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3D Printing in Pharmacy- Pixels to Pills: A Review

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ABSTRACT:

Recently, 3D printing appeared to be a game-changer in the field of pharmacy, thus giving rise to new possibilities regarding medication delivery, customization of dosage forms and personal medicine.

The properties of 3D printings in pharmacy are:

1. Its ability to produce complex structures in layer-by-layer manner; this means that one can control how much of drug is added into it as well as its distribution. Such methods have been limited by common practices like batch processing and standardized formulations.

2. They also allow for Kinetics – precisely controlling when certain drugs will be released so that they work better and make it easier for patients to comply.

3. In addition, we can customize the formulations for the needs of different individuals and ensuring the treatment is effective while minimizing side effects known as Patient-Specific Dosage Form

4. Additionally, the process of drug development is accelerated by 3D printing and its rapid prototyping techniques.

Its applications encompass anything from fabricating patient-specific dosage forms to producing sophisticated drug delivery systems.

In addition, 3D printing facilitates the development of paediatric and geriatric dosage forms that have modified shapes and sizes which are tailored to children and elderly respectively, who represent vulnerable patient groups.

Keywords:

Customization of Dosage Forms, Layer-by-Layer, Patient-Specific Dosage Form, Rapid Prototyping.

1. Introduction:

First applied to the development of pharmaceuticals in 1996, 3D printing of pharmaceuticals has been the source of much research and considerable advancement. Much of the research conducted since that period is centered on exploring and refining 3D printing technology for pharmaceutical applications. Still, development of commercial scale capabilities has advanced substantially in recent years. FDA approval of the first 3D printed pharmaceutical, Spritam, this research in 3D printing, coupled with its commercial scale of manufacturing, gives evidence of the fact that the method of 3D printing can be used in large-scale manufacturing pharmaceuticals.[1]

Today, three-dimensional printing remains one of the fastest developing branches of technology, art, and science; it does not stop expanding its applications. The International Standard Organization explains the term "three-dimensional printing" as: "fabrication of objects through the deposition of a material using a print head, nozzle, or another printer technology". [2]

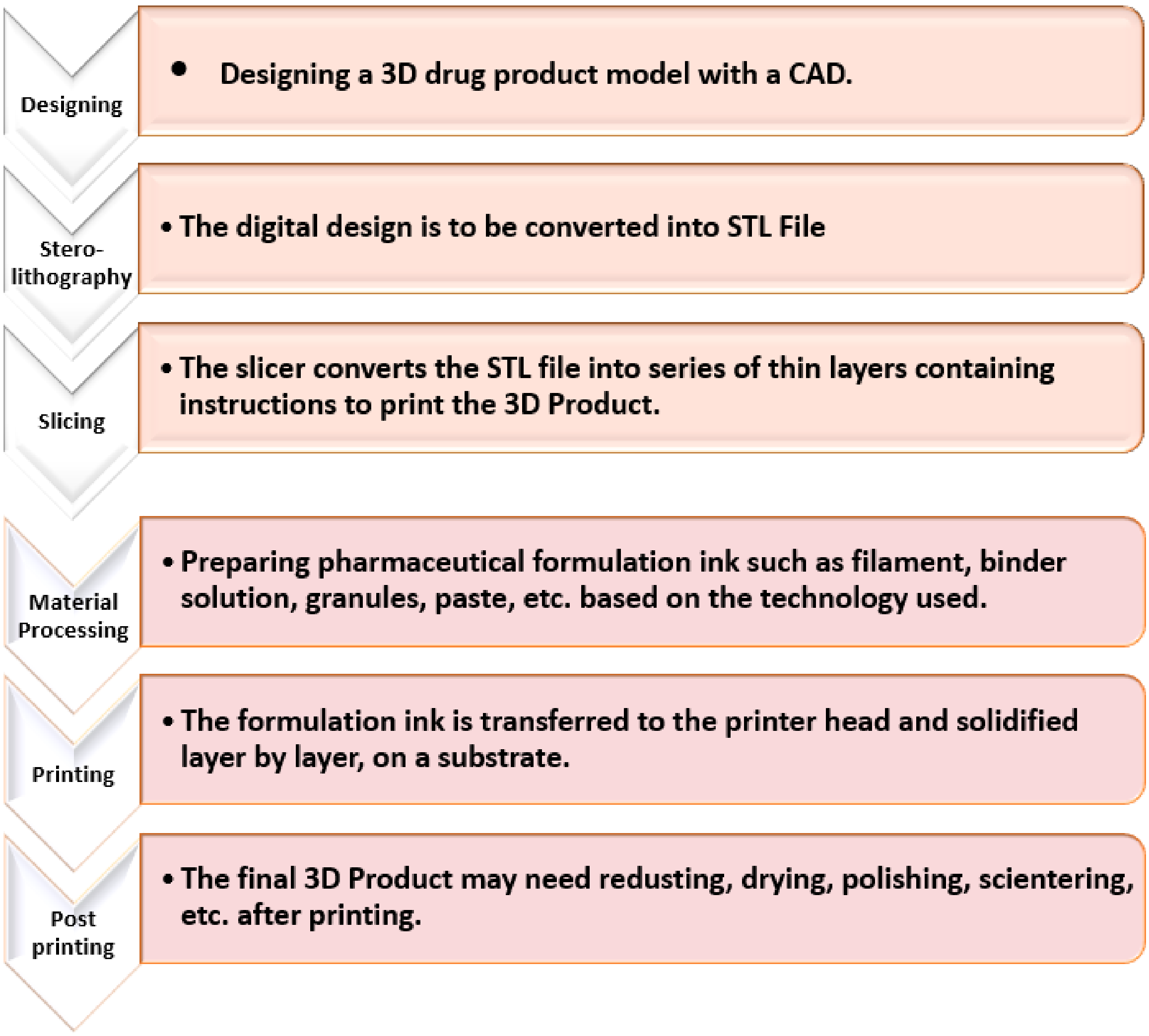
These actions show how to abandon 'one size fits all' framework in favour of personalisation, which demands that medications be adjusted according to human beings' physical makeup, medications already taken simultaneously by the patients concern, how they respond to drugs, and their DNA makeup among others (such as gender , age, weight). For instance; Personalised medicine through administering drugs differently i.e. having two or more medicines combined in one pill, appropriate doses among others provides numerous advantages such like increased medicine adherence decreased adverse drug reactions and better treatment outcomes.

