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ADDITIVE MANUFACTURING TECHNOLOGIES, APPLICATION AND FUTURE CHALLENGES OF 3D PRINTING

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ABSTRACT
3D printing is a method of rapid and productive prototyping when objects are inserted into each other into three-dimensional production layers. Although 3D printing was introduced in the 1980s and technology has received many applications from the manufacturing industry from automotive parts to machinery, its use in the pharmaceutical area is still limited. However, the power of 3D printing in the pharmaceutical industry is now evident. The ability of 3D printing to produce drugs with specific specifications tailored to the needs of individual patients has shown the possibility of making customized drugs. The technology allows volume forms to be accurately printed in a variety of ways, sizes and formats that are difficult to produce using traditional techniques. However, there are various challenges associated with the proper use of 3D printing in the field of pharmaceutical that must be overcome in order to make the most of this technology. In this review, we are given an overview of the various 3D printing technologies used in the construction of complex simulation forms and their capabilities and limitations.

KEYWORD: 3D Printing Technologies, Additive Manufacturing, Application, Future Challenges.

1. INTRODUCTION

Three-dimensional printing technology (3DP) relies on computer-assisted architecture to achieve unparalleled flexibility, time saving, and the unique production capacity of pharmaceutical drug products. This process incorporates 3D proto-typing of layer-by-layer fabrication (with computer-assisted design models) to form the wood material into the desired size form.[1] Since its development at the Massachusetts Institute of Technology (1992)[2], 3DP is receiving increasing attention in the development of the pharmaceutical design as an effective strategy to overcome some common challenges of conventional pharmaceutical unit operations. For example, the normal operation of a production unit involving grinding, mixing, granulation and compression can lead to different product final requirements in terms of drug loading, drug extraction, drug stability and pharmaceutical dosage form stability.[4-8] Efforts to improve 3DP in product development, pharmaceutical have led to significant FDA approval. In this report, we will explore the strengths, challenges and prospects of 3DP in pharmaceutical product development by paying close attention to rigid dosage forms and drug schemes that can be planted.

A BIT OF HISTORY

The concept of 3DP has evolved since the early 70 'of the twentieth century when Pierre A. L. Ciraud described the use of powdered material and the subsequent solidifica tion for each crust using the action of a large power beam. In this case solvents such as plastic or metal can be used in theory to prepare the material for repair. In the early 80's' patent right: The BA process of forming an article with a line size ^, Ross Housholder described the idea of tying sand with a variety of materials and Carl Deckard devised a method of reinforcing a powder bed with a laser beam called a selected laser. sintering (SLS).[4,4] The first commercially available technology created by Chuck Hull was stereolithography (SLA). This method was based on the photopolymerization of liquid resin by ultraviolet light. In the late 80's Scott Crump filed a patent for mixed modeling (FDM) - a process that used thermal moplastic equipment to prepare an object. 90's Emanuel Sachs - A collaborative MIT scientist with BThree-dimensional printing techniques

based on joining the selected regions of powder by binding material.[3,4]

