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3 D PRINTING TECHNOLOGY IN PHARMACEUTICALS: A REVIEW

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Abstract:

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. The introduction of 3D printing technology in the pharmaceutical industry has opened new horizons in the research and development of printed materials and devices. The main benefits of 3D printing technology lie in the production of small batches of medicines, each with tailored dosages, shapes, sizes, and release characteristics. The manufacture of medicines in this way may finally lead to the concept of personalized medicines becoming a reality. This chapter provides an overview of how 3D printed technology has extended from initial unit operations to developed final products.

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INTRODUCTION:

Three-dimensional printing (3DP) is an emerging technology used to describe 3D products manufactured on a digital design platform in a layer-by-layer fashion. 3D printing was originally developed with industrial application purposes and has progressively become a promising technology within past few years. Emergence of 3D printing in the pharmaceutical industry has led to radicaI shifts in the manufacturing process of drug products and has markedly enabled non-digitalized medical products to turn into digital 3D content. 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 dimensions. It is also known as additive manufacturing and solid free form fabrication. 3D printing technology has enabled unprecedented flexibility in the design and manufacturing of complex objects, which can be utilized in personalized and programmable medicine.

Advantages of 3D Printed Drug Delivery

1. Enhanced productivity: 3D printing works more quickly in contrast to traditional methods especially when it comes to fabrication of items like prosthetics and implants with an additional benefit of better resolution, repeatability, more accuracy, and reliability.
2. Customization and personalization: One of the pioneer benefits of this technology is the liberty of fabrication of customized medical equipment and products. Customized implants, prosthetics, surgical tools, fixtures can be a great boon to patients as well as physicians.
3. Increased cost efficiency: Objects produced by 3D printing are of low cost. It is an advantage for small-scale production units or for companies that produce highly complex products or parts because almost all ingredients are inexpensive.
4. 3DP allows controlled size of droplets, complex drug release profiles, strength of dosage and multi-dosing.

Disadvantages of 3D Printing

1. In inkjet printing, proper flow of ink can only be achieved with ink that has precise viscosity.
2. Ink formulation material should have the property of self-binding but should not bind to other printer elements. In some formulation when the ink does not possess adequate self-binding property or it binds with other elements of printer then the resultant formulation does not have required hardness.
3. Rate of drug release may get affected due to binding of ink with another printer

3D PRINTING PROCEDURE

First, a virtual 3D design of an object using digital design software like Onshape, Solidworks, Creo parametric, Autocad, Autodesk etc. is created

↓

This digital model is then converted to (.STL) digital file format which stands for standard tessallation language or stereolithography

↓

Triangulated facets give information regarding the surface of the 3D model that is present in the (.STL) file

↓

The (.STL) file is converted into G file by slicing the design into a series of 2D horizontal cross-sections by the help of specialized slicer software, which is installed in the 3D printer

↓

Now the print head is moved in the x-y axis to create the base of the 3D object.

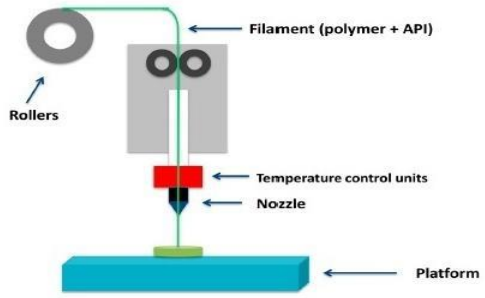
↓

The print head is now allowed to move in the z-axis, thereby depositing the layers sequentially of the desired material, hence creating a complete 3D object

Types of 3D printing technology

1. Fused deposition modeling (FDM)

This is the extruding a thermoplastic filament through high temperature nozzle into semi-solid fused state filament in layer-by-layer fashion. The object is formed by layers of melted or softened thermoplastic filament extruded from the printer's head at specific directions as dictated by computer software. The material is heated to just above its softening point which is then extruded through a nozzle, and deposited layer by layer, solidifying in a second. This is why it is also called Fused Filament Fabrication Drug loading in the filament is usually achieved through incubation in organic solvents and poor drug loading may limit its use to low-dosed drugs.



