THE BOMBAY TECHNOLOGIST

ARTICLE

A Review Study on 3D Printing in Tablets

Nidhi Rajkondawar[a*], Vaishnavi Patil[a], Vidhi Thakur[a]

[a]Department of Pharmaceutical Science and Technology, Institute of Chemical Technology, Matunga, Mumbai, 400019, India

Abstract

The growing need for tablet production as a personalized dosage form led to the use of 3D printing for tablet production. In this technique, pills are printed to control the release rate with complex structures and to print the on-demand personalized dosage drugs formulations. Different steps involved in 3D printing start from model designing to 3D Printed tablets. Each technique has been discussed in the article along with its principle and examples. Material extrusion uses temperature or pressure to extrude tablet material. Vat polymerization, Material Jetting and Selective Laser Sintering use UV light and laser for 3D printing of tablets. In Binder jetting, the binder solution acts as an adhesive to form a tablet. For selecting the right kind of 3D printing technology, it is important to analyze the characteristic properties of each tablet using various methods, this includes their importance in tablet formulation. 3D printing of tablets includes some challenges which should be taken into consideration while preparing tablets. Challenges faced during 3D printing of tablets include powder agglomeration, incompatibility of the drug substance leading to structural imperfections in the final product, lack of constant and consistent flow, clogging of the 3D printer head in terms of powder-based 3D printing, concerns related to resin toxicity in case of Vat photopolymerization, thermal stability(SLS) and as current 3D printing technology is slow therefore mass production of tablet printing is a challenge.

Key Words

CAD- computer-aided design, 3D printing, solidification, tablets.

1. Introduction

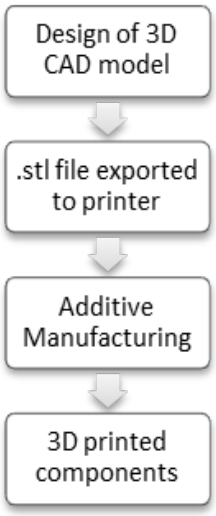
Engineer Charles Hull first proposed 3D printing (additive manufacturing technology) in the early 1980s. In 3D printing, a 3D digital model is created with the help of material by placing it layer by layer[1] The first oral 3D-printed drug is Spritam®; it got approval from the United States Food and Drugs Administration (U.S FDA) in 2015 [2]. In oral dosage form, *Tablets* are most widely used due to their versatility for formulating any drug. It is a dosage

A Review Study on 3D Printing in Tablets

form used by the adult population because of its potential benefits of quicker action with minimum stability problems [3]. The traditional method of production of the tablet is by compression of the powdered formulation. On large-scale manufacturing, pressure needs to be applied to give the powder a shape and also helps to keep the formulation intact.

Therefore, if we want a tablet that can be prepared immediately when needed, such technology will be helpful. Many people are currently suffering from various ailments that require them to take multiple medications [1]. These sometimes can lead to forgetfulness and missing out on a dose. Hence, formulating a combination of several drugs as and when needed through the help of 3D printing will help in solving the problem, for example, in the case of diabetes.

Tablet formulation which is aesthetically tailored to the customer's demand and polypill production has added to the technique's advantage [4]. 3D printing creates digital models using computer-aided design software. The medical practitioner analyses the reports and suggests the possible causes of the abnormality and the target organ. The right kind of medication is selected, and with the help of computer-aided design software, a correct formulation can be designed [5]. Using 3d printers, either single blend or multilayer printed tablets can be produced. The ability to use 3D printing to develop new treatments for many chronic conditions (e.g Asthma, arthritis, and diabetes) is immense[3]. 3D printing has been proposed as a promising set of techniques for producing tailored oral solid dosage forms. For example, a heat-based fused deposition modelling 3D printer was used to make simple tablets with sustained-release profiles [6]. Previous research shows that 3D printing of small tablets boosts capacity, individual performance, and behavioural variations of output depending on the size, as, and when the polymer is used [7]. This review article discusses the various techniques and challenges of 3D printing to design tablets as a dosage form.



