

Emerging Frontiers of 3D Printing in Drug Delivery and Tissue Regeneration

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Abstract: In the fields of pharmaceutical sciences and biomedical engineering, additive manufacturing—also known as three-dimensional (3D) printing—has emerged as a revolutionary technology [1]. This technology, in contrast to traditional manufacturing methods, makes it possible to produce complicated dosage forms, biomedical implants, tissue scaffolds, and customized drug delivery systems with exact control over drug dose and release characteristics [3]. Its uses in organ restoration, tissue engineering, wound healing, oral dosage forms, and ocular medication administration have increased recently. Additionally, living tissues and organ models for drug screening and regenerative medicine have been made possible by 3D bioprinting. Notwithstanding its encouraging promise, issues with pricing, scalability, and regulatory approval still exist. This article examines the leading pharmaceutical company and emphasizes its contribution to the advancement of regenerative medicine and sophisticated drug delivery technologies.

Keywords: 3D Printing, Additive Manufacturing, Tissue Engineering, Personalized Medicine, Bioprinting.

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I. INTRODUCTION

By depositing materials sequentially in accordance with computer models, three-dimensional printing is an advanced manufacturing process that creates items[4].In pharmaceutical sciences, this technology offers significant advantages over traditional manufacturing methods by enabling precise control over dosage, geometry, and drug release patterns [5]. The ability to fabricate patient-specific formulations has made 3D printing a promising approach for personalized medicine [6]. Additionally, the technology enables the production of complex drug delivery devices, implants, and scaffolds that cannot be easily produced by conventional methods. The pharmaceutical industry has increasingly explored 3D printing for developing customized drug delivery systems, improving drug bioavailability, and enhancing therapeutic outcomes. Beyond drug delivery, 3D

printing also plays a critical role in tissue engineering, regenerative medicine, and biomedical device fabrication. The main uses of 3D printing technology in the biomedical and pharmaceutical industries are covered in the sections that follow.

In recent years, the rapid advancement of additive manufacturing technologies has significantly expanded the possibilities of pharmaceutical product design and development. Traditional pharmaceutical manufacturing generally follows a “one-size-fits-all” approach, which may not be suitable for patients with varying physiological conditions, age groups, and disease states [7]. In contrast, 3D printing enables the fabrication of individualized dosage forms with tailored drug release profiles, dosage strengths, and geometrical designs [8]. This flexibility makes it

especially helpful for elderly and young patients, who frequently need customized dosage schedules.

Furthermore, the integration of computer-aided design (CAD) with advanced printing techniques allows researchers to develop sophisticated drug delivery systems with

controlled porosity, internal structures, and drug distribution patterns [9]. These characteristics improve drug stability, dissolution rate, and therapeutic efficiency. As a result, 3D printing has gained considerable attention from researchers and pharmaceutical industries worldwide as a potential tool for the next generation of drug delivery technologies.

