

# A Review on 3D Printing Technology Used in Pharmaceutical Industry

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**Abstract:** *Three-dimensional printing (3DP) makes it possible to create a variety of geometries using computer-aided design with various materials and procedures for intended uses, such pharmaceutical drug delivery systems. Despite the fact that 3D printing was patented in 1986, 3DP research did not gain traction until the past 10 years. The expectations of regulatory bodies, constraints, challenges in setting up such facilities for the manufacturing of pharmaceutical goods, benefits, drawbacks, uses, techniques, and related manufacturing hazards are all presented here. FDA. When compared to conventional drug preparation methods, 3D printing technology offers substantial benefits for customized drug production, making it simple to create preparations with intricate structures or drug release characteristics and enabling quick production of tiny quantities of medications. It also offers a thorough analysis of the state of this platform's research and development at the moment. The present review aims to provide an overview of the benefits, limitations, and uses of 3D printing in pharmaceutical technology by outlining several techniques (such as thermal ink jet printing, ink jet printing, fused deposition modeling, extrusion 3D printing, zip dose, hot melt extrusion, 3D printer, stereolithography, selective laser sintering, laser-based writing system, continuous layer interface production, and powder-based 3D printing). [15]*

**Keywords:** Structure, Laser, Pharmaceutical, Drugs, Computer-aided design, Printing, Modeling, 3D printing and Three-dimensional printing

## I. INTRODUCTION

Drug delivery is the effective and secure passage of a pharmacologically active chemical, or the drug, within the body to achieve the necessary therapeutic efficacy. Modifying the drug's release profile to change its pharmacokinetics contributes to increasing both the medication's safety and effectiveness. Using 3D printing, turn become one of the leading technologies in the pharmaceutical industry. Growing in popularity, three-dimensional printing (3DP) is used in the aerospace, automotive, biomedical, dental, defense, industrial, and commercial sectors. It has made rapid prototyping and small-scale manufacturing more accessible, affordable, and easy sectors that are consumable. The term "three-dimensional" (3D) printing refers to a manufacturing process wherein objects are created by layering together materials (such plastic, metal, ceramics, powders, liquids, or even living cells) to create a three-dimensional object. The creation of tangible models through three-dimensional computer-aided design (CAD) is known as rapid prototyping. It is also known as solid free-form fabrication and additive manufacturing because material is applied layer by layer under computer control. The field of 3DP medical applications is predicted to undergo a revolution as its applications grow. The application of 3DP in the medical field will have numerous benefits, including enhanced collaboration, economic efficiency, better productivity, democratic architecture and production, and the invention and personalization of medical equipment, medications, and appliances. [28]

"Structuring a three-dimensional object in its physical configuration from its digital form"  
is the definition of 3D printing :-

- The progressive addition of materials, 3D printing, also known as additive manufacturing, turns geometric representations into tangible items.
- With the use of 3D printing technology, an object can be printed directly from a computer-aided design (CAD) model, layer by layer, by depositing material.

3D printing is characterized by :-

“Constructing a three-dimensional item from its digital form to its physical configuration”

1. Additive manufacturing, also known as 3D printing, uses incremental material additions to produce tangible items from a geometric representation.
2. Using a computer-aided design (CAD), 3D printing technology can print an object layer by layer by depositing material. [28]

### 3D PRINTING PRINCIPLES

Modeling- Computer-aided designs (CAD) into virtual blueprints.

Printers- That print materials read the design and apply layers of material one after another.

Completing- The supports are eliminated or dissolved to obtain the finished product after printing.[7]

### Merits of 3D Printing Technology :-

1. Its high drug loading capacity in comparison to traditional dosage forms.
2. Small doses of powerful medications are given with accuracy and precision.
3. lowers production costs because there is less material waste.
4. Appropriate medication administration for challenging to synthesize active components, such as low water solubility.
5. Limited time for therapy.
6. Genetic variances, ethnic differences, age, gender, and environmental factors can all be taken into account when customizing medication for a patient.
7. The course of treatment can be altered to enhance patient adherence when administering numerous drugs under different dose regimens.
8. The 3D models can be made with a variety of materials. It makes the process of creating prototypes or construction models for a wide range of projects across numerous sectors relatively simple.
8. Excellent surface-finish items are produced. [10]

