ISSN No:-2456-2165

Recent Approaches on 3D Printing (3DP) in Pharmaceuticals as Dominance Role in Traditional Formulation

Rahul Pal*[1], Prachi Pandey[2],
Arsh Chanana[5], Ravindra Pal Singh[6]
*[1,2,5,6] Department of Pharmaceutics,
NIMS Institute of Pharmacy, NIMS University
Jaipur, Rajasthan, India

Saman Waheed[3], Aparna Katiyar[4]
[3,4] Shri Ram Murti Smarak College of
Engineering and Technology,
Bareilly, UP, India

Abstract:- 3D Printing drug is to design and develop medicine that are suited to an individual. Pharmaceutical product is designed in three dimensions with computer. The three-dimensional printing (3DP) is an advance technique which used to describe 3D products manufactured on a digital platform designing and, in a layer-by-layer fashion of the given pharmaceutical product and object. The 3D Printing technology generally used to formulate the medicines that are tailored to a patient's therapeutic requirements (e.g., dosage, drug and drug release profiles). The aspects associated with 3D printing such as less material wastage, ease of manufacturing, less human involvement, very less post processing and energy efficiency makes the process sustainable for industrial use. 3D Printing technology has appeared as a major technological revolution of the recent years leading to the manufacturing and production of novel medical products and devices in pharmaceutical industry. In 3D Printing the Deposition of medicaments and excipients which may resulting in a shift in perspective in drug configuration, production, and use. These dosage forms address on-demand manufacturing, feasibility, improved size, dosage, and geometry, increased bioavailability with desired drug release profiles, and minimal toxicity or adverse drug reaction issues. However, it may help to address specific issues for various subgroups, such as paediatrics, geriatric, visually impaired, and chronic disease patients. Although several articles highlight the various applications of 3DP techniques. This review highlights the recent dominance role of 3D Printing technology such as including fused deposition modelling (FDM, Stereolithography (SL) and binder jetting has described the advancements in pharmaceuticals formulations with latest technology and enhancing drug therapeutic activity against the particular disease within less of time, show therapeutic approaches to bring in a vast array of useful applications and benefits to human.

Keyword:- *Pharmaceuticals, 3D-Printing (3DP), Traditional Formulation, DOD, Rapid Prototyping and DOS.*

I. INTRODUCTION

In the developing world, growing major demand on customized pharmaceutics which is especially for drug formulation or drug designing and medical devices makes the impact of additive manufacturing of pharmaceutical products has increased rapidly in the recently working years in pharmaceuticals. The 3D Printing has become one of the developing and powerful tools for serving as a technology of precise manufacturing of individually developed dosage forms, tissue engineering and disease modeling medicament. 3D Printing (3DP) is also known as *Rapid Prototyping*, is forecast to revolutionise the pharmaceutical sector, changing the mode of medicinal products development, manufacture and their use for the patients. The concept of the delivery of the drug has highly shifted over the years from conventional oral dosage form towards the targeted release of the drug. A constant motivation is on the rise, for the empowerment towards drug design, material property knowledge, manufacturing and processing of pharmaceutical dosage forms using a novel approach. Physico-chemical and biopharmaceutical properties of the active ingredient as well as auxiliary substances needs to be considered before the development of a dosage form [1]. An increased attention is being received by personalized medicines and the dose of the drug to be administered due to their elevated chances of adverse effects. Geriatrics and paediatrics have a high risk of adverse reactions during the manufacturing of pharmaceuticals for the general population [2]. In the last few decades, the focus has highly been shifted towards the personalization of the medicines for the disease. Therefore, Advancements is essentials for the novel dosage forms formulation and 3DP technologies have risen to a considerable extent recently. Three-dimensional printing (3DP) is considered to be a highly revolutionized, versatile and powerful technology so as to mark its steps towards the novelty in the pharmaceutical field for the formulation. It is highly helpful in engineering sector for medications, tissues and organs as well as in the modelling of the disease against the pharmaceuticals [3].

Three-dimensional printing (3DP) is one of the fastest developing areas of advance technology, science, pharmaceuticals and still it has the broader the applications. The term three-dimensional printing was defined by

ISSN No:-2456-2165

International Standard Organization (ISO) as: "Fabrication of objects through the deposition of a material using a print head, nozzle, or another printer technology''. [4] Although several conventional dosage forms (*Tablets or Capsules*) and formulations have been developed over the working years, they fail into the individual needs of the patient with their respective disease treatment. 3DP technology addresses these issues and contributes to the upgrading and development of conventional pharmaceutical formulation techniques. 3D printing is a manufacturing process in which materials are deposited layer by layer to form an entity. Based on a pre-designed 3D digital model, it accumulates the printed layers layer by layer to complete the construction of a 3D object. The main benefits including firstly reduced prototyping time and costs, easy product modifications at the designed level, the ability to manufacture small objects, and structures that are impossible to form using subtractive techniques [5].

3D Printing commonly extremely flexible, allowing local control of material composition and microstructure. Compared with traditional formulation processes, 3D printing has great advantages in producing highly complex and custom-designed products, so it is more economical and time-saving. Currently, the 3D printing technologies applied in the pharmaceutical preparation field mainly include **Fused Deposition Modeling** (FDM), **Stereo Lithography Appearance** (SLA) and **Binder Extrusion Printing**, etc. are the techniques involving in the drug modeling's and object build.[6]

- *FDM (Fused Deposition Modeling)*

Fused deposition modelling (FDM) 3D printing, also known as fused filament fabrication (FFF), is a material extrusion additive manufacturing (AM) process. FDM builds parts layer by layer by selectively depositing melted material in a predetermined path. The final physical objects are formed using thermoplastic polymers in the form of filaments. Composing the largest installed base of 3D printers worldwide, FDM is the most widely used technology across most industries, and likely the first process you think of when 3D printing comes up. The machinery of FDM focused on the (**Fig. 01**) below-