II. UTILIZING 3D PRINTING IN DOSAGE FORMS FOR PHARMACEUTICALS

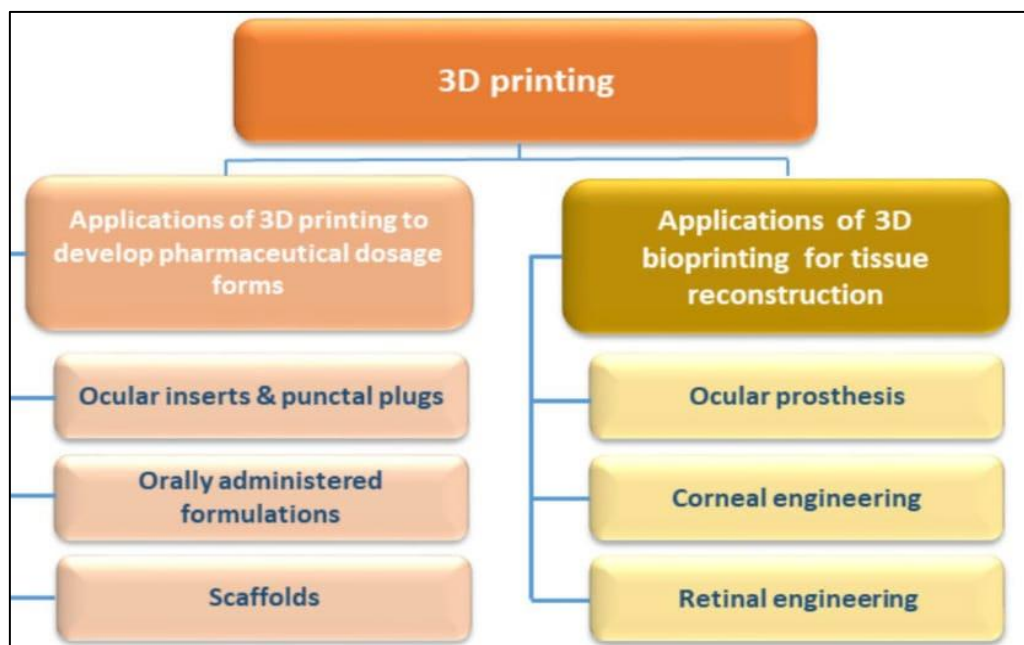


Fig 1 Utilizing 3D Printing in Dosage Forms for Pharmaceuticals

➤ Ocular Drug Delivery Systems

Conventional ocular dosage forms such as eye drops suffer from poor bioavailability due to rapid tear drainage, blinking, and limited corneal residence time [10]. To overcome these drawbacks, 3D printing technology provides a promising approach by enabling the fabrication of patient-specific ocular inserts and punctal plugs with controlled geometry, drug loading, and release profiles [11]. Using computer-aided design, complex and tailored dosage forms can be produced layer by layer with high precision. This technology supports personalized medicine by adjusting size, shape, and drug concentration according to patient needs. Moreover, 3D printing allows the use of biodegradable and biocompatible polymers that enhance ocular residence time and therapeutic efficacy [12]. Therefore, in the treatment of ocular illnesses, 3D-printed ocular dosage forms offer a novel substitute for traditional eye drops by increasing patient compliance, lowering dosing frequency, and improving medication retention.

• 3D-Printed Ciprofloxacin HCL Ocular inserts

3D printing technology has been utilized to fabricate drug-loaded ocular inserts designed to improve drug retention and therapeutic efficiency in ocular diseases. The production of patient-specific ciprofloxacin hydrochloride ocular inserts was achieved using fused deposition modeling (FDM) combined with hot-melt extrusion [13]. Hydroxypropyl cellulose (KluCEL™) was selected as the polymer due to its biodegradable and bioadhesive properties [14]. The produced

inserts showed no drug-polymer incompatibility, a smooth surface shape, and good mucoadhesive strength. The drug was found in an amorphous form and showed prolonged release for up to 24 hours, according to studies assessing drug-excipient compatibility, thermal properties, drug content, and in vitro drug release [15]. Furthermore, the formulation demonstrated effective antibacterial activity and enhanced trans-corneal penetration compared with conventional eye drops. Stability studies indicated that the formulation remained stable for three months at room temperature, allowing once-daily administration for the treatment of bacterial ocular infections [16].

• Ganciclovir-Loaded Ocular Systems

The combination of ultra-flexible nanovesicles and 3D printing technology has been explored as a promising strategy for treating cytomegalovirus (CMV) retinitis, a severe ocular infection that commonly affects immunocompromised patients such as those with HIV/AIDS or organ transplant recipients. Conventional therapies frequently exhibit low ocular bioavailability because of restricted corneal permeability and quick drug removal. Therefore, to increase therapeutic efficacy, sophisticated drug delivery devices are required [12]. This method used ultra-flexible glycerosomes (phospholipids + glycerol + water) to encapsulate ganciclovir. Its optimization and preparation were carried out using Design-Expert® software.

[17, 18]. These vesicles were incorporated into a polylactic acid (PLA)-based 3D-printed ocular insert designed using CAD software [2]. The biodegradable insert provided controlled and sustained drug release, improving drug stability and delivery to ocular tissues. Confocal laser scanning microscopy showed enhanced corneal penetration, while pharmacokinetic studies in rabbits demonstrated that therapeutic drug levels in the aqueous humor were maintained for up to five days. Histopathological analysis confirmed good biocompatibility without ocular irritation [17]. Overall, this 3D-printed ganciclovir-loaded ocular system offers a promising non-invasive platform for cytomegalovirus (CMV) retinitis treatment by improving drug penetration, prolonging release, and reducing dosing frequency.

- *Dexamethasone-Loaded Punctal Plugs*

To improve ocular hydration and maintain more tear film, punctal plugs—tiny biological devices—are placed into the tear ducts. Digital light processing (DLP) 3D printing technology was used to create punctal plugs filled with dexamethasone [19]. Semi-interpenetrating polymer networks were made with polyethylene glycol (PEG) and polyethylene glycol diacrylate (PEGDA) [20]. The study showed that the medication release time was extended to more than 21 days by increasing the content of polyethylene glycol diacrylate. BALB/3T3 fibroblast cells were used in cell compatibility experiments, which demonstrated satisfactory cell viability [21]. To increase biocompatibility, more post-curing and cleaning procedures were suggested.

III. 3D PRINTING FOR ORAL DRUG DELIVERY SYSTEMS

- *Immediate-Release Tablets*

3D printing has been applied in the development of immediate-release oral tablets with improved drug dissolution characteristics [22]. Lopez-Vidal and co-workers reported the incorporation of albendazole nanocrystals into 3D-printed tablets using melting solidification printing technology [23]. Polyethylene glycol and propylene glycol were used as carrier materials. The inclusion of nanocrystals significantly enhanced drug dissolution compared to conventional tablets. Another study utilized fused deposition modeling to produce personalized hydrocortisone tablets for children with congenital adrenal hyperplasia. Drug content was monitored using near-infrared spectroscopy to ensure compliance with pharmacopeial limits. This approach demonstrated the feasibility of producing personalized pediatric medications using 3D printing technology [24].

