Additive manufacturing – A futuristic approach

Dornala Chaitanya Dixit*
* *M.Pharm, (Ph.D) Associate Professor. Dr. KV Subba Reddy Institute of Pharmacy*
Co-Authors: Dr. M Sri ramachandra, Gangula Neeraja Reddy, Teppali Jyothi, Neerukattu Sandhya

Abstract: Additive manufacturing (AM), also referred to as 3D printing, is an innovative method of production that is poised to redefine the future of manufacturing in various sectors. This state-of-the-art technology enables the fabrication of intricate and tailored items by adding material layer by layer, as opposed to traditional subtractive techniques. AM has found application in industries such as aerospace, healthcare, automotive, and consumer goods, where precision and customization are crucial.

Despite existing limitations such as material restrictions, production speed, and high expenses, advancements in technologies like metal 3D printing, bio-printing, and 4D printing hold potential for addressing these obstacles. As AM becomes more integrated into global supply chains, it offers advantages in terms of sustainability, reduced waste, and decentralized production models. This piece explores the development, benefits, challenges, and future trends of additive manufacturing, providing a thorough understanding of its transformative potential for industries and the global economy.

Key words: additive Manufacturing (AM), 3DPrinting Technology, Industrial Applications of 3D Printing, Customization in Manufacturing, Rapid Prototyping, Material Efficiency, Bio-Printing, Sustainability in Manufacturing, Industry 4.0Future of Manufacturing.

1.0 INTRODUCTION

Additive manufacturing (AM), also known as 3D printing, is quickly becoming a revolutionary technology in the pharmaceutical sector. Traditionally linked with manufacturing and prototyping, AM is now being investigated for its ability to transform drug development, production, and delivery systems. By constructing products layer by layer using digital designs, additive manufacturing permits the precise production of intricate structures and personalized dosage forms that were previously unachievable with traditional pharmaceutical manufacturing techniques. In pharmacy, AM allows for the creation of tailored medications customized to meet individual patient requirements, optimizing drug dosage and release profiles, and even consolidating multiple medications into a single pill.[1] This technology also facilitates swift prototyping in drug research and development, enabling faster testing of new drug formulations. Furthermore, 3D-printed implants, devices, and drug delivery systems are opening up new opportunities in personalized medicine and targeted treatments. Despite its potential, the implementation of AM in pharmacy faces challenges such as regulatory approval, ensuring consistent quality control, and scaling up production for widespread use. Nevertheless, as technology progresses and regulatory frameworks evolve, additive manufacturing is set to play a pivotal role in the future of personalized medicine, enhancing healthcare efficiency, patient-cantered care, and fostering innovation.[2]

2.0 HISTORY

A literal examination of cumulative manufacturing (AM) traces its origins back to print form in the 1860s and geomorphology in the 1890s. These foundational ways paved the way for the “print- icon recording” system, which was patented in 1951 and involves the picky exposure of layers within a transparent print conflation as cross- sections of the object are scrutinized for replication.[3]

Cumulative manufacturing is revolutionizing medical practices and simplifying tasks for engineers. In 2004, the Society of Manufacturing Engineers distributed the colourful technologies related to AM, and by 2012, at least four other significant technologies had surfaced. [4]

In 2009, Bourell and associates published a roadmap for AM that surfaced from a factory attended by 65 influential numbers in the field [5]." Direct Digital Manufacturing (DDM) of metallic factors affordable, durable, and structurally effective aircraft" was the caption of a Navy factory that Frazier covered in 2010[6].

Three- dimensional printing, also appertained to as cumulative manufacturing, involves the creation of three- dimensional objects with the guidance of a 3D printer and a computer or digital train. DeSimone responded," 3D printing is 2D printing and over again," in a 2015 TED talk, describing the technology. The generality of Stereo lithography or 3D printing was first put forth by Prof. Charles Hull in 1983. In the 1980s, rapid-fire- fire- fire prototyping was a more precise term for what we now call 3D printing, which at that time was primarily used for creating functional or visually appealing prototypes.

As of 2022, the expressions cumulative manufacturing and 3D printing can be used synonymously due to the advancements in delicacy, repetition, and material diversity in the technology, allowing certain 3D printing styles to be supposed suitable for artificial product.[7]

2.1 Comparison of Traditional Manufacturing:

The three technologies are Photo sculpture, Topography, and Material Deposition. They use manual labour to construct parts in an additive fashion without the use of tools. Photo sculpture, demonstrated in 1860, used photography and hand craftsmanship to create sculptures. Topography, dating back to 1892, involved creating 3D topographical maps from aerial photos. Material deposition, dating back to 1925, used a moving deposition source to create 3D parts. These approaches demonstrate the early stages of additive manufacturing before the invention of the computer.[8]

3.0 ROLE OF ADDITIVE MANUFACTURING IN PHARMACY TODAY

3.1 Personalised medicine:

Personalized medicine is a medical approach that uses individuals' characteristics and genetic information, along with lifestyle and medical data, to customize the most suitable treatment for each person at the right time. It also helps in identifying susceptibility to diseases and providing targeted prevention.[10] This approach addresses the limitations of traditional medicines, which may not work for many patients, and helps in reducing healthcare costs associated with trial-and-error treatments. Other terms used to describe this concept include individualized medicine, precision medicine, stratified medicine, pharmacogenomics, genomic medicine, and P4 medicine (personalized, predictive, preventive, and participatory).[9]

3.2 3D Printing Drugs:

