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3D Printing Technology: The Impetus Concept in the Drug Delivery

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ABSTRACT

The 3D printing technique is a highly turbulent approach nowadays in pharmaceutical technology. It is the continuous improvements towards the latest concept in the drug improvement to understand the better quality of the raw material as well as the production process. In the current era, it is the fastest growing technology. It is advantageous in different aspects like reducing the need of the prototyping, reduce the time & costs, helps in the easy modification of the process. It is a versatile & powerful manufacturing tool. A 3D printing technique in the field of the biomedical field is known as the bio-printing. Different techniques are used during the 3D- printing process which is as follows- Binder deposition, Inkjet printing, Material jetting, Power bed fusion, photopolymerization, Power bed, etc. The need for 3D printing technology is due to the technological advancement in therapy advancement. It also helps in the development of the Novel Drug Delivery System (NDDS). It has been applied for the manufacturing of the pharmaceutical solid dosage form as well as the combination of the solid & liquid dosage form. It is mainly used to form personalized medicine which is the combination of the different pharmaceutical ingredients which are used in the treatment of the different diseases. Nowadays this technique has been followed up by the different pharmaceutical vendors so as to provide the patient's customized medicinal treatments day by day. This technique has also been used to customized the release profile of the different drugs like to produce the sustain as well as extended release formulations. From all the above data we concluded that 3D printing is the versatile technique which is used to enhance the use of the combination therapy nowadays.

Keywords: ***3D-*** *3 Dimensional,* ***NDDS****- New Drug Delivery System,* ***FDM****- Fused Deposiion Modeling,* ***DDD*** *- Drug Delivery Devices,* ***AM****- Additive Manufacturing,* ***RP*** *- Rapid Prototyping*

Introduction

Nowadays, 3D- printing technology is a highly turbulent approach in the sector of pharmaceutical technology. The main asset of 3D- printing technology in the pharmaceutical sector is to produce the customized dosage forms which allied with the tailored dosages, shapes, sizes & due to its release characteristics. 3D- printing technique covers the drug development process, preclinical development & clinical trials, through to crucial medical care. **(Trenfield *et.al.,* 2018).** 3D- printing technique is the continuous impetus towards the latest concept in drug design for better understanding of the raw materials properties used in the production & during the various processes to assure the better quality of dosage forms. Physiochemical & Biopharmaceutical characteristics of API's (Active Pharmaceutical Ingredients) was considered & studied during each stage of product development **(Tariq et.al 2019).** By-product development, we are mainly focusing on novel dosage forms & various technological processes. We observed that day by day the demand of the conventional medicines over the different diseases overcoming by the demand of the customized personal medicines like different layered 3D- printing tablets etc., which is the most revolutionary concept in the current era. In the current era, the 3D printing technique is the fastest developing technology, but the present development nowadays still needs to broaden the application. The fabrication of the 3D-printing products was defined by ISO i.e., International Standard Organization. 3D- printing tablets have different advantages like-

1. Reduce the need for prototyping
2. Reduce Time & Costs
3. Helps in easy modifications of the product

Moreover, the applications of the 3D printing tablets in the different departments like Science & Engineering enhanced since 2012. The number of the scientific papers also increased by the 27% since the last five years i.e., 2012 to 2017 from 59 to 1573, these hike shows the revolutionary use of the 3D- printing technology in the pharmaceutical product development. 3D- printing technique also have achievement in the biomedical research field as well. The approach of the 3D- printing in the biomedical research field is known as bioprinting. The issue only related to this approach is the regulatory related issue due to its

