THE FUTURE IS LAYERED: UNDERSTANDING THE IMPACT OF 3D PRINTING TECHNOLOGY

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Abstract

With its unmatched versatility in creating patient-specific dose forms, three-dimensional (3D) printing has become a game-changing technology in pharmaceutical manufacturing. 3D printing enables the on-demand creation of medications with configurable geometries, drug-release profiles, and dosage strengths, in contrast to conventional manufacturing techniques that rely on large-scale batch production. This change is beneficial for handling complex therapeutic needs, such as pediatric dose modifications, tailored oncology treatments, and polypharmacy in geriatrics. Fused deposition modelling (FDM), stereolithography (SLA), selective laser sintering (SLS), and inkjet printing are just a few of the 3D printing methods that make it possible to produce dosage forms with increased structural diversity and precision. To create tablets, implants, transdermal systems, and controlled-release matrices, these technologies can modify excipients and active pharmaceutical ingredients (APIs). A significant turning point in the field was reached when the U.S. FDA approved Spritam® (levetiracetam), the first 3D-printed medication, demonstrating the clinical and regulatory viability of 3D-printed drugs. The use of 3D printing in personalised medicine is further strengthened by its

benefits, including rapid prototyping, waste minimisation, and high drug-loading efficiency. However, there are still issues with material compatibility, process validation, regulatory standards, and scalability for broad clinical application. Multi-material printing is anticipated to be the primary focus of future developments.

Keywords: 3D printing, additive manufacturing, personalised medicine, binder jetting, stereolithography (SLA), drug delivery systems.

1. Introduction

Additive manufacturing, also known as three-dimensional (3D) printing, is a revolutionary technical development that is changing the pharmaceutical sciences. In contrast to traditional production methods such as compression, granulation, or moulding, 3D printing enables the use of computer-aided design (CAD) models to build pharmaceutical products layer by layer. This layer-wise fabrication enables an unparalleled level of precision, structural complexity, and personalisation in dosage form development (Norman et al., 2017).

The potential of 3D printing to create highly customised dose forms that satisfy specific patient needs is one of its most noteworthy benefits. By modifying drug dosage, release kinetics, and formulation properties based on patient-specific variables such as age, weight, genetics, and illness state, personalised medicine aims to maximise therapeutic outcomes. While 3D printing enables rapid and precise adjustments to dosage strength, form, and internal arrangement, traditional mass-production techniques struggle to achieve this level of flexibility (Khaled et al., 2021). Additionally, this technology makes it easier to combine multiple active pharmaceutical ingredients (APIs) into a single dosage form, creating "polypills" that streamline prescription regimens, enhance adherence, and reduce errors—especially in patients with chronic conditions that require intricate multidrug therapies (Goyanes et al., 2015). Precise control over drug release profiles, from immediate to prolonged or even pulsatile release, is made possible by the capacity to design tablets with different densities, porosities, and multilayer architectures. The approval of the first 3D-printed medication, Spritam® (levetiracetam), by the U.S. Food and Drug Administration (FDA) in 2015 established the practicality of this technology. It sparked global interest in improving additive manufacturing for pharmaceuticals (Aprecia Pharmaceuticals, 2015). Since then, research has grown rapidly, investigating a variety of printing methods, such as stereolithography (SLA), fused deposition modelling (FDM), selective laser sintering (SLS), and inkjet printing, each with distinct

potential for drug formulation and design (Wang et al., 2020). 3D printing stands out as a disruptive, revolutionary tool with enormous potential to transform how medicines are designed, manufactured, and delivered as the pharmaceutical industry shifts toward individualised therapeutics, decentralised production, and rapid prototyping.

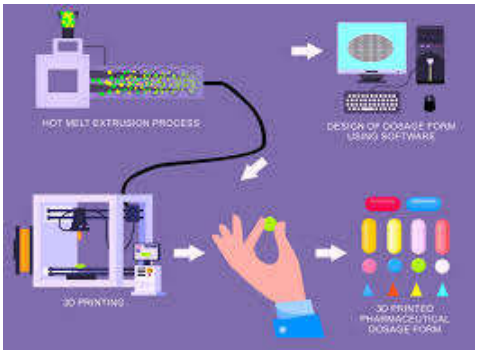

Fig:(1) Introduction to 3D Printing

2. Principles of 3D Printing in Pharmaceuticals

Drug goods are manufactured layer by layer from a digital blueprint, usually generated with computer-aided design (CAD) software, via three-dimensional (3D) printing, a form of additive manufacturing. This method is very different from conventional pharmaceutical manufacturing, which uses bulk or subtractive techniques such as compression, granulation, and milling. Drug formulations' physical structure, dosage, and release properties can be better controlled thanks to 3D printing's accuracy and digital nature.

1. Customizable Dose and Geometry

Customising the drug product's dosage strength and physical form is one of the main benefits of 3D printing in the pharmaceutical industry. To achieve personalised medicine, customisation is essential, especially for populations such as children, elderly patients, and people with metabolic abnormalities who need individualised doses.

Tablet geometry, including size, porosity, infill density, and shape, can be altered via 3D printing to affect swallowing ease, dissolution behaviour, and disintegration time.

For instance:

• Lattice or porous architectures promote quick disintegration;

• Higher infill density permits delayed drug release.

• Geometric shapes like spheres, rings, and pyramids can control surface area exposure.

Geometric modifications have a significant impact on pharmacokinetics and therapeutic effectiveness, according to studies. Goyanes et al. (2015) showed that drug release profiles can be modulated in 3D-printed tablets without altering their composition by altering their internal structure. It is not easy to attain this degree of accuracy with conventional techniques.