### Demerits of 3D Printing Technology :-

1. At the moment, size restrictions are the only thing limiting 3D printing technology. Even with 3D printers, really huge items are still unattainable.
2. The typical householder still cannot afford to purchase a 3D printer due to its high cost. Various 3D printers are needed to produce different kinds of items, and color printers are more expensive than monochrome printers.
3. Manufacturing employment will go, as is the case with all new technologies. [12]

### 3D PRINTING TECHNIQUE

First, a simulated 3D modeling of an object using digital design applications like SolidWorks, On shape, Creo parametric, AutoCAD, Autodesk, etc.

↓

The electronic file format (.STL), which stands for stereolithography or standard tessellation language, is subsequently applied to the digital model.

↓

Triangle facets add detail to the 3D model (STL) image's surface. [5]

↓

Using specialist software that is installed in a 3D printer and splits the design into a sequence of 2D horizontal cross-sections, the (STL) file has been converted into a G file.

↓

It is now possible to move the printer head in the x-y axis to the base of the 3D item. Upon shifting into the z-axis, the print head will progressively deposit the desired content layers, creating a complete three-dimensional object.

↓

The maximum 3DP technology numbers are compatible with the STL file format. When the 3D models are transformed into a digital format, very few errors may occur. STL; errors made during converting can be fixed using tools like

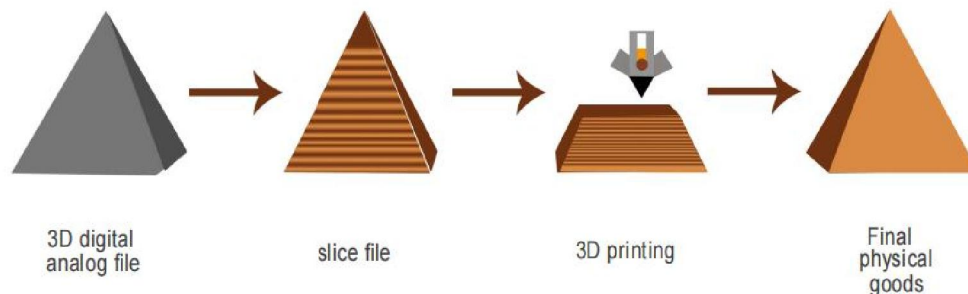
Magics (Materialize). The material type, color, texture, properties, and other details are not specified in depth in STL. [8]

### 3D PRINTING PROCEDURE

Initially, an object's virtual 3D design is produced utilizing digital design programs such as On Shape, SolidWorks, Creo Parametric, AutoCAD, Autodesk, etc. After that, this digital model is transformed into a digital file in the (STL) format, which is an acronym for stereolithography or standard tessellation language.

Triangulated facets provide details about the 3D model's surface that is contained in the (STL) file. The design is cut into a number of slices to transform the (STL) file into a G file.

3D horizontal cross-sections using specialist software for slicers, which is included inside the 3D printer. To produce the 3D object's basis, the print head is now moved along the x-y axis. The one that currently permits the print head to travel along the z-axis, depositing the required material's layers one after the other, resulting in a finished 3D object. The greatest number of 3D printing technologies that work with (STL) file's structure. When converting the 3D model to an STL digital file, some mistakes could happen; thus, software for example, Magics (Materialize) can be used to fix conversion mistakes. different file types STL such as 3D manufacturing format (MF) and additive manufacturing file format (AMF). STL doesn't possess details on the kind of material, including its qualities, color, texture, and other characteristics.



**Fig. 1. Process of 3D Printing.**

### 3D PRINTING TECHNOLOGY TYPES

According to variables including drug packaging, drug release, drug stabilization, and pharmaceutical dose stability, the conventional pharmaceutical industry operations of milling, grinding, granulation, and compression frequently result in uneven finishing quality. On the other hand, 3DP offers strategic benefits as a potent tool technology, including improved R&D efficiency, security, efficacy, and medication accessibility.

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#### I. Thermal Printing using Inkjet

Using a micro-resistor to heat the ink fluid until it turns into vapor and expands to force the ink drop out of a nozzle is the process of thermal inkjet printing.

