Ingredients and Excipients for the production of Personalised Medicine (PM) as per need of the individual patient. The techniques used to formulate 3-D printing objects include Stereolithography, Inkjet printing, and fused deposition modelling. Inkjet printig is again divided into continues jet printing and drop on demand. Different polymers are used to formulate such dosage forms like polyvinyl alcohol, poly-caprolactone, poly-lactic acid, etc. ***Conclusion:*** In this mini-review analysis, we have reviewed about 3-D printing technology. We have reviewed different dosage forms prepared using 3-D printing technology and discussed different technologies used in the 3-D printing technique.

GRAPHICAL ABSTRACT



Keywords: Three-dimensional printing, Personalised medicine, Computer-aided software, Standard triangle language, Controlled devices, Personalised Medicine.

1. INTRODUCTION

Drug development was seen broadly and in growth, which produce more efficient and safe medicines. Customised drugs have the ability for the high safety measures of treatment. Personalized Medicine (PM) aims to change the drug choices, doses, and inventions for individual patients. It also offers improved healthcare, promotes testing and the discovery of diagnostics and treatments, predicts the human propensity to suffer from a specific illness or disease (Mancinelli, Cronin, & Sadée, 2000; Vogenberg, Barash, Pursel, & Therapeutics, 2010). PM allows doctors to move beyond one-size-fits-all models of administering medications for proper treatment choices to particular patients regardless of the patient has inherited gene differences that result in different gene responses to specific drugs that may vary from person to person. As a result, personalised medicine is a novel technology which has developed a novel disciplinary specialisation known as "Pharmacogenomics" (Mancinelli *et al*., 2000; Soni, Jain, Gupta, & Jain, 2015; Vogenberg *et al*., 2010).

Importance of 3 Dimensional Printing Technology

3-DP technology for the pharma companies is a powerful and future method that leads to precision medicine focusing on individual requirements.

The manufacturing method of 3D Printing has revolutionised. It increases design output and reduces lead times and cost of tools for new goods.

1.1. Personalised Medicine (PM)

These are defined as a part of medical treatment for each patient's characteristics that improving the ability of the patient to identify and cure a disease, and providing opportunities for early detection and better treatment of the disease.

PM includes facts about genes, proteins, pathology and illness of an organism, according to the National Cancer Institute.

It is a kind of drug that uses patient genotype information to take a preventive action against the occurrence of diseases or conditions.

This PM uses biomarkers, which measures the genes and proteins to diagnose and treat disease(K. K. J. C. o. i. m. t. Jain, 2002).

Importance of Personalized Medicine

Personalized medicine begins to transcend the shortcomings of conventional medicine as it is dependent on the particular genetic structure of each individual. Progressively, the priority is being shifted from the response to avoidance in medicine. Predict disease sensitivity.

2. HISTORY

Charles Hull is credited with the introduction of 3DP after inventing, patenting, and commercialising the first 3D shape printer apparatus in the mid-1980s and invented the Standard Triangle Language (STL) file format which was interfaced with the current Computer-Aided Design (CAD) software. In this method, stereolithography (SL) Consists of a laser that passes through the droplet surface polymer, drying the polymer before the process is blurred again to facilitate the drying of the other side, and this cycle is continued printed object till the intended design is achieved(C. W. Hull, 1990; C. W. Hull *et al.*, 1993; C. Hull, 1986).

In the early '90s, 3-D printing was initiated in the pharmaceutical industry at Massachusetts Institute of Technology (MIT, Cambridge, MA, USA) to develop the manufacturing technologies and patented by the three-dimensional techniques for printing, Sachs *et al*., The first 3-D technology printed tablet was prepared with Levetiracetam's anticonvulsant drug as spiratam was authorised by USFDA in Aug 2015 and marketed. The spiratam tablet is given to the patients who have epilepsy with high dose and no water in emergencies for fast onset of action(El Aita, Ponsar, & Quodbach, 2018; Norman, Madurawe, Moore, Khan, & Khairuzzaman, 2017).

In that year, Charles filed a licence regarding the stereolithography apparatus. At the same time, the researcher and UT consultant Austin applied for a licence for the selective laser sintering process, in which the beam of light is transmitted via the powder bed to sinter the powder. The powder layer is dropped, and a sheet of fresh powder is added, and the procedure is carried till the solid object is prepared(Deckard, 1989).

In 1989, Scott Crump, Stratasys co-founder, applied for a patent on the development of fuses (FDM). By extracting solidifying materials (wax, thermoplastic resin, molten metals) until the desired structure is formed, this technique creates an object.(Crump, 1992). In 1996 Helisys innovators designed a laminated object in groundbreaking cubic technologies, processing method to manufacture objects, and organise sheets with adjacent layers bonded by adhesive welding(Feygin, Shkolnik, Diamond, & Dvorskiy, 1998).

Nowadays, 3-D printing is gaining more attention, which can develop the pharmaceutical technologies by increasing the efficacy, preciseness and individualisation, and reducing the wastage cost. Also, have the authority to process novel oral dosage forms in the existence and medical devices(Liaw & Guvendiren, 2017; Peng *et al*., 2017; Prasad, Smyth, & pharmacy, 2016). The aim of 3-D printing can replace the conventional manufacturing process. 3-D printing

technology is positively trending and has the remarkable innovation of various drug development processes (Daly, Harrington, Martin, & Hutchings, 2015; Ursan, Chiu, & Pierce, 2013).

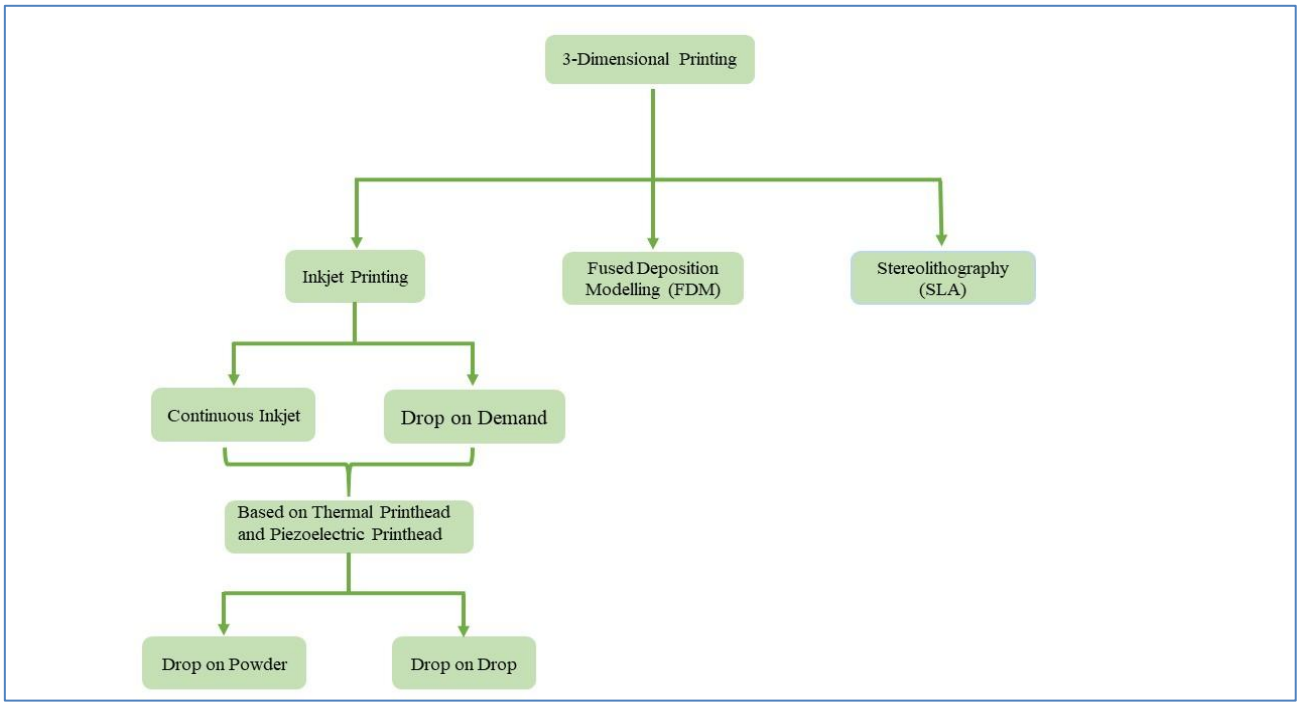
Three-Dimensional Printing

3 dimensional printing is an additive production process, and it is a novel rapid prototyping technology in which the application of several layers defines stable complexes in order(Konta, García-Piña, & Serrano, 2017). The production of 3-D objects is done from digital design using Computer-aided software(Belhabib & Guessasma, 2017; Gross, Erkal, Lockwood, Chen, & Spence, 2014). 3-D printing process also adapted the unexplained opportunity to alter its design and manufacture of complicated objects that could be used in personalised medicine. It has an effective strategy to address some of the difficulties of traditional pharmaceutical unit operations*(Alhnan et al., 2016; Norman et al.,* 2017). Increased patient compliance with the least adverse effects resulting in a ground-breaking improvement in medication design and treatment choices(Khaled, Burley, Alexander, & Roberts, 2014; Ventola & Therapeutics, 2014).

