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Overview of 3D Printing Technologies In Pharmaceutics

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Abstract: 3D printing, also referred to as Additive Manufacturing, emerged in the 1980s. In August 2015, the FDA granted approval for a 3D-printed drug product, marking a significant milestone in the global commercialization of 3D-printed pharmaceuticals. This development highlights the challenges and issues faced by the industry, while also reflecting the evolving trends within the 3D-printed drug sector. It serves as a valuable resource for researchers involved in the field of 3D-printed pharmaceuticals. The technology, which utilizes computer-aided design to create customized 3D-printed medications, operates on a layer-by-layer basis to transform digital models into tangible drug products. This advancement in 3D-printed pharmaceuticals is crucial for the development of solid oral dosage forms. As a versatile platform technology, 3D printing offers distinct advantages for creating complex, personalized, and on-demand products. This review provides an overview of the mechanisms behind the most prevalent 3D printing technologies, detailing their features, benefits, drawbacks, and applications within the pharmaceutical industry, while also assessing the current progress in this innovative field.

Keywords: 3D printed drug products; 3D printing technology; Additive Manufacturing (AM); Personalize medicine; Three-dimensional printed drug.

1. Introduction

Three-dimensional printing (3DP) is a technique for creating 3D objects from digital designs by layering materials, enabling the production of items with diverse geometries through an additive process. Commonly referred to as additive manufacturing (AM), 3D printing (3DP) was first realized in 1984 by Charles W. Hull of 3-D Systems Corp. This technology encompasses various methods, including fused deposition modeling (FDM), solid state extrusion (SSE), stereo lithography apparatus (SLA), selective laser sintering (SLS), and binder jetting (BJ 3DP). This paper will explore and compare some of the most prevalent 3D printing technologies, examining their historical context, current status, and future market outlook based on specific criteria related to accuracy, functionality, and usability. Initially, the technology was prohibitively expensive and impractical for widespread use. However, as we entered the 21st century, prices significantly dropped, making 3D printers more accessible. Although additive manufacturing has been around for over three decades, it has only recently gained traction and attracted the attention of both industry professionals and the general public.

The adoption of additive manufacturing (AM) has significantly advanced the pharmaceutical sector towards the realm of personalized medicine. This approach may reduce the likelihood of adverse reactions or ineffective treatments caused by dosages that fall outside the therapeutic range, ultimately enhancing patient compliance and satisfaction. Personalized medicine also encompasses appropriate dosage forms tailored for specific populations, including paediatric, geriatric, and dysphasic patients, ensuring they can effectively use their medications. In contrast, traditional manufacturing methods fail to offer personalized dosing solutions due to cost and practicality constraints, whereas AM boasts high precision, adaptability, and serves as a viable manufacturing alternative. Three-dimensional printing technologies have been employed to create a diverse array of medicinal products, including immediate-release tablets, controlled-release tablets, dispersible films, micro-needles, implants, and transdermal.

2. History

The history of 3D printing, which began in the 1980s, marks a significant evolution in technology. In 1986, Charles Hull patented Stereo lithography (SLA), the first of its kind in 3D printing. By 1989, Scott Crump, co-founder of Stratasys Ltd., invented and patented Fused Deposition Modeling (FDM). The early 1990s saw academic research delve into the applications of 3D printing in drug delivery and tissue engineering, with MIT developing binder jetting in 1993, laying the groundwork for future advancements in drug printing. The first paper on 3D printed drug delivery systems emerged in 1995, and by 1999, scientists achieved a breakthrough by successfully printing a human bladder scaffold, marking a pivotal moment in biomedical 3D printing. The year 2000 ushered in experiments with inkjet-based printing of pharmaceutical compounds, focusing on personalized medicine and controlled release systems. The RepRap Project, an open-source 3D printer, launched in 2005, followed by the first demonstrations of powder bed printing in 2007. The expiration of a key FDM patent in 2009 led to an influx of affordable consumer 3D printers, democratizing the technology. In 2013, President Barack Obama acknowledged 3D printing's potential in his State of the Union address, while 2014 saw metal printing gaining momentum in aerospace and medical fields. A landmark moment occurred in 2015 when the FDA approved 3D printing technology, with Spritam, developed by Aprecia Pharmaceuticals, becoming the first 3D printed drug approved for use, showcasing the technology's viability in drug manufacturing.