- It is employed in the production of drug-loaded liposomes.
- Drug-loaded biodegradable microspheres.
- Drug-eluting stents are coated and loaded using patterned microelectrode arrays.
- Generating biological films without affecting protein activity injecting.
- Av spontaneously prepared or dissolved medication onto three-dimensional scaffolds

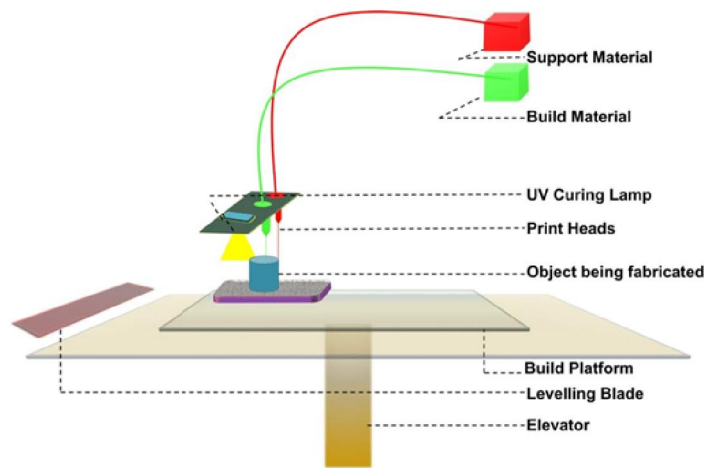
**Inkjet Printing:**

The same method used in computer-operated inkjet printing is the source of this personalized medicine approach. It was modified for use in pharmaceutical applications by substituting pharmaceutical solutions containing medications for the ink and regular paper with edible substrate sheets. The two primary printing types used under inkjet printing are thermal inkjet printers and piezoelectric inkjet printers. Dose alterations are accomplished by changing the area to be printed or the number of layers printed in given area. Printing-based inkjet systems encompass two types of techniques: Continuous inkjet printing and Drop-on-demand printing. In continuous inkjet printing, the liquid ink is directed through an orifice of 50-80 μ m diameter creating a continuous ink flow. These parameters are controlled by creating an electrostatic field. Thus, the droplets are charged and separated by “droplets of guard” to minimize the electrostatic repulsion between them. The electrostatic field created directs the charged droplets to the substrate. [29,30]

Inkjet drug printing offers a significant advantage of accurate control of dose combination and pattern of drug release. Ink jet printing requires the starting materials to possess certain characteristics mainly; particle size needs to be <1 μ m to avoid clogging the printer head, viscosity needs to be < 20 c P and surface tension between 30 and 70 nm/m for efficient flow.

Merits of Inkjet printing include -

- low cost of processing.
- Quick processing speeds.
- It produces very little waste, provides CAD data in a "direct write" fashion.
- Large areas of material are processed with little contamination.

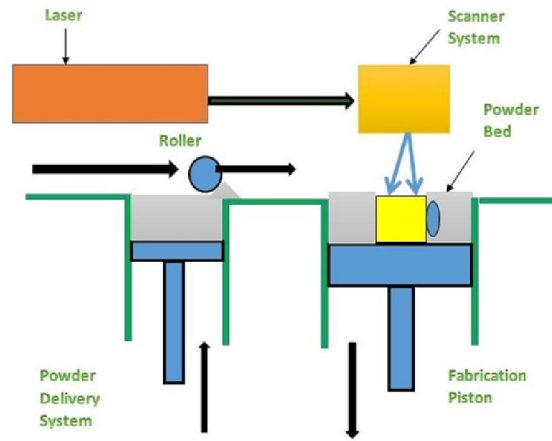


**Fig. 2.1. Inkjet Printing in 3D Printing.**

**II. SELECTIVE LASER SINTERING**

A fast-manufacturing method called selective laser sintering, which is typically employed for rapid prototyping, is based on the utilization of powder-coated metal additives. For the scan. Then positioning the particles in the specified sizes and forms. The layers are heated by a constant laser beam. The scanned layers' shape matches the source to individual parts of the models developed by design with computer assistance or from files created by Stereo-Lithography printing. Upon completing the initial layer scan, the scanning of Overlying the first layer is the second layer moving from the bottom to the top and continuing the procedure until the finished product is complete.