3-D printing can produce various dosage formulations with different masses and weigh a material, intricate inner geometrics, more than one drug and additives. 3-DP can be used for poorly soluble medicines in water, peptides, potent medicines, etc(Moulton & Wallace, 2014). It offers economic benefits by delivering cost-effective drugs to the patient and economic benefits for the manufacturer of 3-D printed tablets compared to traditional dosage types. However, to ensure this intervention's effectiveness includes a well-controlled software system to ensure data protection and patient profile safety(Awad, Trenfield, Gaisford, & Basit, 2018). 3-D printers are simple to manage, and correct deposition of API and excipients can be obtained through this accurate dosing and design (Chen *et al*., 2015).

3. 3-Dimensional Printing technology for personalised drug delivery system

3-D inkjet printing and Fused Deposition Modelling (FDM) techniques have been developed for the research and production of drug processes. The execution of these techniques in the dosage form design has a spiking device that helps develop unique, multifunctional and modified dosage forms.



3.1. Inkjet Printing

Inkjet printing is based on Lord Rayleigh's theory of instability, developed in 1878(Strutt & Rayleigh, 1878), defined with the assistance of a pattern-generating machine capable of developing and producing digitally regulated formulation and positioning of small liquid droplets in the substrate(Goole & Amighi, 2016).

The Inkjet printing is again classified into two types. They are: 1) Continuous jet printing (CJ) and 2) Drop on Demand (DOD) printing(Goole & Amighi, 2016).

The CJ and DOD printing techniques both contain the printer heads of thermal and piezoelectric which triggered to produce drop or bubble formation by trigger mechanisms and control the viscosity of the

characteristics of liquid and droplet formation(Ihalainen, Määttänen, & Sandler, 2015).

3.1.1. Continuous Jet (CJ) Printing

CJ printing uses a high-pressure stream to create a continuous stream of loaded particles. Electromagnetic layers in device retain particles on layer, and waste is collected, recirculated again, as shown in fig.**1**(Acosta-Vélez & Wu, 2016; Derby, 2010).

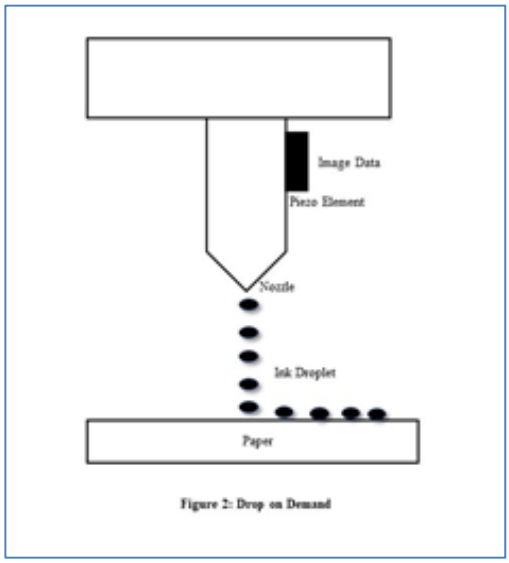


Fig-1: Continuous jet printing

3.1.2. Drop on Demand (DOD) Printing

DOD printing has a high accuracy and less wastage compared to CJ printing. It has got 1000 nozzles. The induction of electrical current generates heat in the thermal printhead so that the bubble is formed in volatile material and printed on the substrate, as shown in fig.2. This technique's downside is the heat liable for active biological ingredients due to the usage of high vapour pressure solvents that contain high temperatures(Acosta-Vélez & Wu, 2016; Alomari, Mohamed, Basit, & Gaisford, 2015). In contrast, piezoelectric printheads are connected with piezoelectric materials, extended and contracted by electrical current supply (Tekin, Smith, & Schubert, 2008).

The Drop on Demand is again sub-classified into two types based on thermal and piezoelectric printheads. They are: 1) Drop on drop and 2) Drop on powder.

As the formulated layer deposits on each other, it produces a solidifying layer of the substance. This process is known as drop on drop deposition, and when the printer head deposits the droplets on the solid material, it is known as drop on powder deposition(Dimitrov, Schreve, & de Beer, 2006). Drop on powder deposition is again graded into subtypes, (a) drop on drop deposition, and (b) drop on solid deposition, as shown in table 1. The decrease in solid deposition is also known as the "Powder Bed Fusion" In which the droplets themselves produce a separate layer of architecture; the droplets are written explicitly on the solid substance(Acosta-Vélez & Wu, 2016; Fina, Goyanes, Gaisford, & Basit, 2017; Goole & Amighi, 2016; Konta *et al*., 2017).

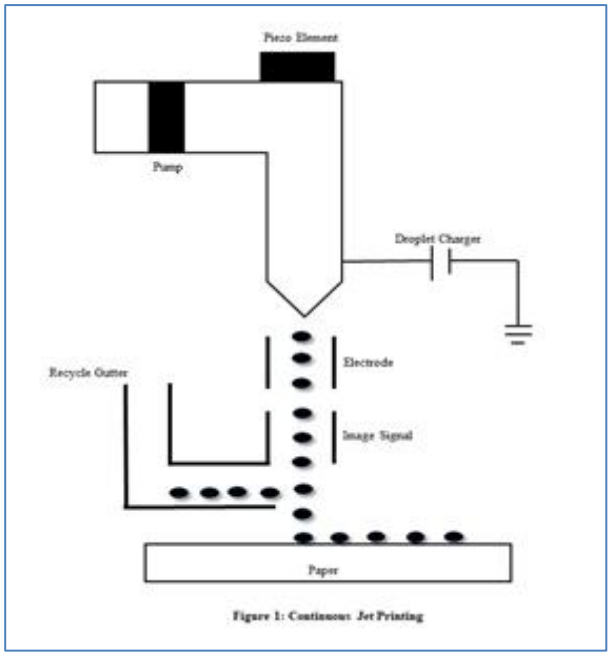


Fig-2: Drop on Demand

Table-1: Interplay between drop on drop and drop on solid deposition(V. Jain, Haider, & Jain, 2018)

Drop on Drop Deposition	Drop on Solid Deposition
The solid layer formed by the droplet deposition is based on the binder.	Deposition of droplets on powder bed is done by binding of high melting particles and low melting particles.
Binding content, Droplet size, Cooling, their interaction and solidification can have an effect on the process.	The properties of powder may affect the process.
No licenced application.	Have the licenced application (TheriForm™).
High drug loading can be possible.	Regulated delivery of drugs, including different sizes, can be accomplished.
Process is difficult for the execution.	Low drug loading can limit the use of drugs.

3.2. Fused Deposition Modelling (FDM)

FDM printers are also used with the same cost-effective method as 3-D inkjet printing. In this method, molten plastics' pellets were expelled from its printers, forming a thin film of prototyping (Hoy, 2013). This procedure includes thermoplastic polymers such as polylactic acid (PLA), polyvinyl alcohol (PVA) and acrylonitrile butadiene styrene(Prasad *et al*., 2016; Ratheesh *et al.*, 2017). Hot-melt extrusion (HME) is inserted upstream from the printer nozzle, deposited on the platform in the shape of filaments, settles the filament after hardening. The technique is also known as Fused Filament Fabrication, as shown in fig. 3. The material deposition depends on the nozzle's size, the nozzle diameter, the pressure drops and the feed rate. This technology's benefit is the development of multi-faceted scaffolds with a specific dosage, the proper mechanical strength by adjusting the different kinetics of the infill percentage, preventing the use of temperature-sensitive APIs and minimal thermoplastic content(Konta *et al.*, 2017; J. Wang, Goyanes, Gaisford, & Basit, 2016).