In 2017, the first study on the acceptability of 3D printed medicine was conducted. By 2019, researchers began integrating Artificial Intelligence to enhance drug formulations and optimize 3D printing parameters. The COVID-19 pandemic in 2020 significantly accelerated the use of 3D printing technology for producing essential items such as masks, swabs, and ventilator components. Fast forward to 2023, Indian institutions and companies, including NIPER, IITs, and Sun Pharma, initiated research and development projects focused on the 3D printing of personalized tablets and implants.

In 2024, regulatory agencies like the FDA and EMA started formulating guidelines for 3D printing practices. Finally, in 2025, clinical trials commenced for the implementation of on-demand drug printing within hospital settings.

3. Objectives

The objectives outlined focus on advancing personalized medicine, which aims to customize drug formulations to meet the unique needs of individual patients, thereby enhancing treatment efficacy and safety. The impact of this approach is significant, as 3D printing facilitates the precise adjustment of dosages and formulations tailored to each patient, particularly benefiting those with chronic conditions or rare diseases, ultimately leading to improved health outcomes. The utilization of 3D printing technology for the fabrication of tissue models aimed at drug testing and the development of bioactive scaffolds for tissue repair holds the potential to greatly enhance clinical research and introduce innovative treatments for organ failure and other conditions that necessitate regenerative therapies. This advancement can lead to improved drug testing and preclinical trials by facilitating the creation of more precise and lifelike models of human tissues and organs, which in turn allows for more effective preclinical evaluations and may decrease the dependence on animal testing. Furthermore, the focus on enhancing patient compliance through the design of user-friendly dosage forms can significantly boost adherence to prescribed medication regimens, particularly among vulnerable populations such as children and the elderly. Additionally, the commitment to sustainability in pharmaceutical manufacturing is addressed through the adoption of 3D printing, which employs additive manufacturing techniques that reduce waste and promote the use of biodegradable materials, thereby fostering more environmentally responsible production methods. Lastly, the capability of 3D printing to mitigate drug shortages by facilitating localized, on-demand production of essential medications presents a vital solution, ensuring that critical healthcare needs are met, especially in underserved regions.

4. Technologies

Stereolithography (SL) Technology

The 3D printing revolution began in the late 20th century, with Stereolithography being the first 3D printing technique to emerge in the market. The initial 3D printers that were developed were SL machines, which were utilized for creating 3D models, prototypes, components, and patterns. While numerous research efforts in 3D printing took place during the 1970s, it was Charles Hull who introduced and patented this innovative process in 1984. To understand the concept of Stereolithography, it is essential to first grasp the workings of the SL process. The procedure begins with the creation of a CAD file, which is then converted into an STL file format. This STL file contains the geometric information necessary for a 3D printer to fabricate an object. The process involves four key components: a UV-curable photopolymer liquid, a perforated build platform, a laser source, and a computer system for process control. Once the STL file is processed, the 3D printer operates by submerging the perforated platform into the liquid polymer tank. As the platform descends, the liquid polymer flows through the perforations and, upon contact, is exposed to a UV laser that instantly cures the polymer. The platform continues to lower, building the object layer by layer, with each new layer bonding to the previous one, starting from the base. After the final layer is completed, the printed object is placed in a different resin to facilitate its separation from the liquid polymer. This step enhances the adhesion between the layers within the resin, and the model is then cured in a UV oven at a specified temperature, solidifying all layers and achieving the desired finish. Consequently, these steps culminate in the creation of the final product. Therefore, Stereolithography (SL) can be defined as a 3D printing technique that transforms liquid photopolymer into three-dimensional objects using a Stereolithographic machine.