personalized dose variation from person to person. 3D-printing technique is the versatile & powerful tool in the manufacturing of various devices. 3D- printing technique is the most favorable example of the additive manufacturing (AM) in which various layers are prepared separately from the 3D- model data & then the various materials are joined layer by layer by the use of the joining material. **(Jamroz W., Szafraniec J., Kurek M., Jachowicz R., 2018).** Nowadays, 3D- printing technology gets matured enough for the ease of the peoples may apply online with the help of the open source software with relatively lower cost. The evolved form of the 3D-printing technology used in the broad range of applications like tissue engineering, dentistry. Although after the above evolution in the pharmaceutical field this technology is still at its infancy stage & its full potential has needed to be explored still. In the pharmaceutical field 3D-printing technique overcome the different challenges which we are facing in the conventional dosage forms manufacturing like milling, mixing, granulation & compression which affects the grade of the finally developed dosage form & it's different characteristic properties like drug loading, drug release, drug stability, etc. **(Horst J.D., *et. al.,* 2018).**

Techniques Used in the 3D- Printing pharmaceutical manufacturing:-

There are different techniques of 3D- printing which we follow during the pharmaceutical products manufacturing which is as follows:-

1. Binder Deposition
2. Inkjet Printing
3. Material Jetting
4. Powder Bed Fusion
5. Photo-polymerization
6. Pen-based 3D- printing & modeling
7. Fused Deposition Modelling (FDM)

From all the above techniques FDM is one of the most recently discovered & precise method for the manufacturing of the personalized pharmaceutical oral solid dosage form. But on the other hand, the challenge we are facing in this technique is about the availability of the materials used in this technique like thermoplastic polymers & not ideal for optimizing the dosage amount for the poorly water-soluble drugs.

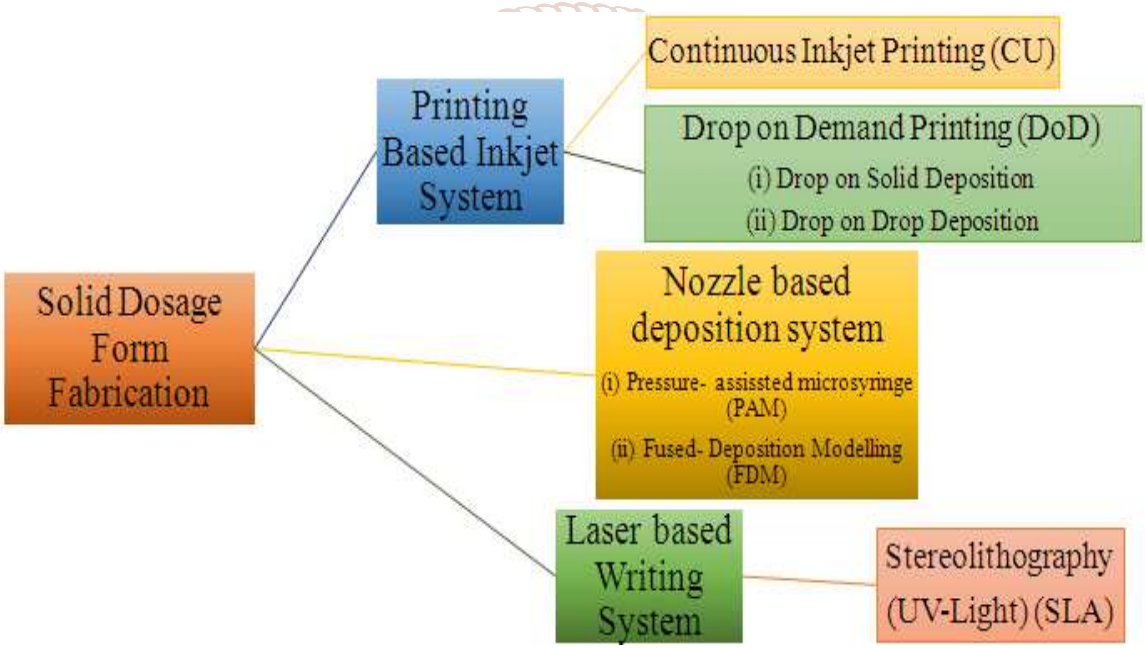

Figure1.1. Schematic Diagram Representing different 3D- Printing Techniques used to fabricate Drug