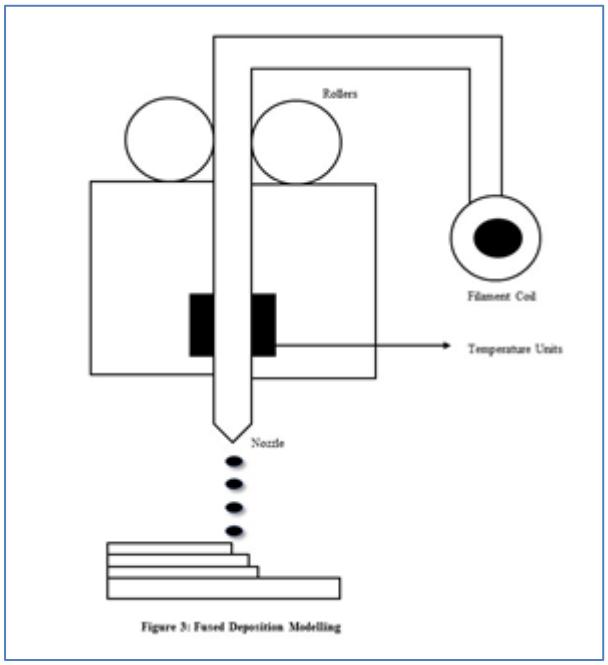


Fig-3: Fused Deposition Modelling

3.3. Stereolithography 3-D Printing

As described in the introduction, this technique was invented by Charles Hull in the 1980s, often known as the Laser-based method of writing(Ventola & Therapeutics, 2014). The principle involved is 'photo-polymerisation' in which free radicles are released after interaction with the photo-inhibitor and the UV radiation(Goole & Amighi, 2016).

The method requires an unreacted functional group on the solidifying structure in the first layer of polymers with the illuminated resin in the next layer, ensuring adhesion and forming the layer, as shown in fig.4. Post-printing processing is often necessary to cure the final product, boost the mechanical integrity and remove the manufactured item's attached support (Melchels, Feijen, & Grijpma, 2010).

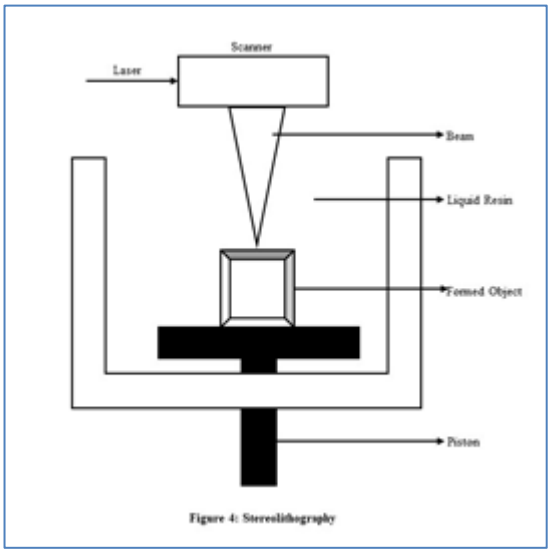
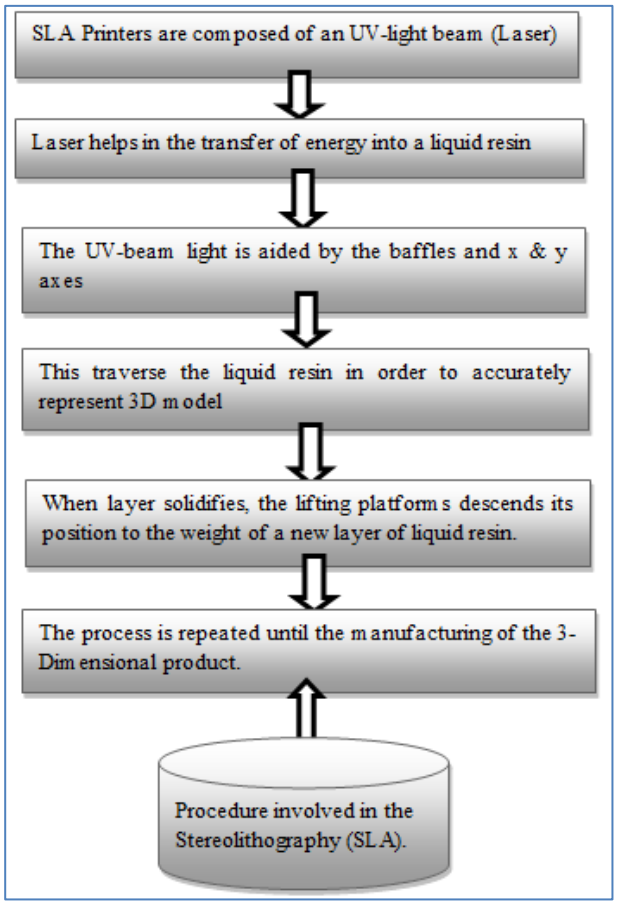


Fig-4: Stereolithography

This technique's downside is a health threat in the form of possible carcinogenic resins and a prolonged operation.



4. ADVANTAGES OF 3-D PRINTING

4.1. Customization

Any template can quickly be printed with 3D printing regardless of how intricate it is.

4.2. Constant prototyping and Increased Productivity

By the use of 3d printing with less time it allows rapid development of a greater proportion of prototypes of the actual thing than scientific models. This helps the designer develop their designs in case of design defects which may impact quality of the product.

4.3. Affordability

The initial cost for setting up a 3D printing facility is definitely high. Besides that, it is much cheaper than comparable to labour productivity and costs of production rather than using the conventional techniques. Further, the fact that 3D printing is equivalent to small-scale and mass-produced goods for production or production of products.

4.4. Storage

Standard output produces extra goods that you probably know, such that storage issues occur. 3D printing technology will however 'print' items where appropriate, thus removing surplus products and no storage costs.

4.5. Employment Opportunities

The universal application of 3d printing techniques would undoubtedly raise a need for engineers required for the design and production of these printers. Engineers trained in troubleshooting and repairs and designers will also be produced to production design plans for goods and further work.

4.6. Health Care

The technological development, a personalised individual area of the body and organ can now be created. It's called bioprinting this technology. Even though this is all experimental right now, the promise is immense. In addition to addressing the lack of donor organs, this development also addresses organ refusal as the building organ would consist of individual uniqueness and DNA.

5. DISADVANTAGES OF 3-D PRINTING

5.1. Decrease in Manufacturing Jobs

The decrease in production employment would have a major impact on the economies of nations with many limited jobs.

5.2. Limited Size

However, the scale of products generated by 3d printing technology is limited in the future, large architectural elements can be produced by using 3d printing.

5.3. Limited Raw Materials

A huge array of raw materials is available in the conventional production. Whereas 3d printers will produce up to around 100 various raw materials and more raw materials are also being developed for production.

5.4. Violation of Copyrights

Misuse is the greatest downside to 3d printing. Everyone that takes a template will quickly misuse goods. It becomes even more popular and it is almost difficult to trace the origins of the forged pieces. Many trademark holders would find it difficult to defend their interests and companies that produce exclusive goods.

5.5 Production of Dangerous Items

With the help 3D printing technology, it is possible to make plastic knives, handguns and other dangerous things. This simplifies the use of a pistol without the detection of militants and criminals.

6. Dosage forms produced by using 3-d printing technology

6.1. Solid Dosage Forms

Solid dosage forms are dose which are mostly used in the pharmaceuticals such as tablets, capsules etc. It contains unit dosage form, in which the composition of active pharmaceutical ingredient and additives, as shown in table 2, 3.

They have been various kinds of oral dosage formulations present on the marketplace. They are:

a. Modified Release
b. Extended-Release
c. Immediate Release
d. Sustained Release
e. Controlled Release
f. Floating Drug Delivery System

6.2. Oro- Dispersible Films

Oro-Dispersible Films (ODF's) are those pharmaceutical dosage forms which hold a novel drug delivery method, with single or multilayer sheets of suitable of excipients and active pharmaceutical ingredient intended for quick release of the dosage form as shown in table 4.

6.3. Topical Dosage Forms

Topical dosage forms are mostly preferred because of their local therapeutic action when applied on the skin or mucous membrane. These are available in the form of creams, pastes etc., as shown in table 5.

6.4. Transdermal Drug Delivery Systems

Transdermal Drug Delivery System is a technique in which the drug-loaded patches are given, and the drug is released through the skin, as shown in table 6.

