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CONCEPT OF THREE DIMENSIONAL PRINTING INPHARMACY

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ABSTRACT

Three dimensional printing enables the development of diverse geometrics through computer aided design (CAD) using different techniques and materials for desired application such as pharmaceutical drug delivery medicine and was approved by food and drug administration in 2015. There has been a growing intrest in 3D printing for drug manufacturing and most of the preoperative models have centred on a dental and craniomaxillo facial area, it applied for surgical planning, prosthetic and other applications. Many researchers have attempted to use computer aided design and computer aided manufacturing (CAM) to realize scaffold that provides a 3dimensional environment for regeneration of tissues and organs. As a result several 3D printing technologies includes stereo-lithography, deposition modelling, inkjet based printing and selective laser sintering have been developed. Due to 3D printing technology precise and unique doses can be engineered and fabricated according to individual prescription. This review composes basics, types and technique used advantages and disadvantages of 3d printing.

KEYWORDS: Three dimensional printing (3DP), Computer aided design, adverse drug reaction, Extrusion, Additive manufacturing.

INTRODUCTION

In a day today life there are various technologies were introduced but three dimensional printing is an additive manufacturing method where by successive layers of material are deposited to form a 3 dimensional structures.[1] It is a method to produce 3D objects from digital model by fusing or depositing material in successive layer correspond to the objects with different geometrics, this process is known as additive manufacturing.[2] It is matchless

method which uses computer aided drafting technology and programming to make 3D object.[3] It is a process creating or making 3D solid object from digital file.[4]

Now a days 3D printing was extent in large amount in market, due to this we make any ranged and structured required object or drug. Because of 3D printing technology different types of drug systems instance oral controlled release system micro pills, microchip, drug implants, fast dissolving tablets and multiphase release dosage forms have been developed.[5] The practical approach of additive manufacturing is called rapid prototyping[6] and its advantages include the reduction of prototyping time and costs, easy modifications of product at designed level, the possibility of manufacturing of smaller objects, individualized of product series or structures impossible to be formed with subtractive technique.[7]

In 2015, the FDA approved SPRITUM® the first 3D printed drug product, which opened a new chapter of pharmaco printing in pharmaceutical manufacturing.[1] The importance of 3D printing in personalized medicine becomes significant with issues reported on ADR, particularly among paediatrics and geriatric patient.[8,9] It had been recorded that the percentage of hospital admission in England due to ADR cases increased by 53.4% from 60055 to 92114 in 2008/2009 to 2014/2015, respectively.[9] Three dimensional printing is forecast to revolutionise the pharmaceutical sector, changing the face of medicine development, manufacture and use. On the basis this review will introduce some 3DP technologies suitable for pharmaceutical manufacturing and also their application to the development of dosage forms indicating the feasibility of this technique in regular commercial product.

HISTORY

Three dimensional printing is a platform for personalized medicine from the beginning of 1990. There are major successes in 3D printed medical device, FDA's centre for device and

radiological health (CDRH) has revised and cleared 3DP medical devices.[10] 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.[11] The idea of 3DP has evolved from early 70's of the 20th centuarywhen Pierre A.L. ciraud described the method of application of powdered material and subsequent solidification of each layer through the action of high energy beam. The first commercially available technology created by CHUCK HULL was stereo-lithography (SLA). This method was based on photo polymerization of liquid resin by ultraviolet light. In 1989 Scott crump field a patent on another 3D printing technology is fused deposition modelling.

3DP TECHNOLOGIES APPLICABLE INPHARMACY

Various 3DP methods have been developed by varying its energy source, material source and other mechanical characters. Among them, the common 3DP technologies applicable for pharmaceutical areas are printing based inkjet (IJ) system, nozzle based deposition system, extrusion 3D printing and laser based writing system.[12] this can be subdivided into several subtypes.