In the current era, there are various pharmaceutical formulations available marketed developed by the use of different 3D-Printing Technique. The list is given below:-

Sr. No.	3D-Printing Technique Used	Dosage Form	Active Pharmaceutical Ingredient	Polymer	Author
1.	SLA	Hydrogel	Ibuprofen, Riboflavin	Polyethylene Glycol, Diacrylate	Martinez *et. al*
2.	FDM	Tablet	Felodipine	PEG, PEO, Eudragit, Tween 80	Alhijjaj *et. al*
3.	FDM & SLA	Nasal Spray	Salicylic Acid	FPLA, PCL	Goyanes *et. al*
4.	FDM	Tablet	Haloperidol	-	Solanki *et. al.*
5.	FDM	Nanocapsules	Deflazacort	PCL (Poly-ethyl- caprolactone)	Beck *et.al.*
6.	FDM	Tablet	Hydro-chloro-thiazide	-	Sadia *et. al*
7.	FDM	Tablet	Nitro-furantoin	Poly-lactic Acid, HPMC	Boetkr *et. al*

Various Developed Pharmaceutical Formulations by the 3D- Printing Technique

Type of 3D process/technique	Dosage form	Active ingredient/polymer	Author
Stereolithography (SLA)	Hydrogel	ibuprofen, riboflavin, polyethylene glycol, diacrylate	Martinez *et al.*
FDM 3D printing	Tablet	felodipine, PEG, PEO, Tween 80, Eudragit EPO	Alhijjaj *et al.*
UV inkjet 3D printed	Tablet	ropinirole, cross-linked poly(ethylene glycol diacrylate) (PEGDA)	Clark *et al.*
semi-solid extrusion 3D printing technique in combination with UV- LED crosslinking	Tablet	prednisolone, polydimethylsiloxane (PDMS)	Hollander *et al.*
(FDM) and (SLA)	model of a nose adapted to the morphology of an individual	FPLA-salicylic acid and PCL-salicylic acid	Goyanes *et al.*
FDM	Tablet	haloperidol	Solanki *et al.*
Thermal Inkjet (TIJ) Printing	Solid dosage forms	Rasagiline mesylate	Genina *et al*.
(FDM) and Hot Melt Extrusion (HME)	Tablet	domperidone, hydroxypropyl cellulose (HPC)	Chai *et al.*
FDM	Nano-capsules	deflazacort, poly(ε-caprolactone) (PCL)	Beck *et al.*
FDM and HME	Compartmentalized shells	rifampicin (RIF) and isoniazi (ISO)	Genina *et al*.
FDM	Tablet	Hydrochlorothiazide	Sadia *et al.*