6.5. Implants

Implants are defined as a medical device to replace, fix, or set securely to replace the body's missing biological structures, as shown in table 7.

Table-2: Solid dosage forms

S. No	Drug	Excipients	3-DP Technique	Dosage Form	Conclusion
1.	5-aminosalicylic acid, 4-aminosalicylic acid	PVA Filament	FDM	Modified release	The dissolution profiles of tablets on infill percentage at 10% shows the drug release with in 4h whereas,50% & 90% shows burst of tablet and slow release and there should be a quicker release of medications acquired by decreasing the infill percentage of tablets(Goyanes, Buanz, *et al*., 2015).
2.	Paracetamol	PEG-Diacrylate, Diphenyl (2,4,6-trimethylbenzoyl) phosphine oxide, 4-aminosalicylic acid, PEG-300.	Stereolitho graphy	Modified release	SLA printing is a technique to manufacture drug-loaded tablets of top quality Resolve. Comparison to FDM 3D printing, it decreases oxidative damage of drug and so on. Provides an alternative direction for the development of tablets containing thermo-sensible medications(J. Wang *et al*., 2016).
3.	Prednisolone	PVA, Glycerol, Acetonitrile, Methanol	FDM	Extended release	Prednisolone deliver from a 3DP tablet was expanded to 386. About 24 hours. The medication control accuracy usually ranges between 88.7 %. and that's 107 %(Skowyra, Pietrzak, & Alhnan, 2015).
4.	Theophylline	Eudragit RL, RS, Hydroxypropyl cellulose-SSL grade, TEC	FDM	Extended release & Immediate release	Thermoelectric examination suggested that the maximum of theophylline was developed in the crystalline form of a 3DP tablet. The use of a model drug with a high melting point allowed the fabrication of the 3D printed tablets at significantly lower temperatures than in comparison with previous studies(Pietrzak, Isreb, Alhnan, & biopharmaceutics, 2015).
5.	Theophylline (or) Dipyridamole	PVP, Talc, Tri	FDM	Immediate release	The tablets are ideal for two different medications and obtained instantaneous drug release. The tablet demonstrated high mechanical properties and reasonable in-batch differentiation(Okwuosa *et al*., 2016).
6.	Haloperidol	Kollidon VA64, Kollicoat IR, HPMC-HME 15 Cp, HPMCAS	FDM	Immediate release	Miscibility of drug polymer, screening of polymer for drug release and the printability of tablets(Solanki, Tahsin, Shah, & Serajuddin, 2018).
7.	Paracetamol	PVP K25, sodium phosphate monobasic, Croscarmellose sodium	FDM	Immediate release	The 3DP tablets produced more than 90 % of the effective dose within 10 minutes. The results indicate that the printing did not influence the type of paracetamol(Khaled *et al*., 2018).
8.	Propranolol HCl	Cellulose acetate, D-mannitol, PEG 6000, Ethanol, Acetone, Dimethyl sulfoxide	FDM	Immediate release	This technique offers the opportunity to use excipients of pharmaceutical grade in Various ratios without compromising the consistency of the printed product. The use of varying proportions of different excipient proportions for the development of the encapsulation shell demonstrated the ability to regulate the encapsulation shell. The volume and rate of propranolol Hcl released from the off-the-shelf tablet(Algahtani, Mohammed, Ahmad, & Saleh, 2020).
9.	5-ASA, Captopril, Theophylline, Prednisolone	Eudragit-E, Triethyl citrate, Tribasic calcium phosphate, MCC	FDM	Immediate release	A multiple dosage form with four different physicochemical properties were prepared and tablets improved mechanical properties and appropriate batch differentiation. The inclusion of a pharmaceutical grade non-melting factor is added to allow for smooth flow(Sadia *et al*., 2016).

10.	Ondansetron	B-Cyclodextrin cavamax, Kollidon VA-64, Mannitol, MCC, Crospovidone, Magnesium stearate, Silicon dioxide, Aspartame	Selective laser sintering 3D printing	Oral dispersible tablets	It was concluded that, it shows fast disintegration and drug release more than 90% in 5 mins(Allahham *et al*., 2020).
11.	Glimepiride & Metformin	PVA, PLA, Eudragit RL, PEG 400, Citric acid monohydrate, Triethyl citrate	FDM	Immediate release & Sustained release respectively	Dynamic nano-indentation Testing has permitted the mechanical evaluation of the generated polymers to take place at a more basic level than traditional methods(Gioumouxouzis *et al*., 2018).
12.	Ibuprofen	EC, HPMC, Sodium alginate, xanthan gum	FDM	Sustained release	24 hours drug released was accomplished by incorporating release modifications and changing the pattern composition of the designs. The FDM printability was significantly influenced by a molten viscosities and physical characteristics of the filaments fed to the FDM printer(Yang, Wang, Li, Ou, & Yang, 2018).
13.	Captopril, Nifedipine, Glipizide	PEG 6000, HPMC 2910, HPMC K100MCR, Nacl, Tromethamine, D-mannitol, Croscarmellose sodium, MCC, Sodium starch glycolate	FDM	Sustained release & Controlled release	A complex multi-compartmental tablet is prepared and is able to deliver the drug with defined two different mechanisms. Captopril shows zero order and remaining drugs first order drug release(Khaled, Burley, Alexander, Yang, & Roberts, 2015).
14.	Paracetamol, Caffeine, Naproxen, Chloramphenicol, Prednisolone and Aspirin	PEG 300, PEG Diacrylate, Diphenyl(2,4,6-trimethylbenzoyl) phosphine oxide	Stereolithography	Sustained release & Controlled release	It was concluded that, successfully prepared multi-layer polypill containing six different APIs and demonstrated acceptable physicochemical characteristics and different drug release profiles(Robles-Martinez *et al.*, 2019).
15.	Hydrochlorothiazide	PVA, PLA, Mannitol	FDM	Controlled release	Formulations are prepared in hallow shape and these exhibits the zero-order drug release(Gioumouxouzis, Katsamenis, Bouropoulos, Fatouros, & Technology, 2017).
16.	Acetaminophen	HPMC E5, HPC EF and LF, EC N14, Soluplus (PCL-PVA-PEG), Eudragit L100	FDM	Controlled release	This research indicates that, the combination of FDM-based 3DP with HME provides a possible novel approach for the development of customised dosage forms, and also improved prolonged release of drug profiles than directly compressed tablets(Zhang, Feng, Patil, Tiwari, & Repka, 2017).
17.	Rifampicin and Isoniazid	PEO, PLA, PVA	FDM	Controlled release	The physical isolation and spatial containment of interactive drugs in tightly sealed dcDU compartments prolonged and hindered release profile and absorption relative to open filaments in both in vitro and in vivo experiments(Genina *et al*., 2017).
18.	Glipizide	PVA	FDM	Controlled release	Drug release test revealed a 5h controlled-release pattern based on the configuration of the system; Glipizide inserted in the outer surface were released first then the release behaviour of glipizide inserted in the inner part occurred after a lag period based on the properties of the outer surface(Li *et al.*, 2017).
19.	Budesonide	PVA, Eudragit L100, Talc, Isopropanol	FDM	Controlled release	The delivery aspects of the novel product have shown that it has been launched. Opportunities for the prevention of irritable bowel syndrome(Goyanes, Chang, *et al*., 2015).
20.	Guaifenesin	Trisodium phosphate dodecahydrate, HPMC 2910, PAA, Carbopol 974P NF, HPMC 2208, Microcrystalline cellulose, Sodium Starch Glycolate	Desktop 3D Printing	Controlled release	The production of relatively complex formulations printed into bilayer tablets matches with the commercial Guaifenesin(Khaled *et al*., 2014).