Nevertheless, with personalized medicine from mirage into actuality there is an urgent need for technologies that will enable moving from traditional large batch production of fixed dose medicines to flexible personalized dosages, different doses combinations systems on demand. Therefore, this movement can be supported through three-dimensional printing techniques. 3D printing enables the production of printlets (3D tablets) which are specific to the medical necessities (e.g. dosage forms, mixes of drugs and release pattern) and personal tastes such as shape, size, feel and taste sensations by print layer by print layer approach. [3]

In Contrary to the normally used subtractive and formative manufacturing methodologies, this technique is one of the methods of Additive Manufacturing in which parts are prepared from 3D model data in the process of joining materials layer by layer. The practical approach of AM is called rapid prototyping (RP), and the advantages are: reduction of prototyping time and costs, easy modifications of a product at designed level, possibility to manufacture small objects, individualized product series, or structures impossible to form with subtractive techniques. [2]

Owing to the portable, compact and user-friendly nature of 3D printers, as well as the ability for 3D printing to manufacture medicines on demand, the technology could be easily integrated into healthcare settings, including hospital wards, in-patient pharmacies, and community pharmacies.

- **How does 3d printing work?**



2. Manufacturing Techniques of Drugs By 3D Printing:

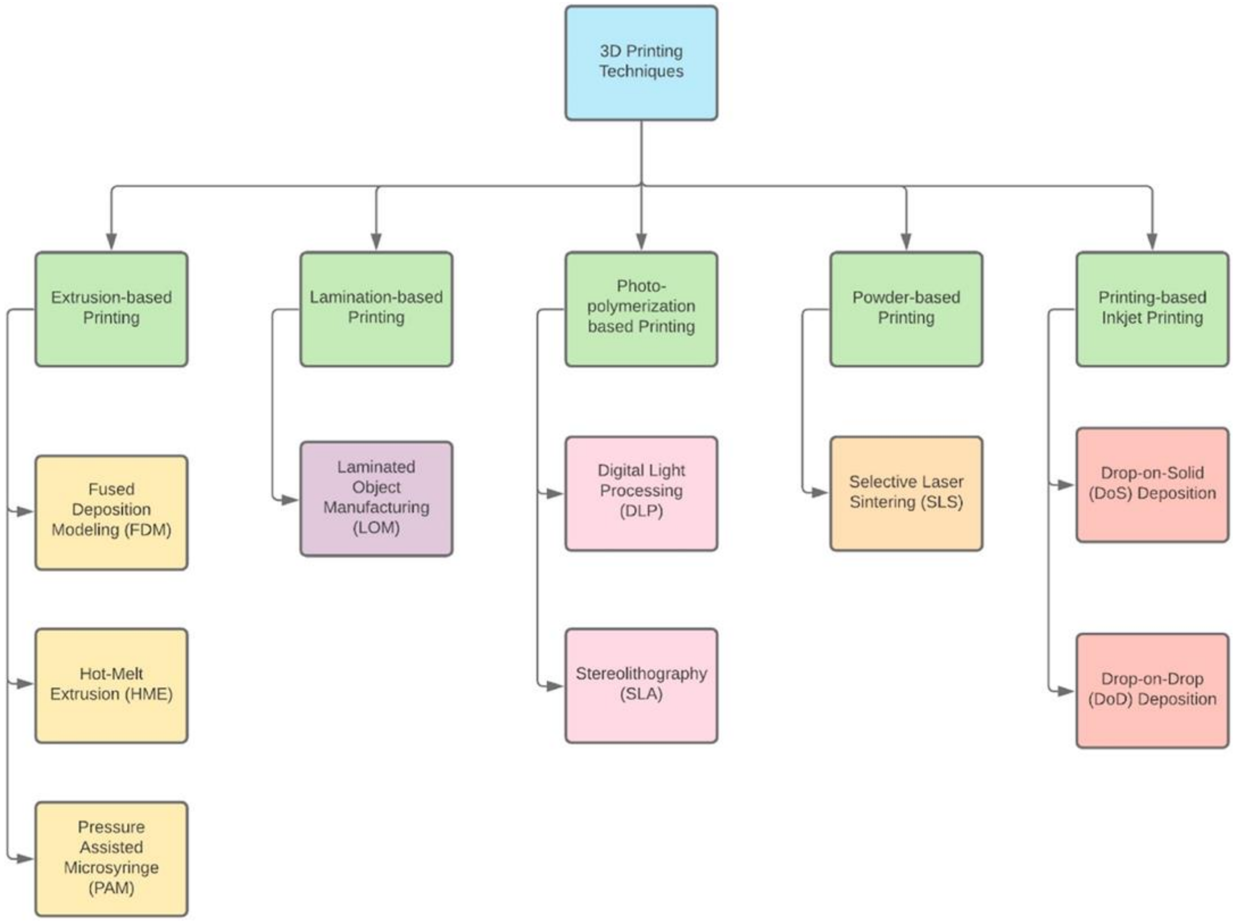


Fig-1 : Different Techniques Involved In 3D Printing of Drugs

2.1 Extrusion Based Printing:

Extrusion-based printing is a widely used method in the 3D printing of drugs, where a filament or paste containing the active pharmaceutical ingredient (API) and excipients is extruded through a nozzle to form layers that build up the final dosage form. This technique allows for precise control over the drug's geometry, enabling the creation of complex dosage forms with tailored drug release profiles. The method is particularly effective for producing multi-layer tablets and personalized medicine, as it can easily incorporate different drugs and release mechanisms into a single dosage form.

➢ **Fused Deposition Modelling(FDM):**

Fused Deposition Modelling (FDM) is a popular 3D printing technique used in drug manufacturing that involves the layer-by-layer deposition of thermoplastic materials loaded with active pharmaceutical ingredients (APIs). In FDM, a filament of drug-loaded polymer is heated and extruded through a nozzle, forming successive layers to create solid dosage forms such as tablets or capsules.