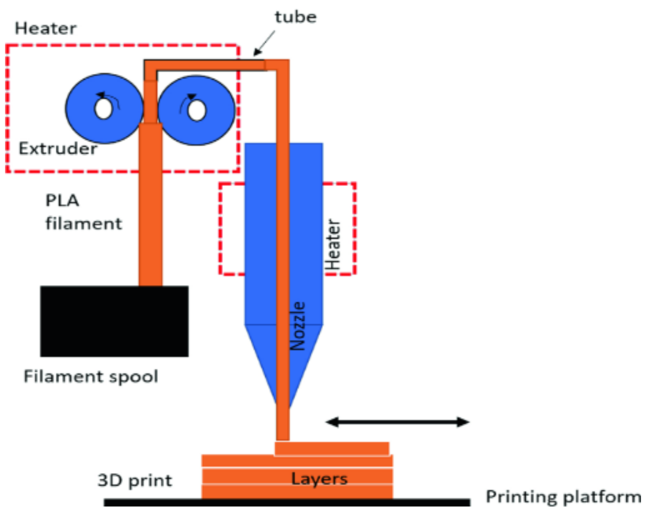

Fig 1 Fused Deposition Modelling's

FDM uses digital design files that are uploaded to the machine itself and translates them into physical dimensions. Polymers such as ABS, PLA, PETG, and PEI are used in FDM, and the machine feeds them as threads through a heated nozzle. [6]

To operate an FDM machine, you first load a spool of this thermoplastic filament into the printer. Once the nozzle hits the desired temperature, the printer feeds the filament through an extrusion head and nozzle. Multiple passes are required to fill an area, similar to colouring in a shape with a marker. When a layer is completed, the build platform descends and the machine moves on to the next layer. In some machine setups, the extrusion head moves up. This process repeats until the part is finished. [6-7]

- *(SLA) Stereo Lithography Appearance*

Stereolithography is a 3D Printing process which uses a computer-controlled moving laser beam, pre-programmed using CAM/CADD for object modelling. Stereolithography (SL) is a 3D printing process used in industry to create concept, models, cosmetic-rapid prototypes, and complex parts with intricate geometries in as little as one day. Stereolithography parts can be produced in a wide selection of materials, extremely high features resolution, and **quality surface finishes** are possible with SLA. SLA incorporates critical design considerations to help improve part manufacturability, cosmetic appearance, and overall production time. [8]

Stereolithography (SL) is an excellent choice for rapid prototyping and project designs that require the production of very accurate and finely detailed parts. Infrastructure of SL machine in 3D Printing show in (**Figure. 02**)

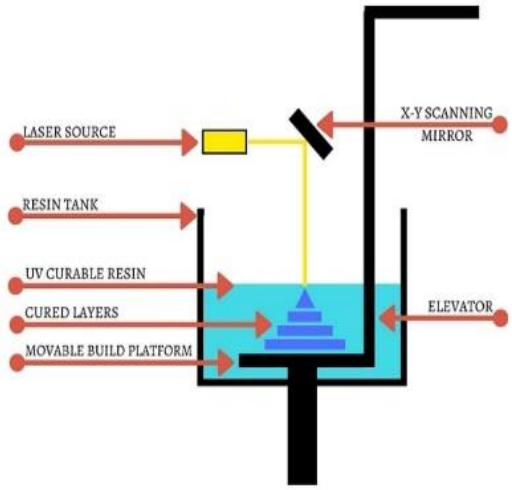

Fig 2 Stereolithography (SL) in 3D Printing

The working of Stereolithography machine begins the 3D printing process by drawing the layers of the support structures, followed by the part itself, with an ultraviolet laser aimed onto the surface of a liquid thermoset resin. After a layer is imaged on the resin surface the build platform shifts down and a recoating bar moves across the platform to apply the next layer of resin. The process is repeated layer-by-layer until the build is complete the production under 3D Printing. [9]

➢ *Binder Extrusion Printing*

Binder Jetting is a family of additive manufacturing processes. Binder Jetting involves depositing a binder selectively onto a powder bed and bonding these areas together to form a solid part one layer at a time. The materials commonly used in Binder Jetting are metals, sand, and ceramics that come in a granular form. Binder Jetting is used in various applications, including the fabrication of **full-color prototypes**, the production of **large sand casting cores and molds** and the manufacture of low-cost 3D printed metal parts. [10]

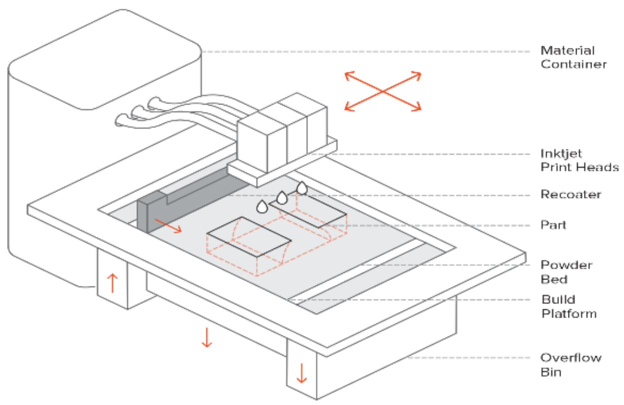

Fig 3 The Binder Jetting (Binder Extrusion) Process

➢ *The Working of Binder Jetting Process Consisting Some Steps* -

- *STEP. I.* The build platform is first covered with a thin layer of powder using a recoating blade.
- *STEP. II.* Then, a carriage with inkjet nozzles (which are similar to the nozzles used in desktop 2D printers) passes over the bed, selectively depositing droplets of a binding agent (glue) that bond the powder particles together. The size of each drop is approximately 80 µm in diameter, so good resolution can be achieved.
- *STEP. III.* When the layer is complete, the build platform moves downwards and the blade re-coats the surface. The process then repeats until the whole part is complete.
- *STEP. IV.* After printing, the part is encapsulated in the powder and is left to cure and gain strength. Then the part is removed from the powder bin and the unbound, excess powder is cleaned via pressurized air.

Depending on the material, a post-processing step is usually required. For example, metal Binder Jetting parts need to be **sintered** (or otherwise heat treated) or **infiltrated** with a low-melting-temperature metal (typically bronze). Full-color prototypes are also infiltrated with acrylic and coated to improve the vibrancy of colors. Sand casting cores and molds are typically ready to use after 3D printing. [11]

The completion of data of techniques used in 3D Printing (3DP) majorly used for the production of modeling's, of the given material which are generally thermostat, and follow lots of feature to build the 3D Printing object. These all techniques commonly work with the using of some material for the proper manufacturing such described in the given (**Table. 01**)

Table 1 List of 3D Printing Techniques and Material Used

Sr. No.	3D Printing Technique	Material Used
01.	FDM (Fused Deposition Modelling)	ABS, Polycarbonate and ULTEM™ 9085 Resin
02.	Stereolithography (SL)	Polypropylene, ABS (*Acrylonitrile Butadiene Styrene*) And Polycarbonate
03.	Binder Extrusion Printing	Gypsum, sand, ceramics, metals or polymers in granular forms.

