# Building the next frontier: Artificial intelligence in 3D-printed medicines

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# **ABSTRACT**

Artificial intelligence (AI) and 3D printing are transforming pharmaceutical manufacturing by enabling the production of personalized medications. AI supports real-time decision-making in diagnostics and robotics, although its application in pharmaceutical research remains at an early stage. 3D printing, particularly additive manufacturing, provides precise control over drug formulation, allowing the design of patient-specific dosage forms with tailored release profiles. Machine learning and deep neural networks are used to predict formulation parameters, optimize processing conditions, and support the design of innovative drug delivery geometries. Technological platforms such as cloud computing and blockchain enhance data security, transparency, and scalability. Printable materials—including thermoplastic polymers, hydrogels, and bioinks—demonstrate utility in AI-assisted manufacturing systems. The integration of AI, smart materials, and 3D printing advances intelligent drug production technologies aligned with Industry 4.0 principles. Key considerations include regulatory compliance, data reliability, ethical implications, and pathways for clinical translation. Clinical medicine is rapidly advancing through the adoption of 3D printing and AI, enabling personalized prosthetics, accurate surgical planning, and bioprinted tissues. AI-driven segmentation and optimization enhance the accuracy and efficiency of 3D-printed anatomical models for pre-operative preparations and medical training. Cardiology, oncology, and orthopedics are increasingly adopting these technologies to improve patient outcomes and clinical workflows. Future directions include broader adoption across specialties, bioprinting for regenerative health care, and AI-optimized systems for targeted drug delivery. This review addresses the current challenges and limitations of AI and 3D-printed medicines, pharmaceutical manufacturing, case studies, ethical considerations, and future perspectives.

#### Keywords

Artificial intelligence; 3D printing; Machine learning; Neural networks; Bioprinting; Industry 4.0

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# 1. Introduction

Recent advancements in 3D printing technologies have generated unparalleled prospects for applications in health care, ranging from personalized medicine to tissue engineering. Innovations in materials such as smart polymers, bioinks, and printable drug matrices are revolutionizing how we approach complex medical challenges. 3D printing is an additive manufacturing (AM) method that builds a 3D shape by depositing and solidifying based on a digital model. Personalized and

on-demand medicine production is entering the pharmaceutical industry through the integration of artificial intelligence (AI) and 3D printing. Traditionally, drug production has relied on "one-size-fits-all" formulations designed for broad patient populations. However, this approach generally fails to address interindividual variability in drug response, highlighting the need for more customized therapeutic options.<sup>3</sup> Due to its remarkable versatility, 3D printing can produce drugs with accurate concentrations, controlled release profiles, and customized

shapes, facilitating personalized therapy. This is especially beneficial for pediatric, geriatric, rare disease, and complex combination therapy patients. Developing pharmaceutical formulation is inherently complicated, involving numerous material composition choices, design parameters, and printing conditions.4 This process is both time-consuming and requires significant expertise. Using machine learning (ML) and advanced data analytics, AI can rapidly predict optimal formulations, compositions, and printing parameters, thereby accelerating the design and production of 3D-printed pharmaceuticals. The integration of AI with 3D printing extends beyond formulation optimization. It encompasses real-time quality assurance, automated process monitoring, and predictive maintenance of printing equipment to ensure consistent output.<sup>5</sup> AI-powered vision systems can detect printing defects such as incomplete layers and material inconsistencies and make real-time adjustments. This leads to improved product quality, reduced material waste, and lower production costs. Furthermore, AI-driven systems support the development of intelligent, decentralized manufacturing networks. By incorporating the Internet of Things (IoT) and blockchain technology, electronic prescriptions can be transmitted to local 3D printers for quick, personalized drug dispensing. This digital pharmacy model improves patient access to tailored treatments and accelerates the clinical adoption of 3D-printed pharmaceuticals. In inkjet printing, a liquid containing the medication and additives is jetted onto a designated surface to form a layer. Subsequent layers are created by repeating this process,6 ultimately forming a 3D object. Inkjet printing comprises two main types: Continuous inkjet (CIJ) printing, which emits droplets continuously, and drop-on-demand (DOD) printing, which emits droplets only when triggered. The resulting layers have very fine thickness, offering high resolution but requiring longer print times.7 Nozzle-based technologies rely on the extrusion of medicinal substances through a narrow nozzle. This can be accomplished either by applying pressure, which is referred to as a pressureassisted microsyringe, or by melting the material filaments, a process referred to as fused deposition modeling (FDM).8 Pharmacies, hospitals, and rural clinics can become part of a decentralized manufacturing network, reducing reliance on centralized production and shortening supply chains.

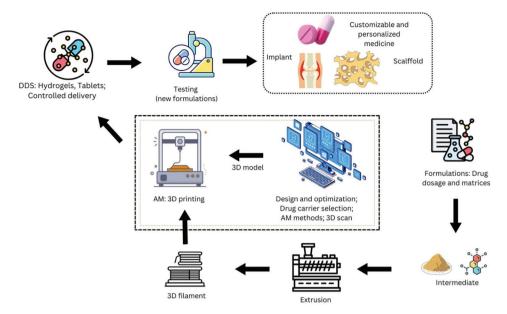
Future AI-3D printing convergence could overcome pharmaceutical development constraints, eliminate the need for expert intervention, and produce safer, more effective treatments tailored to patient needs. AI can estimate drug release kinetics, forecast patient adherence, and uncover drug interactions, thereby personalizing treatment regimens. Patient feedback loops, which monitor therapy outcomes and feed back into AI models, can also enhance formulations and

dosing regimens.9 This technological convergence should spur innovation in regulatory science beyond manufacturing. Regulatory bodies are exploring ways to certify AI-driven, 3D-printed pharmaceuticals, balancing both safety and effectiveness with rapid customization and innovation. Industry, academics, and regulators must collaborate to ensure data integrity, procedure validation, and post-market surveillance requirements. This transformation has farreaching effects. By enabling on-demand, patient-specific drug production, AI combined with 3D printing can address global health issues such as medicine shortages, antibiotic resistance, and rapid response to infectious diseases. 10 Portable 3D printers using AI-driven composition tools could generate life-saving pharmaceuticals during disasters or humanitarian situations. The collective impact of these technologies will make the pharmaceutical sector more sustainable. By producing medicines only when needed and minimizing recyclables, 3D printing and AI could reduce the environmental impact of drug manufacturing. Digital inventory systems and justin-time production also reduce the occurrence of expired and unused drugs. Creating the next frontiers in medicine requires the integration of these technologies to establish a smart, autonomous, and patient-focused drug production ecosystem.<sup>11</sup> Although technical, regulatory, and ethical challenges exist, the potential to improve health care is vast. With ongoing research and collaboration, AI and 3D printing are set to transform pharmaceutical science, providing more secure, more effective, and fully personalized treatments to patients worldwide.

**Figure 1** shows the conceptual process of making personalized medicines using AM-assisted design and fabrication of a drug delivery system (DDS). As research continues to evolve, the potential applications of AI in 3D-printed medicines are likely to expand further, contributing to a new era of healthcare innovation. The intersection of AI and 3D printing in pharmaceuticals presents a promising frontier, yet significant research gaps remain. These gaps primarily concern the integration of AI technologies into the 3D printing processes for drug development and manufacturing. This review addresses AI research gaps in drug discovery and AI–3D printing integration in medicine. **Table 1** shows the materials used with different AM techniques in biomedical fields.

In medical imaging, AI and 3D printing have promoted innovation. Combining these two technologies has the potential to increase diagnostic precision, streamline clinical workflows, and ultimately improve patient outcomes. AI has made significant strides in medical imaging by aiding the automation of processes that were previously manual and time-consuming. By utilizing AI-based algorithms, medical professionals can analyze and interpret images more quickly

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**Figure 1.** Conceptual process for creating personalized medicines using additive manufacturing (AM)-assisted design and fabrication. This complete workflow outlines the creation of customizable and personalized drug delivery systems using 3D printing and AM. Drug delivery solutions such as hydrogels and controlled-release tablets are initially created. These innovative compositions are thoroughly evaluated before being customized into implants and scaffolds. The resulting drug doses and matrices are then converted into a precise recipe, which guides 3D printing filament extrusion. To produce an accurate 3D model, 3D printing uses filament alongside design and optimization techniques, including medication carrier optimization and 3D scanning. A personalized drug delivery device created by 3D printing completes a cycle of patient-specific medical innovation and improvement. The figure was created by the authors using Canva

**Table 1.** Materials used with different AM techniques in biomedical fields

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AM technique	Materials used	Application	References
Material extrusion	PLA	Prosthetics	14
(FDM)	ABS	Surgical models	
	Nylon	Custom implants	
PBF	Titanium alloys	Orthopedic implants	14
	Cobalt- chromium alloys	Dental implants	
	Magnesium alloys	Bone scaffolds	
Directed energy	Titanium	Implants	15
deposition	Cobalt- chromium	Repairing structures	
Material jetting (PolyJet)	Photopolymers	Dental applications	15
		Surgical guides	
Binder jetting	Stainless steel	Bone implants	16
	Ceramics	Dental applications	
Vat photopolymerization	Photopolymer resins	Custom dental appliances	16
		Surgical models	

Abbreviations: ABS: Acrylonitrile butadiene styrene; AM: Additive manufacturing; FDM: Fused deposition modeling; PBF: Powder bed fusion; PLA: Polylactic acid.

and accurately, leading to earlier detection of diseases and improved patient care.<sup>17</sup> Recently, three-dimensional printing, often known as 3D printing or 3DP, has paved the way for

the manufacturing of entirely individualized medications on demand. When it comes to formulation creation, pharmaceutical 3DP provides infinite alternatives because of its versatility. However, successful navigation of these options typically requires experienced oversight. Utilizing AI within pharmaceutical 3D printing eliminates the need for human expertise, as ML can reliably predict optimal process parameters. 18 This frees up human resources for other tasks. AI may also be integrated into a pharmaceutical 3DP IoT, transforming the personalized creation of pharmaceuticals into an intelligent, efficient, and autonomous production pipeline. The cloud and distributed ledger technology (blockchain) are examples of supporting infrastructure that will play an important role.<sup>19</sup> Importantly, the use of pharmaceutical 3D printing in clinical settings will be accelerated by these technologies, which will also drive the global shift toward personalized medicine and Industry 4.0.20 A multi-stage approach uses AI algorithms and 3D printing technology to improve design, optimization, and manufacturing. In AI, implementation begins with problem definition and algorithm selection, including supervised learning for regression and classification tasks or reinforcement learning for adaptive control systems. For robust model performance, data are gathered, cleaned, and labeled before being partitioned into sets for training, validation, and testing. Model development may use pre-trained models for rapid implementation or bespoke models for domain-dependent requirements, with precision, accuracy, and recall evaluated.<sup>21</sup> After training, AI models can automate or optimize 3D printing workflow tasks such as defect identification, material selection, and parameter optimization.