3D printing of drugs is revolutionizing the pharmaceutical industry by enabling personalized, patient-specific medications. This technology allows for precise control over drug dosages, shapes, and release profiles, leading to customized treatments. The FDAapproved Sprit Am (levetiracetam) was the first 3D-printed drug, offering fast-dissolving medication for epilepsy patients.[11] Benefits include tailoring doses for specific groups like children or the elderly, combining multiple drugs into one pill, and accelerating drug development by allowing rapid prototyping of new formulations. Additionally, 3D printing supports on-demand manufacturing, potentially allowing pharmacies and hospitals to produce medications locally. Challenges remain in regulatory approvals and scaling production for mass use, but 3D-printed drugs have the potential to transform personalized medicine, making treatments more accessible and tailored to individual needs.[12]

3.2.1 Technology method of 3D printing PM -

Creating a completely PM requires a dynamic manufacturing process whereby administration route, product size and shape, and drug release kinetics can be quickly and simply modified to suit the individual patient's needs and preferences. 3D printing, the process by which an object is built up in a layer-by-layer method, according to instructions from a computer-aided design (CAD) software, offers a solution to the limitations current pharmaceutical manufacturing methods impose on the development of PM.[13]

3.2.1.1 Fused Deposition Modelling (FDM):

The FDM technique involves using a movable head to deposit a thread of molten thermoplastic material onto a substrate. The material is heated up to 1°C above its melting point, allowing it to solidify right after extrusion and then weld to the previous layers. The FDM system head typically includes two nozzles: one for the part material and one for the support material. This system can be seen as a desktop prototyping facility because it uses inexpensive, non-toxic, and odourless materials in a variety of colours and types, such as acrylonitrile butadiene styrene (ABS), medical ABS, PLA, investment casting wax, and elastomers.

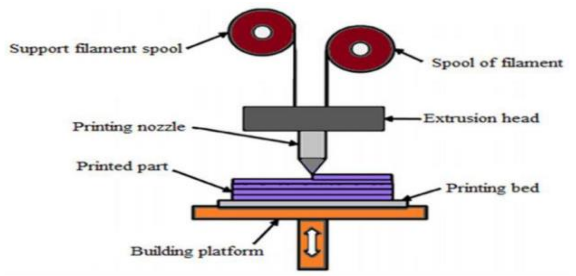


Figure 1: Fused Deposition Modelling

The simplicity of the FDM process, along with the relatively low cost of equipment and raw materials, makes it ideal for use by hobbyists and to produce low-cost plastic parts. However, the accuracy and surface quality of FDM parts are relatively poor when compared to those produced by powder-based plastic AM processes.[14]

The main advantages of this process are that no chemical post-processing is required, there are no resins to cure, and it involves less expensive machines and materials, resulting in a more cost-effective process.[15]

Future Perspectives: The potential applications of FDM 3D printing in pharmaceutical product development are illustrated in Fig:1. As not all necessary dosage regimens for personalized pharmacotherapy are readily available, pharmacy-based dosage printing offers an alternative to traditional industrial manufacturing. Additionally, 3D printing of pharmaceuticals presents a viable solution in scenarios such as on-demand production of required medications at clinics, during disaster relief efforts, and in operating rooms.[16]

3.2.1.2 Hot Melt Extrusion [HME]:

The hot-melt extrusion (HME) process was developed in the early 1930s and quickly became widely used in the plastic, rubber, and food industries. In the 1970s, its application expanded to the pharmaceutical industry for formulation, product development, and manufacturing. The first use of HME as a manufacturing tool in the pharmaceutical industry. [17]

Hot-melt extrusion involves mixing polymeric material in a chamber using a rotating screw at high temperatures. Active pharmaceutical ingredients (API) and other excipients can be added with a polymer to the chamber. When the chamber is heated above the polymer's melting point or glass transition temperature, molecular-level mixing occurs, resulting in a final amorphous product. This extrudate can be used as a drug-loaded filament for other techniques.[13]

The extruder is made up of four distinct parts:

1. An opening through which material enters the barrel. This opening may have a hopper filled with the material(s) to be extruded, or the material may be continuously supplied in a controlled manner by one or more external feeders.
2. A conveying (process) section, which includes the barrel and the screw(s) that transport and, where applicable, mix the material.
3. An orifice (die) for shaping the material as it leaves the extruder.
4. Downstream auxiliary equipment for cooling, cutting, and/or collecting the finished product fig:2.[18]

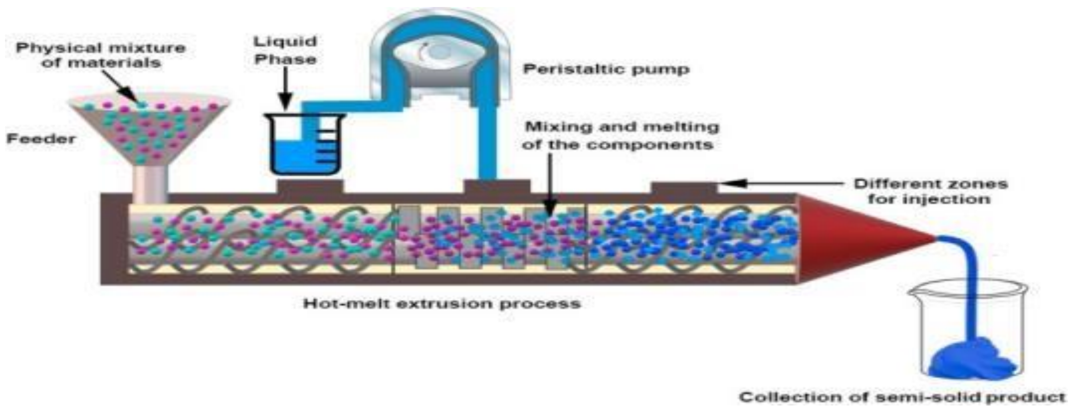


Figure 2: Hot Melt Extrusion

3.2.1.3 Semi -Solid Extrusion [SSE]:

The semi-solid extrusion (SSE) process involves pushing a semi-solid starting material (in the form of gel or paste) through an opening using compressed air pressure, a syringe plunger, or a screw, depending on the specific equipment used. The material is deposited layer by layer, as shown in Fig:3.

