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A REVIEW ON 3D PRINTING

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ABSTRACT:

Three-dimensional printing is a revolutionary technique that uses computer aided design software and programming to create three dimensional objects by placing material on a substrate. 3D printing is an additive layer manufacturing techniques, where consecutive layers of material are deposited or solidified to form a 3D structure. Medicinal substances is configured in three dimensional with computer assisted design module and transformed to a machine legible form which suggests the exterior emerge of the 3D dose form, then it sliced this surface into number of different printable coats and convey these layers to the machine. The different 3D printing techniques has been developing and developed to fabricate novel solid dosage forms, which are among the most well-known and discrete products today. The 3D PRINTING technology has caught the attention of medical devices industry and pharmaceutical industry due to its applications on various platform in health care industry. Even though this technology exists for a long time it is of public interest highly now due to the approval of 3-D printed tablet and other medical devices and also with the advent of USFDA's guidance on technical considerations specific to devices using additive manufacturing which encompasses 3-dimensional (3D) printing has triggered many thoughts about this technology which needs to be considered for successful delivery of intended product. This paper presents regulatory agencies expectations, limitations, problems in establishing such setups for production of drug products, advantages, disadvantages, applications, methods and associated risks involved in manufacturing. It also provides the comprehensive review of the current status of research and development on this platform.

INTRODUCTION:

Drug delivery is the technology and formulation developed to efficiently transport a pharmacologically active compound in the body to achieve therapeutic efficiency in a safe manner. The efficiency and safety of a pharmaceutical product can be improved by controlling the release profile which in turn modulates the pharmacokinetics of a drug. The interspecies variability is an obstacle frequently faced in the clinical scenario. Customized medicine and dosing receives increasing attention because of the high chances of undesirable side effects. The probability of adverse reactions is higher in the pediatric and geriatric populations when the bulk manufacturing of pharmaceuticals concentrates on the average population [1, 2]. 3D printing can play a significant role in multiple active ingredient dosage forms, where the formulation can be as a single blend or multi layer printed

tablets with sustained release properties. This reduces the frequency and number of dosage form units consumed by the patient on a daily routine. 3D printing technology has high potential in individualized dosage form concept called the polypill concept. This brings about the possibility of all the drugs required for the therapy into a single dosage form unit. Three dimensional printing technology is a novel rapid prototyping technique in which solid objects are constructed by depositing several layers in sequence. The rapid prototyping involves the construction of physical models using computer-aided design in three dimension. It is also known as additive manufacturing and solid free form fabrication [3]. 3D printing technology has enabled unprecedented flexibility in the design and manufacturing of complex objects, which can be utilized in personalized and programmable medicine. It is an effective strategy to overcome some challenges of conventional pharmaceutical unit operations. [1, 4]

History:

3D Printing is a platform for personalized medicine from the beginning of 1990. There are major successes in 3D printed medical device, FDA's Center for Device and Radiological Health (CDRH) has revised and cleared 3DP medical devices.[6]The first 3D printing method used in pharmaceutics was attained by inkjet printing, a binder solution onto a powder bed, therefore the particles bind together. The technique was repeated until the final desired structure was obtained. This first happened in the early 90's at the Massachusetts Institute Technology developed and patented by Sachs et al.7 In 1989 Scott Crump filed a patent on another 3D printing technology, fused deposition modeling, to harden the surface where extruded polymer filaments heated into a semi-liquid state and extruded through a heated nozzle and deposited onto a build platform as layer by layer.8,9 Inkjet printing was the technique used to manufacture Spritam tablets (levetiracetam) for oral use, the first 3D printed drug approved by the Food and Drug Administration (FDA) in 2016 by Aprecia Pharmaceuticals. 3D printing is most advanced technique in the fields such as automobiles, aerospace, biomedical, tissue engineering and now in the pharmaceutical industry (initial phase). FDA motivates the development of advanced manufacturing technologies such as 3Dprinting and by means of risk-based approaches.