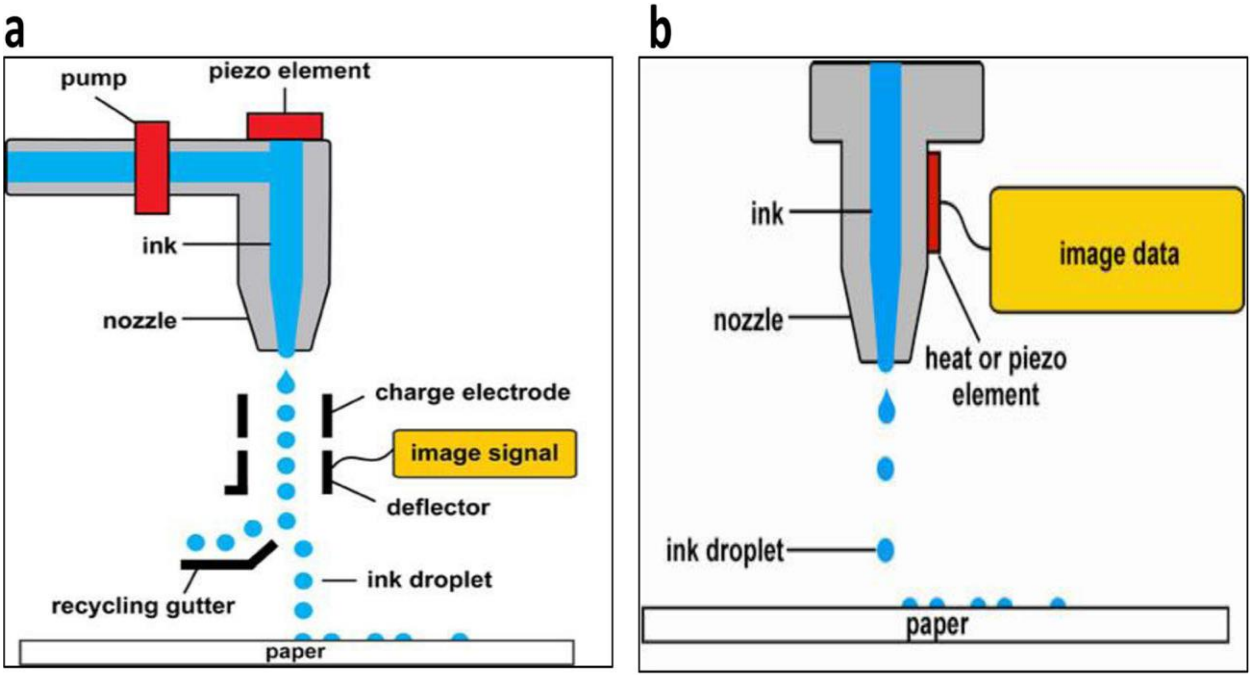
Fused deposition modelling (FDM) Printing system.

2. Thermal inkjet (TIJ) printing

It involves the heating of ink fluid by the help of micro-resistor, thereby creating a bubble of vapor that nucleates and upon expansion forces the ink to drop out of the nozzle. Dispensing of extemporaneous preparation/solution of drug onto 3D scaffolds is an area where this technique can be employed.