Fused Deposition Modelling (FDM) Technology

A technique that employs thermoplastic filament heated to its melting point, which is then extruded layer by layer to create a 3D object. This technology was pioneered by Scott Crump in the early 1990s and introduced by Stratasys INC in the USA. FDM 3D printers feature a support base that allows for vertical movement and includes an extruder that feeds the filament, heating it to its melting point before extruding it through a nozzle to build the desired object layer by layer. The extruder is capable of moving in three dimensions (x, y, and z). The term 'fused deposition modeling' refers to the process where adjacent layers fuse together during deposition by the extruder, with the 3D printer responsible for shaping the final product. Depending on the desired surface finish, the completed object may be dipped in resin, similar to the Depending on the desired surface finish, the completed object may be dipped in resin, similar to the Stereolithography (SL) method

Powder Bed Fusion (PBF) Technology

A technique that employs a thin layer of powder to construct a component. An energy source, such as a laser or electron beam, is utilized to fuse the powder in accordance with the component's geometry. This method enables the laser to selectively melt the powder layer by layer, creating three-dimensional structures. The PBF process involves distributing pulverized material over the previously formed layer, preparing it for the next layer, which results in a distinct output rather than a continuous one, although each layer is connected to its neighboring layers. A hopper feeds the pulverized powder, which is then evenly spread across the powder bed using a roller or brush. The optimal thickness of each powder layer is determined by the specific process conditions and materials used. Various techniques under the Powder Bed Fusion umbrella include Selective Laser Sintering (SLS), Electron Beam Melting (EBM), Selective Laser Melting (SLM), Direct Metal Laser Melting (DMLM), and Direct Metal Laser Sintering (DMLS). Selective Laser Sintering (SLS) is a rapid prototyping technique developed in the mid-1980s by Dr. Carl Deckard and Dr. Joe Beaman at the University of Texas at Austin. This method allows for the creation of intricate geometries by layering and consolidating powdered materials. The solidification process is facilitated by CO2 or nitrogen lasers, depending on the desired surface finish and fusion characteristics. Various types of powders, including thermoplastics, ceramics, glass, and metals, can be utilized in this process. When metal powders are used, the technique is referred to as Direct Metal Laser Sintering (DMLS). SLS printers consist of two chambers, with the first chamber transferring power to the second, where the actual manufacturing takes place. The powder is heated

to a temperature below its melting point, and a leveling roller spreads the powder to form layers. Once the manufacturing process is complete, additional finishing operations are necessary.

Selective Laser Sintering (SLS) Technology

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Binder jetting (BJ) Technology

A technique that employs an adapted form of inkjet technology, first introduced by the Massachusetts Institute of Technology (MIT). Unlike traditional methods that utilize lasers for binding, this process relies on an inkjet system to adhere objects together. It operates on a 2D printing technology, building up layers to create a 3D object. The process begins similarly to other 3D printing methods, starting with the creation of a 3D model that is then imported into the printer's software. To maintain a continuous supply during printing, a dispenser is used to provide the necessary powder. After applying a powder layer of varying thickness, the printhead deposits the binder according to the design specifications. Before proceeding to the next layer, the binder solvent is dried using fluorescent or electric lamps. Subsequently, the powder bed is lowered, and a new layer of powder is added. Once the printing cycle is complete, the binder is placed in a furnace, with the required temperature and duration depending on the binder's composition. Metal and ceramic components typically undergo processes such as sintering, infiltration, heat treatment, or hot isostatic pressing before they can be utilized. In contrast, most metals and plastics do not need any post-processing and can be used immediately after exiting the printing system.

