Review Article

A BRIEF REVIEW ON 3D PRINTING IN PHARMACY

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ABSTRACT:
3D printing , also known as additive manufacturing has gained significant attention in the pharmaceutical industry due to its potential to revolutionize drug development and delivery. This technology allows for the creation of complex drug formulations , personalized dosage forms , and customized drug release profiles. By priting medications layer by layer , 3D printing offers precision in design , scalability in production , and the possibility for on – specific doses, enhance bioavailability , and improve the convenience and compliance of drug regimens. However , challenges such as regulatory hurdles , material limitations , and the need for standardized quality control processes remain. Despite these obstacles , 3D printing holds great promise for the future of pharmaceutical manufacturing , making it a promising area of research and innovation in personalized medicine.

INTRODUCTION:
3D printing is also known as additive manufacturing, it is a method of creating a three dimensional object layer-by-layer using a computer created design. It was first developed by Charls Haul, in 1984. 3DP has a wide range of applications like tissue design, printing of organ, diagnostics, manufacture of biomedical devices and the design of drug and delivery systems in the medical field. Replacing and repairing the defective organs like kidney, heart, etc or all together creating a new organ that mimics the same functions as that of original are some additional uses of this technology. The application of 3D printing in medicine can provide many benefits, including the customization and personalization of Medical products, drugs and equipment, cost effectiveness, increased productivity, the democratization of design and manufacturing and enhanced collaboration. 3DP has been used in anti-cancer therapy, for the production of stimuli responsive hydrogels, nanogels and drug loaded implants with great flexibility and a wide variety of shapes that allow dose customization and targeted treatment with minimum side effects. Different types of drug delivery systems for instance oral controlled release systems, micro pills, microchip, drug implants, fast dissolving tablets and multiphase release dosage forms have been developed using 3 dimensional printing technology.3D printing is an additive layer manufacturing techniques, where consecutive layers of material are deposited or solidified to form a 3D structure. In this review, the most information was available on different review articles published in different international journals. Several approaches have been taken to ensure a high-quality literature review dissertation of 3D printed oral pharmaceutical formulations, focusing on their mechanical properties. Databases from Research gate and Google Scholar were used for an initial comprehensive and a second in-depth search of the topic. The main keywords used in the search were: 3D printed tablets, 3D printed oral dosage forms, additive manufacturing, 3D printing in personalized drug dosage forms, bioprinting organs for clinical trial. Number of articles analyzed in detail in the Results, websites were also used to obtain reliable information on the guidelines.

LITERATURE SURVEY:
1) Essyrose Mathew, Giulia Pitzanti, Eneko Larraneta and Dimitrios A. Lamprou in 2020 studied 3D Printing of Pharmaceuticals and Drug Delivery Devices which is published by MDPI Journal in 2020. 2) Danae Karalia, Angeliki Siamidi , Vangelis Karalis and Marilena Vlachou in 2021 studied 3D-Printed Oral Dosage Forms: Mechanical Properties, Computational Approaches and Applications which is published in MDPI Journal in 2021. 3) Byeong Ju Park, Ho Jae Choi, Sang Ji Moon, Seong Jun Kim, Rajiv Bajracharya, Jeong Youn Min, Hyo-Kyung Han in 2018 studied Pharmaceutical applications of 3D printing technology: current understanding and future perspectives which is published by Springer an American publishing company in 2018. 4) Nasim Samiei in 2020 studied Recent trends on applications of 3D printing technology on the design and manufacture of pharmaceutical oral formulation which is published by Beni-Suef University Journal of Basic and Applied Sciences in 2020. 5) Witold Jamroz, Joanna Szafraniec, Mateusz Kurek, Renata Jachowicz in 2018 studied 3D Printing in Pharmaceutical and Medical Applications– Recent Achievements and Challenges which is published by Springer an American publishing company in 2018. 6) Asad Ali, Usama Ahmad and Juber Akhtar published 3D Printing in Pharmaceutical Sector: An Overview by intechopen. 7) C. Lee Ventola, MS. in 2014 studied Medical Applications for 3D Printing,

Current and Projected Uses published by P&T publisher in 2014. 8) Ravikumar Tamil Ponni, Mahalingam Swamivelmanickam, Sivagnanam Sivakrishnan in 2020 studied 3D Printing in Pharmaceutical Technology and published an article by research gate in international journal in 2020.