The compound annual growth rate of the AM for Additive manufacturing (AM) or additive layer manufacturing (ALM) is the industrial production name for 3D printing, **a computer-controlled process that creates three dimensional objects by depositing materials, usually in layers** industry, including all services and products worldwide, has grown by 26.2% over the last 27 years to $5.1 billion in 2015 [12]. When compared with the other segments of AM industry, the healthcare (or medical) industry is the third largest market, with approximately 16% of the overall revenue, following automotive and consumer electronics (both share 20% of the overall revenue).

3D Printing (3DP) is gaining considerable attention as a potential technology enhancing efficacy, preciseness, and individualization while reducing wastage cost. The new technology also enables creation of novel oral dosage forms and medical devices which are otherwise challenging to be produced using conventional manufacturing technologies [13-14].

The advent of 3D printing technology in the pharmaceutical industry has made it possible to design and manufacture novel complex drug products, as well as multiple active drug pharmaceutical ingredients (API) into one dosage form with customized release trends and individualized design adapted to patients' specific needs. A 3D modelling application or 3D scanner is used by CADD (Computer Aided Drug Designing) in the first stages of the 3DP to virtually create the drug items or medications. [15]

➢ *Flow Chart of 3d Printing*

Explains by the definition 3DP is a step-by-step fabrication of the layers and finally form the medicament as similarly this 3DP as a software which slice the final model or the conventional dosage form into hundreds or thousands of horizontal layers of the medicines. When creating the medication formulation, the printer builds up the objects layer by layer, creating a single three-dimensional object. Above the description is the basics of that how's the 3DP printing performed in the pharmaceuticals for the medicament development [16]. The given below chart explain (**Fig. 04**) the basic 3D Printing performance-

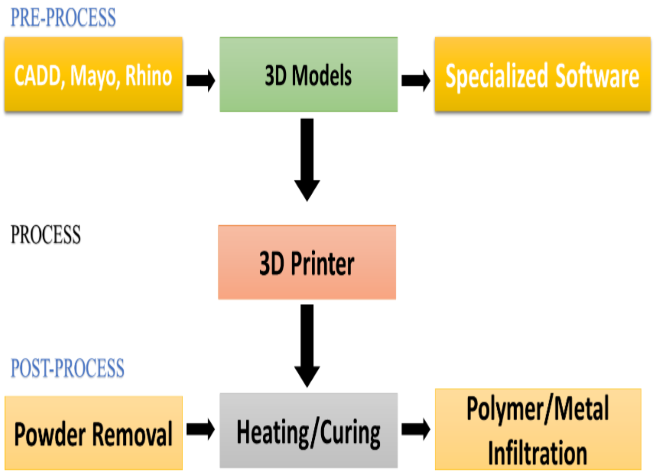

Fig 4 Flow Model of 3D Printing for Drug Modelling

These all process play an important role for the drug designing and drug development, as per the CADD and other software using the object build. Above (**Fig. 04**) the flow chart is necessary to understanding the basics of the 3D Printing of the given material products.

➢ *Merits of 3d Printed Drug Delivery*

The drug designing is the cost effective as well as the less time-consuming processing for the drug development or formulation of the drug, this type of 3DP is commonly for enhancing the therapeutic effect and especially for accuracy. Further 3D Printing is consisting numbers of merits in the formulation such as they describe as below section-

- High drug loading capability compared to conventional dosage forms.
- Accurate and precise dosing of powerful medications that are given in small amounts to promote activity.
- Reduced production cost due to less wastage of materials.
- Medication can be tailored to a patient in particular based on age, gender.
- Treatment can be customized to improve patient adherence in case of multi-drug therapy with multiple dosing regimen.
- Manufacture of small batch is feasible and the process can be completed in a single run.
- 3D printers capture minimal space and are affordable. [16-17]

➢ *Demerits of 3d Printing*

Including the numbers of merits in 3D Printing, it consists some disadvantages which are generally, size limitation and many more, discussed below data-

- Problems related to nozzle are a major challenge as stopping of the print head which affects the final products structure.
- Powder printing clogging is another hurdle. Possibility of modifying the final structure on to mechanical stress, storage condition adaptions and ink formulations effects.
- Printer related parameters and these effects on printing quality and printer cost.[18]

II. REASON BEHIND THE INITIATION OF 3D PRINTING

The FDA's Center for Device and Radiological Health (CDRH) has amended and approved 3D printed medical devices, which represent significant in advancements of the product in pharmaceuticals. The first 3D printing method used in pharmaceutics was attained by inkjet printing, a binder solution onto a powder bed, therefore the particles bind together. The technique was repeated until the final desired structure was obtained. [17-18] *Inkjet printing* was the technique used to manufacture Spritam tablets (*levetiracetam*) for oral use, the first 3D printed drug approved by the *Food and Drug Administration* (FDA) in 2016 by Aprecia Pharmaceuticals. 3D printing is the most advanced technique in many fields, including automobiles, aerospace, biomedicine, tissue engineering, and now the pharmaceutical industry (initial phase). [18]

III. COMMONALITIES AMONG 3D PRINTING (3DP) METHODS AND COMPARISON TO TRADITIONAL MANUFACTURING

3D printing has been predicted to replace traditional manufacturing technologies. However, the real power of the technology may lie not in competing with, but in complementing and augmenting conventional manufacturing methods. Several different 3D printing methods exist with different input materials and operating principles. Most 3D printing processes follow the same basic procedure for manufacturing solid products from digital designs:

➢ *Design*

The intended product design is rendered digitally. Designs can be rendered in 3D with computer-aided design (CADD) or digital 3D model software or in 2D as a series of images corresponding to the to-be-printed layers.

➢ *Conversion of the Design to a Machine-Readable Format*

3D designs are typically converted to the STL file format, which describes the external surface of a 3D model. 3D printing programs "slices" these surfaces into distinct printable layers and transfers layer-by-layer instructions digitally to the printer. Software can automatically suggest where to print support material to provide scaffolding for the in-process print for 3D printing methods that produce free-standing objects. [19]

➢ *Raw Material Processing*

Nylon, polycarbonate, ABS (acrylonitrile butadiene styrene), and PLA (polylactide) including soft PLA - as well as recycled alternatives- are all common plastics that can be used in 3D printing. Polymers like these are typically distributed in wire feedstock and used in material extrusion printers. Raw materials may be processed into granules, filaments, or binder solutions to facilitate the printing process.

➢ *Printing*

Raw materials are added and solidified in an automatic, layer-by-layer manner to produce the desired product. [20]

➢ *Removal and Post-Processing*

Products May Require Drying, sintering, polishing, or other post-processing steps after printing. Unprinted material can now be harvested and recycled for use in the printing process.