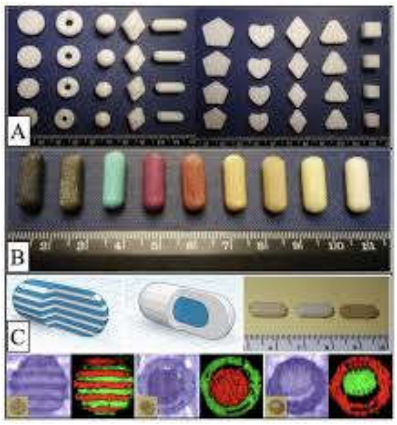

Fig: (2) Customizable Dose and Geometry

2. On-Demand Production

Point-of-care manufacturing is enabled by 3D printing, which allows clinical facilities, pharmacies, and hospitals to produce medications on-site and as needed. This reduces reliance on large-scale production and enables prompt fabrication of customised dosages. On-demand printing supports emergency or remote healthcare, reduces storage needs, and addresses medication shortages (Khaled et al., 2021).
This idea aligns with the future decentralised pharmaceutical production model, in which digital prescriptions are converted directly into printed dosage forms.

3. Flexibility in Combining Multiple Drugs (Polypill Capability)

Multiple active pharmaceutical ingredients (APIs) with distinct release profiles can be combined into a single dose unit via 3D printing. This is accomplished by printing multilayer arrangements or segmented structures with various medications.
This "polypill" strategy lowers the risk of prescription errors, improves adherence in individuals with polypharmacy, and lessens pill load.
Research has shown that fused deposition modelling (FDM) and inkjet printing techniques can successfully fabricate multi-drug tablets (Goyanes et al., 2016).

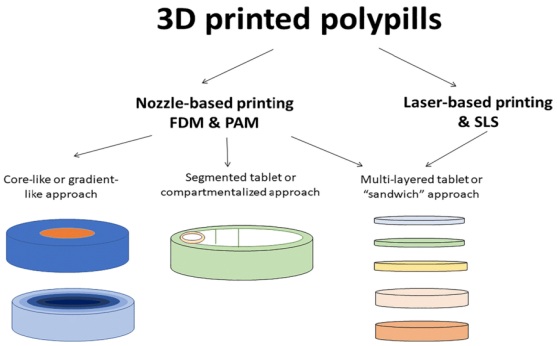

Fig: (3) Flexibility in Combining Multiple Drugs (Polypill Capability)

4. **Reduced Wastage of Raw Materials**

Because only the necessary quantities of API and excipients are used, additive manufacturing naturally reduces material waste. Traditional subtractive manufacturing, on the other hand, often produces excess material through cutting, milling, or other processing steps.
Reduced waste is significant for:
• Drugs with restricted availability;
• High-cost APIs; and
• Customised doses needing small quantities (Awad et al., 2021).
For particular formulas, this increases the sustainability and economic viability of 3D printing.

5. **Improved Therapeutic Outcomes Through Controlled Drug Release**

Diffusion paths, surface area-to-volume ratio, and drug release rates (immediate, sustained, and pulsed) can all be precisely controlled through 3D printing's structural flexibility.
Manufacturers can create complex release profiles by adjusting internal microarchitecture, infill percentage, or polymer composition.

Fig :(4) Reduced Wastage of Raw Materials

3. Major 3D Printing Techniques in Drug Manufacturing (Detailed Explanation)

3D printing technologies used in pharmaceutical manufacturing differ in their mechanisms of material deposition, energy source, and compatibility with drug and excipient properties. Each technique offers unique advantages in terms of precision, material versatility, and formulation

Fig: (5) Major 3D Printing Techniques in Drug Manufacturing

a. Fused Deposition Modelling (FDM)

Due to its ease of use, low operating costs, and compatibility with a wide range of pharmaceutical-grade polymers, fused deposition modelling (FDM) is one of the most popular 3D printing methods in the pharmaceutical industry. In FDM, a thermoplastic polymer is heated until it softens, then extruded through a nozzle. This polymer is frequently combined with an active pharmaceutical ingredient (API). The final dose form is created by layering the extruded material (Goyanes et al., 2015).

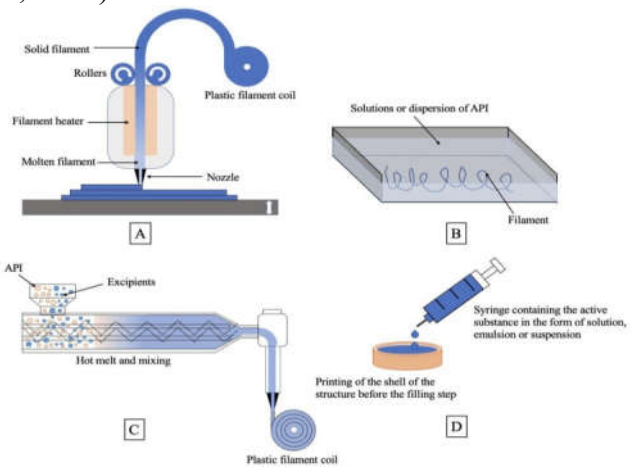

Fig: (6) Fused Deposition Modelling (FDM)

Commonly used polymers include:

- Polyvinyl alcohol (PVA),
- polylactic acid (PLA),
- hydroxypropyl cellulose (HPC),
- ethyl cellulose (EC)

Advantages of FDM

• Suitable for developing controlled-release and immediate-release formulations;

• Enables multi-layered or compartmentalised drug structures;

• Permits alteration of infill density, tablet shape, and surface area

Limitations

The thermal degradation of heat-sensitive APIs at high extrusion temperatures (typically 150–250°C) is a significant disadvantage. FDM is therefore best suited for thermostable medications. Despite this drawback, FDM's versatility in drug manufacture has been

demonstrated by its successful fabrication of modified-release tablets, polypills, and gastroretentive systems.

b. Stereolithography (SLA)

A UV or laser light source is used in stereolithography (SLA), an advanced 3D printing technology, to cure photosensitive liquid resins through photopolymerization. Layer by layer, the resin solidifies, enabling the creation of intricate and sophisticated drug delivery systems (Wang et al., 2020).