AIM:

The role of 3D printing technology in pharmaceutical industry for production of personalized drug dosage forms and in bioprinting for clinical trials. Importance of 3D manufacturing technique it's advantages and disadvantages. Recent trends in 3d printing and future prospects. Regulatory guidelines for this technology.

OBJECTIVES:

To describe how 3D printing process in formulation of drug delivery is better than conventional manufacturing techniques. Different types of techniques used in 3DP. Working of 3D printing, the steps involved in 3D printing. Advantages and disadvantages of 3DP. Recent trends and 6development in 3D printing technology. Future prospects and limitatregulatory guidelines

HISTORY:

3D Printing was invented by Charles Hull in 1980 which he called "Stereolithography". Year and Major development in the field of 3D printing 1980:- Dr. Hideo Kodama filed firstpatent for RP technology 1984:- Stereo lithography apparatus (SLA) was invented by Charles Hull1986:- Carl Deckard invented apparatus for producing parts by selective sintering 1989:- Patent was granted to Carl Deckard for SLA 1990:- Fused deposition modeling (FDM) 1992:- First SLA machine was produced using 3D system 1993:- 3D printing patent was granted to E.M Sachs 1996:- Clinical application of biomaterials for tissue regeneration 1999:- Luke Massella received first 3D printed bladder which was an amalgamation of 3D. p . rinted biomaterials and his own cells 2000:- MCP technologies introduced the SLM technology 2002:- Miniature functional kidney was fabricated 2003:- Term organ printing was coined 2004:- Dr. Bowyer conceived the RepRap concept of an open-source, self-replicating 3D printer 2005:- First color 3D printer was introduced by Z Corp 2007:- Selective layer customization and on-demand manufacturing of industrial parts 2009:- Organovo, Inc., announced the release of data on the first fully bioprinted blood vessels 2011:- 3D printing was applied in gold and silver World's first 3D printed car, robotic aircarft was introduced 2012:- Extrusion-based bioprinting for an artificial liver 3D printed prosthetic jaw was implanted2013:- SolidConcepts produced a 3D printed metal gun 2014:- Implementation of multi-arm bioprinter to integrate tissue fabrication with printed vasculature 2015:- First 3D printed pill was approved by US FDA Organovo announced the release of data on the first fully bioprinted kidney

MATERIALS AND METHODS:

Tablets are divided manually using hands, knives, or tablet splitters, which leads to uneven weight distribution after division and drug release problems (e.g., premature drug release, breakage of coating system, etc.). 3D printing, on the other hand, can effectively solve these problems by moving away from the "one- size-fits-all" approach and mass production toward personalized pharmacotherapy. Five main techniques have been used to produce pharmaceutical dosage forms: binder jet printing, fused deposition modeling (FDM), semi-solid extrusion (SSE), selective laser sintering (SLS), and stereolithography. 3D screen printing is based on the transfer of API-containing printing paste through specific openings of the printing screen onto a given substrate.

3D PRINTING AND CONVENTIONAL MANUFACTURING:

Conventionally tablets are produced by mass fabrication which involves multiples processes such as blending, mixing, milling, and finally compression into tablets. conventional manufacturing techniques are intended to be a large-scale mass production with a one-dose-fit-all approach which may not necessarily consider the individual needs of a patient. The major disadvantages of the traditional manufacturing process include being time-consuming and costly while also requiring highly skilled technicians.

Parameters	3D printing	Traditional manufacturing
Cost	Upton 70% savings due on Prototyping costs	Higher cost of manufacturing and shipping
Design	Allows for easy yet inexpensive innovation in design	Less innovative designs due to cost constraints
Speed	Lesser time taken due to compressed design cycles	More time to build final product
Quality	Lighter and smaller amount to waste; Higher precision with layer by layer manufacturing	Creates more waste; subtractive process will compromise on precision

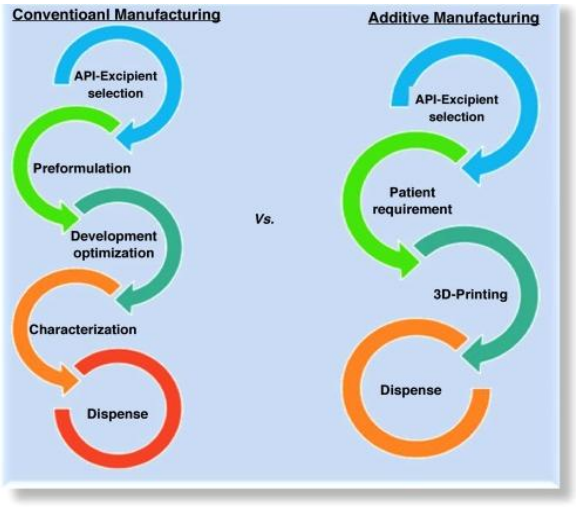


Figure 1 - Conventional tablet manufacturing process (A). 3D printing manufacturing process (additive manufacturing) (B).