This method is particularly advantageous for producing personalized medication with complex geometries and tailored drug release profiles. FDM is also noted for its precision, ease of use, and cost-effectiveness, making it suitable for on-demand production of customized pharmaceuticals.

The disadvantage is that it may be unsuitable for thermosensitive drugs, it can be challenging to formulate the initial filament feedstock, it can be challenging to scale up and it has low drug loading capacity. [5]

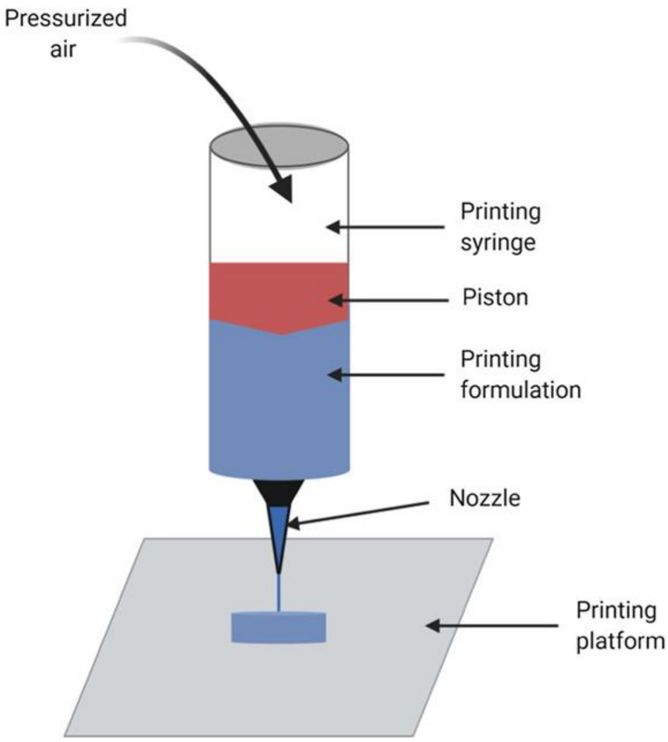


Fig-2 : Fused deposition modelling

➢ **Hot Melt Extrusion (HME):**

Hot Melt Extrusion (HME) is a key technique in 3D printing for drug manufacturing, especially for producing solid dosage forms. In this process, a blend of pharmaceutical ingredients, including the active pharmaceutical ingredient (API) and polymeric excipients, is heated and melted. The molten mixture is then forced through a die to form a continuous strand, which can be cut into specific shapes or further processed in 3D printers to create customized drug formulations.

HME offers excellent control over drug release profiles, improves the solubility of poorly water-soluble drugs, and enables the production of complex, multi-layered structures. It's particularly useful in creating dosage forms with tailored drug release characteristics, making it a promising method for personalized medicine.[6]

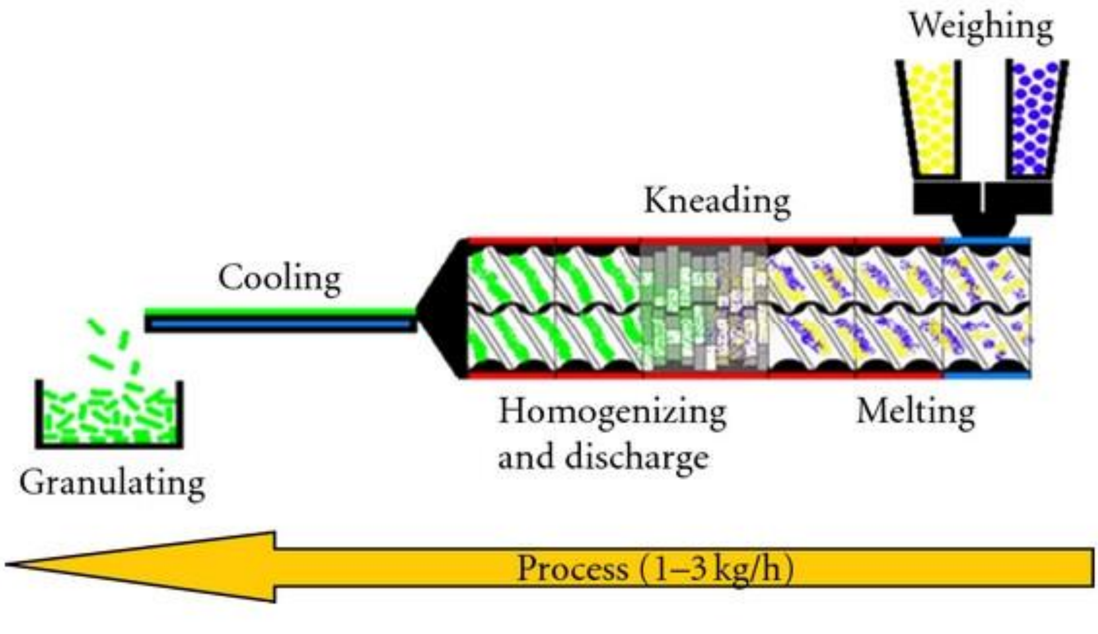


Fig-3 : Fused deposition modelling

- **Pressure Assisted Microsyringe (PAM):**

The Pressure-Assisted Micro Syringe (PAM) method is a specialized 3D printing technique used in drug manufacturing that involves the extrusion of semi-solid formulations through a fine nozzle. In this method, pressure is applied to a syringe filled with a drug-loaded paste or gel, allowing precise deposition layer by layer to create intricate drug delivery systems or dosage forms. The PAM method is particularly advantageous for printing materials that are too viscous for other 3D printing techniques, making it ideal for producing controlled-release drug formulations and personalized medicines.[7]

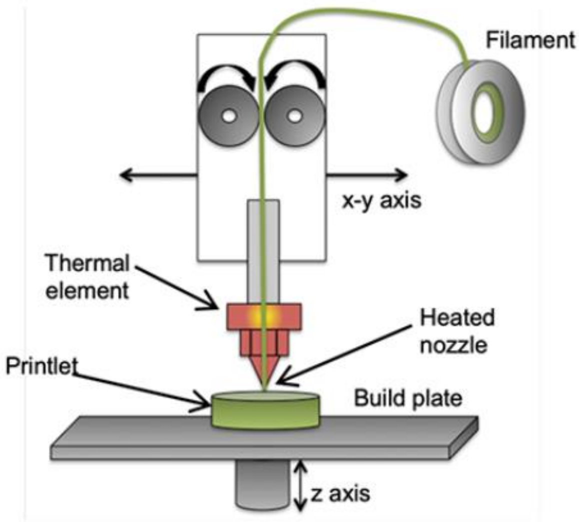


Fig-4 : Pressure Assisted Microsyringe

2.2 Lamination based printing:

Lamination-based printing, also known as laminated object manufacturing (LOM), is a 3D printing technique where layers of material are bonded together to form a solid object. In drug manufacturing, this method involves the stacking and bonding of drug-containing layers to create a dosage form. Each layer can contain different drugs or excipients, allowing for the creation of complex, multi-drug delivery systems.