Discussion

The technological advancements in the pharmaceutical field are constantly improving and provide various possibilities for meeting the needs of personalized drug therapy. The three-dimensional (3D) printing technology has endless potential in the fabrication of patient-specific drug delivery devices (DDD) and dosage forms as technological development are progressing. Moreover, the rapidly evolving research on 3D printed DDD has enabled us to determine several challenges related to the manufacturing and marketing of personalized drug delivery systems. The 3D printing has enabled the fabrication of prototypes of DDD with varying complexity and shows that customization of drug products is possible. There is potential to improve patient-specific drug therapies of the future using printing technologies. The technological advancements, new scientific concepts, interdisciplinary work, and defined regulatory guidelines will continue to support and strengthen the prospects of 3D printing as an option in the manufacture of medical products. (Sandler N. *et. al.*, 2016) Three-dimensional printing (3DP) is a unique prototyping technology that has advanced over the past 35 years and has the great potential to revolutionize the field of drug delivery with its inherent advantages of customizability and the ability to fabricate complex solid dosage forms with high accuracy and precision. 3DP can fabricate solid dosage forms with variable densities and diffusivities, complex internal geometries, multiple drugs, and excipients. 3DP can successfully address the issues relating to the drug delivery of poorly water-soluble drugs, peptides, potent drugs and the release of multi-drugs, etc. However, there are some problems that restrict the applications of 3DP in the commercial market, such as the selections of suitable binders, excipients and the pharmaco-technical properties of final products. Further advancement in process performance is required to overcome these issues where 3DP technology can be successfully combined with a novel drug delivery system (NDDS). (Moulton SE *et.al.,* 2014) 3D printing encompasses a range of different techniques, each involving advantages and open issues. Particularly, solidification of powder, extrusion, and stereolithography have been applied to the manufacturing of drug products. The main challenge to their exploitation for personalized pharmacologic therapy is likely to be related to the regulatory issues involved and to implementation of production models that may allow to efficiently turn the therapeutic needs of individual patients into small batches of appropriate drug products meeting preset quality requirements. (A**precia Pharmaceuticals, 2015)** Three-dimensional printing has become a useful and potential tool for the pharmaceutical sector, leading to personalized medicine focused on the patients' needs. It offers numerous advantages, such as increasing the cost efficiency and the manufacturing speed, since rapid prototyping (RP) can be done in a matter of minutes. However, there is still a significant barrier to ensure that 3D printed medicines have the same efficacy, safety, and stability as the pharmaceuticals conventionally manufactured by the Pharmaceutical Industry. Regarding the establishment of guidelines, laws, quality systems and safety of use and consumption of 3D printed medicines, it is a great challenge for the regulatory authorities entailing great obstacles, given the traditional requirements by the pharmaceutical sector. **(Konta AA *et. al.*, 2017)** The use of various types of printing technologies offer potential solutions for personalized medicine and tailored dosage forms to meet the needs of individual treatments of the future. Many types of the scenario for printed dosage form exist and the concepts include, on the simplest level, accurately deposited doses of drug substances. In addition, computer design allows for endless opportunities to create suitable geometries with tailored functionality and different levels of complexity to control the release properties of one or multiple drug substances. It will take some time to convert these technological developments in printing to better treatments for patients because challenges exist. However, printing technologies are developing fast and have the potential to allow the use of versatile materials to manufacture sophisticated drug-delivery systems and biofunctional constructs for personalized treatments. (Beck RCR *et. al.,* 2017) 3D printing technology can handle complex internal structure such as internal walls, hollow channels, porosity, multiple material regions, and multiple drug

distributions. This is a feature traditional pharmaceutical manufacturing processes do not share, which ensures the feasibility of realizing rapid release, sustained release, controlled release, multiple drug delivery systems and personalized medicine based on structure design. (Boetkar J. *et. al.,* 2016)

Conclusion

It is evidenced that through its versatility, speed of production and precision, the use of three-dimensional printing for the elaboration and distribution of controlled drugs plays a key role in the current pharmaceutical industry, considering that drugs can be designed according to the patient's need. The fused deposition modeling (FDM) technique and hot melt extrusion (HME) of filaments for 3DP still excels in relation to the other printing techniques, such as binder deposition, inkjet printing, material jetting, powder bed fusion, photopolymerization, pen-based 3D, printing and molding have been gaining more and more space. The use of 3DP in pharmaceutical formulation development is an effective strategy to overcome challenges of conventional pharmaceutical unit operations since the conventional manufacturing operation can result in disparate qualities of the final products with respect to drug loading, drug release, drug stability, and pharmaceutical dosage form stability. 3DP offers significant potential benefits in the field of drug delivery and pharmaceutical/medical device manufacturer. (Diogo J. H. *et. al.*, 2018)

Acknowledgment

3D- printing is one of the emerging technique in our daily world. By the use of this technique, we can take multiple numbers of the medications in just only a single dose by prohibiting their interactions. This can enhance the formulation experiences in the today world. We can manage the multiple dosage profile with the help of this technique. Nowadays, not only the tablets but the capsules & the suspension also formulated with the multiple active ingredients. 3D -printing technology helps us to redefine the unit dosage form of the different formulations.

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