2. BENEFITS AND APPLICATIONS OF 3DP AT PHARMACEUTICAL DRUGS DELIVERY

3D Objects can be found in many techniques such as inkjet design, Direct-Write, Zipdose, Thermal inkjet (TIJ Printing and Fused Deposition Modeling (FDM).[1,5,13,16] Compared with the standard production process, 3DP offers many attractive features, such as, (a) high production levels due to its fast-moving systems., (b) the ability to achieve high drug loads in the quantities required for precision and precision especially for strong drugs used in small doses, (c) to reduce the waste of material that can save on production costs and (d) to be available in a wide range of Pharmaceutical Active ingredients that include water soluble, peptides and proteins, as well as a drug with small therapeutic windows.[1-7,10,14,15,21] 3DP at Pharmaceutical drug delivery is expected to be well done mostly in place of personalized medicine. We have come to the time of practice and medicine where "one size does not fit all" because the drug must suit the needs of each patient while taking into account genetic profiles, age, race, gender, epigenetic and environmental characteristics. Also, there are cases where treatment regimens should be customized to improve patient adherence to treatment. This is especially important in the treatment of chronic diseases in which patients have to follow complex treatment regimens that include multiple medications and high frequency of dosage couples with side effects. In all these cases, customization can be achieved with 3DP technology. This may be due to the flexibility in the design, development and manufacture of one or more products with built-in and easily controlled layers that can be adapted to different patient conditions.[22] Therefore, we assume that with customized 3DP drugs, health professionals will have the opportunity to consider the patient's pharmacogenetic profile before choosing a treatment option.[1,6,5,9,14,22] It is expected that 3DP will continue to receive a lot of attention in robust rating forms as the most popular forms of drug dosage. Strong measurement forms gained popularity with many factors such as: simplification, pain avoidance, direct measurement, and the ability to obtain patient adherence to treatment. However, many of the steps for the production of solid dosage formulas are hampered by many challenges such as long-acting processes, batch-to-batch variations due to reliance on operator judgment, wastage of goods, low drug loading capacity, and suitability for limited components of active ingredients. Many 3DP methods have been investigated to obtain robust measurement forms. We expect that the drug delivery systems that can be planted will also benefit from 3DP technology especially in providing effective strategies to overcome limitations such as batch-to-batch drug combinations during the preparation for implantation and the internal consistency of the resulting implantation. Meanwhile, 3DP techniques have been shown to produce precision-defined implants, large-scale macro-form constructions that can be used effectively in complex drug extraction. In addition, 3DP can provide benefits in increasing the concentration of drugs needed to prepare potential implants in improving drug efficacy and reducing toxicity and side effects.[23,24]

3. ADDITIVE MANUFACTURING TECHNOLOGIES

3.1. LASER BASED WRITING SYSTEMS

3.1.1. Stereolithography

The first commercial application of stereolithography as a robust formulation of forms dates back to the late 1980s.[3,13,14] This method was patented by Charles Hull, founder of 3D Systems, Inc., in 1986. The printing process involves a specially designed 3D printing machine called a stereolithograph apparatus (SLA), which converts liquid plastic into solid 3D materials.[3,15] The SLA has been found to be widely used in the preparation of customized scaffolding and drug-carrying scaffolding. In terms of accuracy and resolution, stereolithography is superior to all other solid forms of form factor (FFF) with an accuracy of up to 20µm.[3,13] Patient-specific models with functional components, implanted devices, tissue engineering, and cell-containing hydrogels are possible with this technology.[3,15]

Stereolithography is based on the polymerization of photopolymers (frames) treated with ultraviolet light.[3,13,16] In line with the same goal the two approaches are defined by STL technology: the way to the top and the way to the top, as shown in Fig. 1. In a downward direction UV light heals the surface or a very thin layer of photopolymer coating above the construction platform. After the reinforcement of the first layer, the platform is moved down depending on the size of each shortcut phase to produce another layer of photopolymer resin in addition to the reinforced polymer. Thus, a second layer is formed and attached to the first layer. This process continues until the desired construction is completed (Figure 1A). Conversely, on the way down, the construction platform is higher, and the UV source is below the resin tank. The resin tank has a transparent window, which gives the UV laser a resin treatment. Initially, the construction platform was lowered to the bottom of the resin tank leaving only a small layer of resin to be treated. After the first layer is formed, the platform is raised according to the size of each layer. Then a new layer of resin is exposed under the first layer treated and by UV laser, thus forming a second layer (Figure 1B). In both cases, after the construction is complete, the printed product should be washed with alcohol solution to remove excess resin. Finally, sending the treatment to a UV oven can be hired to strengthen the printed parts. The choice of resin is very important depending on the properties of the product (the degree of hardness before UV light) and should be approved by the FDA in the case of pharmaceuticals. A limited amount of available resin is

associated with organic matter, and decaying matter is considered to be the main limitation of this process.[3] The first resins designed for use in stereolithography were derived from molecular weight polyacrylate or epoxy macromers that form glass networks in polymerization established in image and cross-linking. Several frameworks have been developed over the past two decades, and many network structures can be found after healing. Various studies have tested theescope of SLA technology in the pharmaceutical field.

