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3D Printing Technologies for Drug Delivery: A Review

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ABSTRACT
With the FDA's clearance of Spritam, the first 3D printed tablet, precedent has been established for the use of 3D printing in the manufacture of drug delivery systems. Complex compositions and geometries may be prepared thanks to the ability to accurately dispense small quantities, fine spatial control, and layer-by-layer assembly. Because of the great degree of flexibility and control offered by 3D printing, dosage forms including numerous active medicinal components with complicated and customized release profiles may be created. This technology has a one-of-a-kind potential to prepare customized dosages to meet the requirements of specific patients. This study will focus on the 3D printing technologies that are being used to fabricate drug delivery systems, as well as the formulation and processing factors that must be taken into account. This essay will also provide an overview of the many dosage forms that have been created utilizing these technologies in the past ten years.

Keywords
3D, Drug Delivery, Painting, Printing, Technology.

1. INTRODUCTION
Rapid prototyping includes methods for rapidly fabricating models and prototypes, and additive manufacturing is a subset of rapid prototyping; nevertheless, it is increasingly being regarded a scalable manufacturing process. The FDA recently approved a 3D printed or dispersible tablet, Spritam (levetiracetam), demonstrating that these technologies may be used to create complicated and personalized dosage forms [1]. particularly when the commodity is a fresh, emerging, and prospective instrument that may be utilized for both stability and reserves maintenance, with an interesting amount of attraction to speculating speculators seeking unexplained gains. Moving away from historically complicated, sluggish, and costly supply chains, as well as decreasing production to allow for the curing of another layer; this process is continued layer by layer until the required shape is printed, are all business motivations connected with printing medicines [2].
Parallel work on developing alternative additive manufacturing methods was ongoing throughout that time. The year that Hull submitted an invention for his lithographic equipment, a research associate and his consultant from UT Austin filed an intellectual property rights for plasma cutter cutting, a procedure wherein a laser light is digitized over a particle particles to pulse generator or fuse the granules; the concealer bed is then reduced, new particles is expanded, and the process repeats to form a complete object. Researchers at MIT are accredited with inventing "3D printer" after developing a layered approach that uses a typical print heads to drop "ink" or a binding solutions onto a powder particles to bind powdered, then continuing the operation bit by bit to just get the desired form. After that, the totally none or flimsy particles that represents as a computation assistance is excluded. The construction would be additionally modified, such as with heating, to strengthen the connection. 3D printing is the common name for this procedure [3-6].

1.1 History
Charles Hull is known as the "Founder of 3d Printers," since he designed, copyrighted, and commercialized the first 3d - printed hardware in the mid-1980s, and also the STL file structure that allowed current CAD applications to communicate with it. Hull's process, stereoscopic lithographic (SL), includes running a lasers over a fluid resin's interface, cures it, then immersing the stage and applying levels of hardened materials again until required form is achieved. Identity beeswax, flexible plastics, and melted metallic may all be used in this approach. Helisys, which is now Cubic Solutions, devised a layered item manufacture technique in 1996 that includes structuring (usually with lasers) and layering of secretion plates, with adjoining cells bonded by bonds or welds. Figure 1 the Schematic representation of CJ printing. Reprinted with permission from Derby [7].

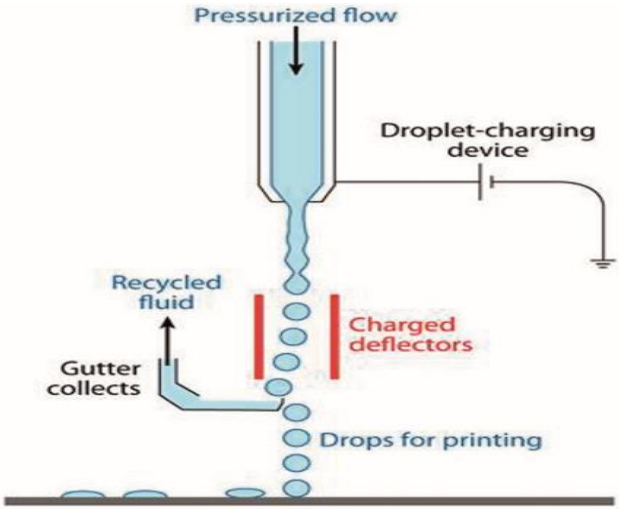

Figure 1: The above figure shows the Schematic representation of CJ printing. Reprinted with permission from Derby

1.2 3D Printing Technologies for Drug Delivery
The use of 3D inkjet printing and FDM methods in drug product research and development is becoming more common. The creation of innovative, versatile, and adaptable solid dosage form has been inspired by the application of these techniques in formulation production.