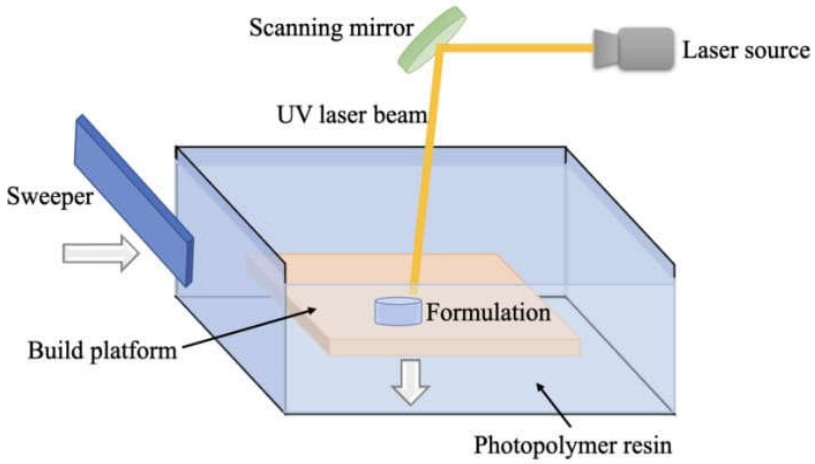

Fig: (7) Stereolithography (SLA)

Advantages of SLA

• Capable of building complex interior channels for modified-release profiles;

• Perfect for making micro-needles, implants, and orodispersible structures;

• Produces high-resolution structures with superior dimensional accuracy

Material Considerations

The need for biocompatible, non-toxic photopolymers is a significant challenge for SLA in the pharmaceutical industry. Currently, only a few photopolymers are suitable for pharmaceutical applications, such as polyethene glycol diacrylate (PEGDA).

Applications

SLA has been investigated for generating:

Customised oral dose forms

• Drug delivery systems that can be implanted

• Sublingual and buccal films

• Patches with transdermal microneedles

SLA is beneficial for patients who need focused, regulated delivery methods due to its high precision.

Selective Laser Sintering (SLS)

A laser beam selectively fuses powdered materials, including polymers, sugars, or drug-loaded excipients, in Selective Laser Sintering (SLS), a powder-based 3D printing technique. Scaffolding materials are not required because the unfused powder supports the printed layers (Fleming et al., 2021).

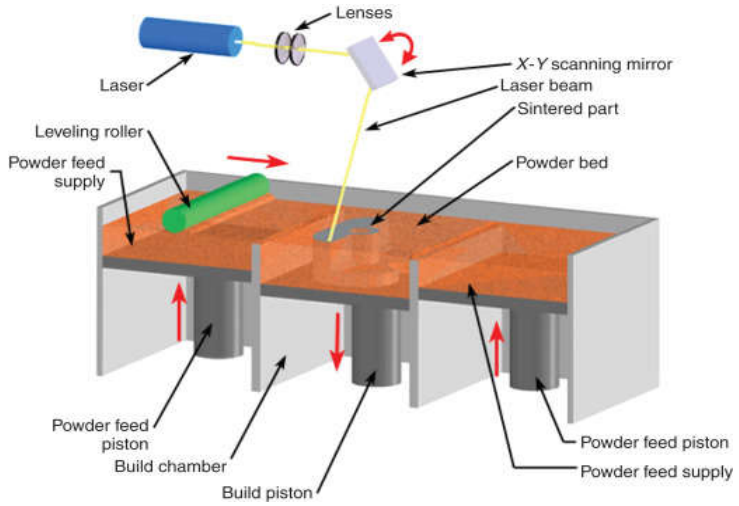

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Fig: (8) Selective Laser Sintering (SLS)

Advantages of SLS

High medication loading capacity; no need for compression force or binders; Because sintering temperatures can be regulated, it is appropriate for thermolabile APIs. Creates porous structures that are perfect for controlled-release or quickly dissolving tablets. Because of SLS's rapid water penetration, its porous nature allows the method to be used to make orodispersible and fast-melting tablets.

Applications in Pharmaceuticals

- Bioactive implants;
- oral solid dose forms with tailored release;
- and quick prototyping of innovative drug delivery systems

SLS offers special advantages in drug formulation science and is particularly promising for medications that require high solubility or rapid dissolution.

a. Inkjet Printing (Binder Jetting and Material Jetting)

One of the first 3D printing methods utilised in the pharmaceutical industry is inkjet printing, which deposits tiny droplets of drug-containing liquids or suspensions layer by layer onto a substrate (Alomari et al., 2015).

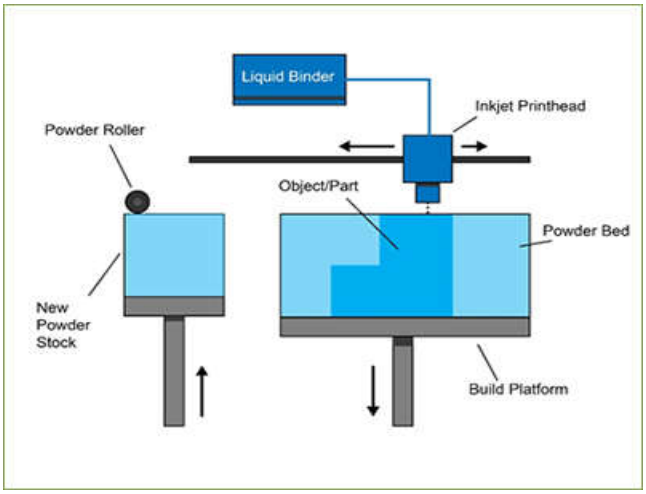

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Fig: (9) Inkjet Printing (Binder Jetting and Material Jetting)

There are two primary methods:

Droplets of a drug-loaded formulation are directly deposited via material jetting.

Binder Jetting creates solid layers by depositing a binding liquid onto a powder bed.

High dosing precision (microgram-level accuracy), the ability to print multiple APIs in layered or spatially separated patterns, suitability for quick prototyping and customised dosing, and the ability to operate at room temperature while protecting heat-sensitive APIs are all benefits of inkjet printing.

Applications

The buccal films, Transdermal patches, pediatric dosages,microdosing tablets, and multi-drug stacked polypills

Additionally, inkjet printing is scalable, appealing to pharmaceutical companies looking to combine mass and customised production.