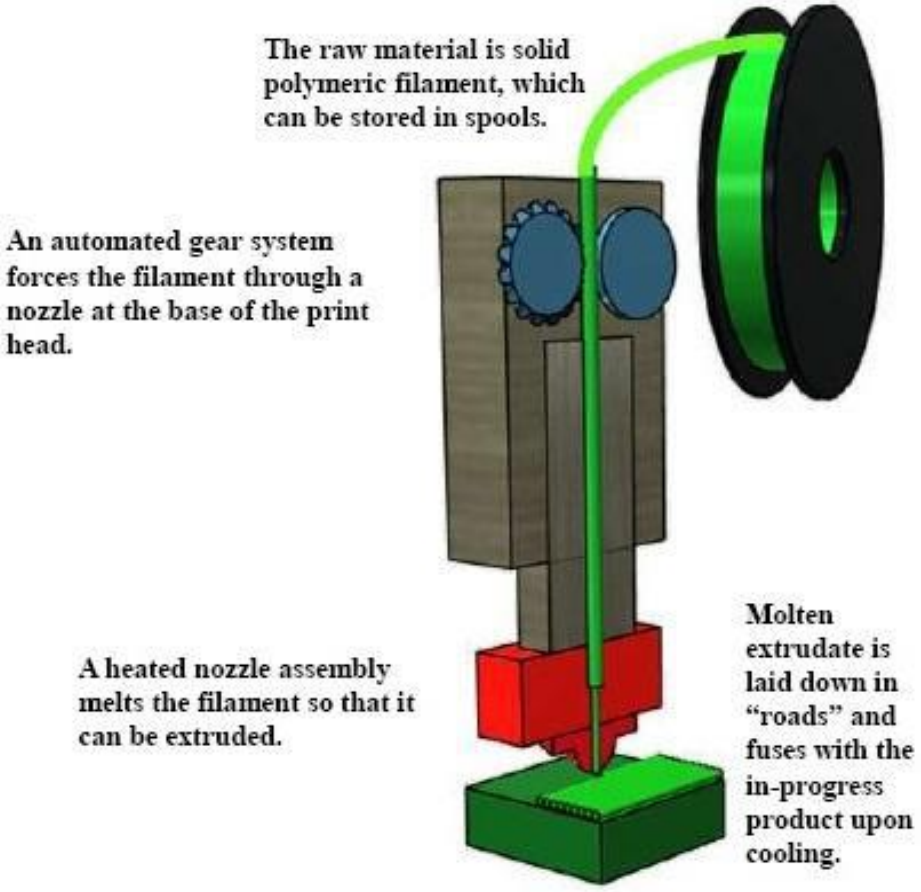
3. Inkjet printing

Another adoption of 3D printing in pharmaceutics is inject printing. This approach is particularly suitable when the formulation of starting materials is liquid. Inject printing is classified into two categories: continuous inject printing (CIJ) and drop on demand (DOD) based on sssthe direction of droplets. In the case of CIJ, the drops are formed by a transducer or a droplet loading apparatus producing a continuous stream of droplets. Then, the droplets are directed to an electrically charged element to obtain the desired charge. Finally, the formed droplets reach onto the substrate and create the 3D product. The main advantage of inject 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 ingredients and personalisation in drug discovery.



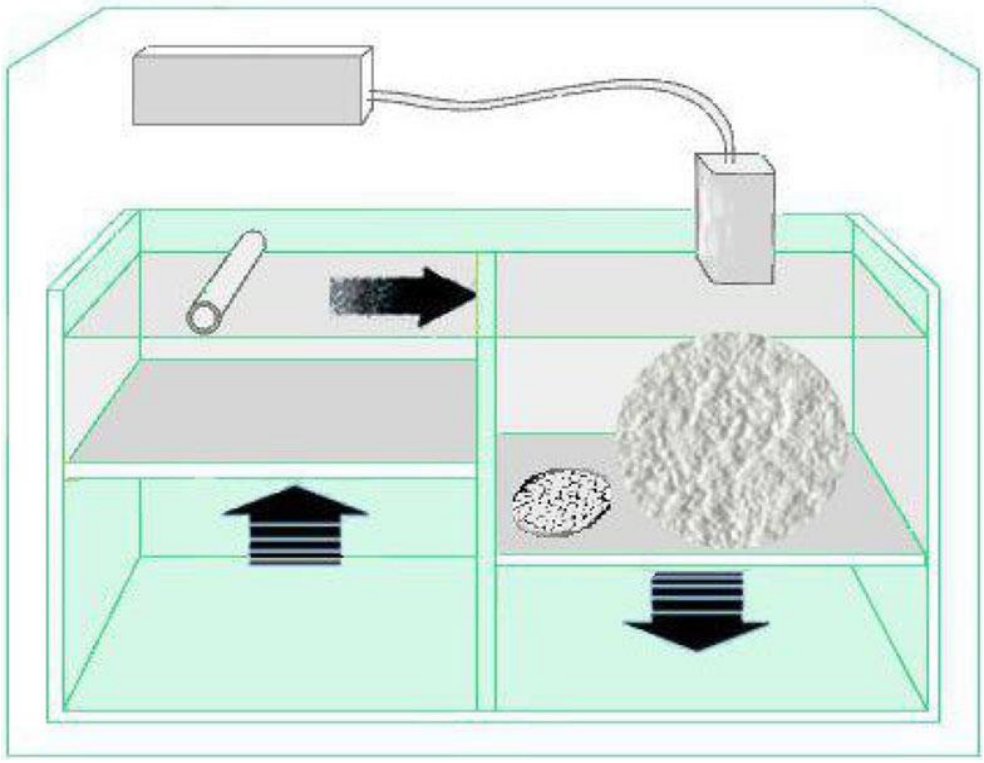
4. Nozzle-Based Deposition Systems

Nozzle-based deposition systems consist on the mixing of drugs and polymers and other solid elements prior to 3D printing. The mixture is passed through a nozzle that definitely originates, layer by layer, the three-dimensional product. There are two types of printings according to the type of material used: Fused Deposition Modelling, which uses melted components, and Pressure-Assisted Microsyringes, which does not require the use of melted materials.