Using a high intensity laser, this method fuses tiny particles of metal, ceramic, glass, or plastic powder into a mass with the required three-dimensional forms. Examining the cross section or layers produced by three dimensions software for modeling on the powder bed's surface, laser fused the powdered material just in certain places so that the One layer of thickness is removed from the powder bed. After that, another layer of material is put on top, and the procedure is carried out repeatedly till the item is finished. [1,10]



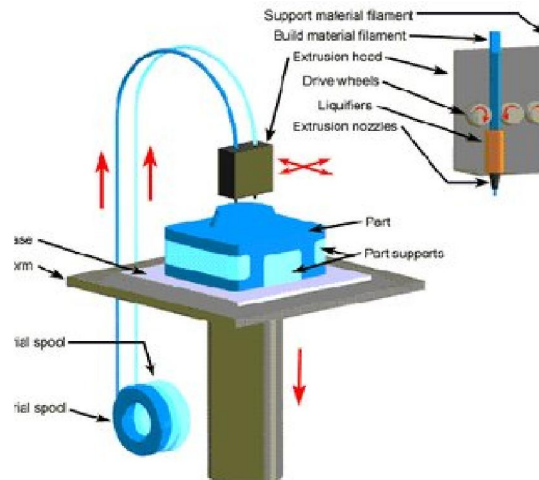
**Fig. 2.1. Selective Laser Sintering Technique.**

### III. FUSED DEPOSITION MODELLING

Selective laser sintering printers are far less widespread and more expensive than fused deposition modeling printers. The printer used for fused deposition modeling has a like the print head of an inkjet printer. However, rather than ink, the print releases hot plastic beads. Moving head, creating the sculpture in thin layers. To form each layer, the procedure is repeatedly carried out exact control over the quantity and placement of each since. For the material to fuse or bond to the layers below, it is heated.

Each layer of plastic solidifies as it cools, forming the solid object piece by piece. Based on a fused deposition modeling's cost and complexity printer, it might have improved capabilities like several Print heads. Deposition of Fused Printers for modeling can make advantage of a range of polymers. Actually, Fused Deposition Modeling in 3D Printed components are frequently created using the same. Thermoplastics utilized for conventional injection molding or machining, so their stability is comparable, durability as well as mechanical characteristics.

The process is choosing the desired polymer, melting it, and then injecting it into a hot dust cloud that is moving. Layer by layer, the polymer is applied on a 3-axis (x-y-z) basis, which, when solidified, gives machine-assisted modeling models a perfect structure. This methodology enables the creation of many dosage methods, including implants, release without order tablets, and so forth. [2]



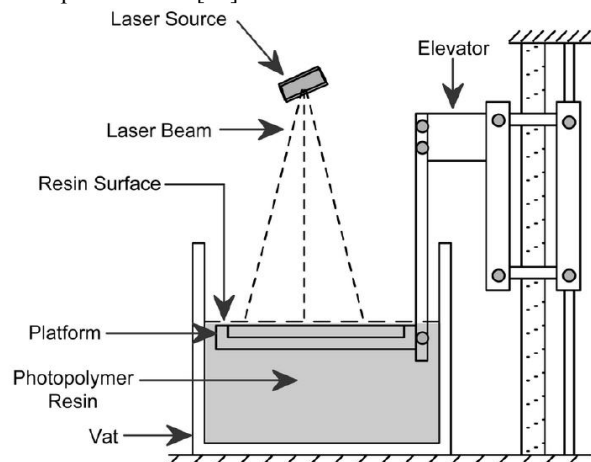
**Fig.2.3. Fused Deposition Modelling.**



#### IV. STEREO LITHOGRAPHY

This method was first discovered by Charles Hull in 1988 as a means of printing three-dimensional systems. Photopolymer materials that can be cured by a UV laser, such as resin or acrylate, were employed in the printing process. This popular and quick prototyping technique can create extremely precise and intricate polymer pieces. By tracing a laser beam on the surface of a vat filled with liquid photopolymer which has a moveable stage within to support the component being built stereolithography creates objects one layer at a time. The photopolymer solidifies rapidly wherever the laser beam hits the liquid's surface. A resulting layer forms on top of the platform after it is lowered by an amount equal to the layer thickness, which is usually between 0.003 and 0.002 inches.