Parallel to 3D printing, Computer-Aided Design software creates a comprehensive 3D model for AM to ensure watertightness. A slicing program transforms stereolithography apparatus (SLA) files into layers and generates printer G-code from the exported model. Fused filament fabrication/FDM, SLA/digital light processing (DLP) methods, and selective laser sintering printers are set up with the appropriate material and build plate for optimal adhesion.<sup>22</sup> The object is printed layer by layer, with AI algorithms checking for anomalies, adjusting conditions in real time, or identifying and fixing faults.

AI improves 3D printing's productivity, reliability, and adaptability, while 3D printing delivers a clear, standardized outcome based on AI-driven design and manufacturing processes.

# 2. Advances in 3D printing for pharmaceuticals

The pharmaceutical industry stands to gain significant advantages from the utilization of 3D printing technology, particularly in the early phase of drug development. The process from the discovery of a medicine to its availability on the market typically takes between 10 and 15 years, with costs reaching £1.3 billion.<sup>23</sup> The recent COVID-19 pandemic, which required rapid medication development and repurposing studies, highlighted the critical need to shorten both the time and cost to market to accelerate drug development timelines. This need became particularly evident during the pandemic.<sup>24</sup> Various 3D printing processes are employed in the pharmaceutical sector, depending on the application and product type. Table 2 compares different 3D printing techniques in the pharmaceutical sector, and Figure 2 shows a schematic representation of the pharmaceutical 3D printing process.

# 2.1. 3D printing process for medicines

Three-dimensional printing can be employed as a rapid prototyping tool for the development of pre-clinical and clinical formulations of medicinal products. This approach allows for the evaluation of one-off or small-batch variations across a range of drug product iterations. The assessment of how various compositions influence key quality attributes, such as drug efficacy in *in vitro* and *in vivo* models, can be accelerated using rapid prototyping.<sup>30</sup> To date, 3D-printed formulations have been evaluated in a wide variety of pre-clinical animal models. As a result, compared to labor-intensive traditional manufacturing methods, 3D printing may facilitate earlier understanding of process and design variables.<sup>31</sup> This, in turn, may enable a quicker entry into first-in-human clinical trials, thereby reducing both development time and cost. In addition, 3D printing could be employed throughout pre-clinical and

early-stage clinical studies to generate small batches of dosage-flexible therapeutic products on demand for evaluating safety and effectiveness. In medicine, AM technologies are widely used, particularly in the production of medical devices and drug formulations.<sup>32</sup> The growing availability of printing technologies and products has made the broad application of 3D printing in the pharmaceutical and medical fields more accessible. Compared to conventional production methods, AM represents an innovative and novel approach to manufacturing medical tools and equipment.<sup>33</sup> Utilizing clinical images of patients, individualized medical devices, and highly customized surgical guides can be fabricated efficiently and precisely. This enables a better anatomical fit for patients and allows surgeons to perform procedures more safely.<sup>34</sup>

# 2.2. Advantages and potential applications of 3D-printed medicines

One of the most significant advantages of 3D printing in pharmaceuticals is the ability to tailor a patient's therapy precisely to their specific medical or lifestyle needs. In the near future, it is possible that patients may be able to choose a formulation type from a catalog.<sup>35</sup> The ability to fabricate medications with precise doses, or even incorporate variable amounts of multiple drugs into a single 3D-printed polyprintlet, can improve treatment efficacy while minimizing the risk of side effects from improper dosing. **Table 3** compares AI-enhanced 3D printing and traditional manufacturing.

# 2.2.1. Enhanced surgical planning and training with 3D printing

The use of 3D printing is becoming increasingly prevalent in medical education and the performance of surgical procedures. Although useful, 2D images offer limited visualization and do not accurately depict the structure of the human body.<sup>41</sup> On the other hand, 3D printing can create models with lifelike appearance and accurate representation. As a result, surgical procedures can become more precise and efficient.<sup>42</sup>

### 2.2.2. Innovative technological development

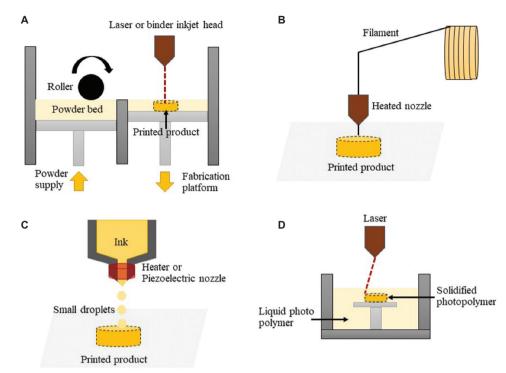
In the future, physicians may be able to train using 3D-printed organs. For example, training on animal organs is not as precise as training with human-like models. The quality of skills acquired by medical students during training, and the overall quality of patient care, can be significantly improved when those skills are practiced on realistic 3D-printed components.<sup>43</sup>

### 2.2.3. Attention to minute detail

Three-dimensional printers can produce low-cost prostheses in areas where they are most needed, such as nations experiencing conflict. For individuals who cannot afford

Table 2. Comparison of different 3D printing techniques in the pharmaceutical sector

Technique	Process description	Pharmaceutical application	Key advantages	References
Powder-based	Layer-by-layer powder binding/sintering	Sustained/immediate release tablets	Customizable release; multidrug	25
Extrusion-based	Paste/filament extrusion	Personalized, complex dosage forms	Versatile; rapid prototyping	26
Inkjet-based	Droplet deposition on powder bed	Fast-dissolving, precise dosage forms	High precision; gentle process	27
Laser-based (selective laser sintering)	Laser sintering/curing of powder/resin	Complex, porous structures (selective laser sintering)	Complex geometries; material versatility	28



**Figure 2.** Schematic representation of the pharmaceutical 3D printing process. (A) Powder-based: A rolling device spreads a thin coating of powder, which is then fused or bound precisely by a laser or binder inkjet tip to form the printed product. (B) Extrusion-based: A filament is inserted into a preheated nozzle that melts and deposits it to form the product. (C) Inkjet-based: A heating element or piezoelectric nozzle ejects microscopic droplets of ink to layer the product. (D) Laser-based: A laser precisely freezes liquid photopolymer as the surface moves to expose and cure additional layers. Reprinted from Huanbutta *et al.*<sup>29</sup> Copyright © 2023, Authors.

**Table 3.** Comparison of AI-enhanced 3D printing and traditional manufacturing

Feature	AI+3D printing	Traditional methods	References
Production scale	On-demand, small-batch production	Large-scale batch processing	16
Customization	Patient-specific dosages, release profiles, and multidrug combinations	Fixed-dose, one-size-fits-all formulations	36
Efficiency	Rapid prototyping (<24 h for new formulations); reduced material waste	Lengthy processes with downtime between steps; higher material waste	37
Drug development	AI-accelerated drug design (<50% time reduction); real-time quality control	Trial-and-error formulation; post-production quality checks	38
Supply chain	Distributed manufacturing (e.g., hospitals/ pharmacies)	Centralized manufacturing plants are vulnerable to disruptions	39
Clinical impact	Personalized release kinetics (e.g., dissolution rate)	Standardized release profiles are often associated with higher adverse events	40

Abbreviation: AI: Artificial intelligence.

traditional prosthetics, 3D printing provides an economical alternative.<sup>44</sup> Access to affordable medical equipment is crucial in economically disadvantaged countries and geographically isolated places. In some areas, poor road infrastructure prevents the timely delivery of medical supplies. The use of 3D printing facilitates the local production of vital equipment, reducing the need for frequent transport.<sup>45</sup> **Table 4** compares CIJ and DOD in 3D-printed medicines.