4. Applications of 3D Printing in Pharmaceuticals (Detailed Explanation)

3D printing provides a revolutionary platform for creating cutting-edge drug delivery systems that can be customised to patient, clinical, and therapeutic demands. The main uses are explained in further depth in the sections that follow.

1. Personalised Dosage Forms

The ability to modify drug dosages, forms, and release properties to meet the needs of specific patients is essential to personalised medicine. Conventional production techniques offer only predetermined dose strengths, which might not be appropriate for patients with specific metabolic or genetic abnormalities or for populations such as children or the elderly.

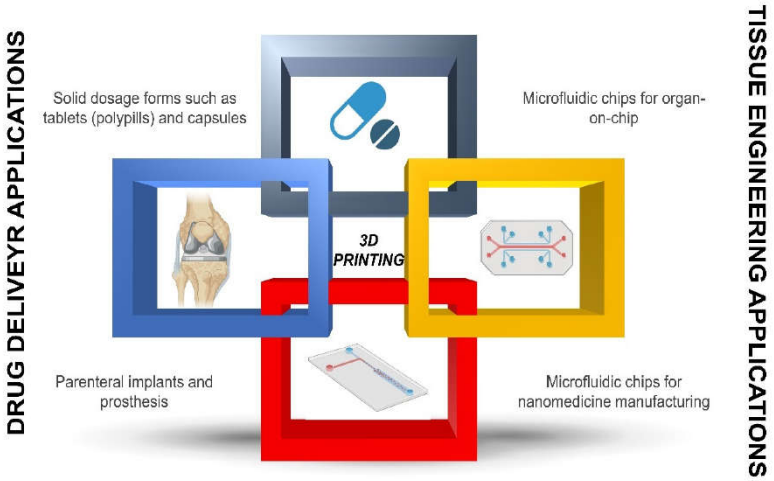

Fig: (10) Personalised Dosage Forms

3D printing provides exact dosage personalisation by modifying:
• Tablet geometry (size, shape)
• Drug loading
• Layer thickness
• Porosity and infill density
For pediatric patients, age-appropriate doses can be made in smaller, easy-to-swallow shapes, boosting medication adherence. To address swallowing issues and polypharmacy concerns, tablets with lower strengths or fast-dissolving constructions can be developed for elderly patients (Trenfield et al., 2018).
Individualised therapy is now more accessible than ever, thanks to the digital nature of 3D printing, which enables therapists to adjust dosage based on therapeutic response quickly.

2. Polypills for Polypharmacy

Polypharmacy—defined as the simultaneous use of multiple medications—is common in chronic conditions such as diabetes, hypertension, and cardiovascular diseases. Managing multiple pills can lead to poor adherence.

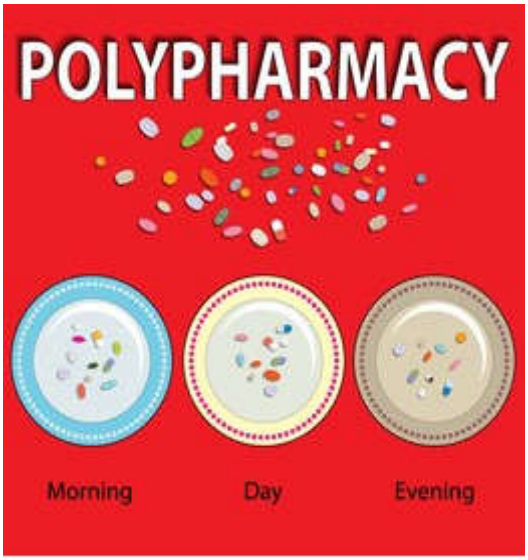

Fig: (11) Polypills for Polypharmacy

• A higher chance of dosage mistakes

• Interactions between drugs

Polypills, single tablets containing multiple active pharmaceutical ingredients (APIs), each with a unique spatial location and controlled-release mechanism, are enabled by 3D printing.

Advantages of 3D-Printed Polypills

Reduced pill load improves patient compliance

allows for a customised API combination selection

lowers errors in the healthcare system, and permits different release profiles (immediate, sustained, and delayed) inside a single tablet.

For instance, Goyanes et al. (2015) used a segmented architecture to successfully create a 3D-printed polypill containing five cardiovascular medications, each released at a different time. Layering and intricate interior design are enabled by methods such as fused deposition modelling (FDM) and inkjet printing.

For patients with chronic illnesses, 3D-printed polypills offer a powerful way to improve therapeutic outcomes and streamline complex medication regimens.

3. Implants and Transdermal Systems

3D printing expands options for designing implants, microneedle patches, and transdermal systems, enabling precise control over medication distribution, shape, and mechanical strength.

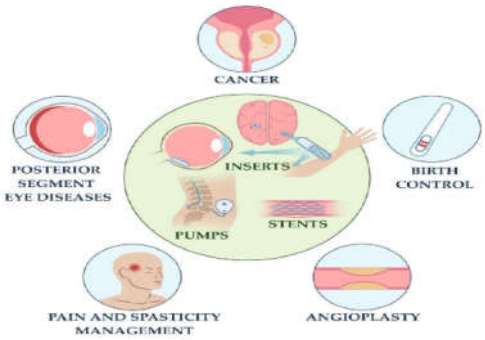

Fig (12): Implants and Transdermal Systems

Implants

3D-printed implants can be:

• Shape-specific for each patient

• Designed for sustained, long-term release

• Made of biodegradable polymers

These implants are beneficial for managing chronic pain, cancer treatment, and contraception.

Microneedle Arrays

Drugs can be delivered painlessly through the skin barrier using microneedles made using digital light projection (DLP) or stereolithography (SLA). High accuracy, customizable length, density, and sharpness, low invasiveness, and increased bioavailability are among its features. 3D-printed microneedles for accurate drug deposition were demonstrated by Uddin et al. (2019), supporting applications in insulin delivery, vaccinations, and dermatological treatments.