As a result, a three-dimensional object made of numerous layers is entirely constructed because of the material's self-adhesive quality, which forces every layer to adhere to every other one. Support structures are required to hold objects with undercuts or overhangs during the fabrication process. These can be designed automatically or manually using a computer program specialized for quick prototyping. After finished, the component is raised over the tank and emptied. The surfaces are cleansed or swabbed clean of any leftover polymer. The part is often given a final cure by placing it in a UV oven. Following the last curing, the part's supports are removed, and its surfaces are polished, sanded, or otherwise completed. The process is carried out repeatedly until a three-dimensional structure takes shape. This approach produces fine-grade three-dimensional structures with great precision. This method has been used thus far to provide oral dosages of aspirin and paracetamol. [13]



**Fig.2.4. Stereo-Lithography.**

#### V. HOT MELT EXTRUSION

The procedure of melting a polymer and a medicine at a high temperature while continually applying pressure inside the device to combine is known as hot melt extrusion. It is a multi-step, continuous manufacturing process that involves feeding, heating, mixing, and shaping. Recent research has demonstrated that Hot Melt Extrusion can increase the solubility and bioavailability of medications that are poorly soluble. [9]

#### VI. EXTRUSION 3D PRINTING

This method does not require higher support material because the material is extruded onto the substrate from an automated nozzle. It is exclusively employed in the production of expectorant tablets containing guaifenesin. Pastes, suspensions, semisolids, and molten polymers are among the materials that can be extruded. [17,24]

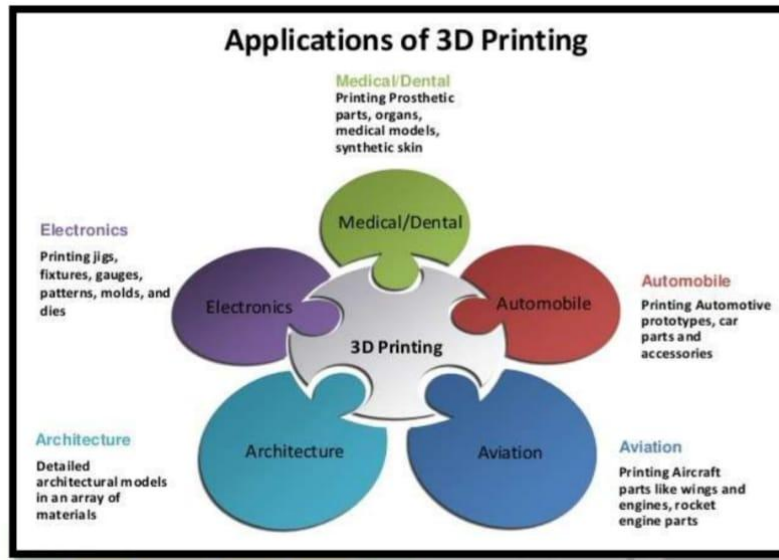
#### VII. PRESSURE-ASSISTED MICRO SYRINGES (PAM)

A micro syringe is used in this instance to drive out fluid stuff that has the proper resistance to flow. With the use of pressurized air, the micro syringe can operate similarly to an inkjet machine and discharge fluid. PAM makes it feasible to have highly advanced medication delivery systems. A similar piston-based device has emerged that uses a stepper motor instead of pressurized air to deliver the printing component. [15]

**APPLICATIONS OF 3D -PRINTING IN PHARMACEUTICALS**

**APPLICATIONS OF 3D PRINTING-**

- Potential applications in pharmaceuticals, medical engineering, tissue engineering, aerospace, industrial design, and architecture for process improvement and performance modification.
- It focuses largely on the two possible locations to advance the development of pharmaceutical products into uncharted territory, producing sophisticated delivery systems, and customized medicine.
- Dental implants in the healthcare sector.
- In the process of creating a multi-drug, organized release implant to treat bone tuberculosis.
- Supports the printing of organs, biomaterials, and materials containing cells. [14]



**Fig 2.1. Application of 3D Printing.**

**3D Printing Applications -**

Despite being an old technology, 3D printing has been quite popular recently in many different industries because of its increased cost-effectiveness, efficiency, and simplicity.