A Review Study on 3D Printing in Tablets

2. Stepwise process of 3D printing

The various steps of this process include the construction of a CAD model (Figure 1). 3D modelling involves skills required for developing a successful 3D model; this is when the concept of CDIO (Conceive, Deceive, Implement, Operate) comes into the picture [8]. Before the transformation of CAD to STL (Standard Triangle Language or Standard Tessellation language), software called "slicer" is required in order to present the model layer by layer [9]. The transformation of the CAD model requires "STL file format", and "correction. STL " format is required to create direction or shape, also used for tool production, manufacturing, and background processing [10].

AM refers to a sub-set of 45-component processes by converting computer-assisted design (CAD), with an STL digital file (common tessellation language), into a visual product. Additive manufacturing (AM) creates the most complex shapes and complexities. This technology breaks the barriers to normal production processes. This technology can be divided into seven sections, providing a detailed structure for separating current and future printing processes. These components include binder jetting, material extrusion, material jet, powder bed assembly, and vat photopolymerization. Although each process is different from the method and material to be processed, every 50 methods are based on a sequential layout of the printed material [11].

Figure 1. Different steps of the 3D printing process[11]

3. Methods

3.1 Material Extrusion (ME)

Material extrusion is characterized by low cost and high speed. It is further divided into two parts based on whether the temperature is applied or pressure is applied [12].

3.1.1 Fused Deposition Modelling (FDM)

In fused deposition modelling (FDM), a prevalent ME technique utilizes high temperature to print tablets. Material like PLA, HPC and HPMC is melted in a liquefier, and then it is extruded from the nozzle on the building platform, after which it is lowered to construct the next layer [13]. Various types of tablets like controlled-release tablets, multiple drug-based tablets and extended and sustained-release tablets can be printed by this technique [14]. Extruded thermoplastic or paste material then falls on the construction stage and solidifies as it cools. FDM has the disadvantage of limiting the use of the thermolabile drug to print tablets [15]. An insoluble weak base, Domperidone(DOM), was chosen as a drug to be used as a Floating Sustained Release(FSR) medicine to increase its bioavailability and reduce its frequency of administration. Hydroxypropyl cellulose was loaded with DOM using FDM. This method was successful in producing rigid shells. Also, slow dissociation of HPC polymer chains had an FSR effect.[16]

3.1.2 Pressure-assisted microsyringe (PAM)

Pressured-assisted micro syringe extrudes semisolid preparation under high pressure based on pneumatic (air or liquid pressure), mechanical and solenoid pistols. The semisolid formulation is added into a syringe-like container with a printing nozzle, allowing the formulation to slide out due to pressure.

A Review Study on 3D Printing in Tablets

Layer-by-layer, this build-up will lead to the formation of a tablet [17]. Another subclass of PAM is also known as solid freeform fabrication (SFF) [18]. Levetiracetam as API, polyvinyl alcohol polyethene glycol graft copolymer and water is used as a solvent to formulate tablets using PAM. Since levetiracetam forms needle-shaped particles under heat, PAM seemed to be a reasonable option. This study focused on fixed-dose combination with different release kinetics, which would decrease the number of tablets taken daily. Hence sustained release is also accomplished[17].

3.2 Vat polymerisation (VP)

VP is a liquid to a solid process. Computer-controlled photopolymerization creates solids from a vat of liquid resins under light radiation [19]. This process chemically synthesizes the selected layer of photosensitive resin and uses UV light to cures it into a solid polymer.
Then the next layer of resin material is uniformly distributed and solidified using a UV light this process is repeated until the model is ready [15]. These techniques include Continuous Liquid Interface Production (CLIP), stereolithography (SLA), and digital light processing (DLP). But since mainly stereolithography is used for oral tablets, it is discussed briefly below.