Direct Energy Deposition (DED) Technology

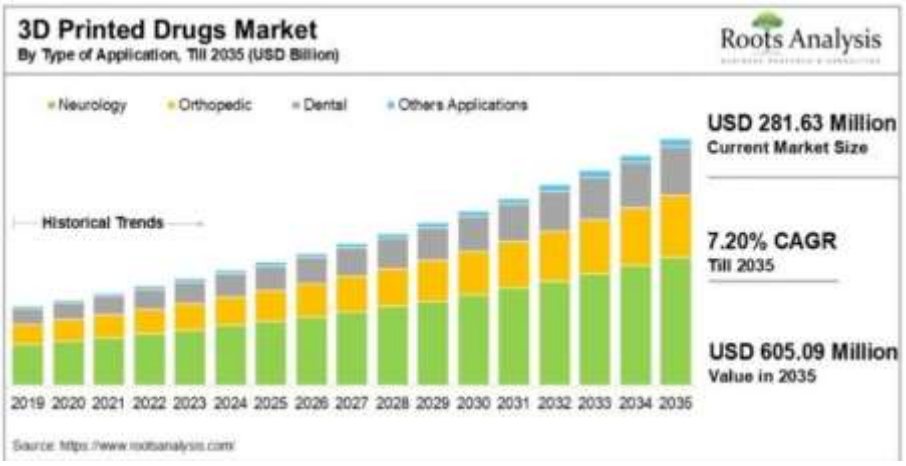
This technique differs from other 3D printing methods as it is primarily utilized for repair and maintenance rather than the creation of new components. DED techniques facilitate material creation by melting the material during deposition. The DED setup includes a deposition head that integrates an energy source with two powder feed nozzles. In this process, either metal powder or a thin wire can be introduced. The component to be fabricated is placed on a platform, and in some instances, inert gas tubing is also utilized. The deposition head, which delivers both the powder and the laser beam, operates on a 4 or 5 axis machine. The DED process employs a focused heat source (either an electron beam or laser), allowing the material to solidify and be built up layer by layer, effectively repairing and creating new material objects on existing products.

Laminated Object Manufacturing (LOM) Technology

It was commercialized by Helisys Inc. (now Cubic Technologies) in 1991, based in California. This rapid prototyping technique creates models using layers of paper, plastic, or metal that are effectively bonded with epoxy. The desired shape of the model is achieved through a laser cutter. The process begins with a sheet attached to a substrate using a heated roller, followed by precise cutting of subsequent layers with either a laser or mechanical cutter. These layers are then glued together in a sequence, either by forming first and then bonding, or vice versa. As each layer is completed, the platform descends, and a new sheet of material is positioned for the next layer, continuing until the prototype is fully formed. Additionally, Ultrasonic Additive Manufacturing (UAM) is a variation of LOM that integrates lamination with ultrasonic metal seam welding and CNC milling.

5. Market overview

The global market for 3D printed drugs is projected to grow from USD 281.63 million in 2024 to USD 605.09 million by 2035, reflecting a compound annual growth rate (CAGR) of 7.20% throughout the forecast period.



3D printed drugs, also referred to as 3D printed pharmaceuticals, represent a revolutionary approach to personalized medicine, utilizing advanced 3D printing technology to create medications with customized release profiles, accurate dosages, and complex structures that traditional drug development methods struggle to achieve. These innovative pharmaceuticals feature a porous design that facilitates easy oral dispersal, eliminating the need for patients to swallow large doses of medication. Importantly, 3D printing technology empowers drug developers to adjust the form, size, and distribution rate of various medications, enabling tailored formulations that cater to individual patient needs, minimize side effects, and enhance adherence to treatment regimens. The demand for 3D printed drugs is driven by the increasing need for personalized therapies, especially among the elderly population suffering from chronic illnesses. Additionally, the rising number of FDA approvals for 3D printed medications has further accelerated their production, providing essential support for patients managing long-term health conditions. Sprit am, created by Aprecia Pharmaceuticals, and marked a significant milestone as the first 3D printed medication to be introduced in the United States in March 2016, serving as an anti-epileptic treatment. In February 2024, Triastek, a Chinese company specializing in 3D printed pharmaceuticals, announced that its T22 gastric retention product has obtained investigational new drug (IND) approval from the FDA. This innovative 3D printed medication is the first to address chronic thromboembolic pulmonary hypertension (CTEPH) and pulmonary arterial hypertension (PAH). With the increasing FDA approvals, numerous stakeholders in the industry are intensifying their research and development initiatives to advance technological innovations in 3D printed drugs. Given the surge in FDA endorsements and the growing collaborations among industry players, we anticipate that the market for 3D printed medications will experience significant growth throughout the forecast period. Furthermore, the market is expected to remain attractive for investment, driven by factors such as the rising demand for cost-effective, customized therapeutic solutions and the expanding use of 3D printing technology within the pharmaceutical sector.