Lamination-based methods offer high precision and the ability to produce dosage forms with unique release profiles, making them particularly suitable for personalized medicine.[8]

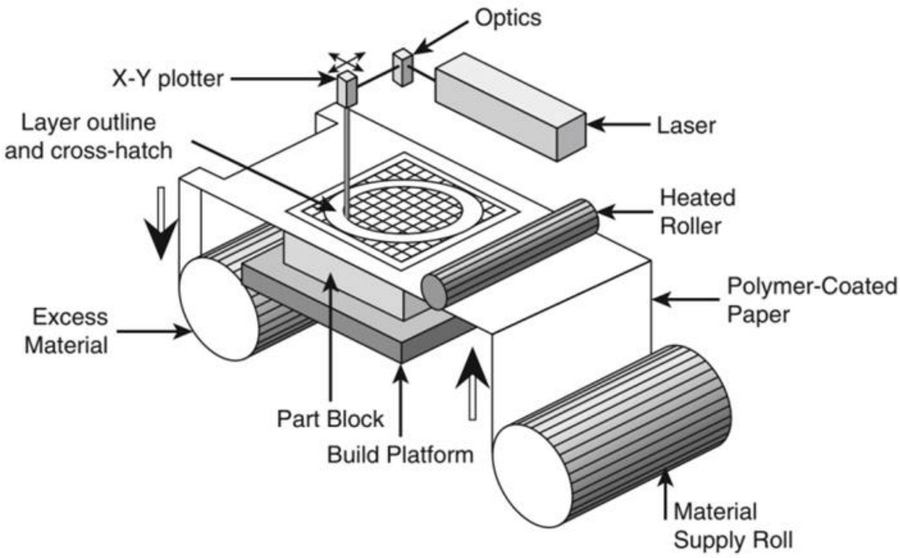


Fig-5 : Lamination based printing

2.3 Photopolymerization-Based Printing:

Photopolymerization-based 3D printing, particularly Stereolithography (SLA), utilizes light to initiate a polymerization reaction in a photosensitive resin, forming solid structures layer by layer. In drug manufacturing, this technique allows for the precise fabrication of intricate drug delivery systems, including microstructures that can control the release of active pharmaceutical ingredients (APIs). The method is highly accurate, making it suitable for producing personalized dosage forms with complex geometries.[9]

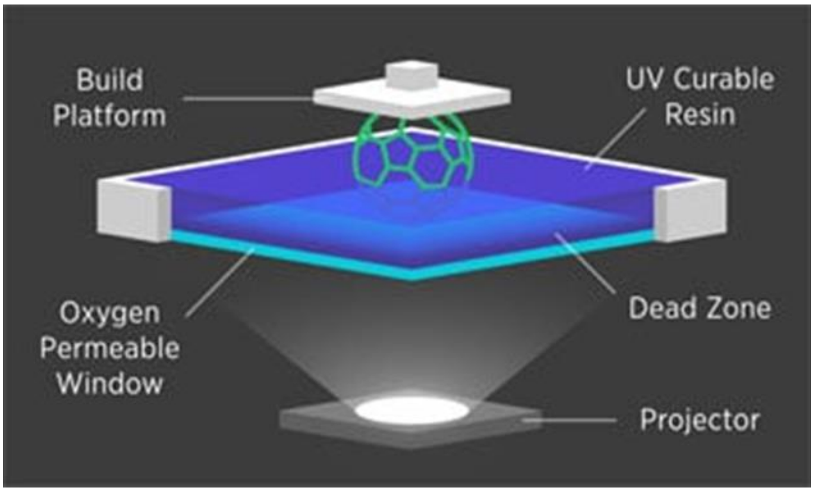


Fig-6 : Photopolymerization-Based Printing

- **Digital Light Processing (DLP):**

Digital Light Processing (DLP) is a photopolymerization-based 3D printing technique that uses a digital light projector to cure photosensitive resins layer by layer, creating highly detailed and precise drug delivery systems.

DLP offers advantages in producing complex geometries, rapid prototyping, and creating multi-drug release profiles within a single dosage form. Its precision makes it particularly suitable for personalized medicine, where tailored dosages and release characteristics are essential.[10]

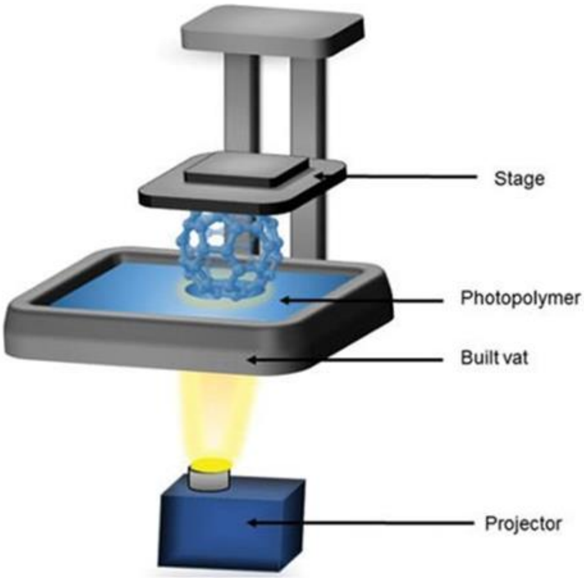


Fig-7 : Digital light processing

- **Stereolithography (SLA):**

Stereolithography (SLA) is a 3D printing technique that utilizes a laser to solidify photocurable resin layer by layer, creating intricate and precise pharmaceutical products.