3.2.1 Stereolithography (SLA)

The principle behind SLA is polymerisation by laser light. In the stereolithography (SLA) printing process, a laser is focused on a specific depth in a vat of resin, which causes localised photopolymerisation leading to solidification of the resin. This photopolymerisation process is repeated layer by layer until a 3D printed tablet is ready. In SLA printing, we can interpret the importance of energy imparted by the laser to cure the resin, which is influenced by the power of the light source, the scanning speed, the exposure time and the amount of polymer and photoinitiator. It is widely used for thermolabile drugs [20,21]. Tablets were prepared using 4-Aminosalicylic acid (4-ASA), paracetamol, Poly(ethylene glycol) diacrylate, Poly(ethylene glycol)and diphenyl(2,4,6-trimethyl benzoyl) phosphine oxide as photoinitiator with an SLA printer. Whether for industrial production or personalised doses, SLA 3D printing can be considered an appropriate method to manufacture modified-release oral dosage forms. [20]

3.3 Binder Jetting (BJ)

Steps for binder jetting (Figure 2.) are as follows:
First, the powder material is distributed over the construction platform using a roller. And then the print head inserts the binder adhesive over the powder where required. The build platform reduces the thickness of the model layer. Another layer of powder is spread over the previous layer. The object is formed when the powder is absorbed into the liquid and unbound powder stays in the area around the object. The process is repeated until the object is made. [22]
Hydrophilic drugs with low partition coefficients can be effectively formulated using binder jetting. One such example is hydrophilic quinapril hydrochloride with short disintegration time, highly porous tablets and excellent mechanical properties. Polyvinylpyrillidoone (PVP), a solvent such as methanol and microcrystalline cellulose(MC), and API were used[23].

Figure.2. Steps for binder jetting[22]

A Review Study on 3D Printing in Tablets

3.4 Material Jetting

Droplets of build material are deposited and dried by solvent evaporation or solidification under ultraviolet (UV) light [14]. Commonly known modes of printing in material jetting include continuous inkjet (CIJ) mode and drop-on-demand (DOD) mode. Both the methods act on the same principle of removing material from a nozzle. As its name suggests, the liquid is pumped through a hose continuously in CIJ mode. Due to the instability of the Rayleigh-Plateau driven by the capillary plane then breaks into the stream of drops. The drops are charged and diverted using heated plates. The CIJ is advantageous on the sole basis of it not clogging the nozzle. Since it is a continuous flow method, there are low chances of the solvent being blocked, making it an easy method. DOD type inkjet printing is widely used, where a drop is produced only as and when required by thermal or piezoelectric actuation. The only drawback of DOD printing is dry ink in the mouth during breaks may lead to the insertion of particles into nozzles, and may lead to clogging [24,25].

Naproxen, a non-steroidal anti-inflammatory agent and the model drug used in this study, was dissolved in the photo-curable formulations. PEGDA, PEG 200 and microcrystalline cellulose were chosen as the diluent for the preform tablet because of its good compressibility and compatibility. Due to its better droplet formation and gelation capacity, it is applicable towards material jetting [26].

3.5 Selective Laser Sintering (SLS)

Selective laser sintering (SLS) is an industrial 3D printing technology that uses a thin layer of bed powder to create a 3D object, similar to PB (Powder Bed). It is a layer manufacturing process that makes it possible to form 3D parts in successive layers. A laser beam uses thermal energy to give it strength [27]. While printing, the laser is directed to draw a selected pattern

on the surface of the powder bed. When the first layer is finished, the roller spreads a new layer of powder over the previous one. The item is built layer by layer [28]. Paracetamol, polyvinyl alcohol units and polyethene glycol units were used for printing with an SLS printer**.** The use of an SLS printer prevents the degradation of drugs. It is successful in being versatile in producing immediate-release

A Review Study on 3D Printing in Tablets

and modified-release formulations.[28]