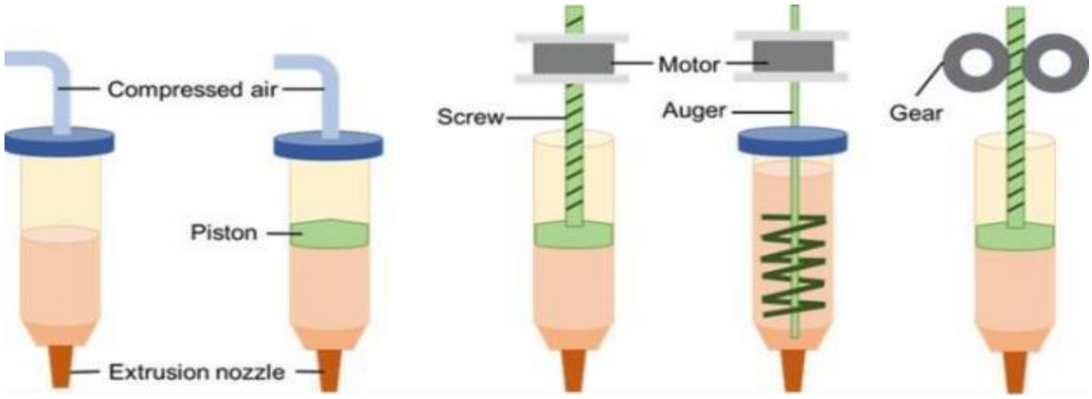


Figure 3: Semi Solid Extrusion

Semi-solid materials can be easily obtained by mixing excipients commonly used in the pharmaceutical industry in optimal ratios with appropriate solvent(s) to achieve a suitable viscosity for printing. SSE does not require high temperatures, but a further drying process is needed when using materials in the form of pastes or gels, which may cause shrinking or deformation of the printed product. Additionally, the fabricated object may collapse during 3D printing if a constructed layer does not harden sufficiently to withstand the confinement of the successive layer.

The technique is usually confined to low resolution since an orifice with a size of 0.4– 0.8 mm is typically employed. However, an accurate parameterization of the dispensing of the semi-solid mass, as well as the use of nozzles smaller in diameter, allows us to obtain dosage forms with good resolution and mass uniformity . The main advantage of SSE is the ability to fabricate dosage forms with high drug loading. By using multi-syringe printing, "polypills" containing 3–5 APIs released with different kinetics can also be obtained.[19]

3.2.1.4 Vat Photo Polymerization (VPP):

The working principle of VPP involves curing a light-curable resin in a vat and creating a solid preform by chains of polymers or crosslinks. VPP methods offer advantages such as smooth surface finish, high part size precision, the ability to produce wall thicknesses from 50 μm to 150 μm, and can be used with a wide range of commercially available materials. This method can be used in machines with different configurations, size scales, and light sources, making it suitable for cost-effective and near-net shape production of multimaterial and FGM components.

The light source for VPP can be a normal laser beam, visible light, or ultraviolet (UV) light spectrum. With light sources, it is possible to cure a full layer of resin; however, with a laser, the whole surface should be illuminated by drawing it. In general, the photopolymer consists of monomers, oligomers, photo initiators, and other additional materials. After curing each layer surface, the part moves upwards or downwards according to the top-down or bottom-up configurations. In the top-down approach, the light source is provided from the top and after the deposition of each layer, the part is moved downwards. In the bottom-up approach, the light source cures the resin at the bottom, and the mechanism moves upwards after curing fig:4.[20]

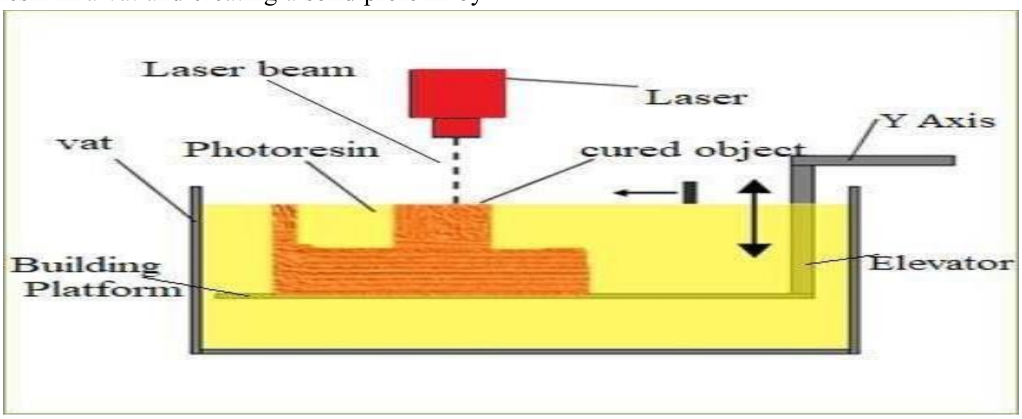


Figure 4:Vat Photo Polymerization

VPP methods have been extensively used for Additive Manufacturing of advanced ceramics. Lithography-based Ceramic Manufacturing (LCM) is a kind of DLP method that was commercialized by Lithoz GmbH, Austria. This method works on the principle of selective curing of ceramic slurry via blue light with a wavelength of 460 nm. LCM method offers manufacturing of very complex and net-shaped structures that have very high resolution up to 100 µm wall thickness. Different sintering methods have been used for stereolithographic Additive Manufacturing of SIC ceramics. It was reported that liquid phase sintering (LPS) offers a promising process for manufacturing dense SIC with good mechanical properties.[21]