### 2.2.4. Cost reduction and faster access to medical equipment

Medical and laboratory equipment can be produced using a 3D printer. For example, plastic components of various apparatuses can be fabricated with a 3D printer. This results in a significant reduction in both expenditures and the time spent waiting for innovative medical equipment from external vendors.<sup>55</sup> In addition, the production process and subsequent applications are simplified. This increases the availability of equipment and enables low-income or remote areas to more easily obtain 3D-printed medical devices.<sup>56</sup>

### 2.2.5. Individualization

The conventional method of fabricating prostheses is extremely costly due to the customization required for each individual patient. With 3D printing, users can choose prosthetic size, form, color, and design,<sup>57</sup> making each 3D-printed component unique. 3D printing has also improved the affordability and accessibility of prostheses. AM is currently being reexplored across health care, aerospace, automotive, maritime, and machinery industries. In pharmaceuticals, personalized

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**Table 4.** Comparison of CIJ and DOD in 3D-printed medicines

Feature	CIJ	DOD	References
Mechanism	High-pressure pump forms a continuous ink stream; droplets are selectively charged and deflected to	Droplets are generated only when needed, using thermal or piezoelectric actuators in the	46
Droplet formation	print areas  Continuous stream breaks into droplets; unused droplets are recycled or discarded	print head Droplets are formed only on demand, reducing waste and improving efficiency	47
Speed	Generally faster for high-throughput applications	Slower than CIJ for large-scale, but more precise and efficient for small, customized batches	48
Precision	Good for marking and coding; less precise for complex pharmaceutical dosing	Very high precision, suitable for exact drug deposition and personalized dosing	49
Material compatibility	Limited by ink properties and recycling requirements	Greater compatibility with a wide range of solvents and APIs, especially in piezoelectric DOD	49
Waste	Higher, due to a continuous stream and the need to recycle or discard unused ink	Minimal, as only required droplets are generated	50
Pharmaceutical applications	Suitable for marking and coding tablets; less common for drug loading or 3D structuring	Widely used for drug loading, personalized tablets, films, and complex 3D structures	51
Automation and flexibility	Good for large-scale, repetitive tasks	Excellent for automation and flexible, patient-specific production	52
Cost	Lower per unit for high volume, but with higher material waste	Higher initial cost, but lower material waste and better suited for small, customized batches	53
Examples in medicine	Tablet marking, packaging	Personalized tablets, orodispersible films, microneedles, capsules, and combination therapies	54

Abbreviations: APIs: Active pharmaceutical ingredients; CIJ: Continuous inkjet; DOD: Drop-on-demand.

medications produced using AM are revolutionizing drug development. The integration of automation and AI improves formulation design, parameter selection, real-time quality control, and defect detection.<sup>58</sup> Together, AM and AI in 3D-printed medicines are accelerating the transition from mass-produced to personalized health care, streamlining production, and enhancing drug quality and availability.

# 3. Smart materials and printable formulations

Printable drug matrices represent a transformative advancement in pharmaceutical manufacturing, enabling precise control over drug delivery and personalized treatment regimens. These innovations address critical limitations in conventional drug production while introducing new capabilities in medication design and administration.

# 3.1. Smart polymers

Smart polymers are a promising technology in medicinal 3D printing. Scientists in Heidelberg have developed polymers with shape memory that can be 3D-printed with excellent precision at both macroscopic and microscopic scales. These novel materials possess lifelike features that advance biological engineering and micro-robotics technologies.<sup>59</sup> Intelligent or stimulus-responsive polymers can change their chemical or physical features in response to external stimuli such as variations in pH, temperature, or electromagnetic fields. These dynamic changes enable smart polymers to perform specialized functions, making them valuable in pharmaceutical and healthcare applications.60 The integration of smart polymers with nanotechnology, bioinformatics, and advanced manufacturing is expected to drive innovative personalized medicine, realtime health monitoring, and less invasive treatments. Smart polymers are revolutionizing health-care diagnostics and therapies by making them more intelligent, safer, and more effective.61

# 3.2. AI-assisted 3D-printed medicine materials

AI-assisted 3D printing is revolutionizing pharmaceutical production by enabling the creation of personalized drugs with precise dosage, release patterns, and medicinal combinations. Pharmaceutical-grade polymers play a crucial role in these applications. Among the most commonly used materials are cellulose derivatives such as hydroxypropyl methylcellulose, hydroxypropyl cellulose, and ethyl cellulose.62 These polymers serve as binding agents, film-forming precursors, and drug release modulators. These biodegradable materials are ideal for extrusion-based and inkjet 3D printing. In pharmaceutical FDM 3D printing, sustainable polylactic acid is widely employed<sup>63</sup> due to its reliability, printability, and tablet-forming properties. SLA and DLP 3D printing use the photopolymerizable material polyethylene glycol diacrylate, which is employed in the production of hydrogels and pliable dosage forms for controlled or prolonged drug release. Polyvinyl alcohol, a water-soluble and biocompatible polymer, is commonly used for immediate-release formulations and as a support material in multimaterial printing.<sup>64</sup> Gelatin and alginate are natural polymers valued for their biocompatibility and ability to form hydrogels, especially in printing chewable

or fast-dissolving dosage forms. Methacrylate copolymers are used for enteric coatings or to achieve targeted drug release in the gastrointestinal tract.<sup>65</sup> **Table 5** lists the materials used in AI-assisted 3D-printed medicines.

### 3.2.1. Material selection and AI integration

AI algorithms play a crucial role in predicting the printability and stability of different material-drug combinations, optimizing formulation parameters such as viscosity, melting point, and drug release profiles, and accelerating the design and quality control of personalized medicines by simulating how materials will behave during and after printing.<sup>69</sup> AI analyzes huge databases of pharmaceutical products to identify ideal formulations for 3D-printed drugs. Advanced AI models, such as conditional generative adversarial networks, can learn from datasets of successful and failed formulations to rapidly explore new material combinations and mass fractions.70 This method accelerates the development of biocompatible and regulatory-compliant materials and optimizes processing settings for printability and drug release characteristics. AI-driven optimization methods, including artificial neural networks (ANNs) and genetic algorithms, can predict the material properties and processing conditions that will work best for a given treatment, thereby eliminating trial-and-error experimentation. This makes pharmaceutical production more effective, safer, and more personalized, enabling patientspecific dosages and improved treatment outcomes.<sup>71</sup>

### 3.2.2 Bioinks for tissue engineering and regenerative medicine

Bioinks are essential for 3D bioprinting of intricate biological components to regenerate malfunctioning organs or tissues. These biomimetic, cell-compatible, and mechanically stable materials assist tissue regeneration.72 They enable precise, layer-by-layer fabrication of complex structures that mimic natural tissues, addressing critical challenges in organ repair and replacement. Bioinks are composed of natural or synthetic biomaterials and living cells, often supplemented with growth regulators such as the growth hormone, transforming growth factor, vascular endothelial growth factor, or exosomes to promote tissue regeneration.<sup>73</sup> They must maintain appropriate viscosity for printability, form stable gels to preserve structure, and exhibit biocompatibility to ensure cell viability. For instance, collagen-based bioinks are widely used due to their resemblance to the extracellular matrix, while exosome-laden bioinks improve cell interactions and extracellular matrix remodeling.<sup>74</sup> Innovations include multi-material bioinks for heterogeneous tissue engineering and physiologically responsive bioinks. Integration with organ-on-a-chip systems and bioreactors is bridging the gap between laboratory-scale prototyping and clinical-scale production. Bioinks enable on-demand tissue transplantation, disease modelling, and drug testing by merging the science of materials, cell biology, and sophisticated manufacturing.<sup>75</sup>

### 3.2.3. Requirements for effective bioinks

Successful bioinks must meet several critical requirements spanning both material and biological properties. From a material standpoint, ideal bioinks should exhibit excellent printability, appropriate mechanical integrity, controlled biodegradation rates, and modifiable surface functional groups. 76 Biologically, they must be biocompatible to maintain cell viability, cytocompatibility to support cellular functions, and capable of preserving the bioactivity of encapsulated cells during and after the printing process. The printability of a bioink depends on factors such as viscosity, surface tension, self-crosslinking ability, and interaction with the printer nozzle. Hydrophilic properties and viscosity of the bioink influence both printing effectiveness and cell encapsulation efficiency. More concentrated bioinks can produce longerlasting 3D structures but require higher extrusion pressures, which may impact flow during direct ink writing through narrow nozzle orifices.77

### 3.2.4. Bioink manufacturing methods

There are two main bioink approaches to bioink formulation for 3D bioprinting: (i) Cell-scaffold based approach, which involves printing 3D tissue constructs using bioink composed of biological materials and living cells. The scaffold material eventually degrades, allowing the embedded cells to proliferate and form functional tissue structures. (ii) Scaffold-free, cell-based approach, which involves printing with living cells to replicate natural embryonic tissue development. Neotissues fuse to create larger, functional tissue structures from selected cell populations. Recently developed supramolecular biomaterials, composed of polymers, have been used as bioinks for 3D printing. These advanced materials offer enhanced printing speeds, configurable surface properties for improved cell-material interactions, and precisely programmable mechanical properties through biomaterial gradients.

# ${\it 3.2.5. Limitations \ and \ future \ prospects}$

Bioink technology continues to advance but faces several challenges. Bioinks must exhibit high resolution, *in situ* gelation, appropriate viscoelasticity, mechanical stability, and

Table 5. Materials for artificial intelligence-assisted 3D-printed medicines

Material type	Examples	Printing method	Key role in 3D-printed medicines	References
Cellulose derivatives	НРМС, НРС	Extrusion, inkjet	Binder, film former, controlled release	66
PLA	Polylactic acid	FDM	Solid dosage forms, biodegradable	66
PEGDA	PEG diacrylate	SLA, DLP	Hydrogels, flexible forms, sustained release	67
PVA	Polyvinyl alcohol	FDM, inkjet	Immediate release, support material	67
Gelatin, alginate	-	Extrusion, inkjet	Hydrogels, chewable/dissolvable forms	68
Eudragit	Methacrylate copolymers	Extrusion, inkjet	Enteric coating, targeted drug release	68

Abbreviations: DLP: Digital light processing; FDM: Fused deposition modeling; HPC: Hydroxypropyl cellulose; HPMC: Hydroxypropyl methylcellulose; PEG: Polyethylene glycol; PEGDA: Polyethylene glycol diacrylate; PLA: Polylactic acid; PVA: Polyvinyl alcohol; SLA: Stereolithography apparatus.