The complete processing for 3D Printing formulation of drug molecules, explained in the given (**Figure. 05**) below of the section such as following-

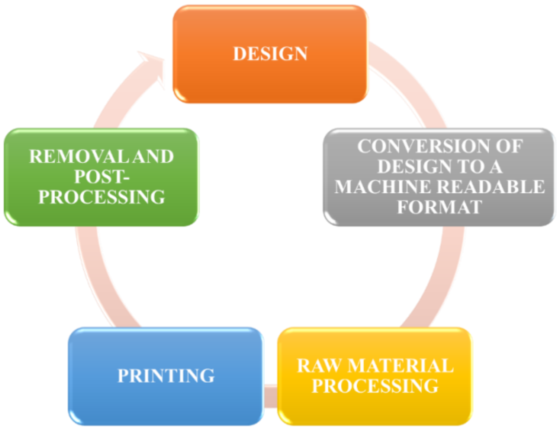

Fig 5 Process Involving in 3D Printing

3D printing in the formulation of material objects includes many steps such as design, conversion of the design to a machine-readable format, raw material processing, printing and removal, and post-processing for the object's construction. [21] The complete processing defined in the below points briefly.

IV. 3D PRINTING (3DP) PROCEDURE IN DIGITAL DESIGNING

3D printing or additive manufacturing is a process of making three dimensional solid objects from a digital file. The creation of a 3D printed object is achieved using additive processes. In an additive process an object is created by laying down successive layers of material until the object is created. Each of these layers can be seen as a thinly sliced cross-section of the object. The 3D Printing performed by the various steps in the below section describes (**Fig. 06**).

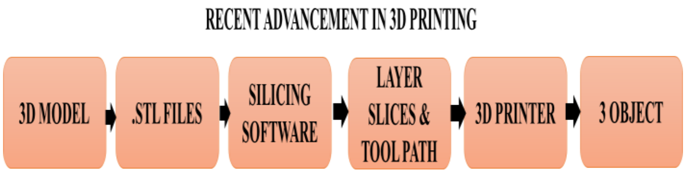

Fig 6 Recent Advancement in 3D Printing Procedure of 3D Printing

V. DIFFERENT TECHNIQUES USED IN 3D PRINTING (3DP)

The applications of 3D printers are one of the most revolutionary and powerful tools for the customized and personalized of pharmaceutical drug product and medicament formulation. 3D Printer have many advantages over the conventional manufacturing technologies for the tablets or capsules. Conventional methods for solid dosage form formulation necessitate a large number of processing steps such as milling, mixing, granulation, and so on. There are numerous techniques involved in 3D Printing for object modelling and build of the given material, such as traditional or tablet and capsule formation [22]. All techniques involving in 3DP describe in the (**Fig. 07**)

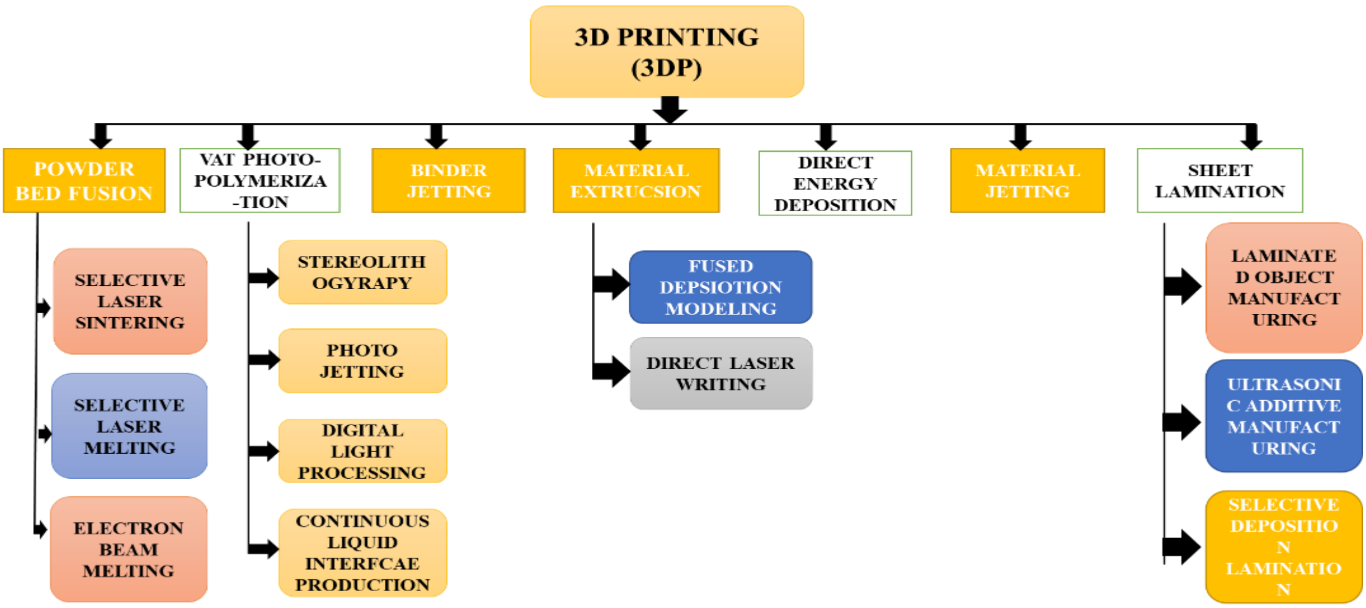

Fig. 7 Different Techniques used in the 3D Printing

The number of steps involved in preparation may increase the chance of batch failure or inadequacy in quality. 3D printing can reduce number of steps involved drastically requiring lesser regulatory and quality control issues. The different 3D Printing techniques utilized for the manufacturing of the medicament or drug products for the recent disease treatment, such defined as below section-

- *Binder Deposition*

This is the primary technique used in the production of pharmaceuticals by 3D printing. In this schematic inkjet printers spray formulations of drugs or binders in small droplets at precise speeds, motions and sizes onto a powder bed. This technique employs binder inks such as polyvinyl alcohol and maltodextrin in small droplets that are sprayed on a powder bed at precise and programmed speed, movement, and size. The ink used may contain only binder solution and the powder bed may contain a mixture of API and excipients to formulate a simplest drug product. Alternative to this API can be used along with binder in solution form or nanoparticulate suspension [22-23]. This technique is mostly suited for poorly soluble drugs i.e., class II and class IV of Biopharmaceutical Classification System (BCS).