3.2.1.5 Ink Jet Printing (IJP):

The IJP technology's key feature is its precise ink deposition, which avoids substrate contact and enables precise control of the printed dose based on the volume ejected through the nozzle Additionally, INKJET provides great flexibility for substrates, as formulated inks can be printed on a wide range of materials, including films, microneedles (MNs), clinical stents, contact lenses, and even nails .IJP is a material jetting technology that entails depositing small liquid ink drops through a nozzle . It can be categorized into two techniques based on how the ink drops are produced: Continuous inkjet printing (CIJP) and drop-ondemand (DOD) IJP.[22]

CIJP operates by utilizing a high-pressure pump to direct the ink through a nozzle, creating a continuous stream. This stream is then fragmented into droplets due to surface tension forces. The frequency can be modified to control the droplet formation.[23] To create a printed pattern, droplets are selectively charged by charging electrodes and pass-through deflector plates that generate an electrostatic field.

On the other hand, DOD methods respond to an electrical stimulus to expel small volumes of liquid. There are two types of DOD print heads: thermal and piezoelectric. In thermal IJP, an electrical signal is applied to a thermal element in the print head, raising the liquid's temperature (i.e., up to 200–300 °C). This temperature increase generates expanding bubbles that eject the fluid through the nozzle, forming a drop. In piezoelectric IJP (PIJP), the print head contains a piezoelectric element that deforms when exposed to an electric current, expelling the drop.[22]

3.2.1.6 Selective Lesar Sintering [SLS]:

This is a description of a three-dimensional printing process that uses a carbon dioxide laser beam to sinter or fuse powder. The process involves heating the chamber to near the material's melting point and using the laser to fuse the powder at specific locations for each layer according to the design. The loose particles are controlled by a piston, which lowers the same amount as the layer thickness for each finished layer (see fig:5).

This process allows for the use of various materials including plastics, metals, combinations of metals, combinations of metals and polymers, and combinations of metals and ceramics.[24] Selective laser sintering (SLS) is similar to binder jetting, but instead of a binder, a laser is used to sinter powder particles together. The primary components of an SLS system are the spreading platform, powder bed, and laser system. This method is advantageous because it is a one-step rapid manufacturing procedure that does not require the use of any solvent and produces high-resolution results due to its laser precision.[25]

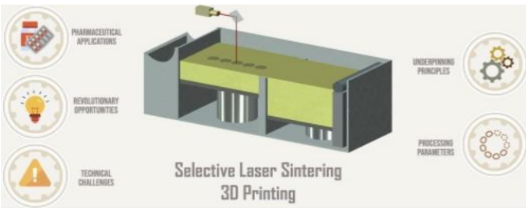


Figure 5: Selective Lesar Sintering

3.2.1.7 Stereolithography (SL):

Additive manufacturing (AM) technologies, also known as three-dimensional (3D) printing, encompass a variety of processes that allow for the layer-by-layer creation of intricate 3D structures using a wide range of materials. These technologies can produce advanced parts with complex geometries, functions, and compositions. AM technologies have been integrated into various fields such as electronics, actuators, biomedical engineering, and sensors. There are three commonly used approaches to AM: extrusion-based 3D printing, selective laser sintering (SLS) or selective laser melting (SLM), and Stereolithography.[26]

Stereolithography (SL), developed by 3D Systems, Inc., was the original and most widely used rapid prototyping process, and in the past, the two terms were used interchangeably. This method involves the solidification of a photosensitive polymer through the application of an ultraviolet laser to the resin. The process begins with a model in a CAD software, which is then converted into an STL file containing slice-by-slice information for each layer. The layer thickness and resolution depend on the specific equipment used. A platform is created to support the piece and any overhanging structures.

The UV laser is used to solidify specific locations of each layer. Once a layer is completed, the platform is lowered, and any excess resin is drained and can be reused. A more advanced version of this process, called micro Stereolithography, has been developed, featuring even higher resolution with a layer thickness of less than 10 μm].

The basic components of a Stereolithography machine are illustrated in Fig:8. The fundamental principle of this process is photopolymerization, where a liquid monomer or polymer transforms into solidified polymer when exposed to ultraviolet light, which serves as a catalyst for the reactions; this process is also known as ultraviolet curing. It is also possible to suspend powders in the liquid, such as ceramics.

Stereolithography introduces errors to the final piece. One such error is over curing, which affects overhanging parts due to the lack of fusion with a bottom layer. Another error is the scanned line shape, which is a result of the scanning process. Because the resin is a highviscosity liquid, the layer thickness varies, leading to errors in border position control. Additionally, the part might require manual surface finishing. These errors are minimized in high-quality equipment. Multiple material Stereolithography allows for the use of different materials in the printing process. To switch materials during printing, all the resin must be drained and replaced with the new material when the process reaches the relevant layer, even if the first material will be used again, as only consecutive layers can be printed. A scheduling process must be specified in the software.[27]

3.3 Prototyping:

This part focuses on developing designs for educational use and innovative suggestions. It covers surgical planning and academic research applications for future medical professionals, creating prototypes to address issues and draw appropriate conclusions for medical complications that may arise in the operating room or due to challenges in the university stage. In the field of surgery, healthcare workers need to be ready for various scenarios. While some procedures are routine and do not vary significantly between patients, there are situations where medical complications necessitate thorough preoperative examination.