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compatibility with various cell types. Sufficient permeability for nutrients, oxygen, and metabolic waste removal is necessary for cell survival within printed structures. Another important factor is that each 3D bioprinting method direct ink writing, inkjet bioprinting, SLA, and laser-induced forward transfer—requires distinct bioink characteristics. To address these challenges, researchers are developing functional polymeric biomaterials, modifying materials, and introducing novel cell—hydrogel blends to create programmable bioinks. These next-generation bioinks are more environmentally friendly, maintain cell viability, offer high-resolution printability, and retain mechanical integrity after printing. Figure 3 shows the advantages and limitations of AI-based 3D-printed medicines.

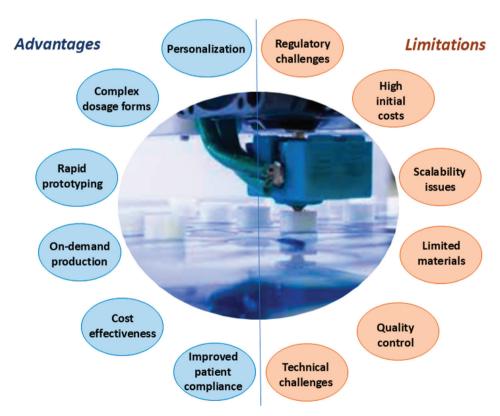
# 4. AI-driven design and optimization in 3D printing

AI-driven design and optimization are revolutionizing 3D printing by enhancing efficiency, enabling the fabrication of complex geometries, and reducing production costs. These advancements include generative design, real-time process adjustments, and enhanced quality control, with applications across aerospace, health care, automotive, and defense industries. He La techniques can predict optimal compositions and process conditions by analyzing large databases of medication formulations, excipient characteristics, and printing parameters, thereby accelerating design and testing

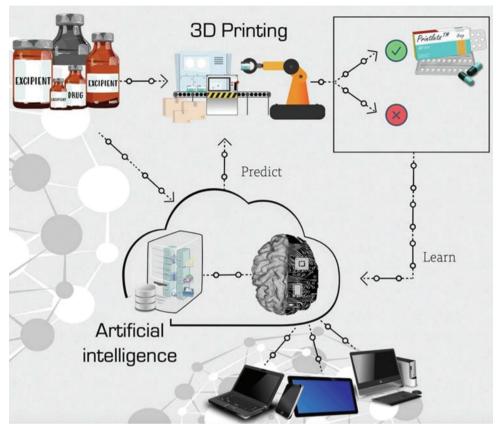
processes. Generative models such as conditional generative adversarial networks can rapidly generate unique, printable pharmaceutical formulations that are both innovative and feasible, often surpassing traditional human-driven approaches in diversity and speed. § Figure 4 shows the ML method for pharmaceutical 3D printability prediction.

# 4.1. AI and its applications in the health-care industry

The remarkable developments in AI technology and ML provide transformative potential for the pharmaceutical industry in areas such as dosage form testing, drug discovery, and formulation. AI systems that analyze genomes and proteomics data help researchers identify disease-related targets and predict how these may interact with potential drug candidates. 86 AI can also reduce development expenses by enhancing both academic and industrial efficiency. ML techniques help design experiments and estimate the pharmacokinetics and toxicology of prospective pharmaceutical compounds. By prioritizing and optimizing lead compounds, extensive animal testing can be reduced, saving both time and resources.87 AI algorithms that analyze realworld data can facilitate the implementation of personalized medicine, leading to more effective treatment outcomes and improved patient adherence. This in-depth analysis explores the various ways AI can be utilized in the pharmaceutical industry, including dosage form design, drug discovery, drug administration, process optimization, and testing.88



**Figure 3.** Advantages and limitations of artificial intelligence-based 3D-printed medicines. The figure compares the pros and cons of pharmaceutical 3D printing. On the left, blue circles emphasize advantages such as personalization, complex dosage design, rapid prototyping, on-demand production, cost effectiveness, and improved patient compliance. On the right, orange circles denote limitations including regulatory concerns, high initial costs, scalability issues, limited material availability, quality control, and technical challenges. The central image of a 3D printer symbolizes the pivotal role of the technology and visually separates the advantages and disadvantages. Reprinted from Bernatoniene *et al.*<sup>83</sup> Copyright 2025, Authors.



**Figure 4.** Machine learning method for pharmaceutical 3D printability prediction. This graphic illustrates the use of artificial intelligence (AI) and 3D printing in pharmaceutical production. In this method, medications and excipients are processed via 3D printing. The printed results are either accepted or rejected based on quality assessments. The AI system continuously learns from both successful and failed outcomes to refine 3D printing predictions. By connecting to databases and computational resources, incorporating both data and user input via digital devices, the AI system improves the efficiency and accuracy of pharmaceutical manufacturing. Reprinted from Elbadawi *et al.*<sup>85</sup> Copyright © 2020, Elsevier B.V.

# 4.2. AI-driven innovations in drug discovery, diagnosis, and personalized medicine

AI shortens drug development timelines and reduces costs while increasing success rates. Innovations such as generative molecular design, lab-in-the-loop validation, and precision targeting are reshaping how diseases are diagnosed and treated. As AI becomes more deeply integrated into health care, it holds the promise of more effective, patient-specific therapies.

# 4.2.1. AI uses in surgical equipment

AI has been incorporated into surgical equipment to assist surgeons during procedures. Robotic surgical devices utilise AI algorithms to support physicians in performing precise and minimally invasive operations. In addition, AI can analyze data from pre-operative and intraoperative procedures to provide real-time guidance and improve surgical outcomes.<sup>89,90</sup>

#### 4.2.2. Toxic effect prediction

AI algorithms can predict the toxic effects of drugs by analyzing molecular structure and attributes. ML models trained on toxicological datasets can anticipate harmful properties and identify potentially dangerous structural features. This capability enables researchers to select safer chemicals and reduce the risk of adverse reactions during clinical trials. 91

### 4.2.3. AI in nanomedicine

AI has the potential to revolutionize nanomedicine by enabling nanoscale therapeutic applications. Nanoparticles are used in imaging, diagnostics, and targeted medical treatments. AI algorithms can predict the physical and chemical properties, stability, and efficacy of nanoparticles, thereby aiding in their synthesis and optimization.<sup>92</sup>

### 4.2.4. Rehabilitation-prosthetics integration

Advanced prosthetic devices now incorporate AI to improve movement and functionality. ML algorithms can analyze user behavior to adapt the prosthesis to better meet individual needs. AI also monitors motion patterns and provides feedback to patients to improve gaits and measure track progress.<sup>93</sup>

### 4.2.5. Medication administration

AI-powered devices help patients manage their medications more effectively. Smart pill dispensers can remind users to take their medication at the correct times and dispense the appropriate dosage. AI algorithms can also analyze patient data, such as medical history and medication usage, to provide personalized treatment recommendations.<sup>94</sup>

### 4.3. Al's pharmaceutical manufacturing potential

AI could accelerate drug development, improve decisionmaking processes, and reduce costs in the pharmaceutical

sector. There are currently numerous applications of AI being utilized within the industry.95 One company is using AI to develop brand-new pharmaceuticals, while another is employing it to analyze existing marketed medications in search of unanticipated applications. 96 Organizations in the biotechnology and pharmaceutical sectors are increasingly turning to AI for support as they compete to bring novel medications to market. AI can speed up the drug development process by automating tasks such as identifying potential therapeutic targets and designing new compounds to act on those targets.<sup>97</sup> It can also analyze large datasets to uncover patterns that may reveal new insights into disease mechanisms. AI is being used to create "virtual patients" capable of testing new treatments and predicting their effectiveness in real patients. Recent advancements highlight AI's widespread influence across the pharmaceutical industry. 98 Drug research, supply chain management, precision medicine, clinical trials, and safety assessment are all being transformed. AI can also support patient engagement by providing information on health and treatment options, potentially improving both compliance and outcomes. The acceleration of target identification, clinical trial planning, and study data analysis can be achieved through AI, helping pharmaceutical companies develop new drugs more efficiently and effectively.<sup>99</sup> In the near future, AI could revolutionize the pharmaceutical sector by expediting drug discovery and development. 100 Using techniques such as virtual screening, vast chemical libraries can be rapidly analyzed, making it easier to identify therapeutic candidates with the desired properties and accelerating lead compound selection. By analyzing genomes, proteomes, and clinical data, AI-enabled precision medicine can classify patients into distinct groups, predict therapeutic responses, and personalize treatment. 101

# 4.4. Improved drug formulation and dosage customization

AI algorithms can optimize 3D-printed dose forms based on patient-specific data such as weight, gender, age, and medical history, enabling customized pharmaceutical therapies. 102 AI can simulate 3D-printed dosing strategies using ML and mathematical modeling on large datasets. Parameters such as geometry, drug diffusion patterns, and dosage strengths can be rapidly prototyped and optimized. Technologies such as binder jetting, fused filament fabrication, and pressure-assisted microsyringe printing are employed to produce 3D-printed pills. 103 Nozzle and platform temperatures, as well as printing speed, significantly affect the quality of 3D-printed tablets. A study using an ANN model demonstrated how processing parameters influenced the performance and drug release profile of 3D-printed diazepam tablets. 104 Conducted postmanufacture, the study evaluated infill pattern, density, and other input parameters to optimize drug-dispersing 3D-printed tablets. For subsequent modeling, infill density, volume ratio, and contact area were identified as the most critical factors. After rigorous testing, ANN modeling, and evaluation, the dissolution performance of the tablets improved.