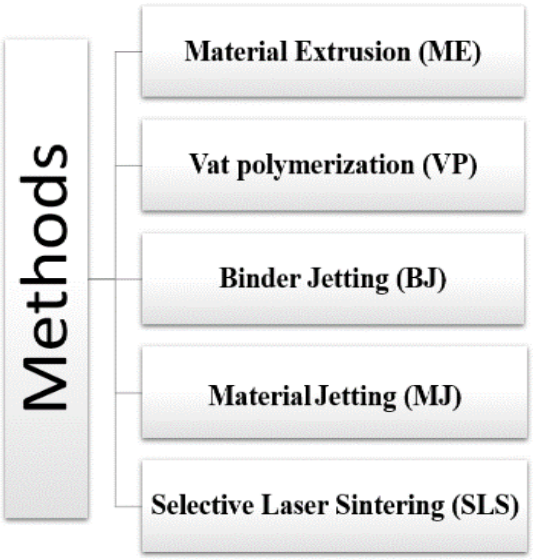


Figure 3. 3D Printing methods

4. Characterisation methods for 3D printed tables

4.1 Differential Scanning calorimetry (DSC) / Temperature analysis

It is used to test start-up power [29]. It estimates fusion and crystallization in detailed analysis. Through DSC major endothermic peaks are obtained which specifies the melting point of the drug. The crystalline or amorphous nature of the drug and the drug-polymer interaction can be analysed by DSC.[7,30] DSC helps estimate the impact of the material's thermal properties on the physical properties of the tablets. [31]As it is evident that DSC records the thermal properties hence those 3D printing methods like FDM uses it to characterize the tablet.[16]

4.2 Powder X-Ray Diffraction

X-ray diffraction (XRD) is an ideal analytical technique that estimates polymeric 3D crystalline structures. Also, it estimates the amorphous or crystalline nature of the drug-polymer combination forming the 3D printed tablet. It is important to the nature of the tablet to estimate its release profile and solubility.[32]XRD is relatively fast and non-destructive. The usefulness of this X-ray diffraction technique is limited to determining crystals and planning temperature treatment steps or characterising the mechanical properties of the tablet [33]. It is also used to determine the polymorphic forms and the angle of orientation of the crystals; practically anything can be found from this method [34]. Powder X-Ray Diffraction characterises tablets made by PAM, SLA, binder jetting and SLS.[17,20,23,28]

4.3 Hardness

Hardness is an important parameter considering the drug release rates and disintegration, especially for bioavailability drugs. An ideal tablet must resist the external damage caused during transportation and storage, and also it must be soft enough to disintegrate and release the drug. In traditional tablet manufacturing, it can be compressed by force. Still, in the case of 3D printing, this needs to be achieved by other methods like drying, changing the composition, laser scanning speed, and other printing parameters.[35] Hardness characterises tablets made by SLS, PAM, binder jetting and SLA.[28,17,20,23]

A Review Study on 3D Printing in Tablets

4.4 Thermogravimetric analysis (TGA)

Thermal stability over a range of temperatures can be checked by TGA analysis. Also, the degradation characteristics of thermo-labile drugs and polymers are studied by this method. [36]As SLS and FDM both use thermal energy to print a tablet hence we need to do Thermogravimetric analysis for the tablets printed by these methods.[28,16]

4.5 Dissolution testing

Dissolution testing is essential to be studied to check for their release profile. Disintegration is desired after taking the tablet to be bioavailable; hence dissolution testing is done. The dissolution of a tablet is influenced by the polymer used in the formulation so this characterisation method helps to decide the category and composition of the tablet. [7,29] Dissolution testing is used to characterise tablets made by using FDM, SLA, binder jetting and PAM as each tablet has to be analysed based on their dissolution for better absorption.[16,20,23,17]

4.6 X-ray computed microtomography

X-ray computed microtomography (XμCT) can be used to gain insight into how changes in the process settings of the 3D printer affect the pore structure of the tablet. Porosity and pore structure are essential characteristics of tablets since they influence mechanical strength and other properties. It is highly suitable to analyze the microstructure of such 3D printed tablets. The X-rays can penetrate all pharmaceutically suitable excipients while undergoing negligible diffraction quickly due to their high energy[37]. Porosity is an essential characteristic in case of SLS as the void space between the binder particles favours the spreading of liquid binder by capillary force.[27] Whereas in case of FDM method showed that tablets with low porosity will have better mechanical properties[38].