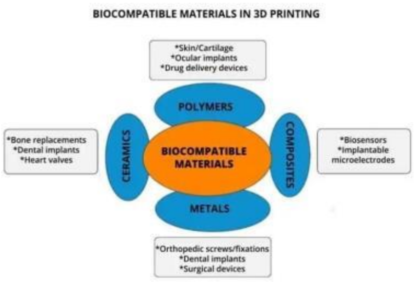
A prototype utilizes real patient scans, an image processor for modelling, and a 3D printer to prepare a surgical plan based on specific requirements. In an academic context, it has been observed that complex systems can be difficult to comprehend during university studies. Among the various options that aid in learning are virtual models, three-dimensional anatomical models, and updated detailed books.

Another available option is the production of 3D models of cases, which helps medical students better grasp the proportions of models on a real or proportional scale. Practising with phantom models allows them to visualize different internal anatomical structures and the representation of complete, partial, or isolated systems of the areas of interest that the student aims to reinforce and understand.[28]

4.0 MATERIALS USED IN ADDITIVE MANUFACTURING

Materials play a vital role in understanding various processes. A wide range of raw materials is currently used for different processes, and significant research is ongoing to develop new materials for specific applications.

Polymeric materials, paper laminates, and waxes are among the initial raw materials used during the origin phase of additive manufacturing (AM). Various types of materials, including polymers, metals, ceramics, composites, and biomaterials, are used as AM materials. The state of their raw forms used as feedstock varies and is discussed below.[29]



4.1 Raw Materials of AM:

Understanding the physical state of raw materials used in the process is crucial for determining their suitability for any additive manufacturing (AM) process. It's essential to grasp the compatibility of different forms of feedstock, such as liquid, powdered, wire, or sheet, for various AM processes. For instance, techniques like Stereolithography rely on curing liquid resins.[30]

4.1.1 Polymers:

Polymers are widely used in additive manufacturing (AM). Plastics, polymeric-graded materials, and polymer matrix composites are the main areas where polymers are utilized in AM. This is due to their lower melting/curing temperatures, improved chemical stability, and their ability to flow smoothly in both molten and softened states. Three commonly used AM techniques are photopolymerization, material extrusion, and material jetting.

The most commonly used polymeric AM materials are thermoplastic polymers and UV-curable polymers. Additionally, FDM, SLS, and inkjet printing are used. Thermoplastic polymers such as polyamide, poly-lactic acid, nylon, acrylonitrile butadiene styrene (ABS), and polycarbonate are commonly used due to their compatibility with the AM process.[31]

4.1.2 Ceramics:

Some raw materials, such as ceramics and concrete, have limited use in additive manufacturing because their individual particles cannot fuse together by being heated to their melting points. In contrast, polymers and metals can fuse sufficiently at their melting points. Ceramics have significantly higher melting points compared to polymers and metals, posing a major challenge for additive manufacturing processes. Therefore, additive manufacturing techniques capable of producing ceramic parts with mechanical properties comparable to those made using traditional manufacturing processes are crucial.

An important example of ceramic additive manufacturing parts is the production of scaffolds made of ceramics for bones and teeth. However, this limitation is significant in applications such as aerospace and construction, where flat external surfaces are essential to prevent stress accumulation at specific points.[32]

4.1.3 Composites:

Composites are a distinct group of materials and are more modern than polymers or metals. Composites can be described as a blend of two or more constituents with final properties significantly different from those of their components. Some additive manufacturing (AM) processes are capable of producing composite parts with greatly improved properties compared to the base constituents. This has led to the widespread use of AM processes for fabrication. Different AM techniques are employed for the reinforcement of composites with fibres. Each technique has varying suitability depending on the base matrix (metal, polymer, ceramics) and reinforcement particles.[33]

4.1.4 Biomaterials:

Additive manufacturing (AM) offers significant opportunities for creating biomaterial constructs with customizable shapes. It allows the manipulation of both external and internal structures, which enhances tissue regeneration and integration.[34] The internal microarchitecture influences the physical, mechanical, and biological properties of porous biomaterials, affecting their performance in terms of stability and permeability. Various AM techniques, like binder jetting and material extrusion, have been used for processing ceramicbased biomaterials.[35]

Selecting the right material for drug delivery systems is essential, as it must be biocompatible, biodegradable, easy to prepare, non-toxic, and affordable. Additionally, finding the correct combination for drug loading into the material is critical.[36]

5.0 APPLICATION OF AM

Additive manufacturing has made its way into many industries and has found diverse applications in aerospace, automotive, dental and medical industries, toys, fashion and accessories, art, and architecture. In this section, we will present some of these applications.[37]

5.1 Aerospace:

When producing aerospace components, it's crucial to achieve the desired material properties. Additive manufacturing (AM) is highly suitable for this purpose as it allows for the production of intricate shapes and small quantities of components. It is particularly beneficial for reducing the weight of aircraft while maintaining safety. AM has been used to print low-volume complex components and spare parts in metals and plastics, leading to significant fuel savings for airlines. For example, General Electric used AM to reduce the number of parts in a jet engine injector from 115 to just two.[38]

5.2 Automation:

Additive manufacturing (AM) has been used in the automotive industry primarily for prototypes and custom parts for high-end vehicles. It helps create innovative, cleaner, lighter, and safer products while reducing lead times and costs. However, the limited build volume of current 3D printers restricts the production of larger components like body panels. Research, such as Materialises development of a large Stereolithography machine (2,100 mm x 680 mm x 800 mm), aims to overcome this. Custom fabrication of tooling is also essential, improving productivity with hand tools that are 72% lighter than traditional ones.[39]

5.3 Medical Applications:

Over the past 20 years, 3D printing has significantly advanced medical technology. It is now used for creating medical devices, implants, prosthetics, bionics, and training models. By combining medical imaging with 3D printing, customization of prosthetics and implants has improved. Stratasys has developed plastic parts for MRI machines using FDM technology, which has reduced costs by up to 78%, manufacturing time by up to 94%, and material waste. Additionally, 3D printing is utilized for orthodontic braces. Aram's Q10plus is designed for orthopaedic implants, while Stratasys employs Polyjet technology to create multi-color anatomical models for training and planning. Another innovative application is 3D bioprinting, which can produce living tissue structures, including bones and organs, with successful tests on animal models.[40]