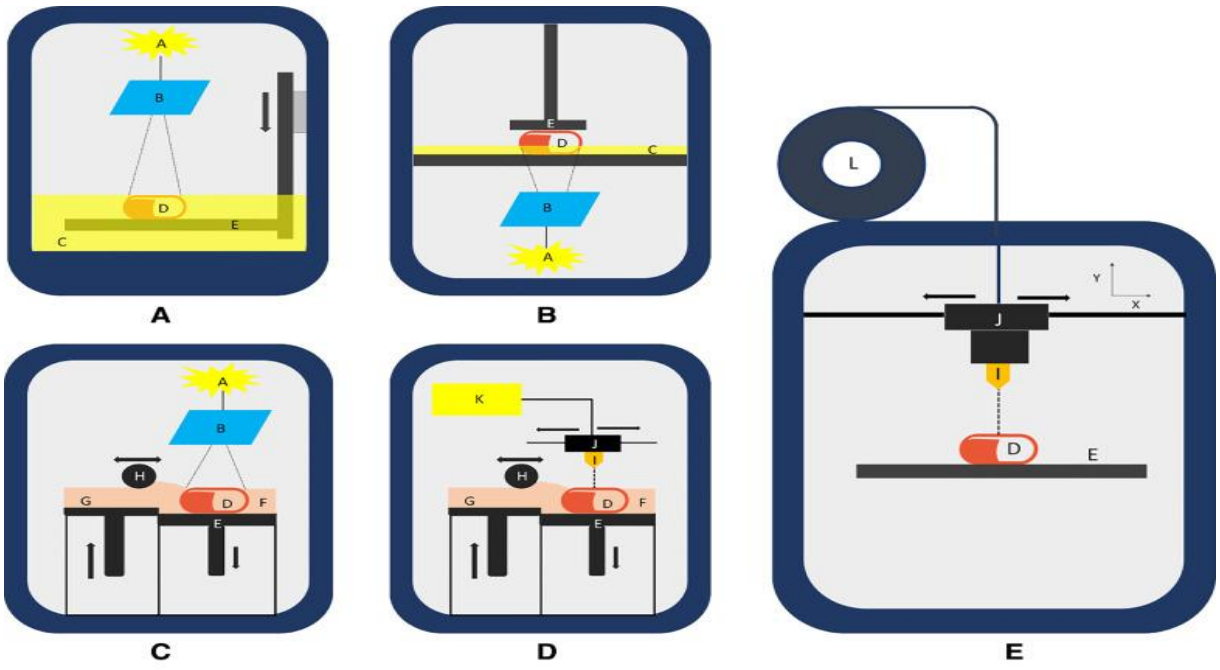

Fig 1: Different 3D printing technologies: (A) SLA bottom-up, (B) SLA top-down, (C) SLS, (D) IJP and (E) FDM.

For example, Goyanes et al. describe a new way of personalizing you to manage your identity using 3D scanning and 3D printing. Patients' noses are scanned with a commercial 3D scanner, and each patient's herbal mask is developed. The selected anti-acne mask was made using SLA and FDM technology and compared. Commercially produced fibers Flex EcoPLA (FPLA) and polycaprolactone (PCL) were loaded with FDM salicylic acid, and by SLA process, salicylic acid was dissolved in poly (ethylene glycol) diacrylate (PSGDA) and poly ethylene glycol PEG. SLA printing revealed 3D-printed (nose position) devices with higher resolution and higher drug loading (1.9%, w / w) than FDM, without drug damage. SLA printing was the most appropriate 3D printing technology to make anti-acne devices with salicylic acid.[3] Martinez et al. SLA print was used to prepare hydrogels loaded with ibuprofen polyethylene glycol diacrylate. Hydrogels containing up to 30% (w / w) water, and 10% (w / w) ibuprofen, are refined. Elimination profiles have shown that drug release rates depend on water content, and high water hydrogels release the drug rapidly.[3] He also used the SLA to prepare a modified release form with acetaminophen and 4-aminosalicylic acid (4-ASA) as model drugs. In their work polyethylene glycol diacrylate (PEGDA) was used as a monomer and diphenyl (2,4,6-trimethylbenzoyl) phosphine oxide was used as an imaging agent. The tablets are successfully printed and the multi-layered construction is made by adding polyethylene glycol 300 (PEG 300) to the printing solution. The paracetamol and 4-ASA loading in printed tablets was 5.69% and 5.40%, respectively. In conclusion, SLA 3D printing technology allows the manufacture of drug-loaded tablets with specific extensor profiles.[3] SLA technologies are known for producing excessive data and have very small cross-sectional layers which is one of the major advantages of this technology. In the case of pharmaceuticals and therapeutic drugs, as discussed earlier, the availability of suitable resin plays a major role in its future use. However, with a proper understanding of the process and the development of SLA resins technology, another method of construction of various rating forms may be proposed.