1] Printing based inkjet (IJ) system

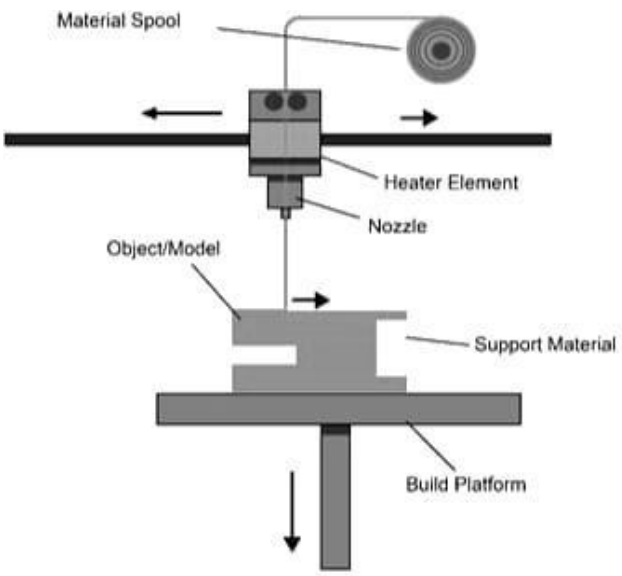
Inkjet Printing:- It comprise two types of technologies namely, continuous inkjet printing (CIJ) and drop on demand printing (DOD). CIJ technology creates a continuous stream of ink through an orifice of 50-80 um diameter by using high pressure pump. DOD technology produce droplets of 10-50 um with a volume of 1-70 pL.[13] The main criterion in developing a formula of API for printing in the inkjet print system is the performance of carrier formulation during printing, which is strongly influenced by rheological parameters such as fluid viscosity, velocity and surface tension.[14,15,16]

The main advantage of inkjet printing method in the pharmaceutical application is its high accuracy in creating 3D drug products. The technology also opens up new possibility for usage of new active pharmaceutical ingredient and personalization in drug discovery.[17]

Thermal Inkjet Printing:- In thermal inkjetprinting, the aqueous ink fluid is transformed to vapours state through heat, expand to push the ink drop out of a nozzle.[18] It is used in the preparation of drug loaded biodegradable microsphere, drug loaded liposomes, patterning microelectrode arrays coating, loading drug eluting stents.[19,20] It is also an effectual and applied method of generating films of biology'swithout negotiating protein activity.[21]

2] Nozzle based deposition system

Fused deposition modelling (FDM) is commonly used method in 3D printing, the materials aresofter or melt by heat to create objects during printing.[22]



Similar to 3DP, the layout for FDM consists of print head able to move along x and y directions above a build platform. The polymer is extruded through theheated nozzle and laid down as filaments according to CAD design. The build platform is then lowered and another layer can be built, until the scaffold is completed.[23]

In this method, thermoplastic materials pass down between two rollers to nozzle tip where it will be subsequently extruded. Before extrusion, the materials are heated by a temperature controlledconditions to ensure their semi-molten form during the extrusion process. Then, the semi-molten polymers solidify, the printing stage is lowered and the same process is repeated until desired 3D objectis obtained.[24, 25]

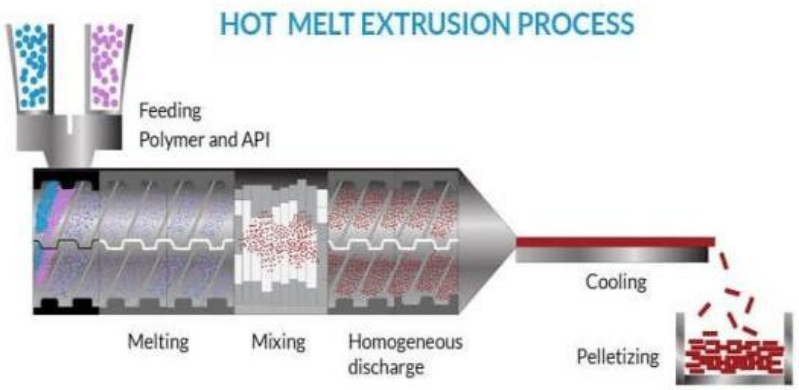
3] Extrusion 3D Printing

In this method the material is extruded from the automated nozzle onto the substrate without any higher supportive material. The components that can be extruded are molten polymer, suspension, semisolids, pastes.[26,27]

Zip Dose:- Personalized 3D printed medicine with ahigh drug load are produced using porous material. The procedure relies on high dissolution and disintegration levels. It is the world's initial and only FDA approved commercial scale 3DP in current therapeutic areas for pharmaceutical manufacturing areas. It has a distinctive digitally coded layering and zero compression practices, used for tablet formulation with large dosage and prompt disintegration. Hence, it helps in over whelming a difficulty in swallowing.[28]

