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A Brief Review on 3D Printing Technology

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Abstract: ***3D printing is associate additive producing technique capable of manufacturing numerous 3D drug merchandise, medical devices, tissues and organs from digital styles. The first federal agency approved 3D drug product was Spritam, has inspired and attracted several analyzers during this during this research undergoing to develop numerous made-to-order dose forms. Three-dimensional printing technologies could be a new fast prototyping technique during which solid objects square measure constructing by depositing many layers in sequence. It becomes one amongst the foremost innovatory and powerful tools serving as a technology of precise producing of developed dose forms, tissue engineering and malady modeling. It's a valuable strategy to beat some challenges of typical pharmaceutical processes. This technology can reform the pharmaceutical producing vogue and formulation techniques. This review aims to introduce 3D printing, its history, advantages, challenges and numerous techniques utilized in fabrication of drug merchandise.***

Keywords: 3D printing, technology, manufacturing process

Nonstandard Abbreviations and Acronyms:
API: active pharmaceutical ingredients
BSA: bovine serum albumin
CAD: computer aided design
CIJ: continuous inkjet printing
DOD: drop-on-demand
EE2: ethinyl estradiol
FDA: Food and Drug Administration
FDM: fused-deposition modeling
FMDe: fused-deposition modeling after extrusion
FMDi: fused-deposition modeling after impregnation
HME: hot melt extrusion
HPMC: hydroxyl propyl methyl cellulose
NSAID: non-steroidal anti-inflammatory drugs
PAM: pressure-assisted microsyringe
PCL: poly (ε-caprolactone)
PEH: pseudoephedrine hydrochloride

1. Introduction

Drug delivery refers to approaches, systems, technologies and formulations for transporting a pharmaceutical compound within the body as needed to soundly come through its desired therapeutic result. The concept of drug delivery has greatly evolved over the years from immediate-release oral dose forms to targeted-release drug delivery systems. Since its initial use, three-dimensional (3D) printing technology has been used as a fast and cost-effective prototyping technique during a big selection of various applications as well as part, automotive, construction, jewelry, and fashion. 3D printing techniques are applied in little production volumes, like prototyping, customization, and also the producing of product with advanced styles, that square measure tough to manufacture with ancient strategies. 3D printing technology is presently utilized in an outsized form of medical applications as well as dental medicine, anatomical models, medical devices, tissue engineering scaffolds, tissue models and drug formulation. The conception targeting has staggeringly advanced throughout the years from prompt elimination through IR dose type to targeted unharness drug delivery systems. Indeed, the necessity of dominant the medication discharge profile to manage the retention, appropriation, digestion, and disposal of the medication quickly showed up as a key issue to reinforce item adequacy, wellbeing, and consistence to the patients.

3D Printing Technologies

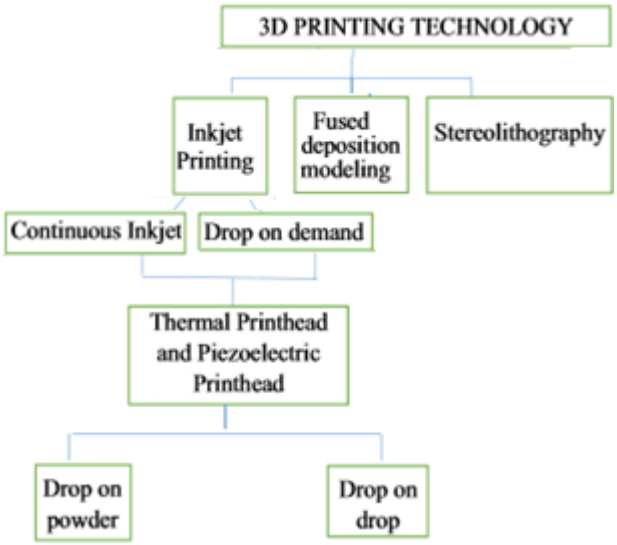

Figure 1: Schematic representation of various 3D printing techniques that are used to design different dosage forms

3D printing is manufacturing process in which drugs, implants and devices could be obtained by depositing material in a layer over layer manner to develop 3D objects. This process is also denoted as additive manufacturing (AM), rapid prototyping (RP), or solid free-form technology (SFF). Today there are number of printing processes available having different printing technologies, designs, speeds and resolutions. An excellent Computer Aided Design and Draft (CADD) software now used to build a design of the drug product. Further the design has been carved in a way to produce standard processing parameter such as extrusion and platform temperature, infill percentage, speed of printing, etc using this software. Once it is done, 3D printer continues to follow instructions to produce the drug product. On the basis of the acquired printing technique, raw materials may be processed into granules, filaments, or binder solutions to assist the printing process. Raw materials are added and solidified in an

automatic, layer-by-layer fashion to produce the desired drug product. After printing, products may then dried, sintered and polished subsequently. At this stage, unprinted material can be harvested and recycled for continued use in printing process. The quality by design technique can also be utilised for varying pharmaceutical manufacturing procedures and drug design parameters. At initial stage, the drug and excipients are used in processing of raw material followed by drying, polishing and packaging.