3.1.2. SELECTED LASER SINTERING (SLS)

SLS, a laser-based technology, as the name suggests it works by causing a mixture of powder bed with a controlled beam of laser beam (Fig. 1C).[3] During the printing process, the laser is directed to draw a specific pattern on the surface of the powder bed. When the first layer is completed, the roller spreads a new layer of powder over the previous one. The object is composed of each layer, and then found under a bed of powder. SLS has been widely used in the construction of scaffolds in

bioengineering with materials associated with suitable materials. There are very few chemicals studied using SLS as a 3D printing technology. In 2017, rapid extraction and modification of paracetamol modified releases as a model drug with Kollicoat IR or Eudragit L100-55 as polymers were printed using SLS technology.[3] SLS uses lasers to solidify polymers by increasing the polymer temperature over melting temperatures. However, there must be a link between the laser beam and the powder particles for the process to take place. In this case, the initial study did not print a paracetamol composition as the polymers used were unable to absorb laser light. Therefore, the Candurin gold sheen, pharmaceutical extracting tablet tablets, was used in various places to print the make-up. Candurin gold sheen is able to absorb laser light that is incorporated into the scanning process. This study has confirmed the use of SLS technology in the development of Pharmaceutical standard forms. But the choice of polymer seems to be very important as the material should be able to absorb the laser light of a given length. Most recently, in 2018, orally dividing pills (ODTs) containing paracetamol as a model drug and hydroxypropylmethylcellulose (HPMC) and kollidon VA 64 as polymers and Candurin gold sheen successfully used SLS technology.[3] SLS has the advantages of printing and high-density pharmaceuticals without the need for solvent. However, high-energy lasers can cause a decrease in drug use and polymers used. By carefully researching this technology for the construction of various measuring forms in the future and the availability of laser light-absorbing polymers can provide an alternative to medical printing using 3D technology.

3.2. INK-BASED PRINTING TECHNOLOGY: INKJET PRINTING

IJP is the collective name for various printing technologies based on the formation and placement of digitally controlled droplets on a substrate. IJP can be broadly differentiated by continuous inkjet separation (CIJ) and drop-on-demand (DoD) ink printing.[3] In addition, the DoD can be subdivided into hot inkjet or piezoelectric inkjet, based on the type of printhead, as well as a solid drop or drop, depending on the substrate in which the print head shoots the formed drops (Fig. 2). When a printhead pulls droplets from one drop to produce a solid object, it is known as a drop-on-drop inkjet, and when it throws into a solid object, it is known as a drop inkjet, also known as a Theriform process. As the descending method is more difficult to apply for treatment, many studies in this field have used the descending method.[3]

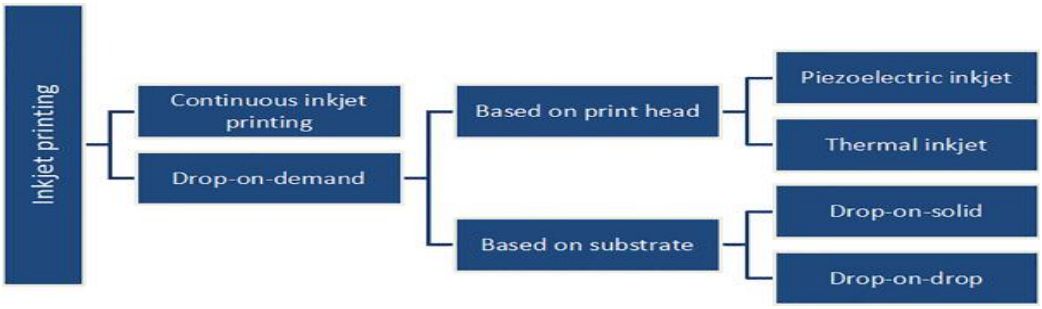

Fig 2: Different types of inkjet printing.

As mentioned earlier, IJP is flexible and uses a variety of technologies. However, the basic rule of printing remains the same for all types of IJP. It consists of a powder bed and a liquid binder. At the beginning of the process, a thin layer of powder is spread over a platform built with the help of a roller. Thereafter the print head releases precisely controlled droplets of liquid binder into the powder bed causing a buildup between the powder particles. After each layer is formed, a new layer of flour is distributed on a platform designed to form a new layer. The secretion of fluid is governed by a variety of mechanisms: piezoelectric, electrostatic and thermal.