SPRITAM-R (anti epilepsy drug) is an oral dispersible tablet, marketed by APRECIA pharmaceutical based on powder bed fusion by layerby layer production system which contain active ingredient, excipients and a binder liquid to producea matrix tablet.[29]

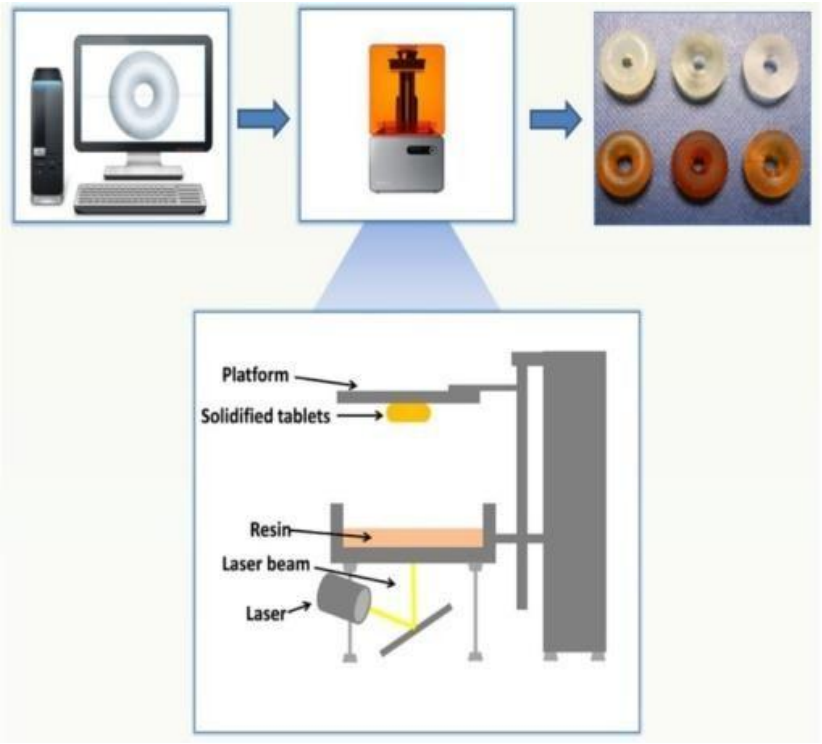
Hot Melt Extrusion:- Hot melt extrusion (HME) is the most popular technique in polymer processing and can be utilized to blend drugs with polymers and extrude the formulation through a circular orifice to form a rod shaped filament for FDM 3D printing.



It is a continuous manufacturing technique that involve feeding, heating, mixing and shaping.[30] In recent years, it has proved that hot melt extrusion capable to optimise the solubility and bioavailabilityof moderately soluble drugs.[31]

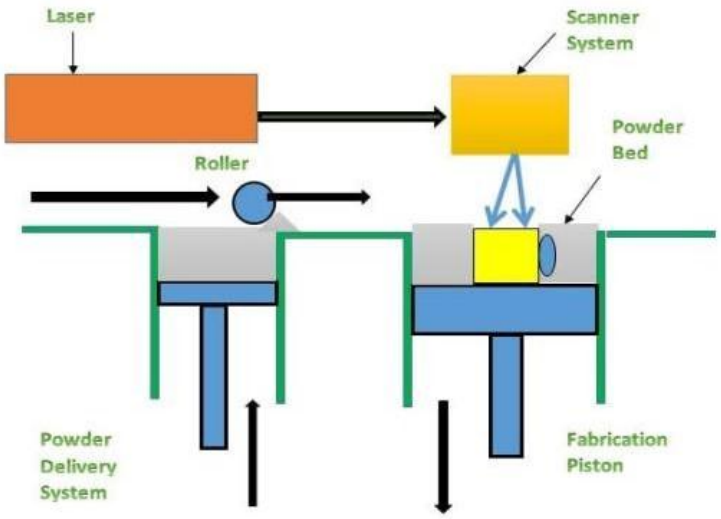
4] Laser based writing system

Stereo-lithography:- Stereo-lithography is the method of computer regulated laser beam is used tomake liquid polymer/resin as solid, means creating a3D structure.[32]



Stereo-lithography requires the use of supporting structures which serve to attach the part to the elevator platform, supports are generated automatically during the preparation of 3D computer aided design model for use on stereo-lithography machine, supports must be removed from the finished product manually, unlike in other, less costly, rapid prototyping technologies.