21.	Acetaminophen	HPMCAS-LG & HG, HPMC E5 & K100M, HPC EF & HF, EC N14	FDM	Controlled release	The polysaccharide based Polymeric materials have been soluble mostly with concept Active Pharmaceutical Ingredient studied, that has been altered through results of release profile in vitro. In regards, physical and chemical characterization revealed that acetaminophen could be dissolved or dispersed. Hydroxypropyl methylcellulose and HPMCAS matrix, forming amorphous solid particles, hSince this drug was only partly distributed into the Ethyl Cellulose and Hydorxypropyl Cellulose matrix(Zhang *et al*., 2019).
22.	Ibuprofen	2-(4-Isobutylphenyl) propionic acid, HPMC-AS, HG, MG, and LG, Filaments of PVA and PLA	FDM	Controlled release	Ibuprofen in HPMC-AS polymers with different infill was prepared successfully and in-vitro studies was carried out. The release of tablet follows the both Fickian and Non-Fickian drug release(Thakkar *et al*., 2020).
23.	Fenofibrate	White beeswax, Potassium phosphate monobasic, Sodium phosphate dibasic, SLS	Inkjet printing	Controlled release	Variation in drug release is observed in a controllable manner by combining geometrics of 3DP and predictive computational approaches. And development of this method is anticipated that another manufacturing process for solid dosage forms with geometry flexibility and complexity for advanced DDS(Kyobula *et al.*, 2017).
24.	Riboflavin sodium phosphate & Propranolol Hcl	Propylene glycol, Glycerol, Ethanol, EC	Inkjet & Flexographic printing	Controlled release	Combination of both printing techniques for CR oral dosage form was successfully prepared. Inkjet-printed solid dosage forms showed a better content uniformity for both Active Pharmaceutical Ingredients, flexographic coating with water insoluble Ethyl Cellulose polymer produced a gastrointestinal tract-insoluble film on top of the printed RSP, which extended the drug release(Genina *et al*., 2012).
25.	Domperidone (DOM)	Hydroxypropyl cellulose (HPC)	FDM	Floating DDS	DOM is successfully loaded, transformed into a solid dispersion with thermally-increasing techniques. Prolonged release has been identified both in vitro and in vivo(Chai *et al*., 2017).
26.	Dipyridamole	HPMC K4M, HPMC E15, MCC PH101, PVP K30,	FDM	Floating DDS	This is possible to produce gastro-floating tablets with a fine internal lattice framework designed by modelling tool Software. Release of drug examination shows at least 8h. Sustained-release pattern based on the infilling frequency of the units, reduced infilling of more floating devices, higher infilling of longer floating devices(Li *et al.*, 2018).
27.	Ropinirole HCl	PEGDA, Irgacure 2959	Inkjet printing & UV Photoinhibition		It was concluded that, amorphous solid dispersions with high degrees of photopolymer curing have been shown. This technique is intended to be used for a variety of API and photo initiator variations, assuming the functionality and permeability of the materials(Clark *et al*., 2017).
28.	Deflazacort	Eudragit RS100 & RL100, Polysorbate 80, Miglyol 812N, PCL	FDM	Tablet loaded with Nano capsule	Conjugation of nanotechnology and 3d printing to produce innovative medicines. Moreover, the drug release and drug loading kinetic are good when compared to tablet dosage form(Beck *et al.*, 2017)
29.	-	PLA, PVA, PEG 400 and 8000, EC, HPMC, HPMCAS and KIR	FDM	Immediate Release	Different drug formulations manufacturing is immediately dissolve, swellable / erodible and enteric dissolved materials were used as beginning thermoplastic materials(Maroni *et al*., 2017).

TABLE 3: ORO-DISPENSABLE FILMS

S. No	Drug	Excipients	3-DP Technique	Dosage Form	Conclusion
1.	Aripiprazole	PVA,	FDM	Oral dispersible films	It was concluded that the drug-loaded filaments were prepared using PVA of good consistency for a 3D printer(Jamróz *et al.*, 2017).
2.	Levocetirizine Hcl	HPMC, Maltitol, Starch (Pregelatinized), Sucralose	Semi-solid extrusion	Oral dispersible films	Different doses of films were prepared successfully with good content uniformity and accuracy, it shows better properties in consistency, viscosity, wetting and flexibility(Yan *et al.*, 2020).
3.	Paclitaxel & Rapamycin or Lidocaine	PLGA, PEG	FDM	Films	Multi layered PLGA and single layered PLGA-PEG-PLGA for paclitaxel & Rapamycin together or lidocaine alone drug release behaviour evaluated in vitro was prepared successfully(Serris, Serris, Frey, & Cho, 2020).
4.	Warfarin	PVA, HPC	Semi-solid extrusion	Oral dispersible films	The relatively slow drug release could be improved by adding the drug concentration, subsequently decreases the amount of polymeric materials and also likely to decrease disintegration time and shows good durability and flexibility(Sjöholm & Sandler, 2019).
5.	Olanzapine	PEO, Kollidon VA-64, Poloxamer 407 & 188	Hot melt pneumatic extrusion	Oral dispersible films	It was concluded that, the drug content shows good printability, strength and fast disintegration and single layered process(Cho, Baek, Lee, & Jin, 2020).
6.	Aripiprazole	PEO, Poloxamer 188, Citric acid	Hot melt pneumatic 3-D printing	Oral dispersible films	It was concluded that, dosage form is flexible, smooth and drug release quick with drug solubility and controlled in terms of its physicochemical properties(Oh, Gang, Park, Park, & Lee, 2020).
7.	Carbamazepine	Hydroxypropyl-β-cyclodextrin, HPMC, PVP, Sodium carboxy methyl cellulose, Croscarmellose sodium, SLS	Semi-solid extrusion 3-D printing	Oral dispersible tablets	This technique provides an innovative approach for the formation of in situ drug cyclodextrin complexes and adequate drug release properties are produced. Wet mass changes are observed due to cellulose ethers(Conceição *et al*., 2019).

Table-4: Topical dosage forms

S. No	Drug	Excipients	3-DP Technique	Dosage Form	Conclusion
1.	Salicylic acid	PLC, PCL, PEG 300, Diphenyl phosphine oxide	FDM & Stereolithography	Topical DDS	In FDM 3DP, the use HME produce filaments of FPLA & PCL-salicylic acid with uniform diameter & SLA involves a one step process with more resolution and more drug loading with no drug degradation than FPCL & PCL-salicylic acid(Goyanes, Det-Amornrat, Wang, Basit, & Gaisford, 2016).

Table-5: Transdermal drug delivery system

S. No	Drug	Excipients	3-DP Technique	Dosage Form	Conclusion
1.	Fluorescein	Acetone, potassium hydroxide, PLA	FDM	Microneedle	MN's are suitable 3d printing by discussing the penetration of the outer layers of skin and delivering a model therapeutic agent(Luzuriaga, Berry, Reagan, Smaldone, & Gassensmith, 2018).
2.	5-Flurouracil	PLG, PCL	FDM	Biodegradable patches	It concludes that, the 3d patches will allow the localized deliver anti-cancer drugs with desired pharmacokinetics(Yi *et al.*, 2016).
3.	Insulin solution from bovine pancreas	Trehalose, mannitol and xylitol	Stereolithography followed by Inkjet coating	MN patches	Insulin solution from bovine pancreas. Franz cell diffusion experiments have shown fast insulin release speeds within 30 min, and it has been shown how 3D printing could be used effectively in the manufacture of Transdermal Drug Delivery microneedles(Pere *et al.*, 2018).
4.	Tetracycline Hcl	PCL, PVP,	Electrohydrodynamic 3D printing	Patches	This 3-D printing technology offers the ability to create single-step pharmaceutical products with limited additives and procedures. Antimicrobial delivery from the PCL-PVP drug substance showed over 5 days but was delayed comparative to pure PCL or PVP, the patch gap size also impacted drug release behaviour(J.-C. Wang, Zheng, Chang, Ahmad, & Li, 2017).