6.0 ADVANTAGES OF AM

6.1 Material Waste Reduction:

One of the advantages of additive manufacturing is its minimal waste production. Traditional manufacturing methods, such as machining, result in a significant amount of waste material due to the removal of excess material from the workpiece. In contrast, additive manufacturing builds objects layer by layer, reducing waste generation. In some cases, the only waste produced is the powder or filament used in the creation of the object. Consequently, additive manufacturing is a more efficient and environmentally friendly process. Additionally, waste material from additive manufacturing processes is often easier to recycle compared to waste from conventional manufacturing processes, providing further cost savings for manufacturers.[41]

6.2 Energy Efficiency:

The operation of traditional manufacturing processes necessitates a substantial amount of energy to fuel the machinery and equipment. These machines often rely on additional tools, like cooling systems, which further increase energy usage. Additive manufacturing processes, on the other hand, are notably more energy efficient. The machines used in additive manufacturing are smaller and consume less energy. Furthermore, minimal auxiliary equipment is necessary, leading to a further reduction in energy consumption. This decreased energy usage can result in significant cost savings for manufacturers. In certain instances, the energy savings can be so significant that the cost of the additive manufacturing equipment can be recouped within just a few years.[41]

6.3 Reduced Costs for Small Production Runs:

Traditional manufacturing can be expensive for small production runs due to fixed setup costs, regardless of the number of products manufactured. Additive manufacturing, on the other hand, does not have setup costs and is efficient for producing small production runs.

This is a significant benefit for manufacturers requiring small quantities of products.[41]

7.0 CHALLENGES AND LIMITATIONS

At present, there are numerous obstacles preventing hospitals and pharmacies from widely adopting 3D printing technology, despite its significant potential in the medical sector.

These barriers encompass various factors.[42]

7.1 Regulatory and Safety Concerns:

The use of 3D printing in healthcare involves creating medical devices, implants, and medications, which raises concerns about regulation and safety. Ensuring the safety and effectiveness of these products is a significant challenge. Regulatory bodies must establish clear guidelines and standards to ensure that 3D-printed healthcare products meet the necessary Quality, safety, and performance requirements.[42]

Pharmaceutical manufacturing is a regulated process that must meet the requirements of current good manufacturing practice (cGMP), such as ensuring the sterility of implants or parenteral products. Printing at home or in a clinic is a key aspect of 3D printing.

However, printing at home or in a doctor's office can halt the entire process due to regulatory issues.

There is a regulatory issue in the process of printing the dosage form.[43]

7.2. Quality Control and Standardization:

Standardization and quality control are crucial in the healthcare sector. The use of 3D printing introduces variability into the production process, which can impact the quality and effectiveness of printed items. It is vital to establish standards for the processes, materials, and quality control procedures of 3D printing in healthcare to guarantee consistent and dependable outcomes.[42]

7.4 Cost and Scalability:

3D printing has the potential to lower healthcare expenses by enabling on-demand production and customization. However, the initial investment in 3D printing equipment and materials can be expensive. Additionally, scaling 3D printing to meet the needs of large healthcare facilities or the general population can be challenging. Overcoming these cost and scalability barriers is crucial for widespread adoption.

Upgrading additive manufacturing techniques on an industrial scale is essential for integrating 3D printing into mainstream usage. Despite significant improvements in the accuracy of 3D printed structures and multifunctional products like polypills, further research is needed to enhance printing speed and increase the size of 3D printers to match the scalability of traditional production methods.[44]

8.0 SUSTAINABILITY AND ENVIRONMENTAL IMPACTS:

Today, "sustainable pharmaceuticals" focuses on reducing environmental impact while promoting public health and social responsibility. This includes eco-friendly manufacturing, waste reduction, and responsible disposal. Companies are urged to balance profitability with environmental concerns to pave the way for a healthier future.

The environmental impact of pharmaceutical production can lead to pollution, contamination of waterways, and antimicrobial resistance. Prioritizing sustainability can help mitigate these issues and protect ecosystems and public health. There is a growing recognition of the need for environmentally friendly practices in pharmaceutical manufacturing, with key initiatives aimed at reducing the sector's environmental footprint.[45]

8.1 Waste Reduction and Circular Economy:

In pharmaceutical manufacturing, the main focus is on reducing waste to address environmental concerns. Companies are working to minimize waste by improving production processes and following principles that support recycling and reusing materials. This focus on the circular economy in the pharmaceutical industry emphasizes the importance of recycling and reusing materials to reduce environmental impact.

Pharmaceutical manufacturing releases harmful pollutants into the air, water, and soil, posing risks to both the environment and human health. Improper disposal of pharmaceutical products, including expired or unused medications, can contaminate water sources, harming aquatic life and contributing to antibiotic resistance. It is crucial to address these environmental concerns.

8.2 Minimizing powder material usage:

This can be accomplished either by recycling the unsintered powder extracted from the finished part and reusing it (if the percentage of contamination is low) or by optimizing the topology of manufactured parts through the use of the proper scanning strategy. Additionally, the amount of powder used is directly proportional to the number of parts on the building plate.[46]

8.4 Reducing manufacturing time:

The time it takes to complete the manufacturing process is influenced by three main factors. One factor is the height and orientation of the manufactured part on the building plate. Another factor is the production volume, which depends on the number of parts on the building plate, their positioning, and the nesting strategy used.