Selective laser sintering:- Selective laser sintering (SLS) act as a way in powder bed to bind. The laser is designed to draw a specific pattern on the surface of powdered bed during the printing process, thus creating a 3D structure.[5]



ADVANTAGES OF 3D PRINTING INPHARMACY

- ✓ The ability to create tablets of any shape and size.
- ✓ The ability to set the dosage individually for each patient.
- ✓ The ability to replace a large number of drugs with one tablet, which also reduces the frequency of medication.
- ✓ High drug loading ability when compared to convectional dosage forms.
- ✓ Accurate and precise dosing of potent drugs which are administered at small doses.
- ✓ Manufacture of small batch is feasible andthe process can be completed a single run.
- ✓ Reduced production cost due to less wastage of material.
- ✓ 3D printers capture minimal space and are affordable.

DISADVANTAGES OF 3D PRINTING INPHARMACY

- ✓ Powder printing clogging is another hurdle.
- ✓ Problems related to nozzle area major challenge as stopping of the print head which affects the final product structure.
- ✓ It is not very Eco-friendly.
- ✓ 3D printing machines are expensive.

CHALLENGES AND APPLICATIONS

1] **Technical Challenges:** Depending on the printing technology applied, the printed material may have inadequate mechanical properties and may have high insignificance making it difficult to further process this dosage form. Defects can occur, especially during the packaging of printed tablets, which can lead to rejection of entire batches. For some 3DP technologies, such as SLA, a lot of unprinted materials produce after process.

2] **Regulatory Challenges:** From a regulatory perspective, 3D printed dosage forms must meet thesame requirements as traditionally manufactured dosage forms. However, at this stage a large gap exists in the regulatory framework while the guidelines for established procedures are well implemented and standardisation there are no guidelines in the 3DP process. Health authorities around the world recognized the lack of guidance and initiated the process of developing standards anddefining practical guidelines.

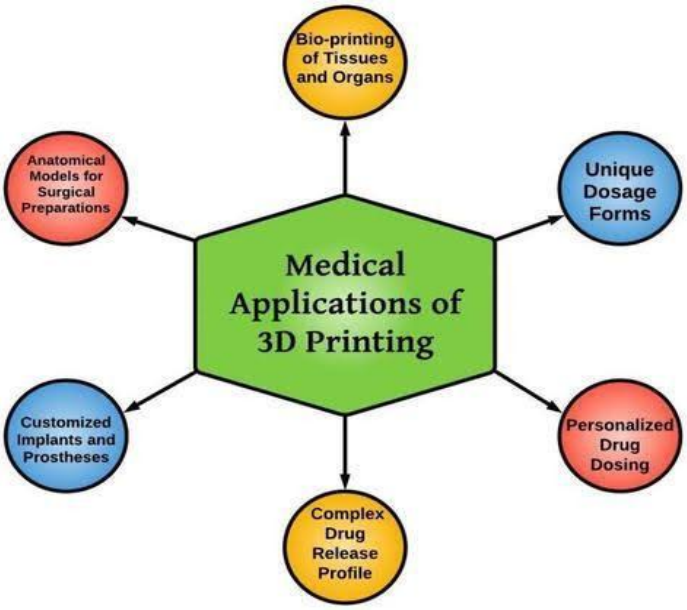
3] **GMP Challenges:** Qualification standards for 3Dprinter manufactures must be defined to meet GMP requirements especially, the topic of cleaningradiation should be addressed to avoid cross contamination. The regulatory and GMP challenges outlined for establishing 3DP as a manufacturing process for pharmaceutical dosage forms should be addressed

jointly by health officials and pharmaceutical manufacturers.

CONCLUSION

Three dimensional technologies can make complex formulations as cost and time efficient. The technology gives better drug spatial distributions, more accurate drug dosing and complex geometrics compared to conventional drugs. 3DP is an innovative and promising way for on demanding personalized dosage manufacturing, which improves patient adherence and effectivity of drugs which reduced the side effects. Above methods to prepare 3D printed drugs are most important in pharmacy to secure the future with rapid manufacturing. It is widely used therefore it accelerate the clinical practice of more patient friendly dose.

In future 3D printing can be regulated and followed by pharmaceutical and all other sectors with neededlevel of safety and security concerns.



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