6. Current Scenarios

1. Global Market Size and Growth
    - Graph : Global Market Size of 3D Printing in Pharmaceutics (USD Million)
    - Projected
    - Source: Grand View Research, 2023; Markets and Markets Report, 2023
    - Interpretation:
    - The 3D printing pharma market is growing at a CAGR of around 20–25%, with

increasing adoption in R&D and niche clinical areas.

2. Regional Market Distribution

- Pie chart : Regional Share of Global 3D Pharmaceutical Printing Market (2023)
- North America – 45%
- Europe – 30%
- Asia-Pacific – 18%
- Rest of the World – 7%
- Source: Allied Market Research, 2023
- Interpretation:
- North America leads due to FDA approval of the first 3D-printed drug (Spritam platform) and advanced R&D infrastructure.

3. Key Market Drivers

- Chart 1: Top Factors Driving Market Growth
- Personalized Medicine Demand – 30%
- Regulatory Support & Pilot Approvals – 20%
- Faster Prototyping & Drug Development – 20%
- Hospital-based On-demand Manufacturing – 15%
- Reduction in Wastage & Cost – 15%
- Source: Global Data Pharmaceutical Insights, 2023

4. Current Situation of 3D Printing in Pharmaceutics

- The pharmaceutical industry is increasingly adopting 3D printing to overcome

- Traditional manufacturing limitations. Applications include:
- Personalized medicine: Tailored drug doses based on patient-specific requirements
- Complex drug-release profiles: Multi-layer or time-released tablets
- Rapid prototyping: Accelerating drug formulation testing
- Implantable devices: Customized transdermal patches and implants
- The U.S. Food and Drug Administration (FDA) approved the first 3D-printed drug,

Spritam (levetiracetam), developed by Aprecia Pharmaceuticals in 2015. This drug
- dissolves rapidly and is used to treat epilepsy

5. Indian Market

- In India, the application of 3D printing in pharmaceutics is still in the research and

pilot stage. However, the potential is significant due to:
- Government support via "Make in India" and "Start-up India"
- Growing pharmaceutical industry with a focus on generics and innovation
- Research institutions actively engaged in 3D printing.
- National Institute of Pharmaceutical Education and Research (NIPER)
- Institute of Chemical Technology (ICT), Mumbai
- JSS College of Pharmacy
- BITS Pilani

7. Significances & Drawbacks

3D printing offers significant benefits, particularly in personalized medicine, manufacturing, and healthcare. It enables the creation of customized drug delivery systems, implants, and organ models tailored to individual patients, improving treatment outcomes. The technology reduces production risks by allowing prototype testing before mass production and speeds up development through rapid prototyping. Modern 3D printers are user-friendly and support complex, flexible designs, leading to high-quality, personalized products. Print-on-demand capabilities reduce storage needs, while the lightweight nature of printed items benefits industries like healthcare and aerospace. Additionally, 3D printing cuts costs by minimizing waste and labour and supports sustainability through efficient material use and eco-friendly options.

3D printing has notable drawbacks, especially in medical and industrial fields. Material optins are limited, and not all meet the standards for strength or biocompatibility. High-end printers and specialized materials are costly, with added expenses for maintenance. Print size is restricted, requiring larger objects to be assembled from smaller parts, potentially weakening them. Additionally, 3D printing is inefficient for mass production and may lead to job losses in traditional manufacturing sectors.

8. Conclusion

This paper provides a comprehensive review of the literature concerning various 3D-printing technologies utilized in the pharmaceutical sector. It clarifies the principles and features of each technology, identifies the appropriate dosage forms, and discusses developmental trends. Additionally, it highlights the commercialization paths of notable companies and institutions involved in 3D-printed pharmaceuticals, detailing their historical progress and significant achievements that are propelling innovations in drug

development models. This technology offers advantages for patients, pharmacists, and the pharmaceutical industry by enhancing the safety and efficacy of treatments. Healthcare professionals, including pharmacists, physicians, and nurses, play a crucial role in facilitating the adoption of this technology and will be instrumental in guiding academics, the pharmaceutical sector, and biotech firms on strategies to innovate the industry through 3D printing.

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