In this process, a computer-controlled laser traces the shape of each layer on the surface of the resin, hardening it. As new layers are added, the build platform descends, allowing the resin to flow beneath the solidified portion.

SLA offers several advantages, including high accuracy, excellent surface finish, and the ability to create complex geometries. These characteristics make it a valuable tool for producing customized dosage forms, implants, and medical devices.[11]

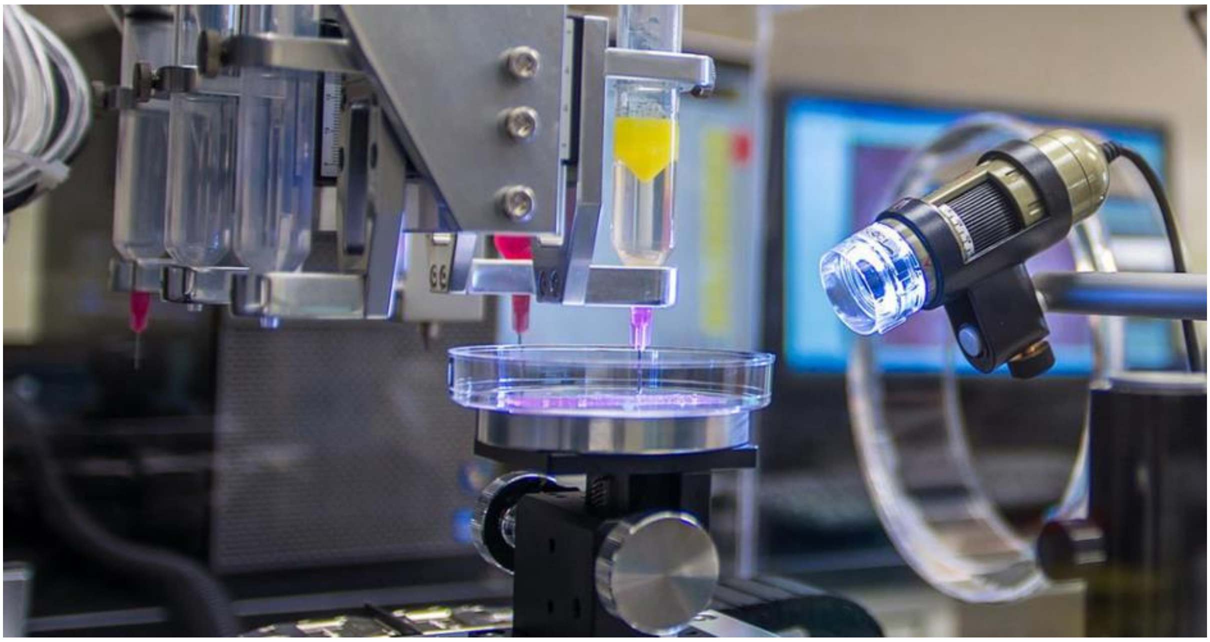


Fig-8 : Stereolithography (SLA)

2.4 Powder based Printing:

Powder-based 3D printing is a revolutionary technique in pharmaceutical manufacturing that involves selectively fusing layers of powdered materials to create complex structures. This method offers unparalleled flexibility in designing and producing customized dosage forms, such as tablets, capsules, and implants. By using a laser beam to selectively melt or sinter the powder, precise control over the structure and composition of the final product is achieved. This technology has the potential to revolutionize drug delivery, enabling personalized medicine and improving patient outcomes.

- **Selective laser sintering (SLS):**

Selective laser sintering (SLS) is a 3D printing technique that has shown great promise in the pharmaceutical industry.

In this process, a laser beam selectively fuses powdered materials, layer by layer, to create a three-dimensional object. SLS offers several advantages for pharmaceutical manufacturing, including the ability to create complex geometries, customize dosage forms, and improve drug delivery. By controlling the laser intensity and scan speed, it's possible to manipulate the porosity and release properties of the printed products. This opens up new possibilities for personalized medicine and the development of innovative drug delivery systems.[12]

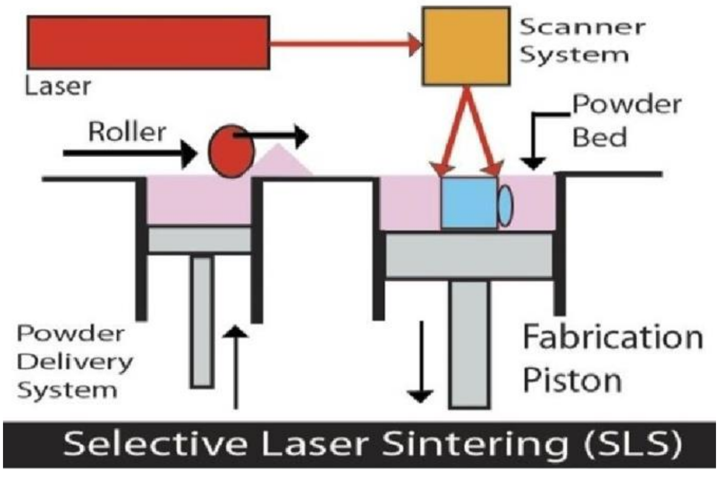


Fig-9 : Selective laser sintering (SLS)

2.5 Printing based inkjet printing:

Inkjet printing is a promising technique in 3D printing of pharmaceutical products due to its precision and versatility. This method involves the controlled deposition of droplets containing pharmaceutical ingredients onto a substrate, layer by layer. By adjusting the droplet size and placement, intricate structures and customized dosage forms can be created. Inkjet printing offers several advantages, including the ability to produce complex geometries, reduce waste, and enable personalized medicine. However, challenges such as ink formulation, nozzle clogging, and regulatory compliance need to be addressed for widespread adoption in the pharmaceutical industry.

- **Drop-on-Solid (DoS) Deposition:**

Drop-on-solid (DoS) deposition is a versatile 3D printing technique that involves depositing individual droplets of a liquid material onto a solid substrate layer-by-layer. In pharmaceutical manufacturing, this method offers precision and control in creating complex dosage forms with tailored properties. By carefully controlling the droplet size, composition, and deposition pattern, DoS can be used to produce a wide range of products, including tablets, capsules, and implants.