Table 1. Difference between 3DP and traditional manufacturing.The 3D printing technology is fundamentally different from the traditional mass production methods. 3D printing in the pharmaceutical industry, it is possible to curtail the process of manufacturing drug products from days to a matter of hours. Speeding up the production process can lead to more rapid release of the drug product into the market. In addition, the ability of 3D printing to rapidly manufacture a drug product causes a substantial cost reduction in the production process, which is highly favorable to the pharmaceutical industry. It promotes creativity, innovation, and customization. The fabrication steps with 3D printing are clean and the material waste is negligible allowing for previously discarded raw materials to be further explored, while also increasing compliance and accessibility of drugs.

PROCEDURE OF 3DP:

Softwares such as onshapes, solidworks, Creo parametric, Autocad, Autodesk, etc. are used for virtual 3D design of objects

The digital design is exported to a readable format for a system which is mainly a stereo lithography (STL) file

Slicer (3D printing software) transfers the STL file into a series of thin layers with the instruction tailored to generate the 3D object.

Preparing pharmaceutical formulation ink such as filament, binder solutions, granules, paste etc. based on technology used.

During the printing, the printer head moves and the formulation ink decomposes onto successive layers on a built tray which will create the basis for the object. The process continues until the desired 3D product is constructed.

Final 3D product may require removal of solvent residues, excess powder, polishing and sintering which occur in the post printing step. Flow chart-Steps involved in 3DP manufacturing process.

TYPES OF 3DP TECHNOLOGY:

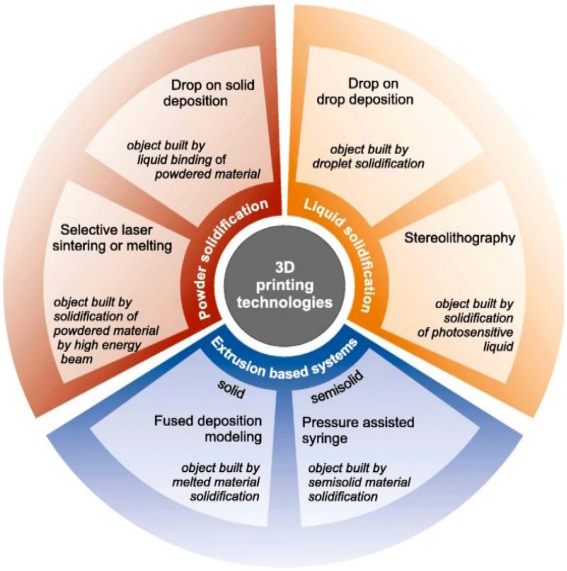


Figure 3 - 3DP methods applied for drug formulation

EXTRUSION BASED SYSTEMS

1. FUSED DEPOSITION MODELING (FDM):
In fused deposition modeling (FDM), drug-loaded thermoplastic polymer filaments are extruded through the print head at a specific temperature in specific directions. The molten filament is then deposited onto the build plate and solidifies in successive layers to form the object. Fused deposition modelling (FDM) is commonly used method in 3D printing, the materials are softer or melt by heat to create objects during printing. Fused deposition modeling 3D printing helps in manufacturing delayed release print lets without an outer enteric coating and also provides personalized medicines doses. This 3D Printing indicates some limitations for system like lack of suitable polymers, slow and often incomplete drug release, because of the drug remain trapped in the polymers, miscibility of drug and additives with the polymers used was not valued. Ethyl cellulose (EC), hydroxypropyl cellulose (HPC), hydroxypropyl methyl cellulose (HPMC), hydroxypropyl methyl cellulose acetate succinate (HPMCAS), ethylated acrylate copolymer (Eudragit® RL and RS), polyethylene glycol (PEG), polyethylene oxide (PEO), polylactic acid (PLA), polyvinyl alcohol (PVA), and polyvinyl pyrrolidone (PVP) are the most commonly used polymers in the FDM 3D printing. Lamichhane et al. used FDM printing technology to develop floating gastro-retentive tablets with controlled release properties.