Piezoelectricity, also known as electrical pressure, is the process by which electricity is generated through the application of pressure. On the other hand, when electrical energy is used, piezoelectric sensors change shape. Therefore, in piezoelectric and electrostatic DoD, the use of current or static electricity causes a rapid change in the state of piezoelectric crystals or mechanical migrations close to the liquid chamber respectively. This creates a change in the liquid state that creates pressure and forces the ink through the microphone. In thermal DoD, the print head is heated by thermal material, and small air bubbles are formed that produce pressure presses to extract ink droplets out of the microphone.

Inkjet printing is the first to use strong FFF in therapeutic medicine.[14] The controlled drug delivery device was made on a desktop type 3D printing machine built at the Massachusetts Institute of Technology in 1996. In that study, a controlled drug delivery tool was developed using Poly-ε-caprolactone (PCL) as the upper and lower layers and polyethylene oxide (PEO) as the middle layer. Subsequently, various complex volume output forms with complex internal geometry, multiple layers with multiple connections and actions were demonstrated in various studies.[16] In addition to conventional formulations, oral films and orally distributed formats were major fields of medical studies using IJP as FFF.[16] Early studies included the application of API (active

pharmaceutical ingredient) in potato starch films using a simple desktop inkjet printer.[17] An aqueous solution of salbutamol was successfully applied to the film. The study also showed the importance of the viscosity of the solution because large viscosities (> 2 mm2 / s) made the extraction of the ink form cartridge difficult. In addition, at low viscosities (<1 mm2 / s), the flow of liquid is influenced by gravity blocking the action of ink design.

Immediately differentiated dose-making methods have been available since the late 1990s and are often sought after by rapid action and patient adherence due to ease of management between children and geriatrics and in cases of dysphasia and incompatible psychiatric patients. To keep pace with demand for new drug delivery systems and advances in 3D printing, the fast-soluble dosage form was patented with levetiracetam as a FDA-approved model drug and was available on the market since early 2016. using Ziprese Technology of Aprecia related to descent technology. This achievement can be considered a major milestone in the use of 3D printing in pharmaceutics. Various methods of rapid elimination have been developed following FDA approval by Spritam.[3]

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Inkjet printing is one of the most advanced 3D printing methods as it can create binder fluid drops in micrometer size. This aids in the precise formation of small particles and a simulation form that would not have been possible with other 3D technologies. Compared to other 3D printing technologies, inkjet printing can transform second-generation production by being able to print injection particles, inhalation or insertion into liquid formulations, rapid dissolving formations and thin films of buccal delivery systems. In addition, inkjet printing has also been used to repair drug delivery devices and packaging materials. In a way, inkjet printing can be used from the preparation of drugs to the final stages of delivery. However, inkjet printing also comes with a number of challenges that need to be addressed in order to make the best use of technology in the production of pharmaceutical products. As mentioned above, the viscosity and surface area of the ink are important for printing using an inkjet printer. API features and assistants and the combination of the API rating and the saver determines the final binding properties. Therefore, an in-depth study may be required to increase ink flow with drops of the desired size and flow. Also, in a strong suction technique, the ink / binder fluid should be able to create a nucleation process in the powder bed where the contact depends on the moisture of the binder-powder, droplet penetration in powder inefficiency and diffuse responsibility behaviour.[22]

3.3. MATERIAL EXTRUSION OR NOZZLE-BASED DEPOSITION SYSTEM: FUSED DEPOSITION MODELING

Material extrusion is the process by which the thread of the desired material is prepared, and the solvent is pushed through a suitable pipe to form the desired product. In this technology, spools of filaments are located on the rollers, which pass through a hot pipe to a temperature high enough to melt the thread. The melted wire is installed on the construction platform according to the design made using the software. The molten material is applied to each layer and glued together because the layers are in a melted state as the construction platform descends to the bottom until a complete product is obtained.