The process typically begins with a powder bed that serves as the base layer.

A liquid material, containing the active pharmaceutical ingredient (API) and excipients, is then dispensed in droplets onto the powder bed. As the liquid solidifies, it bonds with the underlying layers, forming the desired three-dimensional structure. This technique allows for precise control over the drug release profile and the incorporation of multiple components within a single dosage form.[13]

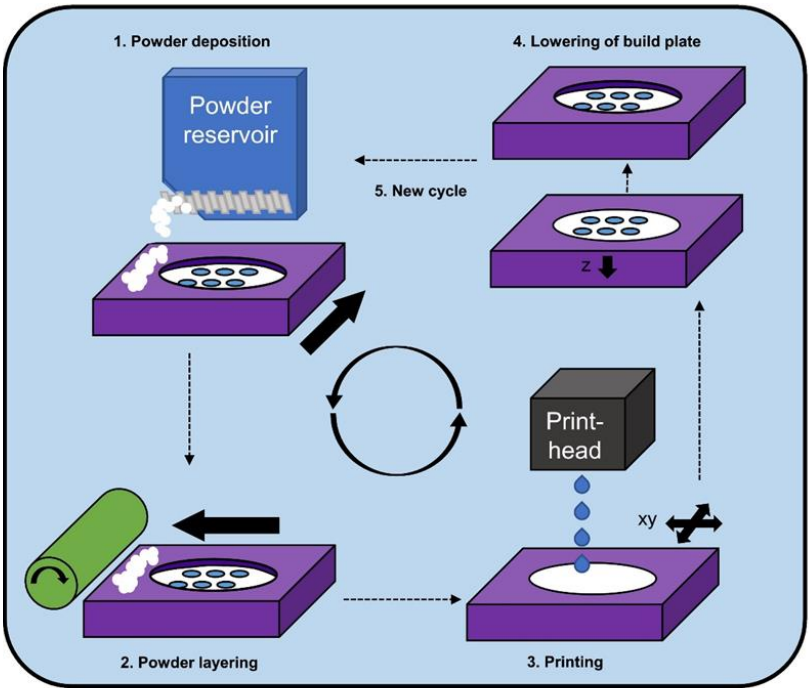


Fig-10 : Drop-on-solid (DoS) deposition

- **Drop-on-Drop (DoD) Deposition:**

Drop-on-drop deposition (DOD) is a 3D printing technique that involves the precise placement of droplets of a liquid material onto a substrate.

In the context of pharmaceutical manufacturing, this method allows for the creation of intricate drug delivery systems with tailored properties. The process involves the use of a printhead that dispenses droplets of a drug-containing ink onto a moving platform. As successive layers are deposited, a three-dimensional structure is formed. This technique offers the potential for personalized medicine by enabling the production of customized dosages and release profiles.[14]

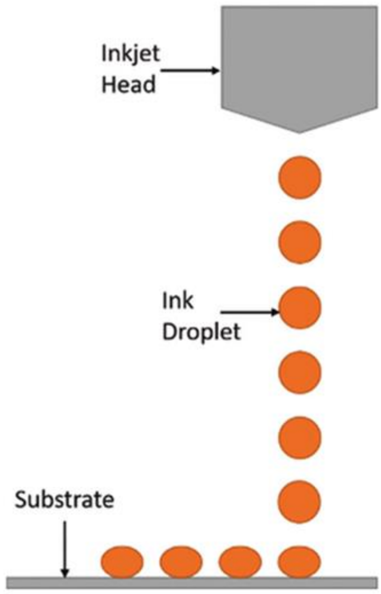


Fig-11 : Drop-on-Drop (DoD) Deposition

3. Advantages:

- **Personalized Medicine:** This technology allows for the customization of drug dosages and combinations tailored to individual patient needs, improving therapeutic outcomes and reducing side effects.
- **On-Demand Manufacturing:** 3D printing enables the on-demand production of pharmaceuticals, which can drastically reduce lead times and minimize waste.
- **Complex Dosage Forms:** The technology allows for the creation of complex drug delivery systems that are difficult to achieve with traditional manufacturing methods. This includes controlled-release formulations, multi-layered tablets, and dosage forms with specific shapes and properties designed to enhance drug absorption and efficacy .
- **Accessibility and Convenience:** By decentralizing drug manufacturing, 3D printing can make medications more accessible. Pharmacies equipped with 3D printers can produce medications locally, reducing the dependence on large pharmaceutical manufacturing plants and improving access in underserved areas .
- Reduces cost of production due to lesser material wastage.
- Narrow therapeutic window
- Accurate and precise dosing of potent drugs which are administered at small doses.
- High drug loading ability when compared to conventional dosage forms.[15]

4. Disadvantages:

- **Material Limitations:** Not all pharmaceutical materials are suitable for 3D printing. The mechanical properties, thermal stability, and rheological characteristics of the materials can significantly impact the printability.
- **Regulatory Hurdles:** The regulatory landscape for 3D-printed pharmaceuticals is still evolving. Ensuring compliance with regulatory standards, such as FDA guidelines, can be complex and time-consuming.
- **Cost and Scalability:** The initial investment in 3D printing equipment and materials can be significant. Additionally, scaling up production for large-scale manufacturing may present challenges.
- **Intellectual Property Concerns**: The ease of replication with 3D printing can raise concerns about intellectual property infringement and counterfeiting.
- **Quality Control and Consistency**: Ensuring consistent product quality and reproducibility can be challenging in 3D printing, especially for complex formulations.[15]

- **Size Limitations:** The 3D printing technology is currently limited by size limitations. Very large objects are still not possible when built using 3D printers.
- As with all new technologies, manufacturing jobs will decrease. This disadvantage can have a large impact to the economies of third world countries. [15]

5. Applications of 3D Printing:

5.1Drug Delivery Systems:

- **Personalized Dosage Forms:** 3D printing can create customized drug delivery systems tailored to individual patient needs, ensuring optimal dosing and therapeutic outcomes.

 Tailoring drug release profiles: Creating dosage forms with specific release rates to match individual patient needs.