### 4.5. Effective medication delivery

AI, in combination with big data, has led to the development of computational pharmaceutics, a field that improves drug delivery using multiscale models. Computational pharmaceutics uses AI and ML to predict drug activity from huge datasets. Simulations of drug formulations and delivery mechanisms allow researchers to evaluate scenarios and optimize drug delivery methods without relying solely on trial-and-error. 105 By saving time in drug development, this approach improves both efficiency and efficacy. Computational pharmaceutics models drug delivery at multiple scales, encompassing chemical interactions and biological behavior. 106 AI-powered systems can predict drug behavior across scales by analyzing complex interactions among pharmacological properties, formulation components, and physiological data. This enhances the design of effective DDSs and deepens understanding of drug dispersion mechanisms. It is particularly useful for estimating physicochemical characteristics of drugs, as well as drug stability and in vitro release profiles. 107 In addition, the same expertise can be applied to improve the predictions of in vivo pharmacokinetic behavior, drug distribution, and in conducting in vivo-in vitro correlation research. By employing appropriate AI technologies, researchers can identify potential risks and challenges associated with DDSs earlier in the development process.<sup>108</sup> This enables proactive adjustments to reduce risks and enhance drug performance. AI and computational modeling reduce the need for timeconsuming and costly trial-and-error experiments, lowering the likelihood of unexpected findings. 109 AI has also improved 3D-printed medicines by enabling the development of patientspecific oral dosage forms, personalized drug delivery implants and instruments, biofabrication of complex tissue structures, scaffold-based tissue regeneration methods, and 3D-printed prosthetics, orthotics, surgical implants, and tools.110 Furthermore, 3D-printed medical equipment and implants offer improved functionality, better patient fit, and enhanced surgical outcomes.

# 4.6. Accelerated drug development and optimization

Due to the failure rate of drugs during the initial stages of research, the pharmaceutical industry bears a significant financial burden. In 2013, the estimated cost of bringing a new chemical entity to market was around \$5 billion, and this figure is expected to continue rising in the coming decade.<sup>111</sup> As a result, there is growing demand for novel technologies to support drug development, particularly those that can rapidly identify potential drug candidates at minimal cost. Using regression models generated by the random forest method, it is now possible to predict the time-dependent release of medications. 112 Tablets are among the most common solid dosage forms in the pharmaceutical industry, available in a wide variety of shapes and sizes, each requiring specific preparation techniques. AI can assist in identifying optimal tablet designs and investigating the desired formulation properties. 113 In addition, it is anticipated that AI will be able to manage tasks with the aid of various automated technologies and algorithms. The integration of AI presents a challenge to regulatory authorities, requiring them to reinterpret regulations related to current good manufacturing practices. 114 To develop solid dosage forms and better understand the relationships between operations and process inputs and

outputs, several AI techniques, including fuzzy logic, neural networks, ANNs, and genetic algorithms, are utilized. Genetic algorithms are employed to predict outcomes based on input parameters, while ANNs improve prediction accuracy for solid dosage forms.<sup>115</sup>

# 4.7. Increased accessibility to personalized medicines

Producing personalized pharmaceuticals via 3D printing is a promising technological approach. It offers the necessary adaptability to customize both the dosage and the physical characteristics (such as size, shape, and color) of DDSs according to individual patient needs. 116 In recent years, several studies have demonstrated the viability of 3D printing in health care as a substitute for traditional compounding, offering advantages in terms of cost, safety, and patient outcomes. These studies have shown that 3D printing could be effectively used in clinical settings to produce medications. In medical environments, 3D-printed chewable drugs appear to be more precise and easily adaptable in terms of size (to achieve various dosages) and organoleptic properties (such as color and taste). 117 3D printing may also be used to construct so-called "polypills," which contain multiple active pharmaceutical ingredients (APIs) with distinct release kinetics and physical separation of each API within a single dosage unit. This opens up the possibility of producing tablets with different flavors, further improving patient adherence.<sup>118</sup> Researchers are currently working to advance the technology, including hardware (printers), software, and suitable excipients, to achieve ideal dosage accuracy, API release, stability, and safety. While these technological advancements are necessary for practical application, it is also vital to take into account the societal factors to gain a comprehensive understanding of the overall success and acceptance of the technology. 119

# 5. Synergistic platforms in personalized medicines

The integration of the IoT, AI, ML, and cloud computing is revolutionizing personalized medicine by enhancing data security, enabling real-time health monitoring, and facilitating tailored treatments. These technologies work synergistically to address longstanding challenges in health care, such as interoperability, scalability, and patient-centric care. AI analyzes genetic, lifestyle, and IoT-generated data to identify optimal therapies, predict disease risks, and recommend preventive measures. For example, ML models can personalise chemotherapy regimens based on tumor genomics. Blockchain technology secures access to sensitive data, ensuring that only authorized providers contribute to treatment plans. Cloud computing provides the computational power needed for AI-driven drug discovery and large-scale genomic analysis. 122

# 5.1. AI techniques to enhance 3D printing for drug development

AI helps ensure the printability, quality, and safety of 3D-printed medicines. This interface enables decentralized, on-demand production of complex and customized dosage

forms, including multi-drug combinations and tailored release profiles, either at the point of care or in pharmacies, supporting the development of digital and personalized medicine. AI-enhanced 3D printing is making drug development more efficient, cost-effective, and patient-specific while maintaining strict safety and quality standards. IoT, AI, ML, and cloud computing continue to drive advances in pharmaceutical 3D printing. By analyzing real-time processing data and automatically modifying parameters to minimize errors and ensure regulatory compliance, these technologies are transforming how personalized medicines are developed and delivered.

#### 5.1.1. IoTs

The IoT refers to technology that connects devices and equipment during manufacturing. IoT devices can monitor environmental parameters such as temperature and humidity in pharmaceutical manufacturing, thereby ensuring product safety and quality. 125 In addition, these devices can track items across the supply chain in real time, allowing for prompt quality interventions. IoT is a leading innovation in information technology. The Internet is a global network of computer systems that links millions of users through the Internet Protocol and Transmission Control Protocol standard suite. Various wireless, online, and optical networking technologies interconnect millions of public, private, educational, commercial, and governmental networks worldwide. 126 Due to a unique addressing scheme, Radio Frequency Identification and other IoT technologies can communicate and adapt to their surroundings to achieve shared objectives. The term IoT was first introduced by computer expert Kevin Ashton. It is best defined as "an openly wide and informational network of electronic devices that can offer data, information, and resources; self-organise; and act and react in response to environmental changes."127 As the pharmaceutical sector is pragmatic about adopting technological advancements, IoT offers significant potential. It can help pharmaceutical companies increase production efficiency, reduce costs, and improve the distribution of medicines to patients. IoT bridges the gap between physicians, manufacturers, distributors, and consumers by monitoring patient compliance with prescriptions via cloud-based platforms. 128 Sensors and smart devices are poised to help the pharmaceutical industry save lives and develop more effective treatments. While IoT increases productivity, resilience, and efficiency, it also presents significant opportunities to transform the pharmaceutical industry.

#### 5.1.2. AI

In the context of Pharma 4.0, AI has the potential to revolutionize drug discovery, development, and production. AI-powered drug discovery tools can identify and validate drug targets more quickly and accurately than traditional approaches, assisting researchers in discovering new medicines. <sup>129</sup> AI can also predict the safety and efficacy of new drug candidates, thereby reducing the need for time-consuming and expensive clinical trials. In manufacturing, AI can forecast and prevent equipment failures, minimize downtime, and reduce waste.

AI-driven automation improves industrial efficiency and quality. <sup>130</sup> In personalized medicine, AI helps optimize therapeutic outcomes by tailoring treatment regimens based on patient-specific data. Overall, AI in the pharmaceutical sector drives innovation and productivity while increasing the potential for safer, more effective therapies.

### 5.1.3. ML

ML is another key technology in Pharma 4.0. It uses algorithms to process data and make predictions or judgments without explicit programming. By analyzing large datasets, ML can uncover patterns that lead to the identification of new therapeutic targets in drug discovery. 131 ML also enhances manufacturing by predicting equipment failures and enabling dynamic adjustment of production schedules. As a subfield of AI, ML develops statistical models and algorithmic techniques that allow computers to perform tasks autonomously. Its transformative potential in drug discovery, development, and production has made ML highly relevant to the pharmaceutical industry. 132 ML algorithms can identify trends, predict potential drug candidates, and optimize drug formulations by processing extensive biological and chemical datasets. This accelerates drug discovery by helping researchers filter through massive data to identify promising compounds. In personalized medicine, ML analyzes patient data to predict therapeutic responses, enhancing treatment outcomes. 133 ML boosts productivity in the health-care sector and may help solve complex medical challenges while facilitating the development of targeted therapies.