5. Challenges

General challenges faced during 3D biomedical products include processing biomaterials, availability of multiple biomaterials, texture, and similarity of colour and organs. Also, printing has low dimensional accuracy, powder agglomeration, and microphone size. However, challenges related to management include providing staff training, high product costs, low business capacity. To avoid the slightest variation and the formation of cracks formed due to heat, highly skilled technicians are required.[10] Also, the biggest challenge is the incompatibility of the drug substance that must be looked at. Structural imperfections may arise in the final product, which can be carried out by developing various production parameters.[39]

3D printing technology (EXT, FDM, and PB) is reliable on a nozzle machine to create consecutive layers at a time. This poses a significant challenge to maintain a constant and consistent flow when needed as the print head stops and restarts during a single print.[40] The nozzle-based system method is used to create volume layers. As the printer head stops and resumes in the middle of the successive layer formation, a continuous flow of printing material is required [10].

A Review Study on 3D Printing in Tablets

In powder-based 3D printing, for example, clogging of the 3D printer head, binder migration, bleeding, improper power supply, and scrubbing are problems that need to be addressed. Powder-based 3D printing mainly requires specialized laboratories to print forms that cause health and work hazards. [40]

In Vat photopolymerization, although the remarkable success in 3D printing is based on photopolymerization, concerns related to resin toxicity and the unintentional reaction of the drug-polymer remain significant issues. On the other hand, photopolymerization may impair the drug's effectiveness in prolonged exposure to intense UV light that may result in drug degradation or an unexpected chemical reaction with a self-acting polymer. The cytotoxicity of photosensitive resin and cell damage during UV radiation poses a challenge to photopolymerization in bioprinting. Therefore, further studies are needed to ensure drug stability during and after printing [41].

The FDM printing method faces many obstacles such as high maintenance because they require a lot of filament to print with, and if the filament isn't kept in good condition, it can cause problems with the printer. The filament can get clogged up if it's not stored correctly or broken if it's mishandled, lack of suitable materials/polymers, and many processing times. Most thermal soluble grade polymers also lack the materials needed to provide good quality construction which is often a significant technical obstacle to developing FDM print applications for pharmaceutical applications. In addition, drug exposure to high temperatures over a long period involved in both the extraction and production of 3D printed equipment can lead to severe drug damage [41].

Various technical and regulatory challenges in SLS technology limit their widespread use in pharmaceutical production. Components tolerate pre-heating and local heating phases during the sintering process, accelerating the deterioration of structural elements, including drug candidates. Therefore, a thorough evaluation of the thermal stability behaviour during the SLS process is needed to understand the degradation mechanisms. The mechanical properties of 3D printed tablets can be modified with flexible design and processing. Therefore, these factors may include extensive research related to the process of various dosage forms. Another challenge that hinders the adoption of this technology is the lack of cGMP compliant 3D printers. In addition, there is no regulatory guide available for drug products produced by 3D printing. Finally, the current 3D printing technology is slow and cannot match the mass production of covary tablet printing machines or capsule filling machines [42].

5.1 Risk Assessment During 3D Printing Process

Risk identification is essential in preventing the failure of quality control parameters such as appearance, content similarities, tests, etc. Risk identification involves using process analysis and flexible verification processes to produce a quality product. If the provided printer can print the provided design, software controls must be used. The thickness of the layer should be controlled by real-time layer thickening monitoring. Improper distribution due to natural conditions should be operated by temperature control and moisture in the production area. The wrong position can be avoided by monitoring print height and head speed during printing. Unequal layers can be avoided by looking at the powder water

A Review Study on 3D Printing in Tablets

content and distribution of powder particle size. Closing the print head can be prevented by confirming particle size distribution and monitoring inkjet flow. Inconsistent agglomeration or binding can cause variation in viscosity of binder or binder surface disagreement. Establishing guidelines, rules, quality systems, and security of use and 3D

printed medicine is a big challenge for regulatory authorities involving significant barriers [43].