5. Powder-based binding method

Rapid prototyping with a powder-based method is of particular interest to the pharmaceutical industry as it has many parallels with current manufacturing processes and may offer a more efficient longer-term printing solution. Multilayers of 3D printing products are constructed by spraying a solution of binder or drug with additional excipients in small droplets from an X-Y print head (in two-dimensional manners) over a powder bed on a built platform. Then, it is lowered along Z-axis based on the height of layers until the subsequent layer is constructed. The layers could be bonded via adhesion or welding in a liquid solution or suspension. Finally, the residual of the solvent and unbound powder is removed under appropriate conditions, allowing for the 3D product to develop properly. Powder bed 3D printing method is fast and compatible for printing a wide range of pharmaceutical substances.



RISK ASSESSMENT DURING 3D PRINTING PROCESS

Risk identification is an important step to prevent failure of quality control parameters like appearance, content uniformity, assay etc. Identifying risk involves through analysis of the process and process variables to assure that a quality product is manufactured.

- When a given printer is unable to print a given design, software controls should be employed
- Variability in layer thickness has to be controlled by real – time layer thickness monitoring
- Improper layering due to environmental conditions should be dealt with controlling the temperature and humidity of the manufacturing area.
- Inaccurate position during printing can be avoided by monitoring print head height and print head speed.
- Uneven layers can be avoided by checking powder water content and powder particle size distribution
- Print head clogging can be prevented by ensuring particle size distribution and monitoring inkjet flow.
- Inconsistent agglomeration or binding can be due to variations in binder viscosity or binder surface tension

CONCLUSION:

3D printing technology is a valuable 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. 3D printing has revolutionized the way in which manufacturing is done. It improves the design manufacturing and reduces lead time and tooling cost for new products. This chapter has summarized different fabrication methods and some notable applications of 3D printing in the healthcare sector, especially in pharmaceutical sciences.

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.

In the near future 3D printing approach will be utilized to fabricate and engineer various novel dosage forms. Although commercial production of such novel dosage forms is still challenging; developing personalized medication, optimized drug release from dosage form, compacting or avoiding drug-drug incompatibilities, protection of biomolecules during manufacture, construction of multiple drug dosage form and multiple release dosage forms will be taken to a new era through 3D printing technology.

REFERENCES:

1. *Norman J, Madurawe R, Moore C, Khan MA, Khairuzzaman A. A new chapter in pharmaceutical manufacturing: 3D-printed drug products. Advanced Drug Delivery Reviews. 2017; 108:39-50*
2. *Diogo JH. 3D Printing of Pharmaceutical Drug Delivery Systems. Archives of Organic and Inorganic Chemical Sciences. 2018; 1(2). AOICS.MS.ID.000109.*
3. *Andrea AK, Marta GP, Dolores RS. Personalised 3D Printed Medicines: Which Techniques and Polymers Are More Successful?. Bioengineering. 2017; 4(79) , 1-16*
4. *Alhnan MA, Okwuosa TC, Muzna S, WaiWan K, Ahmed W, Arafat B. Emergence of 3D Printed Dosage Forms: Opportunities and Challenges. Pharmaceutical Research. 2016);33:1817–325.https://www.fda.gov/MedicalDevices/ProductsandMedicalProcedures/3DPrintingofMedicalDevices/default.htm*
6. *http://cbm.msoe.edu/markMyweb/printResources/documents/historyOf3DPrinting.pdf*
7. *Wang, J, Goyanes A, Gaisford S, Basit AW. Stereolithographic (SLA) 3D printing of oral modified-release dosage forms. International Journal of Pharmaceutics. 2016; 503, 207–212.*
8. *Prasad LK, Smyth H. 3D printing technologies for drug delivery: A review. Drug Development and Industrial Pharmacy. 2016, 42, 1019–31.*
9. *Food and Drug Administration, 2017. Guidance for Industry: Technical Considerations for Additive Manufactured Medical Devices. Center for Devices and Radiological Health Center for Biologics Evaluation and Research, U.S. Department of Health and Human Services. Available online:https://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM499809.pdf*
10. *Food and Drug Administration, 2002, General Principles of Software Validation; Final Guidance for Industry and FDA Staff, Center for Devices and Radiological Health, Center for Biologics Evaluation and Research, U.S. Department Of Health and Human Services. https://www.fda.gov/downloads/medicaldevices/../ucm085371.pdf*
11. Prasad LK, Smyth H (2016) 3D Printing technologies for drug delivery: a review. Drug development and industrial pharmacy 42(7):1019–1031. https://doi.org/10.3109/03639045.2015.1120743
12. Daly R, Harrington TS, Martin GD (2015) Inkjet printing for pharmaceutics – a review of research and manufacturing. Int J Pharm 494(2):554 567.https://doi.org/10.1016/j.ijpharm.2015.03.017
13. Ursan ID, Chiu L (2003) Pierce A (2013) Three-dimensional drug printing: a structured review. J Am Pharm Assoc 53(2):136–144. https://doi.org/10.1331/ JAPhA.2013.12217
14. Jamroz W, Szafraniec J, Kurek M (2018) 3D printing in pharmaceutical and medical applications - recent achievements and challenges. Pharm Res 35(9):176. https://doi.org/10.1007/s11095-018-2454-x
15. Palo M, Hollander J, Suominen J (2017) 3D printed drug delivery devices: perspectives and technical challenges. Expert Rev Med Devices 14(9):685– 696. https://doi.org/10.1080/17434440.2017.1363647
16. Park K (2015) 3D printing of 5-drug polypill. J Control Release 217:352. https://doi.org/10.1016/j.jconrel.2015.10.014
17. Sun Y, Soh S (2015) Printing tablets with fully customizable release profiles for personalized medicine. Advanced materials (Deerfield Beach, Fla.) 27(47):7847-7853. https://doi.org/10.1002/adma.201504122
18. Trenfield SJ, Awad A, Goyanes A (2018) 3D Printing pharmaceuticals: drug development to frontline care. Trends Pharmacol Sci 39:440–451. https:// doi.org/10.1016/j.tips.2018.02.006
19. Goole J, Amighi K (2016) 3D printing in pharmaceutics: a new tool for designing customized drug delivery systems. Int J Pharm 499(1):376–394. https://doi.org/10.1016/j.ijpharm.2015.12.071
20. Osouli-Bostanabad K, Adibkia K (2018) Made-on-demand, complex and personalized 3D-printed drug products. BioImpacts : BI 8 (2):77-79. doi:10.15171/bi.2018.09
21. Khatri P, Shah MK, Vora N (2018) Formulation strategies for solid oral dosage form using 3D printing technology: a mini-review. J DRUG DELIV SCI TEC46:148–155. https://doi.org/10.1016/j.jddst.2018.05.009