In FDM technology, the microphone moves horizontally, and the construction platform moves up and down as the process progresses. After each layer, the construction platform is lowered, and another layer is placed over the previous layer (Fig. 3E). FDM XY fixes are good but Z-fixes are not very good, which is why the size is not even. An additional finishing process may therefore be required if a smooth surface is required. A microphone or small tip used in FDM technology typically ranges from 50-100µm.[11]

The main polymers used in FDM are polylactic acid or polylactide (PLA), polyvinyl alcohol (PVA) and acrylonitrile butadiene styrene (ABS)[5],[17], where PLA and -PVA is also used in the formulation of pharmaceutical dosage forms.[17] The polymers used must be thermal, stable and non-aerosolizing.[8] As a result, there are two major challenges facing FDM technology in the pharmaceutical sector: the acquisition of a suitable cable and the thermal deterioration of the API due to overheating and printing.

In addition to the challenges presented by FDM technology, most 3D printing courses have used the same technology. Various types of scale forms have been investigated to determine the likelihood of a procedure occurring, the first of which is to create PVA filament fibers (Fig. 3A) for controlled release controls. The potential for drug loading in PVA filaments is indicated. Since aqueous solution usually dissolves PVA fiber, an alcohol solution was used to insert the drug into the cord. However, a full load of the drug was not found. Drug withdrawal occurs with soil erosion and was highly dependent on the percentage of drug overflow. Total

drug withdrawal took 20h on a 90% filling tablet.[11] A variety of regulated releases are also designed to use PVA only mixed with desirable APIs such as aminosalicylates (4-ASA and 5-ASA) and prednisolone as tablets and paracetamol or caffeine and budesonide as caplets. However, in a number of formulations such as modified and expanded release pills such as mannitol triethyl citrate, and hydroxypropylcellulose have been used. Goyanes et al. forms two isomers of aminosalicylate used in the treatment of inflammatory bowel disease (IBD), 5-aminosalicylic acid (5-ASA, mesalazine) and 4-aminosalicylic acid (4-ASA), using FDM technology. Commercial PVA fibers were loaded with drugs in an ethanolic drug solution such as the fluorescein control regulation described above. Drug loading was very low in both cases. Final drug loads of 0.06% (w / w) and 0.25% (w / w) were achieved in the 5-ASA and 4-ASA fibers, respectively. Such a small drug was detected as a result of significant temperature reductions (50%) of APIs especially 4-ASAs, which reduced their effectiveness in printing at lower temperatures than in the destructive zone. Therefore, thermolabile drugs may not be suitable for FDM; or temporary heating of the microphone can lead to significant damage to the thermolabile drug. This is a major setback for FDM technology in the pharmaceutical sector. However, to overcome this problem the rapid release of theophylline and dipyridamole tablets as the model drugs were prepared at very low temperatures (90-100 ° C). The use of hydrophilic polymer polyvinyl pyrrolidone (PVP) to reduce printing temperature has been shown to be effective with drug extraction of more than 85% within 30min. In addition, expanding the scope of FDM and increasing its effectiveness in structural scale forms, A. Melocchi et al. designed for various threads using a twin - screw extruder. Fibers based on insoluble substances (ethylcellulose, Eudragit RL), soluble soluble (polyethylene oxide, Kollicoat IR), enteric soluble (Eudragit L, hydroxypropyl methylcellulose acetate succinate) erodible (hydrophilic cellulose derivers, polyviny successfully. Opportunity to design modified output formats with appropriate API has been successfully demonstrated. We have already discussed the possibilities of thread design with different polymers showing different release profiles. However, the first step for FDM producing a thread It is an important step that needs to be studied. Appropriate quality control parameters should also be established to protect FDM technology as one of the manufacturing technologies. Various studies have investigated the possibility of combining a hot extrusion method with 3D printing technology. In order to produce fibers with fine mechanical and rheologic properties al, and tablets with drug reduction and structural cravings J. Zhang et al. controlled output tablets using thermal melt extrusion (HME) technology. When the tablets are 3D printed, the tablets are pressed directly out of the hole, and the tablets prepared from the visible compound are tested for drug release 3D-printed tablets are found to have a better controlled release compared to the other two tablets. In this study, a three-point bending test was introduced as one of the parameters to control the quality of the fibers produced to measure cracking pressure and fracture range as manifestations of thread stiffness and stiffness, respectively. Although high temperatures were used, no API or excessive degradation occurred during HME (140-160°C) and 3D printing process (200 ° C). Acetaminophen was used as a model drug and the polymers used were HPC LF, HPMC E5, Eudragit L100, Soluplus, and EC N14. These studies show that even FDM has the potential to increase the size of 3D printing and the variety of connectivity and APIs.