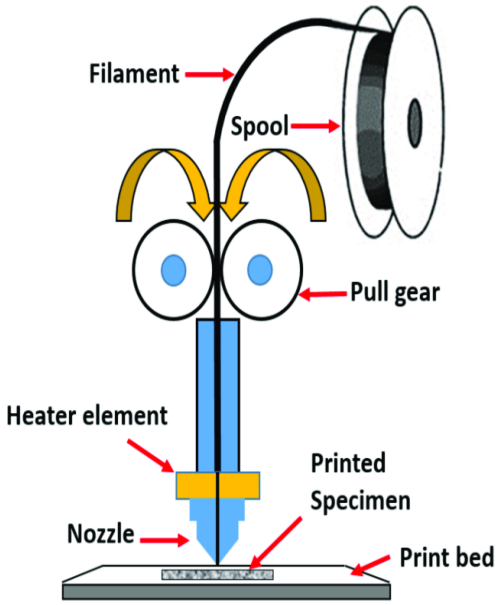


Figure 4 - Fused Deposition Modeling.

2. SEMI-SOLID EXTRUSION:
Semi-solid extrusion (SSE) is a 3D printing technique in which material in semi-solid or semi-molten form is extruded from a syringe-like system in successive layers to form a three-dimensional object. Unlike FDM, which uses solid filaments, SSE prepares the starting material by mixing the ideal ratio of active substances with solvents to form a gel or paste. Moreover, low temperatures are used during the process, therefore, it is suitable for thermolabile active ingredients.

THERMAL INKJET PRINTING (TIJ):
The aqueous ink fluid is transformed to vapours state through heat, expands to push the ink drop out of a nozzle. It is used in the preparation of drug-loaded biodegradable microspheres, drug-loaded liposomes, patterning microelectrode arrays coating, loading drug eluting stents. It is also an effectual and applied method of generating films of biologics without negotiating protein activity.

INKJET PRINTING :
It is also known as ‘mask-less’ or ‘tool-less’ approach for its desired structure formation mainly depends upon the inkjet nozzle movement or substrate movement for an accurate and reproducible formation. The Ink is deposited onto a substrate either in the form of Continuous Inkjet printing / Drop on demand printing. Hence it provides a capability of high-resolution printing. It has a low cost, rate of processing in printing and generation of low level of wastes. It gives CAD information in a ‘direct write’ manner and process material over large areas with minimal contamination.

EXTRUSION 3D PRINTING:
In this method the material is extruded from the automated nozzle onto the substrate without any higher support material. It is only utilized to fabricate tablet containing Guaifenesin act as expectorating. The components that can be extruded are molten polymers, suspensions, semisolids, pastes.

HOT MELT EXTRUSION (HME):
Hot melt extrusion (HME) is the method of melting polymer and drug at elevated temperature and the pressure is employed in the instrument sequentially for blending.27 It is a continuous manufacturing technique that involves feeding, heating, mixing and shaping.28 In recent years, it has proved that Hot melt extrusion capable to optimize the solubility and bioavailability of moderately soluble drugs.

LIQUID SOLIDIFICATION:
1. STEREOLITHOGRAPHY:
Stereolithography is the method of computer regulated laser beam is used to make liquid polymer/resin as solid, by this means creating a 3D structure.30 Stereolithography has several advantages over former types of other 3DP, predominantly it's astonishing resolution and dodging of thermal practices can be harmful for specific drug molecules. Healy et al., used SLA as the AM process to create oral dosage forms of 2.5% and 5% concentration of aspirin and paracetamol. The results from release studies showed that there was an increased in release of active drug when drug loading was increased, this highlights the potential for patient specific drugs to be created with the ability to modulate drug release. Overall, this study effectively highlighted the potential for creating solid dosage forms using SLA printing, with the research leading towards the ability to create personalised medication and the ability to modulate drug release from printed products. Robles-Martinez et al., were able to construct a novel SLA printing method that allowed the production of multi-layered tablets (polypills) that had flexible drug content and shape. The drugs chosen for the work were paracetamol, caffeine, naproxen, chloramphenicol, prednisolone and aspirin. This study showed the possibility to uses SLA 3DP for fabricating multi-drugs tablets to improve personalisation for patients.

DROP ON DROP DEPOSITION:
4. DIRECT WISE:
It encompasses a pattern-generating device that moves as per the guidance of computer-controlled translational stage so that layers after layers are put on in order to achieve a 3D microstructure.