22. Deciding When to Submit a 510(k) for a Change to an Existing Device. Available online: www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm080235.htm)

23. 30-Day Notices, 135-Day Premarket Approval (PMA) Supplements and 75-Day Humanitarian Device Exemption (HDE) Supplements for Manufacturing Method or Process Changes. Available online: www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM080194.pdf

24. Modifications to Devices Subject to Premarket Approval (PMA) - The PMA Supplement Decision-MakingProcess. https://www.fda.gov/downloads/medicaldevices/deviceregulationandguidance/guidancedocuments/ucm089360.pdf

25. Changes or Modifications During the Conduct of a Clinical Investigation. Available online: www.fda.gov/downloads/medicaldevices/deviceregulationandguidance/guidancedocuments/ucm082158.pdf

26. Outterson K. Regulating compounding pharmacies after NECC. The New England Journal of Medicine. 2012; 367(21):1969–72.

27. Drues M. The case of the New England Compounding Center. Healthcare packaging. 8/11/15. Available from: http://www.healthcarepackaging.com/case-new-england-compoundingcenter.

28. Sun L. FDA finds widespread safety issues at compounding pharmacies. In.Washington Post: Health & Science. 2013.

29. Katakam P, Dey B, Assaleh FH, Hwisa NT, Adiki SK, Chandu BR, et al. Top-down and bottom-up approaches in 3D printing technologies for drug delivery challenges. Critical Reviews in Therapeutic Drug Carrier Systems. 2015;**32**(1):61-87

30. Goyanes A, Buanz AB, Hatton GB, Gaisford S, Basit AW. 3D printing of modified-release aminosalicylate (4-ASA and 5-ASA) tablets. European Journal of Pharmaceutics and Biopharmaceutics. 2015;**89**:157-162

31. Masood SH. Application of fused deposition modelling in controlled drug delivery devices. Assembly Automation. 2007 Aug 7;**27**(3):215-221

32. Buanz AB, Saunders MH, Basit AW, Gaisford S. Preparation of personalized-dose salbutamol sulphate oral films with thermal ink-jet printing. Pharmaceutical Research. 2011;**28**(10):2386

33. Meléndez PA, Kane KM, Ashvar CS, Albrecht M, Smith PA. Thermal inkjet application in the preparation of oral dosage forms: Dispensing of prednisolone solutions and polymorphic characterization by solid-state spectroscopic techniques. Journal of Pharmaceutical Sciences. 2008;**97**(7):2619-2636