6. Future scope

3D printing technology and traditional preparation technology are compatible. Traditional preparation technologies have gradually matured after a long practice and have unique advantages in industrial development. On the other hand, like emerging technologies, 3D printing can detect the precise composition of a variety of objects and can overcome the problems of traditional preparation technology in many respects. The development of printing methods in pharmaceutical production expands the scope of 3D printing technology, provides new methods of drug research, and encourages the development of personal drug delivery. It enhances the accuracy and complexity of pharmaceutical manufacturing and provides basic technical support for composite medicines. [25]

The 3D printing method is used to design and engineer various novel dosage forms. Although soon, commercial production of such novel challenging conditions; personal development drugs, drug release in dosage form, combining or avoiding drug interactions, protection of biomolecules during production, the formulation of a multi-drug form. Releasing dosage forms will be moved to a new era of 3D printing technology. [43]

These technologies make your medicine more readily available, as customizable additional production is still an undeniable benefit. Dosage combinations or "polypills" are an emerging possibility afforded by AM. [44]

Table 1: Summary of 3D printing methods[45]

METHODS	MATERIALS	ADVANTAGES	DISADVANTAGES
Binder jet	Binder fluid, powder bed	1. It can be done at room temperature. 2. The use of a variety of materials. 3. Immediately dispersed volume forms can be produced	1. Post-production drying is required. 2. Use of organic solvents. 3. Damage to powdery mildew. 4. It produces weak dosage forms.

A Review Study on 3D Printing in Tablets

Fused deposition modelling	Thermoplastic polymeric filaments	1. A relatively inexpensive process. 2. Non-melting process. 3. No post-production steps. 4. Produces solid dosage forms.	1. The heat involved may slow down certain things. 2. The polymers used should be thermoplastic. 3. Pre-preparation of filaments is required.
Selective laser sintering	Laser energy-absorbing powder	1. One quick production step. 2. It produces high-quality materials.	1. Only laser-absorbing components can be used. 2. High power lasers may undermine drugs.
Inkjet Ink	Ink—drug solution Substrate—polymer bused films	1. Continuous inkjet - prevents closing the nozzle. 2. The much-needed inkjet — high accuracy, low cost, and minimizing waste.	1. Continuous inkjet — waste, low maintenance, and expensive. 2. TIJ — can reduce heat sensitivity.
Stereolithography	Photo-curable liquid resin	1. The process with the highest resolution. 2. Low-temperature stress involved.	1. The starter material should have the treatable features of the image. 2. Treatment measures are required. 3. A small number of polymers are approved for use in pharmacies. 4. Stability issues while storing sensitive resins. 5. The products can be cytotoxic.

8. References

[1]Zhu, X.; Li, H.; Huang, L.; Zhang, M.; Fan, W.; Cui, L *Biomed. Pharmacother.***2020**, *131*.

A Review Study on 3D Printing in Tablets

[2]Jamróz, W.; Kurek, M.; Czech, A.; Szafraniec, J.; Gawlak, K.; Jachowicz, R. *Eur. J. Pharm. Biopharm.*2018, *131*, 44.

[3]Khaled, S. A.; Burley, J. C.; Alexander, M.R.; Roberts, C. J. *Int. J. Pharm.***2014**, *461* (1–2), 105.

[4]Goyanes, A.; Buanz, A. B. M.; Basit, A. W.; Gaisford, S. *Int. J. Pharm.***2014**, *476* (1), 88.