1.3 3D Inkjet and 3D Powder Bed Printing
A pressured flow is used in CJ printing to create a continuous stream of droplets. When the droplets leave the nozzle, they are charged and guided to the substrate or waste to be recirculated

by electrostatic plates. DOD is said to be more accurate and waste-free since it can generate droplet quantities as small as 1–100 pL at high speeds, but only when required. Thermal (also known as bubble) and piezoelectric actuation are the two most prevalent kinds of actuation used in DOD printing. Other techniques of droplet actuation, such as microelectromechanical systems, electrostatic systems, and others, are available or under study, but will not be addressed here. Thermal deterioration of the ink is a minimal danger due to the brief time and limited contact area, but it should be considered.

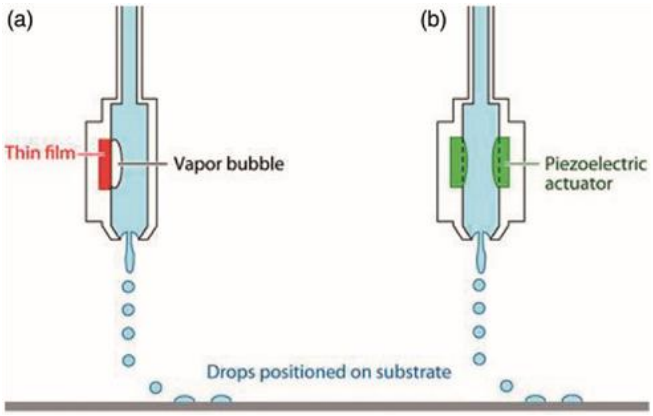

Figure 2: The above figure shows Schematic of DOD printing with (a) thermal and (b) piezoelectric actuation. Reprinted with permission from Derby[1]

When a piezo component, such as a crystalline or ceramics, is given a current, the dynamic component produces muscular device. When the component mainly focused, a compression wave is created, which forces the fluid out of the nozzles. Piezo resistive manufacturing has been shown to have direct monitoring over particle deposition and produces no heat, rendering it more desirable for developing drugs. 3D powder metallurgy painting is the process of depositing a liquid or "ink" onto a metal particle in order to bind the particles. The powder bed is then lowered, a metal powdered layer is applied, and the procedure is performed to attach the powder layers by layers to make the finished form.

1.4 Fused Deposition Modelling

Some commonly used polymers are commercially available as pre-processed, coiled filaments that can be easily fed into FDM printers. Fused filament modelling is another name for this method. The filament is heated to a molten state by heating elements/liquefier as it is passed through the rollers, allowing for extrusion via the nozzle tip. The material cools or is cooled and solidifies after deposition. A hot melt extrusion (HME) may be installed ahead from the printing nozzles for more versatility. This configuration allows for the fabrication of one-of-a-kind compositions, such as semi crystalline suspensions, which may be used as printed technology. Conversely, pinpoint extruded depositing (PED) has been modified to incorporate a tiny auger just before the tip, allowing for the fabrication of system with a dedicated; nonetheless, its use in the manufacturing of pharmacological formulation has yet to be verified. FDM is the depositing of material that would flow though with a nozzles or injection and solidify or be toughened to make a finished structure.