### 5.1.4. Cloud computing

Cloud computing can help the pharmaceutical industry by enabling more efficient data sharing and collaboration. Cloudbased solutions enable organizations to exchange data and insights, thereby improving drug discovery and development. These tools enhance supply chain transparency and collaboration, accelerating responsiveness to quality issues.<sup>134</sup> Cloud computing has revolutionized data management, collaboration, and research in the pharmaceutical sector. Cloud services help pharmaceutical companies streamline operations, secure sensitive data, and accelerate the drug development process. The cloud supports advanced data analysis and ML algorithms for predictive modeling and personalized medicine, along with efficient storage and processing of large datasets and real-time collaboration across geographically dispersed teams. 135 Cloud-based solutions improve scalability, enabling organizations to respond to fluctuating workloads and demands. This flexible and cost-effective strategy optimizes research and development efforts while ensuring regulatory compliance, as cloud providers often offer strong security measures. Overall, cloud computing has driven pharmaceutical innovation, agility, collaboration, and progress in health care.136

# 5.2. Intersection of AI and 3D printing in medicine

Thanks to the advancement of 3D printing technology, it is now feasible to manufacture complex items without human assistance. AI has the potential to further enhance the manufacturing process, despite its complexity. The integration of AI with 3D printers will result in the production of new applications. 137 Several applications will benefit from this technological combination. As adoption becomes more widespread, this integration is expected to revolutionize the manufacturing industry.<sup>138</sup> For example, new prosthetic limbs suitable for surgical applications can be developed using these technologies. Although AI and 3D printing are frequently discussed together, AI can also be utilized independently to improve the quality and performance of manufactured goods. By automating processes, AI can enhance 3D printing performance and minimize human error. 139 This integration may benefit both manufacturing and quality control. In addition, it supports the growth of Industry 4.0 and the IoT in the industrial sector. ML, a subset of AI, can analyze data streams and detect hidden patterns. 140 For example, during the 3D printing of complex materials like titanium, carbon, and other metal alloys, AI is useful for maintaining consistent material properties. Predictive maintenance can also be enabled using trained models. Even in the development of spare parts, ML can assist manufacturers.141

# 5.3. AI-ML-3D printing process for medicines

Three-dimensional printing is a powerful technology capable of creating complex and customized medical devices such as implants, surgical tools, and prosthetics. However, to ensure the safety, performance, and quality of these devices, the printing process must be optimized and comply with specific standards and regulations. <sup>142</sup> AI and ML, when combined with 3D printing, are transforming the pharmaceutical industry, especially in the realm of personalized drugs. This innovative approach improves drug formulation, production processes, and patient treatment outcomes. <sup>143</sup>

# 5.3.1. Pharmaceutical 3D printing

AM, or 3D printing, produces patient-specific pharmaceutical products layer by layer. This method enables the creation of variable formulations with different dosages, shapes, sizes, and release profiles, shifting from mass production to truly personalized medication. Producing customized drugs on demand offers many advantages, including tailoring medications to individual therapeutic needs and patient preferences, and reducing production expenses and time compared to traditional approaches.<sup>144</sup>

# 5.3.2. AI/ML integration in 3D printing

The combination of AI/ML and 3D printing is key to solving pharmaceutical manufacturing problems. One significant application is quality monitoring, where AI algorithms can detect defects in printed dosage forms in real time, ensuring product consistency and safety throughout the production process. <sup>145</sup> In addition, ML can be used to optimize critical printing parameters such as temperature and speed, leading to improved precision and reproducibility. Beyond production, AI also contributes to design innovation by enabling the development of complex dosage forms and multi-drug combinations tailored to individual patient needs. <sup>146</sup> This convergence of AI, ML, and 3D printing facilitates the

advancement of personalized medicine, enhancing drug production efficiency, patient engagement, and treatment adherence. As these technologies continue to mature, their integration into clinical practice is expected to grow, ushering in a new era of data-driven and patient-centric pharmaceutical care.<sup>147</sup>

# 5.4. Successful integration of AI and 3D printing in pharmaceutical manufacturing

Over the past 10 years, AI and 3D printing have driven advancements in the health care industry. New medical equipment, orthopedic implants, and prostheses are being developed by medical specialists using 3D printing technology. 148 In addition, customized models of tissues, bones, and organs are being created with this technology. According to international market research, the medical 3D printing market was valued at more than 1.7 billion US dollars in 2020.149 It is projected to grow at a compound annual growth rate of over 22.3% from 2021 to 2027. 150 Compared to conventional manufacturing approach, AI and AM enables the creation and printing of more intricate designs and a wider range of material.<sup>151</sup> This is facilitated by recent advancements in both technology and materials. Today, medical experts can easily produce customized medical instruments and implants tailored precisely to a patient's anatomy or specific surgical procedure. A more accurate fit of prostheses and implants can significantly reduce the risk of infection, enable pain-free functionality, and accelerate recovery. 152 The integration of AI and 3D printing, also known as AM, is catalyzing a transformative shift across various industries. This synergy enhances efficiency, optimizes design processes, and fosters innovation in manufacturing. The synergistic integration of AI and 3D printing represents a significant leap forward in AM capabilities.<sup>153</sup> By optimizing processes, enhancing design flexibility, and enabling mass customization, this collaboration is set to redefine industry standards and unlock new opportunities for innovation across multiple sectors. As technology evolves, the potential for further advancements remains vast, promising a future where creativity and efficiency are seamlessly intertwined in manufacturing practices. <sup>154</sup> **Table 6** presents the AI algorithms for formulation optimization.

### 6. Clinical translation and case studies

Clinical translation involves translating fundamental biomedical research into health-improving applications, from laboratory innovations to patient care. This translational process encompasses preclinical studies, clinical trials, health-care implementation, and public health outcomes. The goal is to bridge the gap between scientific breakthroughs and widespread clinical application, delivering diagnostics, therapies, and preventive strategies to patients.

### 6.1. Case 1: Advanced AI for diabetics

For instance, Medtronic, a global medical technology company, has developed AI-based tools for diabetes management. The Medtronic Guardian Connected System uses AI and continuous glucose monitoring to provide real-time diabetes support. In 2016, IBM Watson and Medtronic created the *Sugar IQ* app, offering mobile-based personal support for diabetes patients. This diabetes management application uses AI to provide several valuable features, with one of its most important being "Insights." The software performs an in-depth analysis of a user's glucose patterns over time, discovers trends, and delivers personalized alerts to the patient. These insights help individuals understand how certain behaviors, habits, and environmental factors influence their glucose levels. As a result, users can make more informed decisions and take proactive steps toward more effectively managing their diabetes. <sup>160-168</sup>

Table 6. Artificial intelligence algorithms for formulation optimization

Feature/criterion	ANN	GAN	RF	References
Core idea	Mimics biological neurons to model complex relationships	Two networks (generator and discriminator) compete to generate realistic data	Ensemble of decision trees for prediction and classification	155
Use in optimization	Predicts formulation outcomes; used in inverse modeling	Generates novel, optimized formulations by learning data distribution	Selects important variables; predicts outcomes and ranks factors	155
Data requirement	Requires large, labeled datasets	Requires substantial data; can work with unlabeled data for generation	Handles smaller datasets well; less prone to overfitting	156
Strengths	Captures non-linear relationships; flexible model	Can propose entirely new formulation candidates	Robust to noise; interpretable feature importance	156
Weaknesses	Prone to overfitting; requires tuning	Training instability; harder to interpret	May struggle with highly non-linear problems	157
Output type	Predictive model (e.g., concentration vs. response)	New data generation (e.g., novel formulation recipes)	Predictive model with variable importance	157
Optimization role	Response prediction and optimization via simulation	Direct generation of optimized formulations	Response prediction and feature selection	158
Interpretability	Low (black-box model)	Very low (black-box and generative)	High (feature importance is accessible)	158
Computation demand	Moderate to high	High	Low to moderate	159
Common use cases	Pharmaceutical QbD, mixture optimization	New material formulation, drug-like compound generation	Ingredient screening, quality prediction	159

Abbreviations: ANN: Artificial neural network; GAN: Generative adversarial network; QbD: Quality by design; RF: Random forest.

# 6.2. Case 2: Large-scale emergency medical supply production

Ian McHale, a student at Steinert High School in New Jersey, developed a design for a finger splint that can be produced on a 3D printer for less than two cents. Aware of the challenges faced by underdeveloped countries in sourcing medical supplies—especially custom-made items—McHale aimed to create an accessible and low-cost solution. His design enables the production of finger splints using recycled plastic on affordable 3D printers, with each splint taking approximately 10 min to print. Depending on the size of the build platform, a single print run can yield 30–40 splints. The splint is particularly valuable in rural clinics, emergency stations, and field hospitals where medical equipment is limited or unavailable. McHale's innovation won first place in his division at the Mercer Science and Engineering Fair, with the award presented by the US Army and Air Force. He believes this approach allows splints to be fabricated on demand and tailored to individual finger sizes, making them ideal for rapid response and resourcelimited settings.169

# 6.3. Case 3: Bone implants

In 2018, medical professionals at Kunming Medical University (KMU) Hospital in China, in collaboration with the 3D printer company IEMAI 3D, successfully implanted the world's first 3D-printed polyether ether ketone (PEEK) collarbone. This accomplishment was made possible through international collaboration. The procedure was carried out on a 57-yearold patient with advanced cancer to remove cancerous cells from damaged organs and tissues. As part of the operation, the patient's collarbone had to be removed. To reconstruct the collarbone following resection, the medical team at KMU hospital chose to use a PEEK prosthesis rather than the conventional titanium mesh. This decision was made because the PEEK prosthesis would not interfere with the patient's subsequent chemotherapy treatment. In addition, PEEK promotes faster recovery and has shown no adverse effects in patients. The introduction of thermoplastics such as PEEK, polymethyl methacrylate, and others into the medical field has enabled more patients to undergo implant surgeries, as these materials do not compromise potential future treatments. 170

### 6.4. Case 4: Human corneas

In 2018, researchers at Newcastle University in the United Kingdom successfully 3D-printed the first human cornea. They developed a printable solution known as "bio-ink" by combining healthy corneal stem cells with alginate and collagen, allowing for a transparent and printable material. In under 10 min, the bio-ink was effectively extruded using a straightforward 3D bioprinting technique to construct the shape of a human cornea. With 3D printing technology, corneas were customized to the exact specifications of each patient. By using data obtained from scanning a patient's eye, researchers were able to print a cornea that precisely matched the size and shape of the original. The Newcastle researchers anticipated that 3D-printed corneas could help address the global shortage of donor corneas in the near future. However,

further testing is still required before these bioprinted corneas can be approved for transplantation.<sup>171</sup>

### 6.5. Case 5: Heart valves

The 3D tissue printing method was pioneered by Cheung et al. at Cornell University, who succeeded in generating living heart valves with anatomy similar to that of natural valves. Butcher's team developed algorithms that process 3D image datasets of native valves to automatically construct full 3D models of heart valves with high precision. Bioprinting is then performed using a dual syringe system containing a mixture of alginate/ gelatin hydrogel, smooth muscle cells, and valve interstitial cells. The goal is to accurately replicate the composition of the valve root and leaflets. Butcher believed that the fields of tissue engineering and biomedicine would increasingly adopt bioprinting in the future. Patient-specific tissue models would be especially valuable to medical professionals for studying disease pathophysiology, evaluating therapeutic efficacy, and manufacturing living tissue substitutes tailored precisely to individual patient geometry.172

# 7. Challenges and regulatory perspectives

Advanced health-care materials encompass biomaterials, nanotechnology, biofabrication, and biomedical devices aimed at improving diagnostics, therapeutics, and regenerative medicine. These innovations face multifaceted challenges and evolving regulatory landscapes as they transition from research to clinical application. Collaborative efforts between researchers, industry, and regulators are critical to addressing gaps in material characterization, accelerating translational pathways, and ensuring patient safety without stifling innovation.