POWDER SOLIDIFICATION:
This method customs powder jetting/powder bed to feast thin layers of powder and instantaneously applying liquid binder drops with inkjet printers. The ink (binders and APIs or binder solutions) is sprinkled over a powder bed in two-dimensional (2D) approach to make the decisive product in a layer by layer fashion. The adaption of this approach into pharmaceutical manufacturing is at ease than other approaches as powder and binder solutions are broadly used in the pharmaceutical industry. The own disadvantages of this approach are; to remove solvent residues additional drying is required, during printing excess powder accumulates and contributes to wastage and due to the permeable design of the powder the drug delivery system's mechanical strength may poor.

1. SELECTIVE LASER SINTERING:
Selective laser sintering (SLS) act as a way in the powder bed to bind. The laser is designed to draw a specific pattern on the surface of the powdered bed during the printing process, thus creating a 3D structure. For example, Paracetamol is an Orodispersible tablet prepared by this manner. It is currently used for industrial manufacturing of plastic, metallic and ceramic objects. Awad et al., utilised SLS 3DP, for the first time, to produce small oral dosage forms with modified release properties. They fabricated single miniprintlets using paracetamol as a model drug and dual miniprintlets where paracetamol is combined with ibuprofen. For the single miniprintlets, ethyl cellulose (EC) was employed as the main polymer matrix. In the case of dual miniprintlets one layer contained EC for sustained release whereas the second layer containing Kollicoat IR (a graft copolymer comprised of PEG: PVA, 1:3) for immediate release. In order to assess the effect size has on dissolution properties, miniprintlets of two different diameters, 1 mm and 2 mm, were developed. The single miniprintlets exhibited slow paracetamol release, which was reduced when increasing the diameter. For the dual miniprintlets, the diameter does not affect the paracetamol release profile. This work demonstrates the possibility to use SLS 3D printing to combine multiple Active Pharmaceutical Ingredients (APIs) with distinct release properties in a single dosage form.

2. DROP ON SOLID:
ZIP DOSE:
Zip dose is the world's initial and only FDA-approved, commercial-scale 3DP in current therapeutic areas for pharmaceutical manufacturing areas. It has a distinctive digitally coded layering and zero compression practices, used for tablet formulation with large dosage and prompt disintegration. Hence, it helps in overwhelming a difficulty in swallowing. Spritam-R (Anti-epilepsy drug) is an oral dispersible tablet, marketed by Aprecia Pharmaceuticals based on powder bed fusion by layer-by-layer production system. In

which it consists of the active ingredient, excipients and a binder liquid to produce a matrix tablet.

BINDER JETTING:
Binder jetting (BJ) is a 3D printing technique in which a liquid binder solution is precisely applied to a powder substrate using a printer nozzle. The moistened powder particles are then fused together, solidifying the layer. The first layer is printed onto the build platform, then the plunger lowers to the thickness of the following layer and subsequent layers are printed and bonded together. The process is repeated several times until the 3D object is produced.

3DP Technology	Formulation	API
Fused deposition modeling (FDM)	Caplets Tablets Oral films	Caffeine Hydrochlorothiazide Aripiprazole
Thermal inkjet printing (TIJ)	Solution	Salbutamol suspension
Inkjet printing	Implant Nanosuspension Nanoparticle Tablets	Levofloxacin Folic acid Rifampicin Acetaminophen Chlorpheniramine maleate Chlorpheniramine maleate, diclofenac Levetiracetam

Table 2-Pharmaceutical preparations that were developed by 3DP technology.

EFFECT OF 3D PRINTING TECHNIQUE IN DRUG DELIVERY SYSTEMS:
3D printing most likely corresponds to novel architectural innovation and enables designing and fabricating oral dosage forms with different geometrics, complex features such as tablets with a designed internal structure, porosity gradients, torture channels, and multi-compartment systems such as poly-pills containing multiple API in one dosage forms. These features may enable the control of drug release rate by obtaining specific and complex release patterns in response to the patient's needs, thereby enhancing the drug efficacy. Concerning customized medicine, clinical pharmacists or doctors may need patient's individual information such as age, gender, body mass index, and metabolism in order to develop the optimum medical dose. In this way, the patient can receive accurate personalized treatment regimen matching their particular medical profile