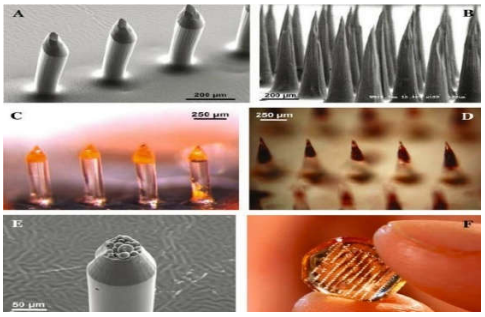

Fig (13): Microneedle Arrays

Transdermal Patches

Hormones, analgesics, and nicotine therapies can benefit from 3D printing's enhanced adhesion, multilayered patches, and uniform drug distribution.

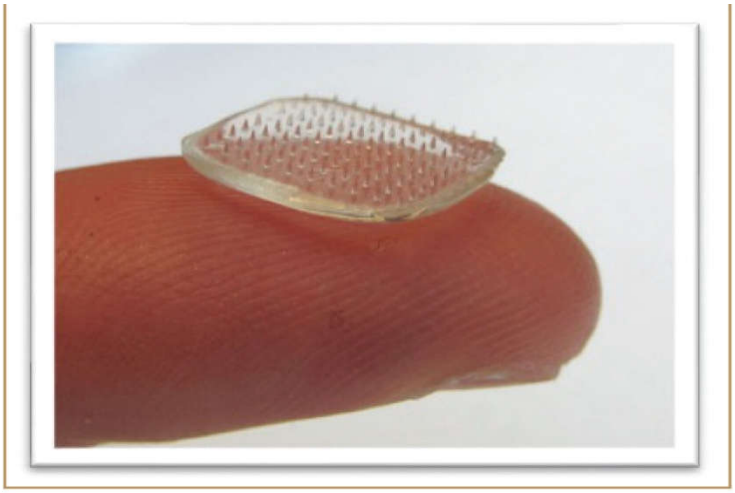

Fig (14): Transdermal Patches

4. Rapid Prototyping

One of the main benefits of 3D printing for formulation scientists is its rapid prototyping capabilities. Researchers can use additive manufacturing to:

• Test various formulation designs quickly

• Change dosage form shape in a matter of minutes

• Cut down on the time and expense of trial-and-error trials.

• Shorten the time it takes to develop drugs

Large-scale tooling and compression equipment are typically required to produce various prototypes. By reducing this to a digital design update, 3D printing, on the other hand, enables faster innovation and minimises material waste (Awad et al., 2021).

Early-stage drug design is also aided by rapid prototyping, which enables researchers to assess mechanical strength and drug-release characteristics before scaling up.

Fig (15): Rapid Prototyping

5. Regulatory Considerations in 3D Printing for Pharmaceuticals (Detailed)

One of the most important factors affecting the uptake and application of 3D printing (3DP) in the pharmaceutical sector is regulatory monitoring. Because 3DP medicinal products differ significantly from traditional dosage forms in terms of material consumption, manufacturing processes, and design flexibility, regulatory bodies like the U.S. The European Medicines Agency (EMA), the Food and Drug Administration (FDA),

Fig: (16) Regulatory Considerations in 3D Printing for Pharmaceuticals

- **Emergence of Regulatory Recognition: The Case of Spritam®**

  Spritam® (levetiracetam) became the first 3D-printed medication to be approved by the FDA in 2015, marking a significant milestone. The approval of Spritam®, a product made with Aprecia Pharmaceuticals' ZipDose® technology, demonstrated that 3D-printed medications could satisfy strict regulatory requirements for manufacturing consistency, safety, and performance (Aprecia Pharmaceuticals, 2015).
  The FDA's openness to assess innovative production techniques was demonstrated by this approval.

• Confirmed that 3DP is feasible for high-dose, quickly dissolving oral drugs.
• Urged pharmaceutical firms to investigate active 3D printing development.

➢ **Quality Consistency**

Because 3DP permits substantial diversity in geometry, infill density, and microstructure, ensuring batch-to-batch and unit-to-unit consistency is a significant regulatory problem. Regulators want proof that:
• The weight, drug content, hardness, and dissolution profiles of printed tablets are all consistent.
• To prevent variations during layer deposition, 3DP hardware (nozzles, lasers, and inkjet systems) is calibrated.
• Printing speed, temperature, layer thickness, and binder deposition are examples of critical process parameters (CPPs) that are verified.
• Throughout production, material characteristics (such as ink viscosity and SLS powder particle size) must stay constant.
Robust quality control is crucial, as variations in printing settings can significantly affect mechanical strength, drug release rate, and porosity (Alhnan et al., 2016).

➢ **Material Safety and Biocompatibility**

Regulators must thoroughly evaluate all materials used in 3DP.
• Plasticisers, resins, polymers, and photopolymers
• Binding agents (for binder jetting or inkjet printing)
• Additives such as colourants, fillers, and stabilisers
These materials must adhere to strict safety regulations set by the FDA and EMA, including:
Biocompatibility (ISO 10993)
For example, the scarcity of photopolymerizable materials approved for medical use makes SLA resins difficult to use (Wang et al., 2020).

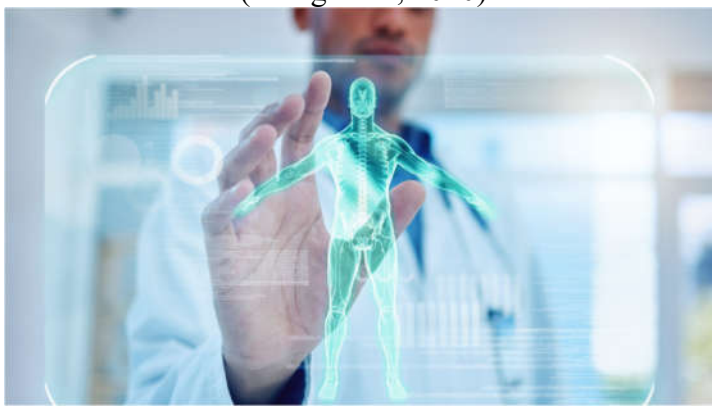

Fig (17): Material Safety and Biocompatibility

➢ **Validation of Printing Parameters**

Since pharmaceutical 3D printing directly determines product geometry, regulators demand
• Documentation of process controls (temperature, deposition rate, laser energy);
• Validation of the digital design file
• Establishment of Process Analytical Technology (PAT) tools for real-time monitoring
• Demonstration of reproducibility under various environmental conditions (temperature, humidity).