 Customizing shapes and sizes: Designing dosage forms that are more comfortable and easier to swallow.

 Combining multiple medications: Incorporating various drugs into a single dosage form, simplifying medication regimens.

 Creating patient-specific dosages: Producing precise doses based on individual requirements, ensuring optimal treatment.

 Addressing specific health conditions: Developing dosage forms for unique patient needs, such as pediatric or geriatric populations.

- **Controlled Release Systems:** 3D printing allows for the precise control of drug release rates, enabling sustained or delayed drug delivery.

 Precise drug release profiles: 3D printing allows for the creation of intricate structures that can control the rate at which drugs are released, ensuring optimal therapeutic effects.

 Customized release patterns: Different printing techniques and materials can be used to achieve various release patterns, such as sustained, pulsed, or delayed release.

 Spatial control of drug delivery: 3D printing enables the precise placement of drugs within a dosage form, allowing for targeted delivery to specific areas of the body.

 Complex drug delivery systems: 3D printing can produce complex drug delivery systems, such as implants, patches, and microspheres, that can be tailored to specific patient needs.

- **Multi-Dose Systems:** Multiple drugs can be incorporated into a single 3D-printed dosage form, simplifying medication regimens. It enables the precise control of drug release profiles, allowing for the delivery of multiple doses of different drugs within a single dosage form. This can simplify medication regimens, improve patient compliance, and enhance therapeutic outcomes. Additionally, 3D printing can be used to create multi-layer systems that release drugs sequentially or simultaneously, providing tailored drug delivery for various therapeutic needs.
- **Oral Disintegrating Tablets:** Rapidly dissolving tablets can be printed for immediate drug absorption, especially for patients with swallowing difficulties.

 Customization: 3D printing allows for the creation of tablets with unique shapes, sizes, and textures, tailored to individual patient needs.

 Rapid Dissolution: The porous structures of 3D-printed tablets can be designed to disintegrate rapidly in the mouth, making them suitable for patients with swallowing difficulties.

 Improved Bioavailability: 3D printing can enhance the bioavailability of poorly soluble drugs by increasing their surface area and promoting dissolution.

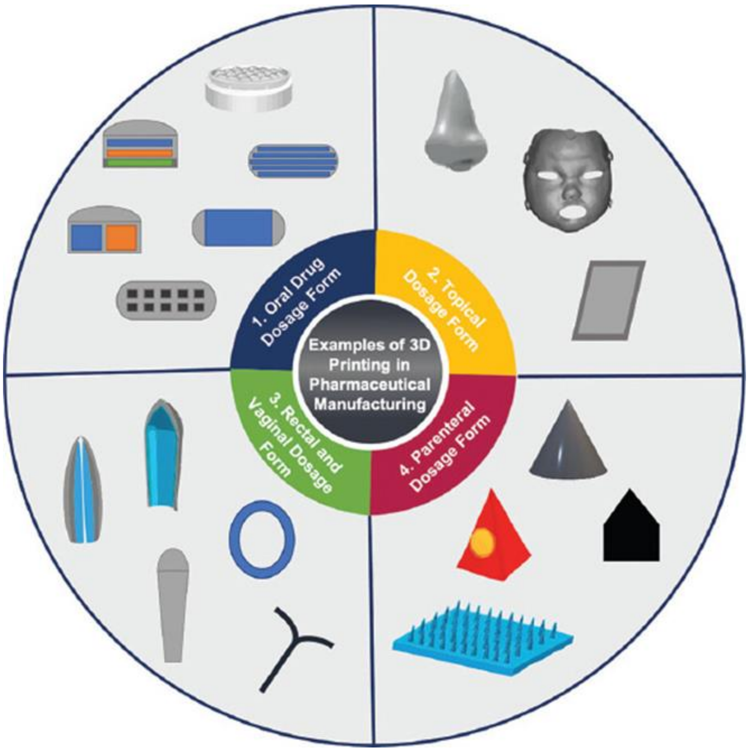


Fig-12 : Applications of 3D Printing in Different Dosage Forms

5.2 Medical Devices:

- **Drug Delivery Devices:** 3D printing can produce intricate drug delivery devices, such as inhalers, pumps, and patches, for various therapeutic applications.

5.3 Research and Development:

- **Rapid Prototyping:** 3D printing enables rapid prototyping of new drug formulations and delivery systems, accelerating the drug development process.

 Accelerating development: Creating physical models of new drug formulations and delivery systems quickly, allowing for early testing and optimization.

 Enhancing design: Iteratively refining designs based on physical prototypes, improving drug efficacy and safety.

 Reducing costs: Minimizing material waste and production time, leading to cost-effective drug development.

 Improving patient outcomes: Facilitating the development of more effective and targeted drug therapies.

- **Organ-on-a-Chip Models:** 3D-printed organ-on-a-chip models can simulate human organs and tissues, providing valuable insights into drug interactions and toxicity.

5.4 Other Applications:

- **Point-of-Care Manufacturing:** 3D printing can enable on-demand manufacturing of medications at the point of care, reducing supply chain complexities and improving access to healthcare.
- **Pharmaceutical Packaging:** 3D-printed packaging can provide unique features, such as tamper-proof seals and customized labeling, enhancing product security and consumer experience.
- **Educational Tools:** 3D-printed models can be used for educational purposes, helping students visualize complex pharmaceutical concepts and processes.
- **Drug Counterfeiting Prevention:** 3D printing can be used to create unique, difficult-to-replicate features on pharmaceutical products, helping to combat counterfeiting.[15,16,17,18]