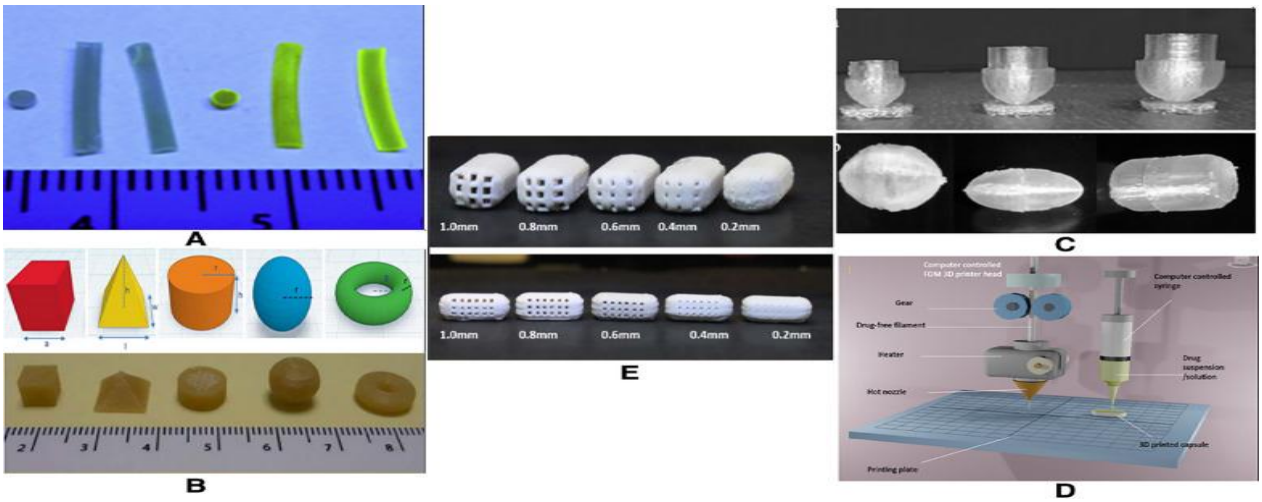

Fig 3: Examples of applications of 3D printing in pharmaceutical sector. (A) Images of PVA filament (left) and fluorescein-loaded filament (right) under UV light (Reproduced with permission from.[3] (B) design and printed tablets of different geometrical shapes using FDM technology (Reproduced with permission from.[3] Copyright 2015 Elsevier B.V.); (C) multicompartment capsular device printed using FDM technology (Reproduced with permission from.[3] Copyright 2015 Elsevier B.V.); (D) dual-nozzle FDM (Reproduced with permission from.[3] Copyright 2018 Elsevier B.V.); (E) channeled tablets (front and side view with channel sizes) (Reproduced with permission from.[3]

Apart from fabricating drugs as modified release systems, capsular devices have also been designed. A. Melocchi et al. manufactured swellable/erodible capsular device using hyproxypropyl cellulose (HPC) filaments (fig. 3C). Furthermore, A. Maroni et al. designed a multi-compartment capsular device using HPC (hydroxypropyl methyl cellulose), KIR (kollicoat IR), HPMCAS (hydroxypropyl methyl cellulose acetate succinate) and PEG (polyethylene glycol) 400 and 8000. To this date, capsule are prepared by injection molding with numerous steps until the finished product is obtained. 3D technology might provide a single-step alternative process for the designing and production of capsule devices of different size and materials.

Recently to help develop personalized medicine and to deliver a poorly soluble drug in a liquid form, a fully automated additive manufacturing process for liquid capsule with the capability to control the dispensed dose has been introduced. In this study, a dual FDM 3D printer was modified to include a syringe-based liquid dispenser (fig. 3D). This was used to fabricate a capsule shell through FDM 3D printing and instantaneously dispense either a suspension or a solution formulation of the model drug. As another recent advancement in FDM technology, the FDM printability of active ingredients ibuprofen-loaded sustained release polymer EC was investigated by introducing indices of melt rheology and mechanical property. Furthermore, sustained release tablets with predesigned scaffold structures were prepared by the FDM process.[3] Although various studies investigated tablets and capsular devices as dosage forms, other dosage forms, such as oral films, were not studied until recently. Fast dissolving films (FDF) of paracetamol were formulated using PVA filaments and PEO as the polymer. Although the disintegration time was slightly higher than that for commercial FDFs, this study proves the applicability of FDM in the formulation of FDFs. Formulations by FDM provides good mechanical strength and high resolution, but the used thermoplastic material should be suitable for extrusion and infill percentage of drug should be optimized to obtain the desired release profile. FDM has been most commonly discussed as the best technology for medicine printing and it can also formulate very complex geometrical dosage forms, which was not feasible with conventional manufacturing process. FDM technology surely opens a new revelation in personalized medicine.