# 7.1. Challenges of 3D-printed drugs in regulatory approval and standardization

Due to the innovative nature of the technology and the lack of established regulatory frameworks for 3D-printed pharmaceuticals, regulatory approval and standardization remain difficult. While 3D printing offers the potential to develop patient-specific doses and multi-drug formulations for personalized medicine, it also complicates regulatory pathways.

### 7.1.1. Regulatory approval issues

Although some regulatory authorities have addressed 3D-printed medical devices, there are no specific regulations for 3D-printed drugs. Even though the Food and Drug Administration approved the first 3D-printed tablets in 2015 and has published guidelines for 3D-printed medical devices, it has not done so for pharmaceuticals. Manufacturers must therefore adapt chemical processes, manufacturing methods, and control procedures to 3D printing in the absence of clear regulatory guidelines. Existing pharmaceutical regulations do not sufficiently cover 3D printing-specific variables such as digital layout files, printing parameters, and material properties, making compliance challenging. Each batch of 3D-printed medication must be tested for safety, efficacy, and quality, further complicating the approval process. In addition, variations in printer models, software, and raw

materials make it difficult to ensure consistent product quality across manufacturing sites or even within the same site.<sup>175</sup> This variability raises concerns about the reproducibility and reliability of drug products, which are key requirements for regulatory approval.

#### 7.1.2. Standardization challenges

Standardization is another major obstacle. The lack of standardized 3D printing operations, materials, and quality control procedures makes it difficult to ensure that all 3D-printed pharmaceuticals are safe and effective. 176 For instance, the absence of current good manufacturing practices specific to 3D printers and the significant variability among devices complicate the achievement of consistent production outcomes. Materials used in 3D printing must be carefully chosen and evaluated for printability, strength, and biocompatibility, but available options remain limited. Traditional pharmaceutical manufacturing relies on validated, controllable methods; however, 3D printing introduces novel factors such as layer thickness, printing speed, and temperature, all of which can influence product quality. 177 Each printed dose must meet stringent criteria, yet real-time, non-destructive quality control procedures are still under development.

### 7.1.3. Ethical and regulatory issues

Beyond technology aspects, regulatory and ethical considerations must also be considered. The possibility of drugs being printed in pharmacies, hospitals, or even at home raises significant concerns regarding regulation and oversight.<sup>178</sup> As the technology evolves, issues such as hacking of printing software, unauthorized replication of medication designs, and intellectual property protection become increasingly relevant. Ethical concerns include equitable access to 3D-printed pharmaceuticals and the prevention of misuse or unsupervised self-treatment.<sup>179</sup> Overall, while 3D printing holds great promise for personalized medicine, the lack of comprehensive regulatory guidelines, standardization issues, and the need for reliable quality control systems continue to hinder its widespread adoption and regulatory approval. Manufacturers and researchers must collaborate to develop new standards and protocols that ensure the safety, efficacy, and quality of these transformative products. 180

# 7.2. Challenges and limitations of implementing AI in 3D-printed medicines

The integration of ML and 3D printing is not without its challenges. To ensure a smooth transition into clinical practice, software developers working on ML-guided 3D printing should proactively investigate and address these potential obstacles. While some of these challenges are specific to the pharmaceutical 3D printing sector, most are common to the broader field of ML. <sup>181</sup> The lack of readily available large datasets for ML training is perhaps the most significant problem faced across industries. In general, ML predictions are more reliable when large amounts of training data are available, although ML algorithms capable of working with small datasets are beginning to emerge. Ideally, unified and easily accessible databases containing relevant 3D printing

data would be available for ML analysis.<sup>182</sup> Despite their numerous advantages, AI-based models suffer from several drawbacks, most notably their lack of interpretability and their requirement for extremely large datasets. As a result, AI models should be employed in conjunction with more conventional experimental methods to ensure both the safety and efficacy of pharmaceuticals. The following sections are examples of some of these limitations.<sup>183</sup>

### 7.2.1. Limited available data

For AI algorithms to make accurate predictions, a substantial amount of data is required. However, there may be insufficient data available for certain demographics or medicines, which could result in less accurate or biased outcomes. <sup>184</sup> For instance, limited data may be available for rare diseases, presenting a substantial challenge when developing AI models. In addition, the data utilized to train AI models may not be representative of the target population, leading to biased findings. <sup>185</sup> In addition, certain types of data, such as longitudinal data or real-world evidence, may not be readily accessible, which can further limit the utility of AI models. Due to these constraints, it is essential to carefully consider both the accuracy and representativeness of the data used to construct AI models. <sup>186</sup>

#### 7.2.2. Analysis and discussion of the results

The outputs produced by AI models are not always easy to interpret, even for subject matter experts. Because these models may not provide a transparent explanation of how their predictions were generated, it can be difficult for physicians and researchers to fully understand and trust the results.<sup>187</sup> In some cases, translating AI-generated findings into actionable insights for clinical practice or drug development may be challenging. Moreover, the use of AI models may require a level of technical expertise that is not readily available to all health-care professionals and researchers, further limiting their practical utility.<sup>188</sup> Consequently, there is a growing need for improved interpretability and explainability of AI models to ensure that their predictions can be clearly understood and effectively applied.<sup>189</sup>

# 7.2.3. Considerations of an ethical nature

As with any application of AI, several considerations must be taken into account in drug development using such technologies. One major concern is patient privacy, especially given the frequent use of sensitive health data in training AI models.<sup>190</sup> Data protection and security are critical issues that require significant attention and cannot be overlooked. It is essential to ensure that patient information is gathered and utilized in ways that safeguard privacy and comply with legal rights. Another ethical issue involves data ownership.<sup>191</sup> In some cases, patient data may be collected without their informed consent, and it may be unclear who owns the data or holds the right to its use. This ambiguity has the potential to cause disputes among patients, researchers, and pharmaceutical companies.<sup>192</sup>

# 7.2.4. Inadequate clinical knowledge and experience

Although AI is capable of detecting correlations, it is vital to recognize that individual patient treatments may differ

despite these associations. AI algorithms often operate within a statistical framework, which may limit their ability to understand the numerous complex factors and far-reaching consequences that various parameters may have. 193 The intricate nature of treatment decisions, shaped by a wide range of individualized characteristics, presents a challenge for AI models that are primarily focused on statistical relationships. As a result, the capacity of AI to fully capture the essential aspects and implications of certain parameters may be limited. 194

### 7.2.5. Systematically complicated biological entities

AI has several limitations in its ability to accurately emulate the complexity of biological systems as a whole. Biological systems are complex and dynamic, consisting of numerous interconnected pathways, feedback loops, and intricate chemical interactions. <sup>195</sup> Because of this complexity, AI models, which frequently oversimplify and generalize biological processes, face significant challenges. These models heavily rely on training data to detect patterns and make predictions; however, the currently available data may not adequately reflect all the intricacies and nuances of biological systems. <sup>196</sup> Real-world complexity and diversity, including genetic variations, environmental influences, and inter-individual variability, may not be well captured by existing AI models. <sup>197</sup>

### 7.2.6. Ethical considerations and regulatory implications

It is essential to recognize and develop specific elements of quality assurance, production challenges, excipient specifications, manufacturing procedures, and related regulatory and technical issues before 3D printing can become a widely adopted therapeutic tool.<sup>198</sup> The creation of personalized pharmaceuticals, with tailored dosing, dosage forms, and drug release kinetics, can be effectively achieved through 3D printing. However, the use of 3D-printed medical devices in home settings presents a significant challenge; to minimize the risk of adverse reactions, such practices must be supervised and managed by qualified professionals.<sup>199</sup> New procedures to govern intellectual property rights related to 3D printing designs are becoming increasingly important. These would provide the flexibility necessary for supporting digital technologies more rapidly and efficiently, especially in the event of a global health emergency. 200 As engineers and healthcare professionals gain experience, the time required to design, manufacture, and implement a 3D-printed personalized medical device (including implants) continues to decrease. Consequently, it is essential for multidisciplinary teams to engage in effective collaboration and foster mutual trust.<sup>201</sup>

### 7.2.7. Material limits and compatibility

Only a limited selection of pharmaceutical-grade components and excipients is currently available for use in 3D printing, which significantly restricts the range of medications and dosage forms that can be produced. <sup>202</sup> Many of these approved materials are mechanically weak or lack the necessary stability, resulting in printed dosage forms that are friable, fragile, and prone to physical degradation. This not only complicates the manufacturing process but also poses challenges for packaging, storage, and transportation, as the risk of breakage or

contamination increases.<sup>203</sup> In addition, the limited availability of suitable materials restricts the development of complex DDSs, such as those with controlled release profiles or multi-drug combinations, further narrowing the potential applications of 3D printing in personalized medicine. Compatibility concerns also arise when considering the chemical and physical interactions between available excipients and APIs, which can impact drug stability and bioavailability.<sup>204</sup> As a result, ongoing research is focused on developing new, robust materials that meet stringent regulatory standards while also supporting innovative dosage form designs.