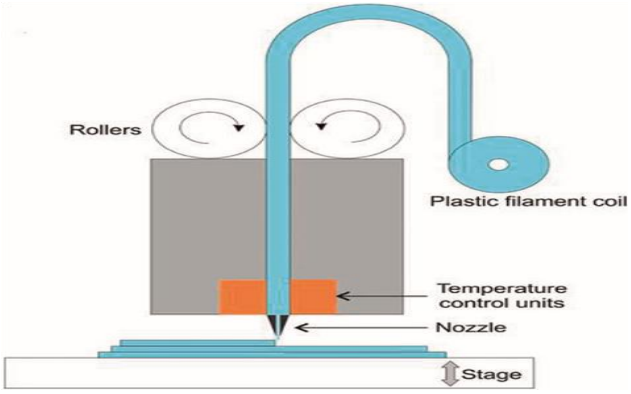

Figure 3: Schematic of fused filament modelling (FDM) printer [1]

1.5 Formulation and Process Parameters for Consideration

FDM creates 3D things by [1] extruding liquid material, [2] depositing it in a layer-by-layer manner to achieve the required shape, and [3] solidifying the molten material, typically by cooling it back to its solid state. FDM and HME are similar seeing as how the input materials should be ejected via a die or nozzles to help with production. As a consequence, the feedstock must possess the requisite viscous properties. These visco plastic features are affected by tube width, volume losses, and rotational speed, as well as the thermodynamic properties of the food, such as heat flux, heat resistance, weight, and crystallinity.

1.6 3D printing or treatment of implants

Immediately after intellectual property rights and published on 3D powder bed conductive ink, MIT engineers created disposable implantation to provide working prototype for their technology for making drug discovery gadgets. These investigations demonstrated the ability to correctly insert small quantity dye solution droplets as well as micro hardness manipulation, such as pipe diameter, as a consequence of cement layering and scanning speed. This approach demonstrated more morphology, contact area, geographical distribution, and other variables that may impact drug loading dynamics. Printable implantation have been shown to reduce or eradicate burst effects and give more regulated zero-order releasing when compared to standard implant fabrication processes such as compressed or blow moulding.

The printed implants had a more porous architecture than the compressed implants, resulting in a quicker and somewhat greater burst release of the medication from the printed implant than the compressed dosage form. Pulsed and bimodal drug release were shown in implants printed with an inner drug reservoir and inner and outside drug layers, respectively. The implants were demonstrated to deliver up to 400 mg in bursts or pulses and maintain a constant level of 120 mg or less for up to 90 days70.

2. DISCUSSION

3D technological improvements are normally configurable, with the capacity to build up tractor trailer or uninterrupted production plants for small volume (orphan items) to significant scale (generics) development and manufacturing, as the author has explained. Precision, limited distribution may increase control, uniformity, and security when using low-dose and/or powerful chemicals. 3D printing allows for the manufacture of various dosing levels in a pharmaceutical or portable setting, providing unrivalled adaptability in tailoring doses to suit patient needs. Furthermore, the ability to print delivery systems at the time of therapy may give patients more

medicinal potential. Because of their awesome comfort and control, 3D printer's techniques are ideal for pharmaceuticals of customizable, complex, and imaginative drug formulations. The use of tailored drug release profiles and personalised dose strengths in injectable screening, testing, and fabrication will only increase as more is understood about and a demand for them grows to better manage complex dosing schedules and various patient demographics.

3. CONCLUSION

A variety of reasons is driving the increasing usage of 3D printing technology in the manufacture of medication delivery systems. The technique enables the creation of multidimensional dose forms with precise material deposition, increased spatial control, and geometric flexibility. These characteristics enable the design and production of extremely creative goods, such as combination medication formulations with multi mechanism release behaviours, which may help patients with complicated dosage regimens comply more effectively. Identification and characterisation of new pharmaceutical materials suitable to processing should be part of future effort to allow medicinal product manufacturing utilizing 3D printing technology. In order to broaden the formulations system development, polymers substances for FDM, in particularly, should indeed be investigated. Both metal powders screen manufacturing and FDM may result in porous and/or partially fused constructions with a poor exterior roughness, reducing the compressive performance of the structural system. This may be handled by adjusting the composition (for example, lowering powdered grain size in the metal powder or enhancing binding ink content) or processing variables. Because of their high adaptability and efficiency, technological improvements are perfect for biopharmaceutical manufacture of bespoke, sophisticated, and novel dosage forms. As more is discovered about medication sustained release and personalised dose concentrations to better manage complex dosing schedules and various patient demographics, the demand for customised release of drug and personalized prescription concentrations grows, their usage in drug delivery system screening, development, and manufacturing will only grow.

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