Table-6: Implants

S. No	Drug	Excipients	3-DP Technique	Dosage Form	Conclusion
1.	Indomethacin	EVA copolymer, PCL, Sodium chloride, Ethanol	FDM	Implant	The suggests that, EVA is applicable for the 3d printing to develop drug charged implantable designs*(Genina et al*., 2016).
2.	Isoniazid and Rifampin	Methyl triethoxysilane, Triethoxysilylpropylsuccinic anhydride	3-D Printing	Implant (ATD)	Modified silica based Mesoporous Hierarchical Scaffold gives well defined porous structure and microenvironment for high API loading and also showed extraordinarily sustained co-release pattern for over 84 days(Zhu, Li, Zhu, Zhang, & Ye, 2015).
3.	calcium phosphate ceramics	PCL	Powdered bed fusion	Implant (Bone tissue engineering DDS)	It was concluded that, complete bone regeneration was not achieved without the addition of osteoinductive elements(Trombetta, Inzana, Schwarz, Kates, & Awad, 2017).
4.	Nitrofurantoin	PLA, HPMC, Metolose	FDM	Implant	This work reveals the promise of custom-made, drug-loaded feedstock materials for 3D printing of customized therapeutic goods for controlled drug release. Nitrofurantoin retained its stability throughout process of 3D printing(Boetker *et al*., 2016).
5.		PCL, Carbon Nanotube, 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide, Chloroform	3D Printing	Tissue (Cardiac tissue)	It was concluded that, 1 percent CNT nanocomposites with PCL-CNT reveal optimum permeability and flexibility for the distribution of H9c2 cells*(Ho et al*., 2017).
6.		PCL, PEG, Gelatine	Stereolithography & Electrospinning technique	Implant (Neural)	3D printed microporous channels embedded with PCL or PCL/gelatin electrospun fibers. 3D printed scaffolds with PCL/gelatin fibers enhanced the neural stem cell differentiation compared to scaffolds with PCL alone fibres(Lee, Nowicki, Harris, & Zhang, 2017).
7.	Tricalcium phosphate	Magnesium, Silicon	3D Printing	Implant	It was concluded that, the addition of magnesium and silicon to 3DP Tricalcium phosphate does not have a detrimental impact on the mechanical strength(Bose, Tarafder, & Bandyopadhyay, 2017).

8.	Mos2, MS-AKT		3DP with Hydrothermal method	Implant	It was concluded that, the nanosheets of MoS2 and MS-AKT. The MS2 layer supplied the scaffolds with controllable photothermal effects and the MS-AKT facilitated the binding, differentiation and osteogenic differentiation of rBMSCs and mediated tissue regeneration(X. Wang *et al.*, 2017).
9.	Zoledronate	PVA, Thermoplastic polyurethane	3-D Printed	Implant	This research reveals, for the first time, the viability of PORO Lay Nanoporous scaffolds to retain and release drugs while inhibiting in vitro diffusion of drugs Patient-derived tissue metastases tumour cells secondary to prostate cancer(Akoury, Weber, & Rosenzweig, 2019).
10.	Cold atmospheric plasma (CAP)	PLA	3-D Printed	Implant (Bone regeneration)	This research used CAP to treat 3D printed PLA scaffolding to enhance bone cell binding and Action. The determined features have reveals that both hydrophilic nature and nanoscale roughness have improved(M. Wang *et al*., 2016).

CONCLUSION

This mini-review analysis from the past research might state that researchers have formulated various dosage types of tablets and capsules, transdermal drug delivery systems, and biomedical scaffolding tissues with maximum safety parameters.

Because of people's lifestyle, today's world focuses solely on medications rather than on a balanced diet, contributing to a rise in disability and addiction on healthcare and medication. 3DP strategies have a significant potential in producing, preparing, and delivering drugs due to their versatility and effectiveness. This PM may provide a good potential for developing formulations as per specific patient specifications that are resistance to disease and its ability to improve a high degree of drug release behaviour to determine the various drug release profiles.

In the future, different people consult doctors with similar disease but based on patient's genomics different doses of medicines are prescribed by the doctor for an individual patient and that medicines are given in the form of powder, and that is formulated into a tablet by patients or dispenser by using 3-D printing technique.

3DP technology improves its formulation development through various printing technologies such as inkjet printing, fused deposition modelling, and stereolithography. Almost all of the compounds are developed using both inkjet printing and fused deposition modelling. However, owing to its high resolution, the formulation's precision is obtained by the FDM printing process.

3DP technology has helped the pharmaceutical sector by offering personalised 3D printing drugs, and the technology has become more attractive in the research and growth of the pharmaceutical industry.

ACKNOWLEDGEMENT

Authors are extremely thankful to Raghavendra Institute of Pharmaceutical Education and Research (RIPER) management, Ananthapuramu for their support.

REFERENCES

- Acosta-Vélez, Giovanny F, & Wu, BM %J Polym. Sci. (2016). 3D pharming: direct printing of personalized pharmaceutical tablets, *2*(1), 11.
- Akoury, E., Weber, M. H., & Rosenzweig, D. H. (2019). 3d-printed nanoporous scaffolds impregnated with zoledronate for the treatment of spinal bone metastases. *MRS Advances*, *4*(21), 1245-1251.
- Algahtani, M. S., Mohammed, A. A., Ahmad, J., & Saleh, E. (2020). Development of a 3D printed coating shell to control the drug release of encapsulated immediate-release tablets. *Polymers*, *12*(6), 1395.
- Alhnan, M. A., Okwuosa, T. C., Sadia, M., Wan, K. W., Ahmed, W., & Arafat, B. (2016). Emergence of 3D printed dosage forms: opportunities and challenges. *Pharmaceutical research*, *33*(8), 1817-1832.
- Allahham, N., Fina, F., Marcuta, C., Kraschew, L., Mohr, W., Gaisford, S., ... & Goyanes, A. (2020). Selective laser sintering 3D printing of orally disintegrating printlets containing ondansetron. *Pharmaceutics*, *12*(2), 110.
- Alomari, M., Mohamed, F. H., Basit, A. W., & Gaisford, S. (2015). Personalised dosing: printing a dose of one's own medicine. *International journal of pharmaceutics*, *494*(2), 568-577.
- Awad, A., Trenfield, S. J., Gaisford, S., & Basit, A. W. (2018). 3D printed medicines: A new branch of digital healthcare. *International journal of pharmaceutics*, *548*(1), 586-596.

- Beck, R. C. R., Chaves, P. S., Goyanes, A., Vukosavljevic, B., Buanz, A., Windbergs, M., ... & Gaisford, S. (2017). 3D printed tablets loaded with polymeric nanocapsules: An innovative approach to produce customized drug delivery systems. *International journal of pharmaceutics*, *528*(1-2), 268-279.
- Belhabib, S., & Guessasma, S. (2017). Compression performance of hollow structures: From topology optimisation to design 3D printing. *International Journal of Mechanical Sciences*, *133*, 728-739.
- Boetker, J., Water, J. J., Aho, J., Arnfast, L., Bohr, A., & Rantanen, J. (2016). Modifying release characteristics from 3D printed drug-eluting products. *European Journal of Pharmaceutical Sciences*, *90*, 47-52.
- Bose, S., Tarafder, S., & Bandyopadhyay, A. (2017). Effect of chemistry on osteogenesis and angiogenesis towards bone tissue engineering using 3D printed scaffolds. *Annals of biomedical engineering*, *45*(1), 261-272.
- Chai, X., Chai, H., Wang, X., Yang, J., Li, J., Zhao, Y., ... & Xiang, X. (2017). Fused deposition modeling (FDM) 3D printed tablets for intragastric floating delivery of domperidone. *Scientific reports*, *7*(1), 1-9.
- Chen, D., Heyer, S., Ibbotson, S., Salonitis, K., Steingrímsson, J. G., & Thiede, S. (2015). Direct digital manufacturing: definition, evolution, and sustainability implications. *Journal of Cleaner Production*, *107*, 615-625.
- Cho, H. W., Baek, S. H., Lee, B. J., & Jin, H. E. (2020). Orodispersible polymer films with the poorly water-soluble drug, olanzapine: hot-melt pneumatic extrusion for single-process 3D printing. *Pharmaceutics*, *12*(8), 692.
- Clark, E. A., Alexander, M. R., Irvine, D. J., Roberts, C. J., Wallace, M. J., Sharpe, S., ... & Wildman, R. D. (2017). 3D printing of tablets using inkjet with UV photoinitiation. *International Journal of Pharmaceutics*, *529*(1-2), 523-530.
- Conceição, J., Farto-Vaamonde, X., Goyanes, A., Adeoye, O., Concheiro, A., Cabral-Marques, H., ... & Alvarez-Lorenzo, C. (2019). Hydroxypropyl-β-cyclodextrin-based fast dissolving carbamazepine printlets prepared by semisolid extrusion 3D printing. *Carbohydrate polymers*, *221*, 55-62.
- Crump, S. S. (1992). *U.S. Patent No. 5,121,329*. Washington, DC: U.S. Patent and Trademark Office.
- Daly, R., Harrington, T. S., Martin, G. D., & Hutchings, I. M. (2015). Inkjet printing for pharmaceutics–a review of research and manufacturing. *International journal of pharmaceutics*, *494*(2), 554-567.
- Deckard, C. R. (1989). *U.S. Patent No. 4,863,538*. Washington, DC: U.S. Patent and Trademark Office.
- Derby, B. (2010). Inkjet printing of functional and structural materials: fluid property requirements, feature stability, and resolution. *Annual Review of Materials Research*, *40*, 395-414.
- Dimitrov, D., Schreve, K., & de Beer, N. (2006). Advances in three dimensional printing–state of the art and future perspectives. *Rapid Prototyping Journal*.
- El Aita, I., Ponsar, H., & Quodbach, J. (2018). A critical review on 3D-printed dosage forms. *Current pharmaceutical design*, *24*(42), 4957-4978.
- Chang, Y. C. (2016). *Design of desktop-scale metal wire-feed prototyping machine* (Doctoral dissertation).
- Fina, F., Goyanes, A., Gaisford, S., & Basit, A. W. (2017). Selective laser sintering (SLS) 3D printing of medicines. *International journal of pharmaceutics*, *529*(1-2), 285-293.
- Genina, N., Boetker, J. P., Colombo, S., Harmankaya, N., Rantanen, J., & Bohr, A. (2017). Anti-tuberculosis drug combination for controlled oral delivery using 3D printed compartmental dosage forms: From drug product design to in vivo testing. *Journal of controlled Release*, *268*, 40-48.
- Genina, N., Fors, D., Vakili, H., Ihalainen, P., Pohjala, L., Ehlers, H., ... & Sandler, N. (2012). Tailoring controlled-release oral dosage forms by combining inkjet and flexographic printing techniques. *European journal of pharmaceutical sciences*, *47*(3), 615-623.
- Genina, N., Holländer, J., Jukarainen, H., Mäkilä, E., Salonen, J., & Sandler, N. (2016). Ethylene vinyl acetate (EVA) as a new drug carrier for 3D printed medical drug delivery devices. *European Journal of Pharmaceutical Sciences*, *90*, 53-63.
- Gioumouxouzis, C. I., Baklavaridis, A., Katsamenis, O. L., Markopoulou, C. K., Bouropoulos, N., Tzetzis, D., & Fatouros, D. G. (2018). A 3D printed bilayer oral solid dosage form combining metformin for prolonged and glimepiride for immediate drug delivery. *European Journal of Pharmaceutical Sciences*, *120*, 40-52.
- Gioumouxouzis, C. I., Katsamenis, O. L., Bouropoulos, N., & Fatouros, D. G. (2017). 3D printed oral solid dosage forms containing hydrochlorothiazide for controlled drug delivery. *Journal of Drug Delivery Science and Technology*, *40*, 164-171.
- Goole, J., & Amighi, K. (2016). 3D printing in pharmaceutics: A new tool for designing customized drug delivery systems. *International journal of pharmaceutics*, *499*(1-2), 376-394.
- Goyanes, A., Buanz, A. B., Hatton, G. B., Gaisford, S., & Basit, A. W. (2015). 3D printing of modified-