ADVANTAGES:
1) Objects produced by 3D printing are of low cost. It is an advantage for small-scale production units or for companies that produce highly complex products or parts because almost all ingredients are inexpensive. 2) Cost efficient due to less wastage of materials. 3) Suitable drug delivery for difficult to formulate active ingredients like poor water solubility and narrow therapeutic windows drugs.
4) Medication can be tailored to a patient in particular based on age, gender, genetic variations, ethnic differences and environment. 5) Treatment can be customized to improve patient adherence in case of multi-drug therapy with multiple dosing regimen. 6) As immediate and controlled release layers can be incorporated owed to flexible designs, manufacturing method of dosage form and it helps in pick out the best therapeutic regimen for an individual. 7) Evades batch-to-batch variations met in bulk manufacturing of conventional dosage forms. 8) Manufacture of small batch is feasible and the process can be completed in a single run.
9) 3D printers capture minimal space and are affordable.

DISADVANTAGES:
1) The fabrication of 3D products require different types of technologies in particular those used in pharmaceutical production, which are often rarely available in the pharma industry. 2) Hackers making alterations to a drug's recipe or doses within a hospital or pharmacy where it's printed, leading to severe health consequences for patients. 3) Problems related to nozzle are a major challenge as stopping of the print head which affects the final products structure. 4) Powder printing clogging is another hurdle. 5)Possibility of modifying the final structure on to mechanical stress, storage condition adaptions and ink formulations effects. 6) Printer related parameters and these effects on printing quality and printercost. 7) In inkjet printing, proper flow of ink can only be achieved with ink that has precise viscosity. 8) Ink formulation material should have the property of self-binding but should not bind to other printer elements. In some formulation when the ink does not possess adequate self-binding property or it binds with other elements of printer then the resultant formulation does not have required hardness. Rate of drug release may get affected due to binding of ink with other printer materials.

APPLICATIONS:
PERSONALIZED DRUG DOSING: Drugs with narrow therapeutic index can easily be prepared

using 3D printing and, by knowing the patient's pharmacogenetic profile and other characteristics like age, race etc., optimal dosage can be given to the patient. Preparation of entirely new formulation is another vital potential of 3D printing for instance fabrications of pills that have a blend of more than one active pharmaceutical ingredient or dispensed as multi-reservoir printed tablets. Hence patients suffering from more than one disease can get their formulation ready in one multi-dose form at the healthcare point itself, thereby providing personalized and accurate dose to the patient with better or best compliance.

1) COMPLEX DRUG RELEASE PROFILE:

In 3D printed dosage forms, a complex drug release profile that allows fabrication of complex geometries that are porous and loaded with multiple drugs surrounded by barrier layers that modulate release of drug. Example. 3D printing has been used to print antibiotic micropatterns on paper, which have been used as drug implants to eradicate Staphylococcus epidermidis, chlorpheniramine maleate was 3D printed onto a cellulose powder substrate in amounts as small as 10–12 moles to demonstrate that even a minute quantity of drug could be released at a specified time. This study displayed improved accuracy for the release of very small drug doses compared with conventionally manufactured medications.

2) CUSTOMIZED IMPLANTS AND PROSTHESES :

By using MRI, CT scan, and X-ray and its translation into .stl 3D print files, implants and prostheses of any possible shape can be made. By using silver nanoparticles, chondrocytes, and silicon, a prosthetic ear was made out of 3D printing technology that was able to detect electromagnetic frequencies. The impact of this technology is so extensive in the field of hearing aids that today 99% of customized hearing aids are made using 3D printers, because, as everyone's ear canal has a different shape, this technology is able to provide perfect fit for each receiver and, moreover, the devices can be produced efficiently and cost effectively.

3)ANATOMICAL MODELS FOR SURGICAL PREPARATIONS:

Organ transplant surgery is expensive and organ transplantation involves the difficult task of finding a donor who is a tissue match. This problem could likely be eliminated by using cells taken from the organ transplant patient's own body to build a replacement organ. This would minimize the risk of tissue rejection, as well as the need to take lifelong immunosuppressants.