The last factor is the scanning pattern, which takes into account the customization and topology improvement capabilities of additive manufacturing (AM). The machine operating time directly affects operational costs and the number of emissions, impacting both economic and environmental aspects.[46]

8.5 Energy consumption:

An energy model was created to compare wire-based and powder-based additivesubtractive manufacturing processes in terms of energy consumption. The study found that both processes consumed similar amounts of energy overall, but the specific energy consumption at different stages varied.

The model proposed a system framework for analyzing the net changes in primary energy use and greenhouse gas emissions with the adoption of additive manufacturing (AM) in the U.S. manufacturing and air transport sectors. The results showed potential savings in primary energy and reductions in greenhouse gas emissions. Additionally, a preliminary analysis of energy consumption in 3D printing processes using an analytical approach was performed, showing significant material and energy savings with the adoption of AM. [47]

8.6 Lightweight designs:

The benefits of sustainability improvements in the use stage of additive manufacturing (AM) parts include fuel consumption reduction and environmental impact savings due to lightweight parts, particularly in transport systems.

A strategic sustainability approach using the life cycle assessment (LCA) method highlights the benefits and challenges of AM technologies. Areas for improvement include concept design, repair and redesign, optimized material usage, value chain management, and social sustainability. Modelling and simulation are important for understanding lightweight component structures.[48]

8.7 Future Trends and Opportunities:

The future of making medicine is looking good. New ideas and technologies are becoming more important. Companies are trying new ways to be more friendly to the environment. They are using smart math, robots, and eco-friendly chemistry. They are also working with other industries to make a better supply chain. This helps them share good ideas, use resources better, and together make the world greener and more responsible.

9.0 FUTURE TRENDS AND INNOVATION

The document offers a comprehensive overview of various 3D printing techniques used to create various polymeric materials. It emphasizes the potential expansion of FDM and DIW methods for multi-material 3D printing by increasing the number of printing nozzles. Additionally, MJ printing technology is a widely used method for multi-material printing. Polyjet is commonly utilized for multi-material MJ printing. Vat photopolymerization processes like SLA and DLP are generally not suitable for multi-material 3D printing due to challenges related to cross-contamination between different material systems.

Nevertheless, the high print resolution, excellent surface finish quality, and diverse material options make vat photopolymerization an appealing option, despite the complexities associated with multi-material printing. Despite significant progress in multi-material 3D printing in recent years, the full potential of this technology has yet to be fully realized.

9.1 Bio printing:

The field of bio printing has seen significant growth and displayed great potential for various medical applications. Bio printing enables the development of intricate 3D structures containing living cells using bio-inks, such as stem cells, tissues, and organs suitable for human use. This technology has the potential to eliminate the reliance on transplants from living donors or cadavers and facilitate the regeneration of organs and tissues.

The bioprinting process, as depicted, commences with a biopsy of an actual organ and utilizes technologies categorized into four groups: extrusion-based, droplet-based, SLAbased, and laser-assisted. While laser-based inkjet bio printers are most suitable for high resolution and precise positioning, extrusion-based, SLA-based, and droplet-based bio printers are more widely used due to their cost-effectiveness and versatility.[49] The design approach techniques are as follows:

1. Biomimicry is the process of replicating cellular and extracellular components of tissues through 3D bio printing.
2. Autonomous self-assembly tissue involves using embryos for organ development to mimic biological tissue.
3. Mini tissues combine the above strategies to create "organs-on-a-chip" for drug screening and disease models using 3D bio printing.[50]

9.2 4D printing:

This method is a type of 3D printing that uses smart materials (SM) capable of changing shape when exposed to outside forces like heat, electricity, magnets, or pressure. A smart design is created to control how the SM behaves when it encounters a specific force. This design helps us understand how the product changes shape, which is important for the printing process.

The printed product can have more than one shape with specific characteristics that can be changed by a force, altering its physical form or properties. The term “4D” refers to the time dimension, meaning the product changes shape after printing due to the force. The diagram shows the 4DP process, which includes five main factors: material, force, AM printing process, modeling, and interaction mechanism.[51]

9.3 Multi- Material Printing:

The rise of 4D multi-material printing signifies an advanced approach to producing components capable of adapting to new functions or shapes after production Nonetheless, this technique encounters obstacles like low printing efficiency and evolution, limited material choices, and inadequate mechanical performance. These challenges arise from the reliance on traditional 3D printing methods such as DLP, DIW, and FDM. Scientific progress has the potential to enable the activation or movement of intelligent structures based on predetermined programs. Moreover, gradient functional materials provide the ability to not only control the microstructural properties of 4D printed structures by strategically adjusting the density and orientation of printed material layer by layer to achieve more intricate geometric transformations but also improve the interface bonding strength of various intelligent compositions. In brief, the advancement in multi-material 4D printing is crucial in driving the progress of the smart materials field.[52]

In addition to the capability of 3D printing methods to fabricate 3D objects with complex geometries, another important potential is the ability to utilize different materials in a single manufacturing platform to create multi-material objects and composites. The adoption of multi-material manufacturing has been seen to enhance functionality and reduce the weight of products, thereby improving the overall performance of the manufactured components. However, multi-material manufacturing does have certain limitations, including dimensional accuracy and size, the need for post-processing, and the inability to process multiple materials under the same conditions, among others. Methods such as FDM and Polyjet printing are predominantly utilized for multi-material additive manufacturing.[53]

9.4 Artificial intelligence and Machine learning:

In the last ten years, there has been a substantial increase in artificial intelligence (AI) and machine learning (ML) due to advances in computational technology. This has led to significant progress in the capabilities for gathering and processing data. Meanwhile, the costs linked to creating and providing new medications to the market and patients have risen excessively. The pharmaceutical industry is drawn to AI/ML techniques because of their automated nature, predictive abilities, and potential for increased efficiency. Enhancing the efficiency of drug development is crucial from both patient and business perspectives, as it can lower expenses, reduce development time, and improve the likelihood of success (POS).