STEPS INVOLVED IN A 3D PRINTED DOSAGE FORM:

Pharmaceutical product is designed in three dimension with computer aided design Design is converted to a machine readable format which describes the external surface of the 3D dosage form. The computer program then slices this surface into several distinct printable layers and transfers that layerby-layer to the machine [1, 3].

Advantages of 3d Printed Drug Delivery:

1. High drug loading ability when compared to conventional dosage forms
2. Accurate and precise dosing of potent drugs which are administered at small doses
3. Reduces cost of production due to lesser material wastage
4. Suitable drug delivery for difficult to formulate active ingredients like poor water solubility, drugs with narrow therapeutic window
5. Medication can be tailored to a patient in particular based on genetic variations, ethnic differences, age, gender and environment.
6. In case of multi drug therapy with multiple dosing regimen, treatment can be customized to improve patient adherence
7. Avoids batch-to-batch variations seen in bulk manufacturing of conventional dosage forms [9].

DISADVANTAGES:

1. Problems related to nozzle are a major challenge as stopping of the print head which affects the final products structure
2. Powder printing clogging is another hurdle
3. Possibility of modifying the final structure on to mechanical stress, storage condition adaptions and ink formulations effects
4. Printer related parameters and these effects on printing quality and printercost.[10]

TECHNIQUES IN 3D PRINTING:

Inkjet Printing:

Inkjet printing known as 'mask-less' or 'tool-less' approach for its desired structure formation mainly depends upon the inkjet nozzle movement or substrate movement for an accurate and reproducible formation. In this methodology, the Ink is deposited onto a substrate either in the form of Continuous Inkjet printing / Drop on demand printing. Hence it provides a capability of high-resolution printing. It has a low cost, rate of processing in printing and generation of low level of wastes. It gives CAD information in a 'direct write' manner and process material over large areas with minimal contamination.

Thermal Ink-Jet Printing:

In thermal inkjet printing, the aqueous ink fluid is transformed to vapours state through heat, expands to push the ink drop out of a nozzle.14 It is used in the preparation of drug-loaded biodegradable microspheres, drug-loaded liposomes, patterning microelectrode arrays coating, loading drug eluting stents. It is also an effectual and applied method of generating films of biologics without negotiating protein activity.

Extrusion 3D Printing:

In this method the material is extruded from the automated nozzle onto the substrate without any higher support material. It is only utilized to fabricate tablet containing Guaifenesin act as expectorating. The components that can be extruded are molten polymers, suspensions, semisolids, pastes.

Powder Based 3D Printing:

This method customs powder jetting/powder bed to feast thin layers of powder and instantaneously applying liquid binder drops with inkjet printers. The ink (binders and APIs or binder solutions) is sprinkled over a powder bed in two-dimensional (2D) approach to make the decisive product in a layer by layer fashion. The adaption of this approach into pharmaceutical manufacturing is at ease than other approaches as powder and binder solutions are broadly used in the pharmaceutical industry. The own disadvantages of this approach are; to remove solvent residues additional drying is required, during printing excess powder accumulates and contributes to wastage and due to the permeable design of the powder the drug delivery system's mechanical strength may poor.

Hot melt extrusion (HME):

Hot melt extrusion (HME) is the method of melting polymer and drug at elevated temperature and the pressure is employed in the instrument sequentially for blending. It is a continuous manufacturing technique that involves feeding, heating, mixing and shaping. In recent years, it has proved that Hot melt extrusion capable to optimize the solubility and bioavailability of moderately soluble drugs.

APPLICATIONS OF 3D PRINTING:

1. Potential use in improving process, modifying performance for industrial design, aerospace, medical engineering, tissue engineering, architecture, pharmaceuticals.

2. It mostly targets on the two potential sites to rise pharmaceutical product development to unexplored areas, manufacturing sophisticated structures for the delivery and personalized medicine.

3.In Healthcare industry to create dental implants.

4. On fabricating an organized release multi-drug implant for bone tuberculosis remedy.

5. Helps in Organ printing, biomaterials and cell-laden materials.[(11)]

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