4) INCREASED COST EFFICIENCY:

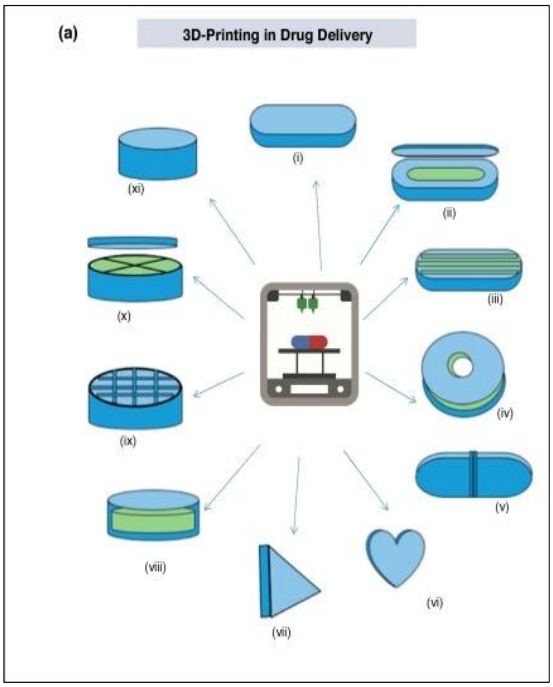
3D printing reduce manufacturing costs by decreasing the use of unnecessary resources. For example, a pharmaceutical tablet weighing 10 mg could potentially be custom fabricated on demand as a 1-mg tablet. Some drugs may also be printed in dosage forms that are easier and more cost-effective to deliver to patients.

5) ENHANCED PRODUCTIVITY:

3D printing works more quickly in contrast to traditional methods especially when it comes to fabrication of items like prosthetics and implants with an additional benefit of better resolution, repeatability, more accuracy, and reliability.

6) DEMOCRATIZATION AND COLLABORATION:

The nature of 3D printing data files also offers an unprecedented opportunity for sharing among researchers. Rather than trying to reproduce parameters that are described in scientific journals, researchers can access downloadable .stl files that are available in open-source databases. By doing so, they can use a 3D printer to create an exact replica of a medical model or device, allowing the precise sharing of designs. Toward this end, the National Institutes of Health established the 3D Print Exchange (3dprint.nih.gov) in 2014 to promote open-source sharing of 3D print files for medical and anatomical models, custom labware, and replicas of proteins, viruses, and bacteria.



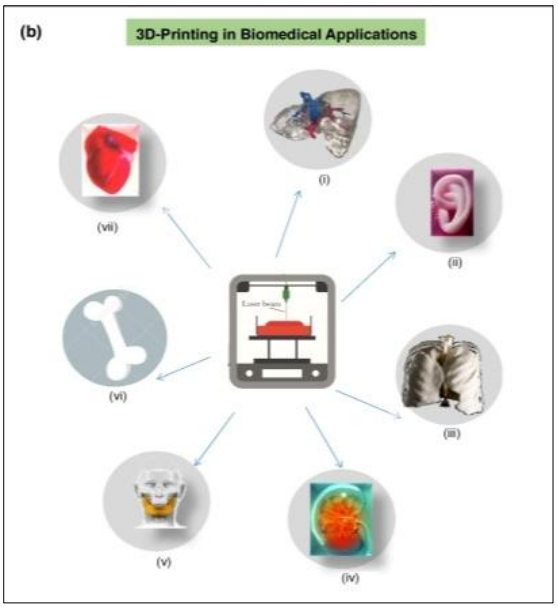


Figure 5 - (a) 3D printing in drug delivery, (b) 3D printing in biomedical applications.

RECENT TRENDS:

PHARMACEUTICAL INDUSTRY:

Spritam (levetiracetam) tablets became the first FDA approved prescription drugs product manufactured using 3D printing technology. Spritam is formulated with Aprecias zip dose technology, which combines the precision of 3D printing and formulation science to produce rapidly disintegrating formulations of medications. An inject printing process produces the water soluble drugs layer by layer by printing aqueous fluid onto layers of powdered medication without compression or traditional molding techniques.

BIOPRINTING COMPANIES:

1) ORGANOVO:

It has been actively developing a line of human tissues for use in medical research and drug discovery. These include both normal tissues and specially designed disease models. They are also working on the development of specific tissues for use in clinical patient care. They successfully printed the liver tissue and kidney tubular tissues.

2) CELLINK:

It develops both bioprinters and bioprinting materials for providing ready-to-print or use models for researchers and healthcare providers. This technology is used to print tissues such as liver, cartilage, skin, and even fully functional cancer tumors that can then be used to develop new cancer treatments.

3) ASPECT BIOSYSTEMS:

Currently the company has been cooperating with the Frampton Lab to create synthetic skin tissue and recently formed a partnership with Johnson & Johnson to develop 3D-printed knee meniscus tissue the thin, fibrous cartilage between some of your joints.