According to Goyanes et al. (2017), even little changes in environmental factors or printer calibration can result in considerable variances in the quality of the finished product.

- **Stability of Printed Formulations**

The effects of 3D printing stressors (heat, laser energy, UV curing, and mechanical pressure), long-term chemical and physical stability, and the moisture sensitivity of porous printed structures must all be taken into account when testing the stability of 3D-printed medications.

• Thermolabile APIs may deteriorate during FDM or SLS processing.

Regulators require complete ICH-compliant stability data, including expedited and long-term studies (ICH Q1A).

In technologies like FDM, where heat deterioration of APIs is a known concern, stability is essential (Jaměz et al., 2018).

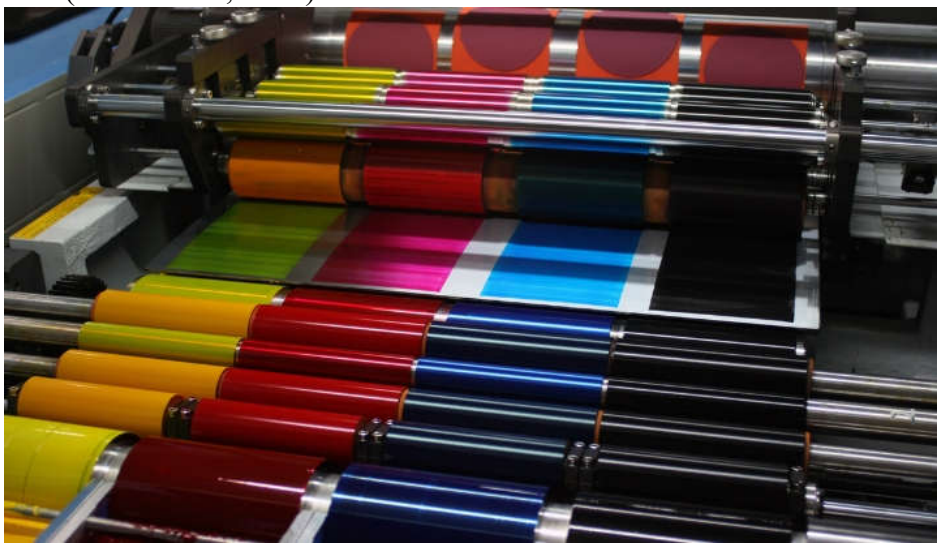

Fig (18): Stability of Printed Formulations

- **Regulatory Pathway Considerations**

3DP pharmaceutical regulations are still being developed. Important points are as follows:

• Because 3DP involves customisation, it could need more paperwork than traditional production.

• The FDA's additive manufacturing guidelines, which are primarily for medical equipment, serve as a foundation; nevertheless, drug-specific criteria are still being developed.

• Regulators concentrate on on-demand production and ensuring that each printed item satisfies predetermined requirements for customised medications.

• To accommodate decentralised or point-of-care printing models, Good Manufacturing Practice (GMP) rules must be modified.

To ensure that the flexibility provided by 3DP does not compromise safety or efficacy, the FDA and EMA place strong emphasis on risk-based strategies (Ventola, 2020).

- **Global Regulatory Outlook**

While the FDA leads in 3DP medical device approvals, other agencies are partnering through international harmonisation bodies such as ICH.

Future regulatory systems will presumably address:

• 3D printing using decentralised hospital pharmacies

• Version control and digital file security
• Requirements for traceability
• Standardisation of materials, printers, and quality testing procedures.

Fig (19): Global Regulatory Outlook

6. Challenges in 3D Printing for Pharmaceutical Manufacturing

Although 3D printing (3DP) has shown promise as a technique for developing sophisticated, customised drug delivery systems, several scientific, technological, financial, and regulatory obstacles prevent its widespread use in the pharmaceutical industry. For 3D-printed pharmaceutical goods to be safe, repeatable, and scalable, these issues must be resolved.

Fig (20): Challenges in 3D Printing for Pharmaceutical Manufacturing

- **Limited Pharmaceutical-Grade Printable Materials**

  The scarcity of appropriate, authorised, and biocompatible materials that satisfy performance and regulatory standards is a significant barrier to pharmaceutical 3DP.

Important Concerns
• Specialised polymers, resins, or powders that can tolerate printing conditions are needed for the majority of 3D printing processes (FDM, SLA, SLS, and inkjet).
• Only a small number of pharmaceutical-grade polymers, such as PVA, PLA, HPMC, and Eudragits, work with 3DP.
• The lack of biocompatible photopolymerizable resins in SLA limits clinical translation.
• FDA/EMA requirements must be met for material toxicity, extractables, leachables, and thermal stability.

Fig (21): Limited Pharmaceutical-Grade Printable Materials

- **Scale-Up Difficulties**

Initially, 3DP was intended for prototypes rather than mass manufacturing. It is still challenging to scale 3DP for commercial manufacturing.
Important Concerns
• Printing times are slow, particularly when dealing with intricate geometries.
With most 3DP technologies, it is currently not feasible to produce millions of tablets on a commercial basis each year.
• When scaling up, variable quality is caused by printer-to-printer variability.
• Maintaining consistent calibration and GMP compliance becomes more difficult with multi-printer configurations.

- **Thermal and Mechanical Stress Affecting Drug Stability**

Numerous 3DP methods subject medications to potentially degrading environments.
Examples of Stressors
• Thermolabile APIs (≥150–200°C) can be degraded by high temperatures in FDM.
• In SLS, laser irradiation may cause structural alterations or thermal deterioration.
• Photodegradation may result from UV curing in SLA.
• Crystallinity may be disturbed by mechanical shear during binder deposition or extrusion.
Consequences
Loss of API efficacy; modifications to drug polymorphism; altered release patterns; and shortened shelf life

- **High Initial Equipment Cost**

One major obstacle remains the high price of pharmaceutical-grade 3D printers and related devices.
Cost-related factors
• High-end biocompatible FDM/SLS/SLA printers are costly.