release aminosalicylate (4-ASA and 5-ASA) tablets. *European Journal of Pharmaceutics and Biopharmaceutics*, *89*, 157-162.

- Goyanes, A., Chang, H., Sedough, D., Hatton, G. B., Wang, J., Buanz, A., ... & Basit, A. W. (2015). Fabrication of controlled-release budesonide tablets via desktop (FDM) 3D printing. *International journal of pharmaceutics*, *496*(2), 414-420.
- Goyanes, A., Det-Amornrat, U., Wang, J., Basit, A. W., & Gaisford, S. (2016). 3D scanning and 3D printing as innovative technologies for fabricating personalized topical drug delivery systems. *Journal of controlled release*, *234*, 41-48.
- Gross, B. C., Erkal, J. L., Lockwood, S. Y., Chen, C., & Spence, D. M. (2014). Evaluation of 3D printing and its potential impact on biotechnology and the chemical sciences.
- Ho, C. M. B., Mishra, A., Lin, P. T. P., Ng, S. H., Yeong, W. Y., Kim, Y. J., & Yoon, Y. J. (2017). 3D printed polycaprolactone carbon nanotube composite scaffolds for cardiac tissue engineering. *Macromolecular bioscience*, *17*(4), 1600250.
- Hoy, M. B. (2013). 3D printing: making things at the library. *Medical reference services quarterly*, *32*(1), 93-99.
- Hull, C. W. (1990). *U.S. Patent No. 4,929,402*. Washington, DC: U.S. Patent and Trademark Office.
- Thayer, J. S. (1996). *Competitive strategic advantage through disruptive innovation dc by Jeffrey S. Thayer* (Doctoral dissertation, Massachusetts Institute of Technology).
- Hull, C. W. (1984). Apparatus for production of three-dimensional objects by stereolithography. *United States Patent, Appl., No. 638905, Filed*.
- Ihalainen, P., Määttänen, A., & Sandler, N. (2015). Printing technologies for biomolecule and cell-based applications. *International journal of pharmaceutics*, *494*(2), 585-592.
- Jain, K. K. (2002). Personalized medicine. *Current opinion in molecular therapeutics*, *4*(6), 548-558.
- Jain, V., Haider, N., & Jain, K. (2018). 3D printing in personalized drug delivery. *Current pharmaceutical design*, *24*(42), 5062-5071.
- Jamróz, W., Kurek, M., Łyszczarz, E., Szafraniec, J., Knapik-Kowalczuk, J., Syrek, K., ... & Jachowicz, R. (2017). 3D printed orodispersible films with Aripiprazole. *International journal of pharmaceutics*, *533*(2), 413-420.
- Khaled, S. A., Alexander, M. R., Wildman, R. D., Wallace, M. J., Sharpe, S., Yoo, J., & Roberts, C. J. (2018). 3D extrusion printing of high drug loading immediate release paracetamol tablets. *International journal of pharmaceutics*, *538*(1-2), 223-230.
- Khaled, S. A., Burley, J. C., Alexander, M. R., & Roberts, C. J. (2014). Desktop 3D printing of controlled release pharmaceutical bilayer tablets. *International journal of pharmaceutics*, *461*(1-2), 105-111.
- Khaled, S. A., Burley, J. C., Alexander, M. R., Yang, J., & Roberts, C. J. (2015). 3D printing of tablets containing multiple drugs with defined release profiles. *International journal of pharmaceutics*, *494*(2), 643-650.
- Konta, A. A., García-Piña, M., & Serrano, D. R. (2017). Personalised 3D printed medicines: which techniques and polymers are more successful?. *Bioengineering*, *4*(4), 79.
- Kyobula, M., Adedeji, A., Alexander, M. R., Saleh, E., Wildman, R., Ashcroft, I., ... & Roberts, C. J. (2017). 3D inkjet printing of tablets exploiting bespoke complex geometries for controlled and tuneable drug release. *Journal of Controlled release*, *261*, 207-215.
- Lee, S. J., Nowicki, M., Harris, B., & Zhang, L. G. (2017). Fabrication of a highly aligned neural scaffold via a table top stereolithography 3D printing and electrospinning. *Tissue Engineering Part A*, *23*(11-12), 491-502.
- Li, Q., Guan, X., Cui, M., Zhu, Z., Chen, K., Wen, H., ... & Pan, W. (2018). Preparation and investigation of novel gastro-floating tablets with 3D extrusion-based printing. *International journal of pharmaceutics*, *535*(1-2), 325-332.
- Li, Q., Wen, H., Jia, D., Guan, X., Pan, H., Yang, Y., ... & Pan, W. (2017). Preparation and investigation of controlled-release glipizide novel oral device with three-dimensional printing. *International journal of pharmaceutics*, *525*(1), 5-11.
- Liaw, C. Y., & Guvendiren, M. (2017). Current and emerging applications of 3D printing in medicine. *Biofabrication*, *9*(2), 024102.
- Luzuriaga, M. A., Berry, D. R., Reagan, J. C., Smaldone, R. A., & Gassensmith, J. J. (2018). Biodegradable 3D printed polymer microneedles for transdermal drug delivery. *Lab on a Chip*, *18*(8), 1223-1230.
- Mancinelli, L., Cronin, M., & Sadée, W. (2000). Pharmacogenomics: the promise of personalized medicine. *Aaps Pharmsci*, *2*(1), 29-41.
- Maroni, A., Melocchi, A., Parietti, F., Foppoli, A., Zema, L., & Gazzaniga, A. (2017). 3D printed multi-compartment capsular devices for two-pulse oral drug delivery. *Journal of Controlled Release*, *268*, 10-18.
- Melchels, F. P., Feijen, J., & Grijpma, D. W. (2010). A review on stereolithography and its applications in biomedical engineering. *Biomaterials*, *31*(24), 6121-6130.
- Moulton, S. E., & Wallace, G. G. (2014). 3-dimensional (3D) fabricated polymer based drug

delivery systems. *Journal of Controlled Release*, *193*, 27-34.