- *Example:* A nanosuspension of folic acid (BCS class IV drug). The mechanism of solidification of drug product is similar to that of wet granulation.

- *Material Jetting*

Powder bed is not necessarily used for inkjet printing. It can print free-form structure by ejecting drop by drop which solidifies simultaneously like stalagmites. Waxes, molten polymers, various resins, suspensions and solutions, and multi component fluids are among the jetting materials used. The entire formulation is designed for jetting, which solidifies quickly, and the final form of the formulation is determined by droplet ejection path, droplet impact, and surface wetting. Deposit single layer and multiple layers of salbutamol sulfate on a potato starch film by thermal inkjet printing within ± 5% of theoretical dose [24-25]. Advantage over binder deposition is smaller layer thickness that enables formulation of micro-particles

- *Example:* Ciprofloxacin (BCS class IV drug) Nanoplexes complexed with dextran sulphate, resulting in nanosuspension on cellulose substrate via inkjet printing [26].

- *Extrusion Based Printing:*

Extrusion based 3D Printing is bifurcation into two techniques, the semisolid extrusion (SSE) and the fused deposition modeling.

(FDM). Extrusion printing technique is governed by two types of printing methods including hot melt extrusion (HME) technique and fused deposition modeling. In the case of HME technique, a homogenous solid dispersion of pharmaceutical excipients such as polymeric materials and plasticizers are prepared in a molten form of polymer and a drug substance is introduced in the polymeric composition. The advantage of hot melt extrusion is that it is a solvent-free method which eliminates the need for a rigorous solvent selection step, making it an environmentally friendly method of production [26-27].

- *Semi-Solid Extrusion (SSE)*

The 3DP process starts by designing the required 3D object using the computer-aided design (CAD) software. The SSE printer is made up of two integrated parts: software and hardware. The software component divides the 3D structure designed in CAD into printable layers. Furthermore, the software system controls the robotic movements of the hardware, as well as the applied pressure and other parameters that influence the printing process.

- *Fused Deposition Modeling (FDM)*

FDM is an additive manufacturing technique also known as fused filament fabrication. It works by extruding of molten mate-rials on a platform layer-by-layer to fabricate the 3D object. The most widely used 3DP technology in the world is FDM. This technique was primarily used for prototyping and engineering, but advances in filament production technology and the variety of materials available for printing have broadened its application to the pharmaceutical field. This FMD well defined in the above section of introduction how's its works and fined product will obtained. The thermoplastic polymers such as polylactic acid (PLA), polyvinyl alcohol (PVA), and ethyl vinyl acetate, 3D printing was introduced as a great adaptation in the pharmaceutical industry. The fused deposition technique is also known as fussed filament (FF) in the literature. [28]

These methods have gained popularity for fabricating 3D drug products in the pharmaceutical industry. The main advantage of the 3D extrusion printing technique is its high flexibility to develop a novel formulation of solid oral dosage forms with a different geometry, complexity and hallow structure product and various drug release profiles, and the ability to print a different range of polymers. Additionally, the extrusion method is a promising way to print materials in an amorphous form that speeds up dissolution and thereby increases the bioavailability of medications that aren't easily soluble.

- *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 (post-printing step). Powder bed 3D printing method is fast and compatible for printing a wide range of pharmaceutical substances. The technique holds considerable promise for producing controlled and quick release medication formulations, high dose drug formulations, and multilayer tablets comprising various and precise active ingredients.

➢ *Drop on Solid Deposition (DOS)*

It is generally, known as *powder-based printing* as well as *desktop inkjet printer*. Powder-based printing technologies include selective laser sintering (SLS), direct metal laser sintering (DMLS), selective laser melting (SLM) and electron beam melting (EBM). Different powder materials and energy sources are used in different powder-based printing techniques, which all rely on localised heating to fuse the powdered ingredients. SLS, DMLS, and SLM employ laser beams directed by mirrors, whereas EBM employs a high-energy electron beam precisely directed by electromagnetic coils, which necessitates vacuum conditions, raising the production cost. DMLS is essentially the same process as SLS, but exclusively utilizes metal alloys. SLS can use a wide range of materials, including polymer and ceramic based powders. SLM and EBM fully melt the materials using a high-energy laser and electron beam, respectively. They primarily use metal alloys and ceramics. There are some subtle but distinct differences between products produced by sintering and melting. In addition, the SLM (or EBM) melting process requires that the candidate materials exhibit similar properties in terms of laser absorption and flow behavior of the liquid phase in order to obtain the desired properties. However, one major advantage of the melting process is that it is capable of producing nearly fully dense parts, thus eliminating lengthy post-processing steps such as thermal treatments or infiltration, which is usually required for the SLS (or DMLS)-printed products [29].

➢ *Photopolymerization:*

It is also known as *stereolithography* (SL) involves exposing liquid resins to ultraviolet or other high-energy light source to induce polymerization reactions. The primary limitation of this technique is the need for photopolymerizable raw materials, which are relatively uncommon in pharmaceutical manufacturing. Furthermore, residual resin can pose a toxicology risk because the uncured material differs chemically from the printed product and may contain functional groups that are plausible structural indicators of genotoxicity. In terms of potential advantages, photopolymerization systems tend to be among the fastest and highest resolution 3D printers available.

- *Example:* Drug delivery application is 3D printing of photopolymerizable hydrogels.

➢ *Printing-Based Inkjet Systems*

In printing-based inkjet system, the ink is deposited onto the substrate mainly in two forms as listed below: -

- *Continuous Inkjet Printing*

In this type, due to the counter mechanisms the drops are continuously driven as needed thereby expelled only when necessary. this method continuous flow of ink is desired during the process. The processing occurs in such a manner that the vibration in the piezoelectric crystals helps in releasing the liquid continuously. The droplet obtained are charged electrostatically and thus, directed towards the substrate. It is mainly useful in printing of packaging.

- *Drop on Demand (DOD)*

DOD is also known as the *Polyjet technology*. In which the droplets of solution which containing the drug or medicament sprayed from the nozzle part of apparatus, the deposition of the thin layer on its formulation. In the DOD printing system, the pharmaceutical-based ink is converted to a droplet form by applying a voltage to a piezoelectric crystal transducer to vibrate the materials or heating the formulation to the temperature higher than the boiling temperature thereby creating droplets. The solution dots are then driven from an orifice to the printer head's nozzle and solidified dropwise. The performance of the carrier formulation during printing, which is strongly influenced by rheological parameters such as fluid viscosity, velocity, and surface tension, is the main criterion in developing an API formula for printing in the inject print system. 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 personalization in drug discovery. [30]

➢ *Other Methods*

- *Powder Bed Fusion*

Sintering (partial surface melting and congealing) of high-melting-point particles with a low-melting-point binder is used in powder bed fusion.