• Additional expenditures include: o Cleanroom infrastructure o Quality testing equipment o Maintenance, calibration, and validation systems o Specialised software for CAD and digital design

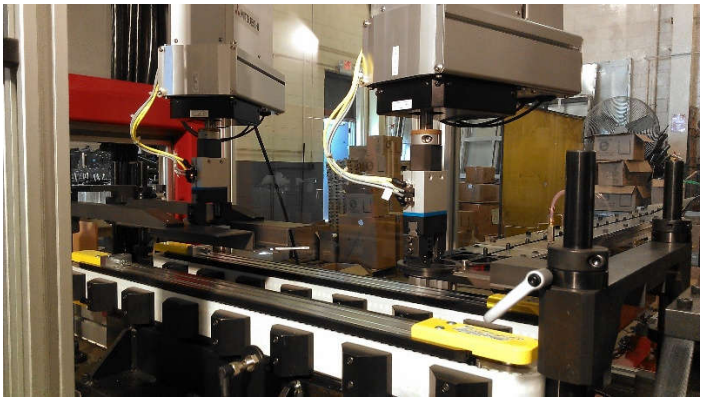

Fig (22): High Initial Equipment Cost

Need for Unified Regulatory Guidelines

Clear and thorough regulatory frameworks for 3D-printed pharmaceutical items are still developing, notwithstanding the FDA's approval of Spritam®.

Difficulties

• Inadequate standards for:

o Material selection

o Printer validation

o Digital file security

Process analytical technology (PAT), decentralised or on-demand printing, and regional variations in regulations (FDA, EMA, PMDA) create ambiguity.

There is still uncertainty regarding GMP adaptation for distributed or hospital-based 3DP.

7. Future Perspectives in 3D Printing for Pharmaceuticals

Pharmaceutical 3D printing (3DP) is a rapidly developing field with ongoing research aimed at overcoming existing constraints and unlocking new uses. Future developments are anticipated to transform drug development and delivery paradigms by emphasising greater personalisation, process automation, material innovation, and sustainability.

➢ AI-Driven Formulation Design

3DP for drug formulation is rapidly using machine learning (ML) and artificial intelligence (AI). AI algorithms can predict the best polymer and excipient combinations for particular APIs.

• To attain the intended drug release profiles, optimise layer design, geometry, and infill density.

• Before printing, model the pharmacokinetic behaviour of customised tablets.
AI-driven design shortens development times and improves formulation accuracy by minimising trial-and-error experimentation. For instance, Trenfield et al. (2020) demonstrated how AI models can improve accuracy and reproducibility by predicting the dissolution profiles of multi-layered 3D-printed tablets.

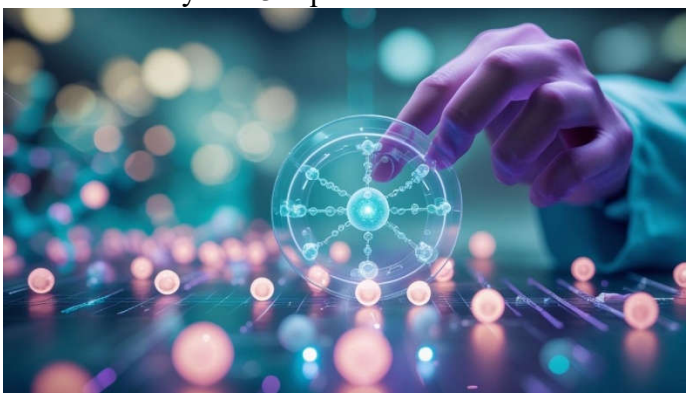

Fig (22): AI-Driven Formulation Design

Multi-Drug, Multi-Release Tablets

Future 3D-printed polypills will progress toward multi-drug, multi-release systems, enabling the concurrent administration of several APIs with varying release kinetics (immediate, delayed, sustained).

Among the main benefits are:

• Making complicated drug schedules for long-term illnesses simpler
• Facilitating combo treatments for metabolic, cardiovascular, and cancer conditions
Compartmentalised or layered constructions, where each layer or module releases a medicine at a set time interval, will be possible thanks to advanced printing processes, such as FDM, inkjet printing, and SLA (Goyanes et al., 2015).

Fig (23): Multi-Drug, Multi-Release Tablets

➢ **Decentralised Hospital-Based Production**

Point-of-care manufacturing in clinics, pharmacies, and hospitals is part of 3DP's future. Personalised medications can be produced on demand, reducing reliance on centralised supply networks and manufacturing.
• Immediate dose adjustments based on patient reaction
• Reduction of medication shortages and waste
For design file management, quality assurance, and regulatory compliance, decentralised production will need integrated digital systems (Norman et al., 2017).

➢ **Bioprinted Tissues for Drug Testing**

A new advancement in pharmaceutical 3DP is 3D bioprinting, which creates organoids and living tissues for drug development. Applications consist of:
• Customised toxicity testing and drug screening
• Reducing animal testing in preclinical experiments
• Evaluating pharmacokinetics and pharmacodynamics in patient-specific tissues
Precision medicine is enabled by this method, which allows more precise prediction of therapeutic efficacy and safety (Melchels et al., 2012).

Fig (24): Bioprinted Tissues for Drug Testing

➢ **Sustainable Materials for Eco-Friendly Printing**

One important upcoming trend in pharmaceutical 3DP is sustainability. Researchers are investigating:
• Renewable and biodegradable polymers
Global initiatives to reduce the environmental impact of medicine manufacturing while preserving therapeutic efficacy align with the use of sustainable printing materials (Awad et al., 2021).