- Norman, J., Madurawe, R. D., Moore, C. M., Khan, M. A., & Khairuzzaman, A. (2017). A new chapter in pharmaceutical manufacturing: 3D-printed drug products. *Advanced drug delivery reviews*, *108*, 39-50.
- Oh, B. C., Jin, G., Park, C., Park, J. B., & Lee, B. J. (2020). Preparation and evaluation of identifiable quick response (QR)-coded orodispersible films using 3D printer with directly feeding nozzle. *International journal of pharmaceutics*, *584*, 119405.
- Okwuosa, T. C., Stefaniak, D., Arafat, B., Isreb, A., Wan, K. W., & Alhnan, M. A. (2016). A lower temperature FDM 3D printing for the manufacture of patient-specific immediate release tablets. *Pharmaceutical research*, *33*(11), 2704-2712.
- Peng, W., Datta, P., Ayan, B., Ozbolat, V., Sosnoski, D., & Ozbolat, I. T. (2017). 3D bioprinting for drug discovery and development in pharmaceutics. *Acta biomaterialia*, *57*, 26-46.
- Pere, C. P. P., Economidou, S. N., Lall, G., Ziraud, C., Boateng, J. S., Alexander, B. D., ... & Douroumis, D. (2018). 3D printed microneedles for insulin skin delivery. *International journal of pharmaceutics*, *544*(2), 425-432.
- Pietrzak, K., Isreb, A., & Alhnan, M. A. (2015). A flexible-dose dispenser for immediate and extended release 3D printed tablets. *European journal of pharmaceutics and biopharmaceutics*, *96*, 380-387.
- Prasad, L. K., & Smyth, H. (2016). 3D Printing technologies for drug delivery: a review. *Drug development and industrial pharmacy*, *42*(7), 1019-1031.
- Ratheesh, G., Venugopal, J. R., Chinappan, A., Ezhilarasu, H., Sadiq, A., & Ramakrishna, S. (2017). 3D fabrication of polymeric scaffolds for regenerative therapy. *ACS Biomaterials Science & Engineering*, *3*(7), 1175-1194.
- Robles-Martinez, P., Xu, X., Trenfield, S. J., Awad, A., Goyanes, A., Telford, R., ... & Gaisford, S. (2019). 3D printing of a multi-layered polypill containing six drugs using a novel stereolithographic method. *Pharmaceutics*, *11*(6), 274.
- Sadia, M., Sośnicka, A., Arafat, B., Isreb, A., Ahmed, W., Kelarakis, A., & Alhnan, M. A. (2016). Adaptation of pharmaceutical excipients to FDM 3D printing for the fabrication of patient-tailored immediate release tablets. *International journal of pharmaceutics*, *513*(1-2), 659-668.
- Serris, I., Serris, P., Frey, K. M., & Cho, H. (2020). Development of 3D-Printed Layered PLGA Films for Drug Delivery and Evaluation of Drug Release Behaviors. *AAPS PharmSciTech*, *21*(7), 1-15.
- Sjöholm, E., & Sandler, N. (2019). Additive manufacturing of personalized orodispersible warfarin films. *International journal of pharmaceutics*, *564*, 117-123.
- Skowyra, J., Pietrzak, K., & Alhnan, M. A. (2015). Fabrication of extended-release patient-tailored prednisolone tablets via fused deposition modelling (FDM) 3D printing. *European Journal of Pharmaceutical Sciences*, *68*, 11-17.
- Solanki, N. G., Tahsin, M., Shah, A. V., & Serajuddin, A. T. (2018). Formulation of 3D printed tablet for rapid drug release by fused deposition modeling: screening polymers for drug release, drug-polymer miscibility and printability. *Journal of pharmaceutical sciences*, *107*(1), 390-401.
- Soni, N., Jain, K., Gupta, U., & Jain, N. K. (2015). Controlled delivery of Gemcitabine Hydrochloride using mannosylated poly (propyleneimine) dendrimers. *Journal of Nanoparticle Research*, *17*(11), 1-17.
- Strutt, J. W., & Rayleigh, L. (1878). On the instability of jets. *Proc. London Math. Soc*, *10*(4).
- Tekin, E., Smith, P. J., & Schubert, U. S. (2008). Inkjet printing as a deposition and patterning tool for polymers and inorganic particles. *Soft Matter*, *4*(4), 703-713.
- Thakkar, R., Pillai, A. R., Zhang, J., Zhang, Y., Kulkarni, V., & Maniruzzaman, M. (2020). Novel on-demand 3-dimensional (3-D) printed tablets using fill density as an effective release-controlling tool. *Polymers*, *12*(9), 1872.
- Trombetta, R., Inzana, J. A., Schwarz, E. M., Kates, S. L., & Awad, H. A. (2017). 3D printing of calcium phosphate ceramics for bone tissue engineering and drug delivery. *Annals of biomedical engineering*, *45*(1), 23-44.
- Ursan, I. D., Chiu, L., & Pierce, A. (2013). Three-dimensional drug printing: a structured review. *Journal of the American Pharmacists Association*, *53*(2), 136-144.
- Ventola, C. L. (2014). Medical applications for 3D printing: current and projected uses. *Pharmacy and Therapeutics*, *39*(10), 704.
- Vogenberg, F. R., Barash, C. I., & Pursel, M. (2010). Personalized medicine: part 1: evolution and development into theranostics. *Pharmacy and Therapeutics*, *35*(10), 560.
- Wang, J., Goyanes, A., Gaisford, S., & Basit, A. W. (2016). Stereolithographic (SLA) 3D printing of oral modified-release dosage forms. *International journal of pharmaceutics*, *503*(1-2), 207-212.
- Wang, J. C., Zheng, H., Chang, M. W., Ahmad, Z., & Li, J. S. (2017). Preparation of active 3D film patches via aligned fiber electrohydrodynamic (EHD) printing. *Scientific reports*, *7*(1), 1-13.
- Wang, M., Favi, P., Cheng, X., Golshan, N. H., Ziemer, K. S., Keidar, M., & Webster, T. J. (2016).

Cold atmospheric plasma (CAP) surface nanomodified 3D printed polylactic acid (PLA) scaffolds for bone regeneration. *Acta biomaterialia*, *46*, 256-265.

- Wang, X., Li, T., Ma, H., Zhai, D., Jiang, C., Chang, J., ... & Wu, C. (2017). A 3D-printed scaffold with MoS 2 nanosheets for tumor therapy and tissue regeneration. *NPG Asia Materials*, *9*(4), e376-e376.
- Yan, T. T., Lv, Z. F., Tian, P., Lin, M. M., Lin, W., Huang, S. Y., & Chen, Y. Z. (2020). Semi-solid extrusion 3D printing ODFs: an individual drug delivery system for small scale pharmacy. *Drug development and industrial pharmacy*, *46*(4), 531-538.
- Yang, Y., Wang, H., Li, H., Ou, Z., & Yang, G. (2018). 3D printed tablets with internal scaffold structure using ethyl cellulose to achieve sustained ibuprofen release. *European journal of pharmaceutical sciences*, *115*, 11-18.
- Yi, H. G., Choi, Y. J., Kang, K. S., Hong, J. M., Pati, R. G., Park, M. N., ... & Cho, D. W. (2016). A 3D-printed local drug delivery patch for pancreatic cancer growth suppression. *Journal of controlled release*, *238*, 231-241.
- Zhang, J., Feng, X., Patil, H., Tiwari, R. V., & Repka, M. A. (2017). Coupling 3D printing with hot-melt extrusion to produce controlled-release tablets. *International journal of pharmaceutics*, *519*(1-2), 186-197.
- Zhang, J., Xu, P., Vo, A. Q., Bandari, S., Yang, F., Durig, T., & Repka, M. A. (2019). Development and evaluation of pharmaceutical 3D printability for hot melt extruded cellulose-based filaments. *Journal of drug delivery science and technology*, *52*, 292.
- Zhu, M., Li, K., Zhu, Y., Zhang, J., & Ye, X. (2015). 3D-printed hierarchical scaffold for localized isoniazid/rifampin drug delivery and osteoarticular tuberculosis therapy. *Acta biomaterialia*, *16*, 145-155.