The most popular uses for 3D printing are:

**1. Construction:**

One of the important uses for 3D printing is construction. Since the 1990s, academics have been investigating concrete 3D printing as a quicker and less expensive method of building structures. Additive welding, powder bonding (reactive bond, polymer bond, sintering), and extrusion (foam, wax, cement/concrete, polymers) are some specific uses of 3D printing in the building industry. Today, site walls and foundations are built using massive 3D printers made to print concrete. Additionally, they have the ability to print concrete parts that are modular for on-site assembly. These technologies save labor costs and waste while enabling increased accuracy, complexity, speedier building, and better functional integration. [17]

**2. Healthcare:**

3D printing is used in the healthcare industry to produce prototypes for innovative dental and medical product development. 3D printing is also used in dentistry for producing tools for making dental aligners and templates for casting metal dental crowns. Additionally, the solution is useful for producing knee and hip implants and other stock items directly, as well as for developing patient-specific products like orthotic insoles, hearing aids, and customized prosthetics. It is being investigated if 3D-printed surgical guidance for certain procedures as well as 3D-printed bone, skin, tissue, organs, and medications are feasible. [11]

In the medical field, instruments are designed to measure the patient's body and can be prepared for operation.

### 3. Aerospace:

3D printing is utilized in the aerospace industry for product development and prototyping. Because it enables researchers to meet the demanding requirements of research and development without sacrificing the high industrial standards, the solution is also extremely beneficial in the development of airplanes. For the flight, several older or non-essential aircraft parts are 3D printed. [3,25]

### 4. Automotive:

Automotive companies use 3D printing to prototype and manufacture specific parts, particularly those who specialize in racing cars like those used in Formula One. Instead of keeping spare parts in store, companies in this sector are investigating the potential of employing 3D printing to meet aftermarket demand by creating them as needed. [4]

### 5. Prototyping and manufacturing:

The production of a single mold using conventional injection-molded prototypes can take weeks and cost hundreds of thousands of dollars. 3D printing was initially developed for quicker and more effective prototyping, as was mentioned before in the text. Prototyping can be finished in a few hours and for a fraction of the price of traditional production lead times thanks to 3D printing technology. This makes it particularly perfect for projects that require users to improve the design at each stage. Products that are often personalized or do not require mass production can also be made using 3D printing. Prototypes are not the only goods that are manufactured quickly using SLS and DMLS. [21,12]

Rapid prototyping is the process of using CAD software to quickly produce a real-scale model of an object.

6. Reconstructing bones and body parts in forensic pathology: Industrial, structural, and fingerprint examinations; accident reconstruction.

7. Personalized dosing: Active pharmaceutical ingredients (API) and excipients are created using digitally controlled equipment.

## CHALLENGES IN 3D PRINTING TECHNOLOGY -

- The technology is still in its early stages of development. As a result, it faces a number of difficulties, including post-treatment procedures, choosing suitable excipients, optimizing the device's performance for a variety of applications, etc.
- To enhance the functionality of 3D printed goods and broaden the scope of innovative drug delivery systems' applications.
- The distance between the nozzles and the powder layer, the printing pace, the duration between two printing layers, and other crucial factors must all be tuned to produce high-quality 3D products.
- Printing rate, passes, print heads line velocity, printing layer interval time, nozzle and powder layer distance, and other key parameters need to be changed in order to increase 3DP quality.
- From a safety perspective, the inherent adaptability may be the most significant liability resource for redesigning using 3D printing.
- There are a number of obstacles to improving 3D printed items and expanding the usage of innovative drug delivery methods, including adaptable use, suitable excipient selections, and post-treatment techniques.
- Drug delivery is still in its early stages of development, despite some encouraging findings. [27]

The printing rate, printing passes, print head line velocity, and interval duration are some crucial characteristics that must be optimized in order to achieve the quality of 3D items. The separation between two printing layers and the nozzles as well as the coating of powder, etc.