4) CYFUSE BIOMEDICAL:

The researchers created 3D printed human liver tissue which stably maintained metabolic functions and thus it might be used for toxicity testing in drugs.

5) TEVIDO BIODEVICES:

They use 3D printers for various reconstructive and cosmetic surgeries and gives hope to breast cancer survivors not to lose their sense of femininity even after serious surgeries. They apply the patients own pigment-producing cells (melanocytes) and tissues during the printing process to lower the chance of rejection and allow patients to have a high quality of life.

6) DIGILAB:

It offers the Cell Jet 3D printer, which has the unique capacity to print cells with 95 percent viability. The 3D-printed cells can be used for stem cell research, cancer biology, automated cell arrays, cell-cell or cell-drug interaction studies, tissue engineering or regenerative medicine.

7) ADVANCED SOLUTIONS LIFE SCIENCES:

Advanced Solutions produces robotic arms for bioprinters, which can print out cell systems and arrays, experimental tissue models, organ models, microfluidic platforms or implant systems. The company offers visualization software, with which medical professionals can create visualizations based on patient data from medical images and print out 3D models with the help of its robotic arm.

FUTURE PROSPECTS:

1) In the medical field bioprinting could be an excellent, fast and life saving solution for creating various tissue structures such as kidney tissue, skin tissue, liver, bone, etc. 2) Bioprinting help to shape the future of healthcare and eliminate animal testing, bioprinting can play a vital role in personalized healthcare for curing diseases, bioprinting organs to eliminate the need to wait, creating skin for burn victims and cosmetic companies for testing. 3) At present, however, the impact of 3D printing in medicine remains small. 3D printing is currently a $700 million industry, with only $11 million (1.6%) invested in medical applications. In the next 10 years, however, 3D printing is expected to grow into an $8.9 billion industry, with $1.9 billion (21%) projected to be spent on medical applications. 4) 3D printing is expected to be especially common in pharmacy settings. The manufacturing and distribution of drugs by pharmaceutical companies could conceivably be replaced by emailing databases of medication formulations to pharmacies for on-demand drug printing. This would cause

existing drug manufacturing and distribution methods to change drastically and become more cost-effective. 5) However, more research does need to be conducted in the field before the production of 3D-printed products on demand can become a reality within a clinical setting, such as the effect of process parameters on the print quality and how reproducibility in 3DP can be improved. FDM is also limited to the number of drugs that can be loaded into filaments, as they need to withstand the high temperatures of the process. However, if research continues to rise in the area of 3DP, due to the versatility of 3D printed products and the number of manufacturing advantages that 3DP offers there is potential for more 3DP to leave the proof-of-concept stage and be developed into a widely used manufacturing tool. 6) Multiple regulatory questions should be addressed. One of the main unanswered questions is the quality assurance if the dosage form/medical device is created on demand for each patient. In order to accelerate the acceptance of this technology, the US FDA published guideline documents for medical devices manufacturing using 3DP technology. Accordingly, we anticipate that more 3D printed pharmaceutical/medical products will reach to the market within the next few years.

REGULATORY LIMITATIONS:

In 2017, the FDA released guidelines for the manufacturing of medical devices and implants; however, there are currently no regulatory guidelines on the 3D printing of other products.The patentability process, especially with regard to intellectual property rights involving 3D printed drug products, should be granted to innovative processes or products. The patent owner has exclusivity on the product or process until the concession expires; in the meantime, other manufactures may not produce, use, or sell without the owner's authorization. Despite this patent right, extemporaneous formulations produced at compounding pharmacies prescribed by professionals to a specific patient are exempted and do not configure patent violation, according to the intellectual property law of several countries, such as UK and Brazil. If the market for compounding pharmacies is not a threat to large pharmaceutical corporations, this technological leap by digital pharmacies can change the global market scenario.

CONCLUSION:

3D printing has become a useful and potentially transformative tool in a number of different fields, including medicine. It is a valuable and potential tool for the pharmaceutical sector, leading to personalized medicine focused on the patients' needs. The regulatory modifcations and considerations may also need to be defned for the approval of pharmaceutical products made by 3DP methods. The number of manuscripts published in this Special Issue focused on 3DP of oral dosage suggests an increasing interest in personalised medicine. Additionally, this Special Issue included several works describing the use of 3DP for other applications such as medical devices. Therefore, 3DP can be applied in a wide variety of fields within biomedical sciences.

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