# 7.2.8. Printer resolution, degradation, and thermal stability

Achieving high-dimensional precision and resolution is difficult for complex or small medicinal items. Nozzle shape, layer thickness, and printer calibration significantly affect product quality. Low-dimensional precision can lead to irregular drug release patterns and dosage inconsistencies, which are critical concerns in pharmaceutical manufacturing. <sup>205</sup> 3D printing currently lacks adequate in-process control, making batch-to-batch uniformity and quality assurance challenging. Variations in printing parameters, environmental conditions, and material properties can affect reproducibility. In addition, techniques such as selective laser sintering may damage thermolabile drugs and excipients due to high temperatures or localized heating. Therefore, thermal stability must be carefully assessed to avoid degradation and to ensure the efficacy and safety of printed medicines. <sup>206</sup>

### 7.2.9. Powder agglomeration and reuse of unused material

Powder agglomeration can lead to irregular microstructures, poor densification, and product defects, which affect the mechanical properties of the printed dosage form and its drug release profile. These issues can result in inconsistencies in tablet strength, dissolution rate, and therapeutic performance.<sup>207</sup> Recyclability and safety are becoming increasingly important in pharmaceutical 3D printing, especially in binder jetting and powder bed processes. Modifications in the particle size distribution, moisture content, or flowability in recycled powders can reduce print quality and compromise product integrity.<sup>208</sup> Continuous reuse of recycled material may introduce impurities or change its physicochemical properties, making it unsuitable for high-quality dosage forms. To reduce these risks and maintain product quality, temperature and humidity must be carefully monitored and controlled during the printing process. Recycled materials must also undergo rigorous quality assurance and in-process monitoring to ensure patient safety and regulatory compliance.9

# 7.3. Implications of industry 4.0 on pharmaceutical manufacturing

Industry 4.0, with its integration of automated processes, real-time data sharing, and smart production systems, is transforming pharmaceutical manufacturing. One of the key implications is improved operational efficiency, as AI and data analytics enable real-time monitoring, optimization, and control of production processes. This leads to reduced waste and enhanced product quality.<sup>209</sup> Predictive quality control is

another critical benefit; generative AI can anticipate potential quality issues during manufacturing, allowing for proactive interventions to ensure compliance with safety standards. In addition, dynamic production scheduling becomes more feasible, as AI systems can adjust schedules in response to real-time demand and changes in supply chain conditions, ensuring timely delivery while minimizing operational costs.<sup>210</sup> Finally, Industry 4.0 supports enhanced regulatory compliance. As regulations continue to evolve, these technologies assist manufacturers in maintaining compliance through advanced tracking, reporting, and documentation systems.<sup>211</sup>

In the not-too-distant future, AI may revolutionize the pharmaceutical sector by accelerating drug discovery and development processes. Using techniques such as virtual screening, vast chemical libraries can be rapidly analyzed, making it easier to identify therapeutic candidates with the desired characteristics. This will expedite the identification of lead compounds. By analyzing genomes, proteomes, and clinical data, AI-enabled precision medicine will be able to classify patients into distinct groups, predict therapeutic responses, and personalize treatment regimens.<sup>212</sup> Deep learning and generative models provide researchers the ability to design novel molecules with target-binding properties, thereby improving the therapeutic efficacy of existing medications while simultaneously reducing adverse effects. In addition, AI will enable the formulation of patientspecific dosages by accounting for individualized drug administration needs.213 By accurately predicting adverse effects and the toxicity of potential drug candidates, AI algorithms are expected to usher in a new era of innovation in safety assessment.

# 8. Limitations of the study

The dynamic and multidisciplinary nature of this research area makes it challenging to provide a comprehensive and up-to-date summary. As AI and 3D printing technologies advance rapidly, many current advancements, algorithms, and applications may be omitted or only briefly addressed due to publication delays or limited availability of peer-reviewed literature. The quality and scope of the available research may also constrain the review, as many studies are preliminary or exploratory and lack large-scale clinical validation. This hinders the ability to draw firm conclusions and develop standardized methodologies. Furthermore, due to the scarcity of literature, regulatory, legal, and data privacy concerns related to AI in pharmaceutical 3D printing may not be fully addressed. The evaluation may also exhibit a technological bias, emphasizing Al's potential and applications rather than examining the feasibility, risks, and constraints of clinical and manufacturing implementation.

# 9. Conclusion and future perspectives

Future research in AI-driven pharmaceutical manufacturing should focus on integrating AI into all stages of drug development and production to improve both efficiency and personalization. Three key sub-points are outlined in the following subsections.

### 9.1. AI in advanced manufacturing technologies

AI should be studied in conjunction with 3D printing and continuous manufacturing. It can optimize printing parameters, predict material behavior, and ensure regulatory compliance in real time, enabling rapid prototyping and scalable production of complex drug formulations tailored to individual patients. By employing AI-driven analytics to dynamically monitor and adjust operations, this integration can address material and regulatory challenges, reduce errors, and ensure product consistency.

# 9.2. Al growth in personalized medicine with on-demand production

By analyzing extensive biological, clinical, and lifestyle data, AI should support the development of customized medications in future research. AI-driven platforms could accelerate the transformation from mass production to on-demand, patient-specific pharmaceuticals by automating drug discovery and fabrication for rare medical conditions or unique patient profiles. This would require advancements in modular production systems and AI-powered real-time quality control mechanisms to enable rapid adaptation.

# 9.3. AI-driven predictive maintenance along with supply chain optimization

Research should focus on AI solutions for predictive maintenance of industrial equipment and smart supply chain management. AI can forecast equipment failures, minimize downtime, and optimize inventory and logistics using IoT devices and real-time data analytics to ensure timely drug delivery. These innovations will strengthen supply chains, reduce waste, and enable more flexible responses to market demands and regulatory changes.

The pharmaceutical industry stands to gain significant advantages from the use of 3D printing technology, particularly in the early phases of drug discovery. The recent COVID-19 pandemic, which required rapid drug development and repurposing efforts, highlighted the urgent need to reduce time and cost to market by shortening drug development timelines. 3D printing can be employed as a rapid prototyping tool during the development of pre-clinical and clinical formulations. This would allow for the evaluation of one-off or small-batch variations of different drug product iterations. Rapid prototyping can accelerate the assessment of how various formulation compositions impact critical quality attributes, such as drug efficacy, in both in vitro and in vivo models. To date, 3D-printed medicines have been evaluated in a range of preclinical animal models to determine their efficacy. Compared to labor-intensive traditional manufacturing methods, 3D printing may facilitate earlier understanding of process and formulation parameters, potentially enabling quicker entry into first-in-human clinical trials, thereby reducing both the time and cost of product development. In addition, 3D printing can be used during pre-clinical and early-phase clinical testing to produce small batches of dose-flexible therapeutic products on demand, allowing for real-time evaluation of their efficacy and safety. Medications could be formulated on demand in

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decentralized locations such as clinics, pharmacies, or even the patient's home using 3D printing technology. This could help pharmaceutical companies reduce transportation and overall logistics expenditures, thereby lowering the carbon footprint associated with distribution and eliminating the need for energy-intensive storage conditions, such as cold-chain systems required for temperature-sensitive medications. However, for 3D printing to be widely adopted in the pharmaceutical sector, a significant transformation in both business models and strategic approaches will be necessary. Despite the fact that many of the opportunities presented by 3D printing remain unexplored, recent developments demonstrate the far-reaching impact AI is already having on the pharmaceutical industry. These impacts extend to precision medicine, drug discovery, clinical studies, formulation optimization, safety evaluation, and supply chain management. AI can enhance the efficiency of drug formulation and delivery. Models powered by AI can predict drug release and absorption, optimizing formulations for efficacy and targeted distribution. Pharmaceutical delivery devices and systems are increasingly leveraging AI to improve patient adherence and convenience. Clinical trials are also being improved through AI, which enhances productivity and reduces costs. AI algorithms support patient recruitment, trial population selection, and trial protocol optimization. In addition, AI can track and evaluate sample data in real time, enabling more flexible trial designs and faster decision-making. Pharmaceutical supply chains are being optimized through AI to improve manufacturing, inventory control, and delivery, forming an integral part of comprehensive supply chain management. AI and ML hold the potential to revolutionize drug administration, especially in the treatment of infectious diseases. This prospective outlook presents exciting opportunities. Nevertheless, it is vital to address challenges related to data quality, legal frameworks, and ethical standards to fully realize AI's potential in pharmaceutical development. AI-driven innovations, on the other hand, have the capacity to transform the pharmaceutical industry and significantly improve patient health outcomes in the coming decades, provided that progress continues through active collaboration among industry stakeholders, academic institutions, and regulatory authorities.

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The authors declare no conflicts of interest.

### Author contributions

Conceptualization: RAK, PS, and SS; Supervision: PS and SS; Writing-original draft: RAK, GK; Writing-review & editing: All authors. All authors have read and approved the final manuscript.

### Ethics approval and consent to participate

Not applicable.

### Consent for publication

Not applicable.

#### Availability of data

Not applicable.

#### Further disclosure

The authors employed ChatGPT to improve the language and readability of the manuscript and have reviewed and edited the paper, as needed, following usage of the AI tool. The authors will take full responsibility for the content of the publication.

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