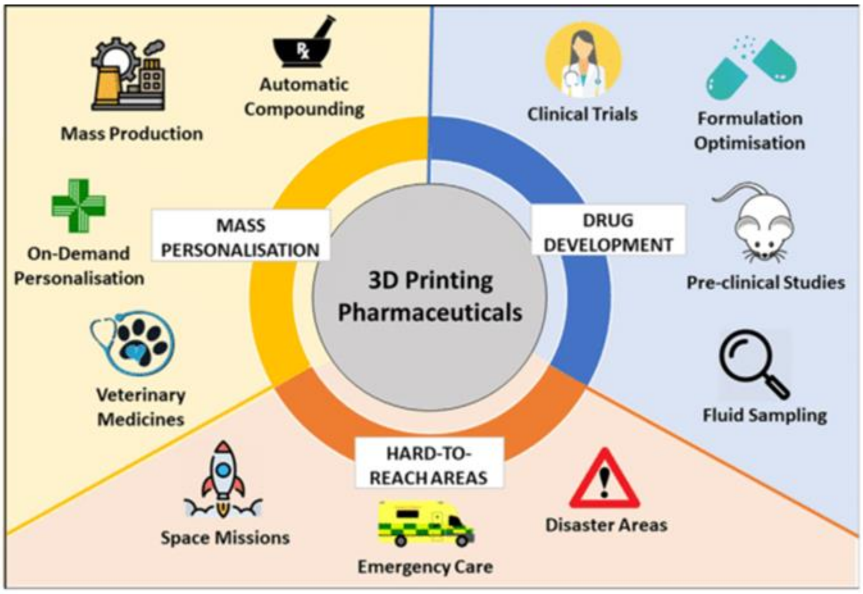


Fig-13 : Applications of 3D Printing

6. Marketed examples of 3D printed drugs:

Active Ingredients	Dosage Forms	3DP Technology
Acetaminophen	*Tablet*	*3DP technology*
Folic Acid	*Nanosuspension*	*Inkjet 3DP*
Levofloxacin	*Implant*	*Inkjet 3DP*
Prednisolone	*Solid dosage forms*	*Thermal Inkjet (TIJ) Printing*
Salbutamol sulphate	*Solution*	*Thermal Inkjet (TIJ) Printing*
Guaifenesin	*Tablet*	*Desktop 3D printer*
Hydrochlorothiazide	*Tablet*	*FDM*

- Spritam, made by US-based pharmaceuticals company Aprecia, is an oral formulation of levetiracetam, which is used to control seizures in people who have epilepsy.
- T19 by China based pharmaceutical and 3D printing technology firm Triastek has been developed in-house and is designed to treat Rheumatoid Arthritis.

7. Conclusion:

3D printing in pharmacy represents a transformative technology that offers numerous benefits. This technology allows for precise control over drug release profiles, potentially improving therapeutic outcomes for patients with complex conditions. Additionally, 3D printing can streamline the production process, reducing waste and enabling on-demand manufacturing, which is particularly advantageous for rare diseases or small patient populations. The capability to design complex drug delivery systems, such as multi-drug combinations and novel dosage forms, further explains the potential of 3D printing in advancing pharmaceutical care. Despite these promising applications, challenges such as regulatory hurdles, scalability, and the need for specialized materials and equipment must be addressed to fully integrate 3D printing into mainstream pharmaceutical practice. Overall, the future of 3D printing in pharmacy is promising, with ongoing research and technological advancements paving the way for innovative and patient-centric therapeutic solutions.

References:

1. Timothy Tracy a,b, Lei Wu a, Xin Liu a, Senping Cheng a, Xiaoling Li a,c,*

3D printing: Innovative solutions for patients and pharmaceutical industry

2. Witold Jamróz1 & Joanna Szafraniec1 & Mateusz Kurek1 & Renata Jachowicz1

3D Printing in Pharmaceutical and Medical Applications – Recent Achievements and Challenges

3. Abdul W Basit & Sarah J Trenfield

3D printing of pharmaceuticals and the role of pharmacy

4. Choonara, Y.E., et al.

3D Printing in Pharmaceutical Manufacturing: Recent Advances and Challenges

5. Abdul W Basit, Sarah J Trenfield

3D printing of pharmaceuticals and the role of pharmacy

6. Maniruzzaman, M., et al.

Hot Melt Extrusion: An Emerging Technique for the Formulation of Personalized Medicines

7. Khaled, S.A., et al.

3D Printing of Drug Formulations: Pressure-Assisted Micro Syringe as a Versatile Tool

DOI: 10.1371/journal.pone.0089432

8. Awad, A., et al.

Recent Advances in 3D Printing of Multilayered Drug Delivery Systems

DOI: 10.1016/j.xphs.2019.12.009

9. Wang, J., et al.

Photopolymerization in 3D Printing of Pharmaceuticals: Challenges and Opportunities

10. Martinez, P.R., et al.

Digital Light Processing (DLP) 3D Printing for Drug Delivery Applications

11. Subhash Deshmane 1, Prakash Kendre 1, Hitendra Mahajan 2, Shirish Jain 1

Stereolithography 3D printing technology in pharmaceuticals: a review

PMID: 34663145 DOI: 10.1080/03639045.2021.1994990

12. Athinarayanan Balasankar 1,†ORCID,Kandasamy Anbazhakan 1, et al.

Recent Advances in the Production of Pharmaceuticals Using Selective Laser Sintering

https://doi.org/10.3390/biomimetics8040330

13. Nadine Gottschalk [a b], et al.

Drop-on-powder 3D printing of amorphous high dose oral dosage forms: Process development, opportunities and printing limitations

https://doi.org/10.1016/j.ijpx.2022.100151

14. Dolores R. Serrano 1,2,*, et al.

3D Printing Technologies in Personalized Medicine, Nanomedicines, and Biopharmaceuticals

https://doi.org/10.3390/pharmaceutics15020313

15. Asad Ali, Usama Ahmad, Juber Akhtar

3D Printing in Pharmaceutical Sector: An Overview

DOI:10.5772/intechopen.90738

16. Essyrose Mathew,[1] et al.

3D Printing of Pharmaceuticals and Drug Delivery Devices

PMCID: PMC7150971 PMID: 32183435 doi: 10.3390/pharmaceutics12030266

17. Jessica Mancilla-De-la-Cruz,[1] Marisela Rodriguez-Salvador,[1,*] Jia An,[2] and Chee Kai Chua[3]

Three-Dimensional Printing Technologies for Drug Delivery Applications: Processes, Materials, and Effects

doi: 10.18063/ijb.v8i4.622 PMCID: PMC9668588 PMID: 36404786

18. Dr. Ganesh R. Godge, Vaishali K. Ghume, Bhakti B. Bidave, Aarti R. Golhar

3D Printing Technology in Pharmaceutical Drug Delivery

DOI:10.47583/ijpsrr.2021.v68i01.003