Both cases necessitate heat, which is typically provided by a laser.

- *Pen-Based 3D Printing*

Pen-based 3D printing is an extension of the extrusion 3D printing process in which the layer-by-layer assembly is controlled manually using a hand-held device.

- *Use of 3D-Printed*

There are limitations to what can be printed using each 3D printing technique in an acceptable length of time.

Molds made from 3D printed objects could allow drug product manufacturers to fabricate complex objects out of non-printable materials. [30-31]

The all steps which are briefly discussed in the above section of the review paper, commonly short-term explaining the techniques with their proper working procedure. The techniques also explained below in the (**Fig. 08**)

ISSN No:-2456-2165

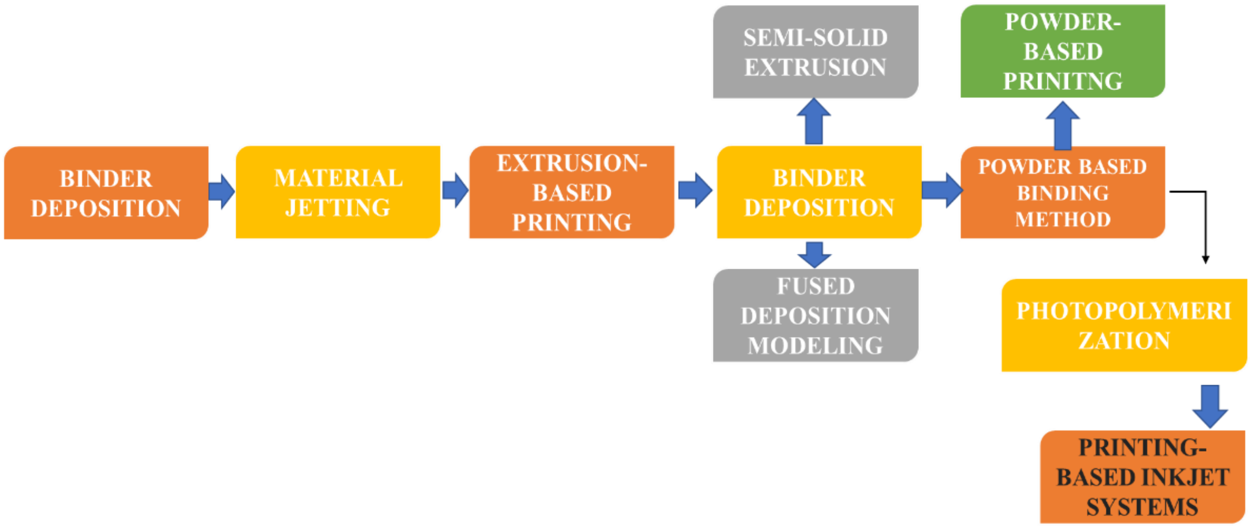

Fig 8 3D Printing Involving Techniques

All the recent and well-developed techniques in the formulation and designing of the object and the model of the given material of the medicines in the following steps. The 3D Printing used in the pharmaceutical formulation broader area of the development, 3D Printing play an important role for the designing. The above (Table 07) define the types of 3D Techniques involving in the designing or 3D image and which dosage form developed in the recently years.

All described in the below section-

Table 2 List of Dosage form and Types of 3D Printing Technique Involving

Sr. No.	3D Technology	Dosage Form	Active Ingredients
01.	Fused Deposition Modeling (FDM)	Tablet	5-Aminosalicylic acid (5-ASA, Mesalazine) and 4-Aminosalicylic acid (4-ASA)
02.	3DP Extrusion-Based Printing	Tablet	Captopril with Nifedipine and Glipizide
03.	A laboratory-scale 3DP Machine	Capsule	Pseudoephedrine hydrochloride
04.	Fused-Filament 3D Printing	Tablet	Fluorescein
05.	Inkjet 3DP	Nanosuspension	Folic acid
06.	3D Powder direct printing technology	Microporous biocermics	Tetracycline, vancomycin and ofloxacin
07.	Piezoelectric inkjet printer	Microparticles	Paclitaxel
08.	Ink-Jet Printer	Solid dispersion	Felodipine
09.	Thermal Inkjet Printer	Oral solid dosage form	Prednisolone

This data is important for understanding which dosage form of different pharmaceutical excipients or medicament used in particular disease and as well as the which type of 3D Printing techniques.

VI. COMPARISON OF TRADITIONAL MANUFACTURING WITH 3D PRINTING

3D printing in pharmaceuticals demonstrates more complexity in dosage forms using layer-upon-layer process. This can be differentiated for personalization in medicine as it is digitally designed and on-demand manufactured using automated and cheap operational methods. It has many benefits over traditional dosage form manufacturing techniques, including high production rates due to its quick operating systems, the ability to achieve high drug loading with the desired precision and accuracy only for powerful drugs that are applied in small doses, a reduction in material waste that can lower production costs, and adaptability to more classes of pharmaceutical active ingredients with poor aqueous solubility. The rationales supporting the increasing research in 3D printing for drug manufacturing are noteworthy. In general, there is a demand for adaptability, a feature that is not often seen in pharmaceuticals [31].

As part of this, it is possible to create dosage forms with intricate geometries and architectural designs, directly increasing the complexity and degree of control over release properties. The adaptability of 3D printing may also be applied for the precise and unique dosing of drugs, whereby drug doses can be printed with the safety of digital control.