ML methods have become more advanced in drug discovery over the past 15-20 years. The latest area in drug development where AI/ML is positively impacting is in the design, operation, and analysis of clinical trials. The COVID-19 pandemic may further accelerate the use of AI/ML in clinical trials due to the increasing reliance on digital technology for collecting patient data. AI involves developing systems that demonstrate human-like behaviour.

ML is a type of AI that utilizes algorithms trained with data. DL is a form of ML that takes loose inspiration from the structure of the human brain, known as artificial neural networks. Human intelligence is linked to the brain’s ability to perceive, understand, and respond to a continuously changing external environment. The field of AI not only seeks to understand the workings of the human brain but also strives to build intelligent systems capable of effectively and safely adapting to dynamic external environments.

Researchers have pursued different approaches to AI, focusing on either replicating human behaviour or prioritizing rationality (making the correct decisions) in both thought and action. AI subfields can be broad, focusing on perception, learning, and reasoning, or narrow, such as in the case of playing chess. Various fields, including philosophy, mathematics, and neuroscience, have contributed to the development of AI technology. ML methods are usually classified as supervised learning, unsupervised learning, and reinforcement learning.[54]

10.0 REGULATORY AND ETHICAL CONSIDERATIONS

10.1 Regulatory considerations:

3D printing technology has greatly advanced in medicine and healthcare. Regulatory agencies worldwide, such as the U.S. Food and Drug Administration (FDA), the European Medicines Agency (EMA), and China's National Medical Products Administration (NMPA), are involved in regulating and approving 3D-printed medical devices.[55]

Some key milestones include the first FDA-cleared 3D printed cranial implant, the OsteoFab Patient-Specific Cranial Device, which received FDA clearance in February 2013. This device was developed by Oxford Performance Materials in the USA. Another important milestone is the first 3D-printed titanium spinal device, the CASCADIA Lateral Interbody System, which received clearance and a CE mark in January 2016. This system was developed by K2M Group Holdings, which Stryker acquired in 2018.

To date, many companies have received FDA clearance for their 3D-printed medical devices based on findings published by the FDA.

10.2 Intellectual Property:

1. Copyright: Copyright law can prevent unauthorized printing of assets and applies to original works like writings, drawings, musical compilations, and sculptures.
Registration is not required for copyright protection, but it provides benefits.
2. Patent right: Patent law protects new, useful, and non-obvious inventions from being copied. Unauthorized use or replication constitutes infringement. Proving patent infringement can be challenging and expensive. Stakeholders may need to consider new claim strategies to protect additive manufacturing inventions.[55]

10.3 Safety concerns And Environmental impacts:

Additive manufacturing processes can create safety risks due to heat, fumes, and airborne particulates. Proper ventilation, cooling time for equipment, and monitoring of oxygen levels are essential for a safe workplace. Metal additive manufacturing, in particular, raises concerns about contaminated gases and electrical hazards.

10.4 Data Security and Privacy:

The integration of 3D printing in healthcare heavily relies on managing and safeguarding patient data. As facilities adopt digital records and 3D imaging, concerns about data security and privacy become crucial. Unauthorized access to this information poses significant risks, potentially compromising patient confidentiality and eroding trust in healthcare providers.

One major concern is the threat of data breaches, as medical data is valuable on the black market. Cybercriminals may target healthcare systems to access patient records, leading to identity theft and other issues. Therefore, healthcare institutions must prioritize data protection through robust security measures, encryption, and continuous monitoring.[55]

Table 1. Concerns about Security and Privacy

Patient Privacy	Protecting patient-specific data used in 3D printing, such as medical imaging scans, to prevent unauthorized access and disclosure of personal and medical information is essential for patient privacy.
Data Breaches	The vulnerability of 3D printing systems to data breaches and cyber-attacks could lead to unauthorized access to patient data or 3D printing files, posing a risk to patient safety and privacy.
Data Ownership and Sharing	Involves complexities in defining data ownership and sharing agreements among different stakeholders involved in the 3D printing process, leading to ethical dilemmas and conflicting interests.[56]
Algorithm Bias and Fairness	The potential for biases in algorithms processing patient data for 3D printing could result in unequal or discriminatory healthcare outcomes for specific populations.

11.0 CONCLUSION

11.1 Long-term Outlook:

Additive manufacturing is poised to revolutionize industries like aerospace, healthcare, automotive, and construction through its capacity for customization, precision, and reduced waste. In aerospace, it enables the creation of lightweight, durable parts; in healthcare, it supports personalized implants and bioprinting. The automotive and construction sectors also benefit from streamlined prototyping and sustainable building. Over time, as AM advances, it will become central to production, reshaping global supply chains, reducing material use, and enabling on-demand manufacturing.

11.2 Adoption Challenges:

Despite its promise, AM adoption is hindered by high equipment costs, material limitations, and slow production speeds. Industries also face challenges integrating AM into existing workflows, requiring investments in skills and infrastructure. Regulatory and certification issues, especially in aerospace and healthcare, add complexity. Intellectual property concerns related to 3D printing designs further slow adoption. However, as technological and regulatory barriers are addressed, adoption will accelerate, with industries already demonstrating the viability of AM.

11.3 Vision of the Future:

In the context of Industry 4.0, AM will play a key role in smart, automated, and decentralized production systems. When combined with AI, robotics, and IoT, AM can enhance production efficiency, enable localized manufacturing, and reduce supply chain dependencies. Smallscale 3D printing hubs could produce goods on demand, offering flexibility and sustainability. In this vision of the future, AM will help create more resilient and adaptive industries, transforming how goods are designed, produced, and delivered globally.

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