The quality of the final 3D printed product is greatly impacted by post-prototyping techniques including drying (hot air heat, microwaves, and infrared). items. To improve the 3D drug loading capacity processed tablet printing, uniaxial compression, and Techniques that are scattered and suspended are used, although this method suffers from congestion and increasing complexity. about the spray nozzle.

## FUTURE PROSPECTS

Future prospects for new possibilities 3D printing will be used in a variety of ways, including-

- Create and design a range of innovative dosage forms.



- Obtain ideal drug release profiles.
- In order to prevent drug incompatibilities, create novel excipients.
- Dose forms for drugs, facilitating delivery,
- Reduce the deterioration of biological molecules or aid in the search for solutions. [22]

New 3D printing technologies might lead to completely new pharmacological research options. 3D printing will be used in many ways in the near future including the fabrication and engineering of new dosage forms, the achievement of optimized drug release profiles, the development of new excipients, the avoidance of drug incompatibilities, the support of delivery, the limitation of biological molecule degradation, and the aiding of cure research. Personalized medicine may provide a whole new range of opportunities because to 3D printing. In its most basic form, experts and researchers envision creating customized oral pills using 3D printing. As an alternative to conventional compounding pharmacies, on-demand printing of pharmaceutical items can be used for treatments that are customized to a patient or for pharmaceuticals having a short shelf life. It could eventually inspire innovations in garage biology. Because 3D printing is still a relatively new technology, there are issues with safety, security, and regulation. Therefore, these issues can be resolved in the near future. [8]

#### **RISK ASSESSMENT DURING 3D PRINTING PROCESS -**

Determining risk is a crucial stage in the development of 3D printing technology. It was primarily done to avoid failure of quality assurance parameters including appearance, assay, and content consistency. To ensure that the products produced in industries meet quality standards, risk factors are determined in conjunction with the process and process variables.

Risk factors are checked in these conditions-

- If a certain printer cannot print a certain pattern, software controls should be used.
- Real-time layer thickness monitoring is required to manage layer thickness variations.
- Improper layering resulted from controlling the production location's temperature and moisture content, mostly due to changes in the surrounding environment.
- It may be possible to prevent incorrect positioning in the printer by monitoring the print head's height and speed during printing.
- It is possible to avoid the uneven layers by keeping an eye on the powder's aqueous content and molecular size distribution.
- Reduced or eliminated print head clogging can be achieved by ensuring the particle size distribution and keeping an eye on the inkjet flow.
- Variations in binder viscosity or binder surface tension cause inconsistent agglomeration. [28]

#### **VIII. CONCLUSION**

Complex structures may be produced quickly and affordably with 3D printing technology. It could enhance its use in biotechnological and pharmaceutical research domains. The pharmaceutical industry uses 3D printing for a variety of technical purposes, including creating new excipients, improving medication compatibility, creating novel drug delivery systems, and creating personalized dosage forms. The pharmaceutical industry, along with all other sectors that require a certain degree of safety and security, may control and follow 3D printing in the future.

In the pharmaceutical industry, 3D printing has emerged as a practical and promising method that might result in patient-centered tailored treatment. With its inherent flexibility, 3D printing technology is opening up new possibilities for sophisticated drug administration that are ideal for individualized or customized treatment. Pharmaceutical formulation methods and production styles will be completely transformed by 3D printing technology.

For pharmaceutical organizations, 3D printing technology might lead to new opportunities in product research, manufacturing, and distribution.

The FDA approved the first medicine made using 3D printing technology, which led to a very quick development of research on topical, oral, and or mucosal dose forms. It is challenging to attain formulation flexibility using traditional technical procedures, but this potential technology gives it.

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**FIGURE REFERENCE**

- Fig.1.1 <https://images.app.goo.gl/rD39AGLfKBp2dTSUA>
- Fig.2.1 <https://images.app.goo.gl/tgf3CwhnmLKBmmQ67>
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- Fig.2.3 <https://app.goo.gl/SpRmvnMDMGU84Csf9>
- Fig.2.4 <https://images.app.goo.gl/nvhTJQbsVuXVJUta7>