Inkjet Printing: Inkjet printing is an umbrella term to describe systems that with the help of pattern-generating device are able to produce digitally controlled formulation and placement of small liquid drops onto a substrate. Inkjet printing technology is basically based on two main droplet formation system: continuous jet (CJ) printing and drop on demand (DOD) printing.

1.1 Continuous Jet (CJ) Printing

CJ printing depends on a pressurized flow to produce a continuous stream of charged droplets. The electrostatic plates in the system projects the droplets on to the substrate where they get deposited. The waste generated during process also gets re-circulated and can be further used. CJ and Drop on Demand (DOD) printing both have embedded printer head either thermal or piezoelectric that has the control over viscosity of liquid and its drop formation characteristics.

1.2 Drop on Demand (DOD)

DOD printing has a more precise and less wasteful execution and contains up to 1000 nozzles. These printheads are primarily triggered by thermal and piezoelectric trigger mechanisms. Induction of electric current produces heat in the thermal printhead leading to generation of bubble in volatile material being printed. This mobilizes small volume of liquid out from the nozzle owing to drop formation. Thermal inkjet printing requires the use of high vapour pressure solvents and produces high temperatures that can results in the degradation of heat-liable bioactive compounds. On the other hand, piezoelectric printheads is associated with piezoelectric materials that expand and contract when electrical current is applied. This change can create enough pressure to eject a droplet due to development of pulse that make fluid of shear rate about 105 demonstrates the two printing systems. When the formulated layer deposits on each other in order to produce a solidified layer of material is known as drop-on-drop deposition and when printer head deposit the droplets onto solid material is known as drop-on-solid deposition. Drop on powder deposition has been divided into two subtypes: drop-on-drop deposition and drop-on solid deposition. The most important benefit with both the system is multiple depositions can be made on same time using different materials and colors which are printed accordingly in a layer by layer manner. The droplet position themselves to produce different layer of design while in “powder bed fusion” the drop on solid deposition which is also known as “powder bed fusion” in which the droplets are directly printed onto the solid material.

Fused Deposition Modelling (FDM):
FDM printers are very common and inexpensive method utilizing a printhead similar to an inkjet printer. However, instead of ink, beads of heated plastic are released from the printhead as it moves, building the prototype in thin layers. This printing technique use thermoplastic polymers such as poly (lactic acid) (PLA), polyvinyl alcohol (PVA) or acrylonitrile butadiene styrene. As demonstrated in Molten materials (API and polymer mixtures) are allowed to pass through the nozzle and deposited on a platform in a layered way in the form of filaments. These filaments settle after hardening. Thus, the process also known as Fused Filament Fabrication. The deposition of material depends on nozzle diameter, the pressure drop and feed rate. Advantage of FDM over powder-bed printing is production of multifaceted scaffolds with accurate dosing system. FDM also offers good mechanical strength with dosage form of different kinetics by modifying the infill percentage, 3D model design or surface area of the formulation Temperature sensitive APIs and limited thermoplastic material limits the use of FDM printing technology.

Stereolithography
Stereolithography was designed by Charles Hullin in 1980 which is also known as Laser based writing system. The principle is based on photopolymerization in which free radicals are released after the interaction between photoinitiator and UV light. In stereolithography apparatus (SLA), specific surface regions of photosensitive liquid resin undergo localized polymerization by exposure to a UV laser. This technology got commercialized in 1986. In stereolithography ultraviolet light is allowed to traverse to the surface of liquid resin leading to x/y axis exposure of each distinct layer modified as the z axis incrementally evolves in the build process. When a layer solidifies, a new layer of liquid resin are again deposited in a way to produce a 3D printed models. These liquid resins are deposited on over one another until a finished product obtained. When the portion is complete, the excess resin is drained off which can be reused again. The formed parts are then washed to remove excess resin and the support structures are removed physically. A UV flood post-curing step may be included for conversion of photopolymer depending on type of resin material used. Usually the finished product has some surface roughness appearing similar to molded parts which is then furnished using treatments with primers, paints, sealant or metallic coatings. Stereolithography uses laser beam developing layers of solidified polymer whereas another technique named Digital Light Processing (DLP) utilize high definition projector which develop cross-sectional objects in form of volumetric pixels (voxels). DLP is usually faster than SLA as the whole layer can be obtained at once. In fact, the laser based printing as a methodology for 3D printing is mainly attractive for several reasons: building high level of resolution, providing smooth parts which do not require finishing processes, enables good z axis strength owing to chemical bonding between layers, time consuming, and printing of clear and high resolution objects. The important parameter needed to be controlled in SLA printing is the thickness of cured layer depending on energy of light to which the resin is exposed.

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