ISSN No:-2456-2165

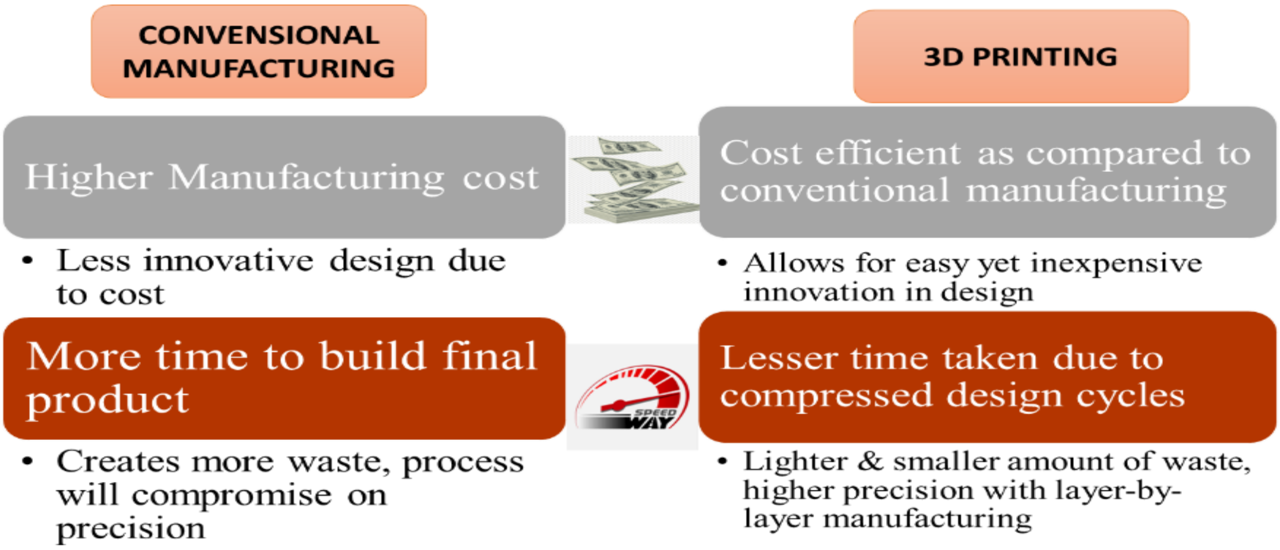

Fig 9 Comparison Between Traditional and 3D Printing (3DP) Manufacturing

Some parameters which well-defined which manufacture is best for the production of the medicament or drug products. Explained in the given above (**Fig. 05**). Additionally, multiple doses or multiple drugs can be printed together in a singular dosage form. Finally, and importantly, 3D printing allows for drug products to be adapted for on-demand, prescription specific production. The ability of on-the-spot drug fabrication will have major implications in emergency medicine and for medications with limited shelf-life [32]. Traditional drugs are manufacturing methods lack the ability to fulfill this necessity, as they focus on large-scale batches [33].

VII. FUTURE ASPECTS & TRENDS IN INDIA

The first product utilising Zip dose techniques for the treatment of epilepsy was released by Apecia Pharmaceutical in August 2015. For the treatment of myoclonic seizures, primary generalized ionic clonic seizures, and partial seizures in both adults and children, the FDA has approved the drug **SPRITAM ZipDose®** *levetiracetam*. Spritam was formulated by Zip dose technology that produced a porous formulation hat disintegrates rapidly [34]. Spritam was designed to fill the needs of the patients who have problems with the current medication therapy. Large doses of up to 1000 mg can be included in a single dosage form thanks to zip dose technology. This method improved patient compliance by making drug delivery simple. Zip dose technology combines the drug formulating science with unique manufacturing capabilities of 3D Printing. According to research conducted in the recent years 6W research, India's 3D printing market is projected to grow at around 20% during 2014-2019. By 2021, the India 3D Printer market is expected to exceed $79 million.

The $6 million facility will allow India's medical device market to become more self-sufficient, reducing total foreign imports from 75% to 10%. 3D Printing having broader area as the future perspective as following charts-

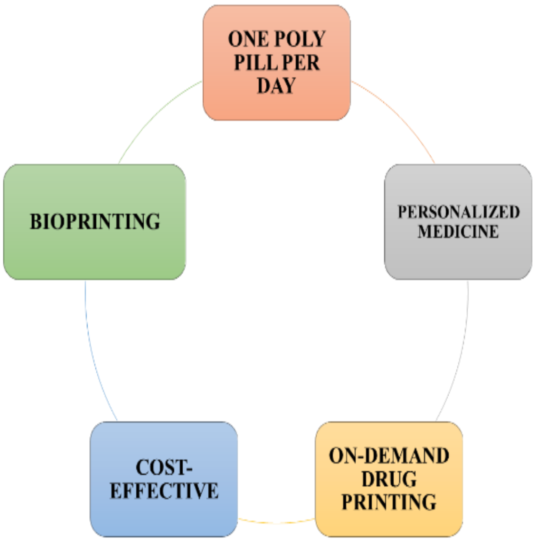

Fig 10 Future Trends of 3D Printing

The Zip Dose mechanism consisting the First, a powder blend is deposited as a single layer. Then an aqueous binding fluid is applied and interactions between the powder and liquids blind these materials together. This process is repeated several times to produce the solid [35].

VIII. CONCLUSION

3D printing in drug formulation is becoming a novel approach for many patients because it brings manufacturing closer to them and allows for personalized therapy. Current technological advancements and increased research in this field can ensure more safe and effective treatment. 3D printing for drug manufacturing represents the future of pharmaceuticals. Current advances in technology and increased research in this field can assure more safe and effective treatment. We believe that with continued research, personalized medicine will reach new levels of possibility, and that this particular application of 3D printing will revolutionise pharmacies. In recent years, researchers proposed dozens of 3D Printing innovations to improve the safety, efficacy and tolerability of medicines. Overall, FDA encourages development of complex dosage forms and manufacturing processes, such as 3D tablet printing, using science and risk-based approaches. The main purpose of the review article to explains the proper techniques involving in the 3D Printing, Traditional compresition of the dosage form. The techniques recently used majorly in the production of the pharmaceutical dosage form production or manufacturing. This 3D Printing could helpful, fulfill the promise of personalized medicament or medicine, a concept that is recently growing in popularity within the pharma industry.