[5]Beer, N.; Hegger, I.; Kaae, S.; de Bruin, M. L.; Genina, N.; Alves, T. L.; Hoebert, J.; Kälvemark Sporrong, S. *Exploratory Research in Clinical and Social Pharmacy* **2021**, *4*, 100073.

[6]Khaled, S. A.; Burley, J. C.; Alexander, M. R.; Yang, J.; Roberts, C. J. *Int. J. Pharm.* **2015**, *494* (2),643.

[7]Krause, J.; Müller, L.; Sarwinska, D.; Seidlitz,A.; Sznitowska, M.; Weitschies, W. *Pharmaceuticals* **2021**,*14*(2), 1.

[8]Huang, T. C.; Lin, C. Y *Telemat. Informatics***2017**, *34* (2), 604.

[9]Gokhare, V. G.; Raut, D. N.; Shinde, D. K. *Int. J. Eng. Tech. Res.***2017**, *6* ((6)), 953.

[10]Kumar, P.; Rajak, D. K.; Abubakar, M.; Ali, S. G. M.; Hussain, M. *J. Mater. Eng. Perform.***2021**, *30* (7), 5342.

[11]Capel, A. J.; Rimington, R. P.; Lewis, M. P.; Christie, S. D. R. *Nat. Rev. Chem.***2018**, *2* (12), 422.

[12]Jamróz, W.; Szafraniec, J.; Kurek, M.; Jachowicz, R. *Pharm. Res.***2018**, *35* (9), 176.

[13] Gao, X.; Yu, N.; Li, J. *Struct. Prop. Addit. Manuf. Polym. Components***2020**, 303.

[14]Mohammed, A.; Elshaer, A.; Sareh, P.; Elsayed, M.; Hassanin, H. *Int. J. Pharm.* **2020**. 580. 119245.

[15]Kollamaram, G.; Croker, D. M.; Walker, G. M.; Goyanes, A.; Basit, A. W.; Gaisford, S. *Int. J. Pharm.***2018**, *545* (1–2), 144.

[16]Chai, X.; Chai, H.; Wang, X.; Yang, J.; Li, J.; Zhao, Y.; Cai, W.; Tao, T.; Xiang, X. *Scientific Reports* **2017**, *7* (1), 1.

[17] el Aita, I.; Rahman, J.; Breitkreutz, J.; Quodbach, JEur. *J. Pharm. Biopharm*. **2020**, *157*, 59.

A Review Study on 3D Printing in Tablets

[18]Elbadawi, M.; Nikjoo, D.; Gustafsson, T.; Gaisford, S.; Basit, A. W. *Int. J. Pharm.***2021**, *595*, 120197.

[19]Xu, X.; Awad, A.; Robles-Martinez, P.; Gaisford, S.; Goyanes, A.; Basit, A. W *J. Control.*, **2021**, pp 743.

[20]Wang, J.; Goyanes, A.; Gaisford, S.; Basit, A. W *Int. J. Pharm*.**2016**, *503* (1–2), 207.

[21]Robles-Martinez, P.; Xu, X.; Trenfield, S. J.; Awad, A.; Goyanes, A.; Telford, R.; Basit, A. W.; Gaisford, S. *Pharmaceutics* **2019**, *11* (6).

[22]**WEBSITE:https://www.lboro.ac.uk/research/amrg/about/the7categoriesofadditivemanufacturing/binderjetting/DateAccessed: 13/03/2022**

[23]Kozakiewicz-Latała, M.; Nartowski, K. P.;Dominik,A.; Malec, K.; Gołkowska, A. M.; Złocińska, A.; Rusińska, M.; Szymczyk-Ziółkowska, P.; Ziółkowski, G.; Górniak, A.; Karolewicz, B. *Eur. J. Pharm. Biopharm.***2022**, *170*, 144.

[24]Guo, Y.; Patanwala, H. S.; Bognet, B.; Ma, A. W. K. *Rapid Prototyp. J*.**2017**, *23* (3), 562.