In addition to making drugs as modified extraction methods, capsular devices are also designed. A. Melocchi et al. developed a flammable / inflatable capsular device using hyproxypropyl cellulose (HPC) fibers (fig 3C). In addition, A. Maroni et al. designed for multi-compact device using HPC (hydroxypropyl methyl cellulose), KIR (kollicoat IR), HPMCAS (hydroxypropyl methyl cellulose acetate succinate) and PEG (polyethylene glycol) and 8000. To date, the capsule is still being injected several times until the final product is obtained. 3D technology can provide a unique step-by-step process for the design and production of capsule devices of different sizes and materials.

More recently to help develop a self-made drug and to deliver a soluble drug in liquid form, a fully automated liquid pill formulation has been introduced that has the potential to control the extracted dose. In this study, a dual FDM 3D printer was modified to insert a syringe-based fluid (Fig. 3D). This was used to form the capsule shell using FDM 3D printing and immediately extract the suspension or formulation of the sample drug solution. As with other recent advances in FDM technology, FDM printing of active ingredients ibuprofen-loaded loaded polymer EC has been investigated by introducing melt rheology and mechanical properties. In addition, solid extraction pills with prefabricated scaffold structures were prepared by the FDM process.[3] Although various studies have investigated tablets and capsular devices as scale forms, other measurement forms, such as oral films, have not been studied until recently. The fast-dissolving (FDF) films of paracetamol are formed using PVA and PEO fibers as a polymer. Although the dispersion time was slightly higher than that of commercial FDFs, this study confirms the effectiveness of FDM in the formation of FDFs. The FDM structure provides good mechanical strength and high refinement, but the thermoplastic equipment that should be used for extraction and the filling percentage of the drug should be designed to obtain the desired output profile. FDM has been widely hailed as the most advanced medical technology and can also create highly sophisticated geometric measurement forms, which could not be used by the standard production process. FDM technology is certainly opening up a new era in customized medicine.

4. CHALLENGES

Our Challenges, Prospects and Vision 3DP technology has many unpredictable benefits; as the ongoing clinical development of 3DP will require vision, money and time.[1,2,10] We anticipate that 3DP-building activities from a comprehensive clinical complaint will include (i) software upgrades and improvements, (ii) new features or testing of old materials used for 3D applications; and (iii) the improvement of the manufacturing process for a variety of drug products, and (iv) clinical studies to evaluate the effectiveness, safety and stability of new 3D-based forms. Aside from the cost of creating new formulas or redesigning existing formats with 3DP, the built-in flexibility can be a great source of responsibility in a security look. It is important to prevent dosage or medication interference with the procedure to ensure that there is no contraindication or mixing of treatment medications to patients. It is also expected that 3DP-regulation control measures will be tougher to prevent illegal printing of drug products.[1] Therefore, depending on the product of the drug, it is expected that the widespread use of 3DP in pharmaceutical drug delivery will be significantly affected by regulatory problems and the need to have a builtin tamper pro-strategic approach.

Although, 3DP is a flexible approach to a wide range of active ingredients of pharmaceutical, it is important to note that the impact of 3DP on the physicochemical properties of the drug and the binding materials must be established in the case by case. This is because it is widely known that the therapeutic efficacy of any drug is influenced by structures such as drug interactions, polymorphic changes and stability in the dosage form. It can be expected that the fastest way to expand 3DP deployments in pharmaceutical drug delivery is to integrate 3DP with standard pharmaceutical technology. Such hybrid systems will work for the guaranteed performance of standard pharmaceutical technology and exploit all the benefits of 3DP in terms of customization, accuracy and minimizing material wastage.

5. CONCLUSION

3DP technology opens the door to a new era of advanced drug delivery with built-in flexibility that is well suited to customized / customized drugs. We believe that with patience and perseverance, 3DP will continue to make changes in developing new generations of pharmaceutical safe and efficient methods.

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