REFERENCES

[1]. Mohapatra S, Kar RK, Biswal PK, Bindhani S. Approaches of 3D printing in current drug delivery. Sensors International. 2022 Jan 1;3:100146.
[2]. Ponni, R. T., Swamivelmanickam, M., & Sivakrishnan, S. (2020). 3D printing in pharmaceutical technology–a review. *International Journal of Pharmaceutical Investigation*, *10*(1), 8-12.
[3]. Varghese R, Sood P, Salvi S, Karsiya J, Kumar D. 3D printing in the pharmaceutical sector: Advances and evidences. Sensors International. 2022 Apr 25:100177.
[4]. Anand N, Singh D, Singh G, Kaur L, Dhawan RK, Kaur N. 3D printing technology in pharmaceutical delivery system: recent advancement in innovative approach. FABAD Journal of Pharmaceutical Sciences. 2020 Dec 1;45(3):253-68.
[5]. Zhu X, Li H, Huang L, Zhang M, Fan W, Cui L. 3D printing promotes the development of drugs. Biomedicine & Pharmacotherapy. 2020 Nov 1;131:110644.
[6]. Li H, Fan W, Zhu X. Three-dimensional printing: The potential technology widely used in medical fields. Journal of Biomedical Materials Research Part A. 2020 Nov 1;108(11):2217-29.
[7]. Kristiawan, R. B., Imaduddin, F., Ariawan, D., & Arifin, Z. (2021). A review on the fused deposition modeling (FDM) 3D printing: Filament processing, materials, and printing parameters. *Open Engineering*, *11*(1), 639-649.
[8]. Samiei, N. (2020). Recent trends on applications of 3D printing technology on the design and manufacture of pharmaceutical oral formulation: a mini review. *Beni-Suef University Journal of Basic and Applied Sciences*, *9*(1), 1-12.
[9]. Samiei N. Recent trends on applications of 3D printing technology on the design and manufacture of pharmaceutical oral formulation: a mini review. Beni-Suef University Journal of Basic and Applied Sciences. 2020 Dec;9(1):1-2.
[10]. Ponni RT, Swamivelmanickam M, Sivakrishnan S. 3D printing in pharmaceutical technology–a review. International Journal of Pharmaceutical Investigation. 2020 Mar 12;10(1):8-12.
[11]. Anand N, Singh D, Singh G, Kaur L, Dhawan RK, Kaur N. 3D printing technology in pharmaceutical delivery system: recent advancement in innovative approach. FABAD Journal of Pharmaceutical Sciences. 2020 Dec 1;45(3):253-68.
[12]. Ali A, Ahmad U, Akhtar J. 3D printing in pharmaceutical sector: an overview. Pharmaceutical Formulation Design-Recent Practices. 2020 Jan 3
[13]. Agrawal A, Gupta AK. 3D Printing technology in pharmaceuticals and biomedical: A review. Journal of Drug Delivery and Therapeutics. 2019 Apr 24;9(2-A):1-4.
[14]. Sjöholm E, Sandler N. Additive manufacturing of personalized orodispersible warfarin films. International Journal of Pharmaceutics. 2019 Jun 10;564:117-23.
[15]. Thabet Y, Lunter D, Breitkreutz J. Continuous inkjet printing of enalapril maleate onto orodispersible film formulations. International journal of pharmaceutics. 2018 Jul 30;546(1-2):180-7.
[16]. Lepowsky E, Tasoglu S. 3D printing for drug manufacturing: A perspective on the future of pharmaceuticals. International journal of bioprinting. 2018;4(1).
[17]. Jamróz W, Szafraniec J, Kurek M, Jachowicz R. 3D printing in pharmaceutical and medical applications–recent achievements and challenges. Pharmaceutical research. 2018 Sep;35(9):1-22.
[18]. Jose PA, GV PC. 3D printing of pharmaceuticals–a potential technology in developing personalized medicine. Asian journal of pharmaceutical research and development. 2018 Jul 10;6(3):46-54.
[19]. Hsiao WK, Lorber B, Reitsamer H, Khinast J. 3D printing of oral drugs: a new reality or hype?. Expert opinion on drug delivery. 2018 Jan 2;15(1):1-4.
[20]. Lim SH, Kathuria H, Tan JJ, Kang L. 3D printed drug delivery and testing systems—a passing fad or the future?. Advanced drug delivery reviews. 2018 Jul 1;132:139-68.
[21]. Cheow WS, Kiew TY, Hadinoto K. Combining inkjet printing and amorphous nanonization to prepare personalized dosage forms of poorly-soluble drugs. European Journal of Pharmaceutics and Biopharmaceutics. 2015 Oct 1;96:314-21.
[22]. Long J, Gholizadeh H, Lu J, Bunt C, Seyfoddin A. Application of fused deposition modelling (FDM) method of 3D printing in drug delivery. Current pharmaceutical design. 2017 Jan 1;23(3):433-9.
[23]. Preis M, Breitkreutz J, Sandler N. Perspective: Concepts of printing technologies for oral film formulations. International journal of pharmaceutics. 2015 Oct 30;494(2):578-84.
[24]. Nematollahi B, Xia M, Sanjayan J. Current progress of 3D concrete printing technologies. InISARC. Proceedings of the international symposium on automation and robotics in construction 2017 (Vol. 34). IAARC Publications.

[25]. Prasad LK, Smyth H. 3D Printing technologies for drug delivery: a review. Drug development and industrial pharmacy. 2016 Jul 2;42(7):1019-31.
[26]. Khaled SA, Burley JC, Alexander MR, Roberts CJ. Desktop 3D printing of controlled release pharmaceutical bilayer tablets. International journal of pharmaceutics. 2014 Jan 30;461(1-2):105-11.
[27]. Agrawal A, Dudhedia M, Deng W, Shepard K, Zhong L, Povilaitis E, Zimny E. Development of tablet formulation of amorphous solid dispersions prepared by hot melt extrusion using quality by design approach. Aaps Pharmscitech. 2016 Feb;17(1):214-32.
[28]. Lee BK, Yun YH, Choi JS, Choi YC, Kim JD, Cho YW. Fabrication of drug-loaded polymer microparticles with arbitrary geometries using a piezoelectric inkjet printing system. International journal of pharmaceutics. 2012 May 10;427(2):305-10.
[29]. Yan, T. T., Lv, Z. F., Tian, P., Lin, M. M., Lin, W., Huang, S. Y., & Chen, Y. Z. (2020). Semi-solid extrusion 3D printing ODFs: an individual drug delivery system for small scale pharmacy. *Drug Development and Industrial Pharmacy*, *46*(4), 531-538.
[30]. Chen, G., Xu, Y., Kwok, P. C. L., & Kang, L. (2020). Pharmaceutical applications of 3D printing. *Additive Manufacturing*, *34*, 101209.
[31]. Wang J, Goyanes A, Gaisford S, Basit AW. Stereolithographic (SLA) 3D printing of oral modified-release dosage forms. International journal of pharmaceutics. 2016 Apr 30;503(1-2):207-12.
[32]. Jandyal, A., Chaturvedi, I., Wazir, I., Raina, A., & Haq, M. I. U. (2022). 3D printing–A review of processes, materials and applications in industry 4.0. *Sustainable Operations and Computers*, *3*, 33-42.
[33]. Gopinathan, J., & Noh, I. (2018). Recent trends in bioinks for 3D printing. *Biomaterials research*, *22*(1), 1-15.
[34]. Redwood, B., Schöffer, F., & Garret, B. (2017). *The 3D printing handbook: technologies, design and applications*. 3D Hubs.
[35]. Lee, J. Y., An, J., & Chua, C. K. (2017). Fundamentals and applications of 3D printing for novel materials. *Applied materials today*, *7*, 120-133.