[25]Cui, M.; Pan, H.; Su, Y.; Fang, D.; Qiao, S.; Ding, P.; Pan, W. *Acta Pharm. Sin. B***2021**, *11* (8), 2488.

[26]Acosta-Vélez, G. F.; Zhu, T. Z.; Linsley, C. S.; Wu, B. M. *Int. J. Pharm.***2018**, *546* (1–2), 145.

[27]Kruth, J.; Mercelis, P.; van Vaerenbergh, J.; Froyen, L.; Rombouts, M. *Rapid Prototyp.J.***2005**, *11* (1), 26.

[28] Fina, F.; Goyanes, A.; Gaisford, S.; Basit, A. W. *Int. J. Pharm.***2017**, *529* (1–2), 285.

[29]**MANUSCRIPT:** Alvaro Goyanes, Asma B.M. Buanz, Simon Gaisford, Grace B. Hatton and Abdul W.Basit.3D printing of modified-release dosage forms loaded with aminosalicylates (4-ASA and 5-ASA).

[30]Hussain, A.; Mahmood, F.; Arshad, M. S.; Abbas, N.; Qamar, N.; Mudassir, J.; Farhaj, S.; Nirwan, J. S.; Ghori, M. U. *Polymers (Basel)* **2020**, *12* (12), 3057.

[31]**WEBSITE:**https://www.azom.com/article.aspx?ArticleID=20724 Date Accessed: **06/03/2022**

[32] Bhatt, U.; Malakar, T. K.; Murty, U. S.; Banerjee, S. *Drug Dev. Ind. Pharm.***2021**, 1.

[33]**WEBSITE:**https://www.thermofisher.com/blog/materials/using-xrd-to-characterize-3d-printed-materials/ Date Accessed: **06/03/2022**

[34]Bunaciu,A.A.;Udriştioiu,E.gabriela;Aboul-Enei.Y. *Crit. Rev. Anal. Chem*.**2015**, *45* (4), 289.

A Review Study on 3D Printing in Tablets

[35]Karalia, D.; Siamidi, A.; Karalis, V.; Vlachou, M. *Pharmaceutics* **2021**, *13* (9).

[36] Diederichs, E.; Picard, M.; Chang, B. P.; Misra, M.; Mohanty, A. *Molecules* **2021**, *26* (14).

[37]Markl, D.; Bøtker, J.; Strobel, A.; Schlossnikl, R. S.; Rantanen, J.; Rades, T.; Zeitler, J. A.; **2017**,(54).

[38]Wang, X.; Zhao, L.; Fuh, J. Y. H.; Lee, H. P.*Polymers (Basel)* **2019**, *11* (7).

[39]Vaz, V. M.; Kumar, L. *AAPS PharmSciTech* **2021**, *22* (1), 49.

[40]Alhnan, M. A.; Okwuosa, T. C.; Sadia, M.; Wan, K. W.; Ahmed, W.; Arafat, B. *Pharm. Res.* **2016**. pp 1817.

[41]Wang, J.; Zhang, Y.; Aghda, N. H.; Pillai, A. R.; Thakkar, R.; Nokhodchi, A.; Maniruzzaman, M. *Adv. Drug Deliv. Rev.***2021**, *174*, 294.

[38]**WEBSITE:**https://www.americanpharmaceuticalreview.com/Featured-Articles/574845-Opportunities-and-Challenges-of-Selective-Laser-Sintering-3D-Printing-in-Personalized-Pharmaceutical-Manufacturing/ Date Accessed: **04/02/2022.**

[39] Ani Jose, P.; Christoper, P. G. Preethy Ani Jose, *Asian J. Pharm. Res. Dev.***2018**, *6* (3), 46.

[40]Kjar, A.; Huang, Y. *Pharmaceutics* **2019**, *11* (8)

[41]Solanki,N.G.;Tahsin,M.;Shah,A.v.;Serajuddin*J .Pharm. Sci*.**2018**, *107* (1), 390.