8. Conclusion

In pharmaceutical manufacturing, three-dimensional (3D) printing has become a game-changing technology, enabling the creation of highly accurate, customised, and patient-specific dose forms. In contrast to conventional batch manufacturing techniques, 3DP enables the layer-by-layer fabrication of tablets, capsules, implants, and transdermal systems, offering previously unheard-of control over dosage strength, geometry, drug-release profiles, and multi-drug inclusion. These skills are especially crucial for the development of personalised medicine, which allows therapeutic approaches to be customised to the particular requirements of patients with polypharmacy, pediatric conditions, and advanced age. Additionally, the technique makes it easier to create polypills, rapid-prototyped formulations, and bioprinted tissues for drug testing, all of which could enhance treatment compliance, maximise pharmacokinetics, and lessen the need for animal models. Additionally, decentralised hospital-based manufacturing and on-demand production promise to improve access, reduce waste, and expedite the delivery of medicines, all of which align with contemporary healthcare objectives.

Future developments, including AI-driven formulation design, sustainable materials, multi-drug and multi-release polypills, and bioprinting applications, are anticipated to overcome present constraints and further incorporate 3D printing into conventional pharmaceutical manufacturing.

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References

1. Aprecia Pharmaceuticals. (2015). *FDA approves first 3D-printed drug*. https://www.aprecia.com

2.Goyanes, A., Wang, J., Buanz, A., Martínez-Pacheco, R., Telford, R., & Basit, A. W. (2015). 3D printing of medicines: Fused deposition modelling of oral drug delivery systems. *International Journal of Pharmaceutics, 487*(1–2), 144–150.

3. Khaled, S. A., Xu, S., & Alexander, M. R. (2021). 3D printing of pharmaceuticals: State of the art. *Materials Today, 47*, 78–91.

4. Norman, J., Madurawe, R. D., Moore, C. M., Khan, M. A., & Khairuzzaman, A. (2017). A new chapter in pharmaceutical manufacturing: 3D-printed drug products. *Advanced Drug Delivery Reviews, 108*, 39–50.

5. Awad, A., Trenfield, S. J., Goyanes, A., Gaisford, S., & Basit, A. W. (2021). Additive manufacturing of pharmaceuticals: An overview of recent advances. *Drug Discovery Today, 26*(1), 365–372.

6. Goyanes, A., Buanz, A., Basit, A. W., & Gaisford, S. (2015). FDM 3D printing of modified-release tablets: Design, characterisation, and testing. *International Journal of Pharmaceutics, 487*(1–2), 144–150.

7.Goyanes, A., et al. (2016). Fabrication of multi-drug polypills using 3D printing technology. *International Journal of Pharmaceutics, 499*(1–2), 394–402.

8. Wang, J., Goyanes, A., Gaisford, S., & Basit, A. W. (2020). Stereolithography 3D printing of oral modified-release dosage forms. *International Journal of Pharmaceutics, 586*, 119–594.

9. Alomari, M., Mohamed, F. H., Basit, A. W., & Gaisford, S. (2015). Personalised dosing: Printing a dose of one's own medicine. *International Journal of Pharmaceutics, 494*(2), 568–577.

10. Fleming, A., Moreno, M., & Forbes, R. T. (2021). Powder-based additive manufacturing for pharmaceuticals: A review. *Advanced Drug Delivery Reviews, 173*, 94–110.

11. Goyanes, A., Chang, H., Sedough, D., Hatton, G. B., Wang, J., Buanz, A., Gaisford, S., & Basit, A. W. (2015). Fabrication of controlled-release 3D-printed polypills for polypharmacy. *International Journal of Pharmaceutics, 494*(2), 657–664.

12. Trenfield, S. J., Awad, A., Goyanes, A., Gaisford, S., & Basit, A. W. (2018). 3D printing pharmaceuticals: Personalised and on-demand manufacturing. *International Journal of Pharmaceutics, 548*(1), 586–596.

13. Uddin, M. J., Scoutaris, N., Ong, J. J., Ahmed, W., & Chowdhry, B. (2019). 3D printed microneedles for transdermal drug delivery: A new era of patient-friendly medication. *Drug Development and Industrial Pharmacy, 45*(1), 1–12.

14. Alhnan, M. A., Okwuosa, T. C., Sadia, M., Wan, K. W., Ahmed, W., & Arafat, B. (2016). Emergence of 3D printed dosage forms: Opportunities and challenges. *Pharmaceutical Research, 33*(8), 1817–1832.

15. Aprecia Pharmaceuticals. (2015). *FDA approves the first 3D-printed drug product*. Aprecia Pharmaceuticals Press Release.

16.Fleming, A., Leng, J., et al. (2021). Selective laser sintering in pharmaceutical development: A review of materials and applications. *International Journal of Pharmaceutics, 593*, 120147.

17.Goyanes, A., Martínez, P. R., Ali, M., et al. (2017). Precision printing of drug-loaded films using 3D printing: Impact of process parameters. *International Journal of Pharmaceutics, 527*(1–2), 285–293.

18.Jamróz, W., Szafraniec, J., Kurek, M., & Jachowicz, R. (2018). 3D printing in pharmaceutical and medical applications. *Pharmaceutics, 10*(4), 1–30.

19.Ventola, C. L. (2020). Medical and pharmaceutical applications of 3D printing. *P&T, 45*(6), 202–211.

20. Wang, J., Goyanes, A., Gaisford, S., & Basit, A. W. (2020). Stereolithography-based 3D printing of pharmaceuticals: Challenges and opportunities. *Advanced Drug Delivery Reviews, 172*, 186–205

21. Trenfield, S. J., Awad, A., Goyanes, A., Gaisford, S., & Basit, A. W. (2019). 3D printing pharmaceuticals: Drug development to frontline care. *Trends in Pharmacological Sciences, 40*(10), 1–14.

22.Melchels, F. P., Domingos, M. A., Klein, T. J., Malda, J., Bartolo, P. J., & Hutmacher, D. W. (2012). Additive manufacturing of tissues and organs. *Progress in Polymer Science, 37*(8), 1079–1104.

23. Trenfield, S. J., Awad, A., Goyanes, A., Gaisford, S., & Basit, A. W. (2020). 3D printing pharmaceuticals: Drug development to frontline care. *Trends in Pharmacological Sciences, 41*(8), 694–705.