- *Colon-Targeted Drug Delivery Systems*

3D printing technology has also been used to fabricate colon-specific drug delivery systems [25]. One study developed a pH-responsive polymeric structure for delivering N-acetylglucosamine to the colon. Tablet shells were composed of Eudragit® FS100 and polylactic acid, while the core contained methyl cellulose hydrogel loaded with the drug [26].

The optimized formulation demonstrated excellent printability, mechanical stability, and controlled drug release

kinetics. This approach supports the concept of personalized medicine by allowing the delivery of different drug combinations in customized doses [27]. Another example involved the fabrication of budesonide-loaded tablets with a pill-in-pill configuration for treating inflammatory bowel disease. These tablets demonstrated accurate dosing and effective colon-targeted drug release compared with conventional formulations [28].

IV. TRENDS OF 3D PRINTING IN SCAFFOLD FABRICATION

3D-printed scaffolds are custom-designed, biocompatible structures fabricated using additive manufacturing to support tissue engineering, bone regeneration, and drug delivery [29]. These scaffolds, which frequently use materials like polymers, ceramics, or hydrogels, imitate the extracellular matrix (ECM) by offering exact porosity, interconnectivity, and structural support for cell growth and tissue remodeling.

Scaffold-Based Strategies for Tissue Repair and Cutaneous Regeneration;

The creation of scaffolds for wound healing and skin tissue regeneration has been extensively researched using 3D printing technology. By combining electrospinning and 3D printing, a layered scaffold structure that resembles the hierarchical organization of skin was created.

- *The Scaffold Consisted of Three Layers:*

- A polyurethane nanofibrous top layer preventing microbial penetration
- A porous middle layer containing quaternized chitosan and silver nanoparticles providing antibacterial activity
- A bottom nanofibrous layer containing mupirocin to enhance tissue regeneration

The developed scaffold demonstrated excellent antibacterial activity against *E. coli* and *Staphylococcus aureus* [30]. High cell adhesion, improved angiogenesis, and accelerated wound healing were also observed.

- *Scaffolds for Bone Disease Treatment*

3D-printed polymeric scaffolds have been investigated for the localized delivery of anticancer drugs in bone cancer treatment. Polyurethane-based scaffolds containing doxorubicin were synthesized using polycaprolactone-polyethylene glycol polymers. Hydroxyapatite nanoparticles were incorporated to enhance bone regeneration [31]. The scaffold exhibited slow hydrolytic degradation and redox-responsive drug release in simulated tumor environments. This strategy allows localized chemotherapy at the surgical resection site while simultaneously promoting bone regeneration [31].

- *Scaffolds for Intravaginal Drug Delivery*

Bacterial vaginosis is a common recurrent infection that often requires prolonged antibiotic therapy. To overcome limitations associated with conventional treatments,

metronidazole-loaded silicone scaffolds were developed using extrusion-based 3D printing. These scaffolds demonstrated high structural stability, minimal swelling, and sustained drug release for up to **14 days** in simulated vaginal fluid. Cytotoxicity studies confirmed minimal toxicity to keratinocyte cells, suggesting that this system could be a promising approach for local intravaginal drug delivery [32].

V. 3D BIOPRINTING AND MEDICAL APPLICATIONS

➤ Ocular prostheses

3D bioprinting is used to manufacture artificial eyes (ocular prostheses) for individuals who have lost an eye. The prosthesis is custom-designed for each patient using digital modeling to ensure proper fit and appearance. It is fabricated through a layer-by-layer printing process using safe and biocompatible materials. To evaluate safety, several tests are performed, including cytotoxicity tests to determine whether the material harms cells, systemic toxicity tests to assess its effects on the body, and sensitization tests to check for possible allergic reactions. The results of these tests have

shown that the prosthesis is safe and biocompatible. Clinical studies further reported no eye irritation and no allergic responses in patients using the prosthesis. Therefore, 3D printing technology plays an important role in personalized eye rehabilitation and significantly improves patients' confidence and overall quality of life [33].

VI. CORNEAL ENGINEERING

Corneal disorders represent a leading cause of visual impairment and blindness across the globe. Currently, corneal transplantation using donor corneas is the most common treatment. However, the availability of donor corneas is limited, and complications such as graft rejection, infection, and high surgical costs may occur. Therefore, researchers have explored 3D bioprinting technology as a promising approach to fabricate artificial corneal tissues for regenerative medicine [34]. An innovative biofabrication method called 3D bioprinting enables the precise deposition of each layer of biomaterials and living cells to produce structures that mimic natural tissues.

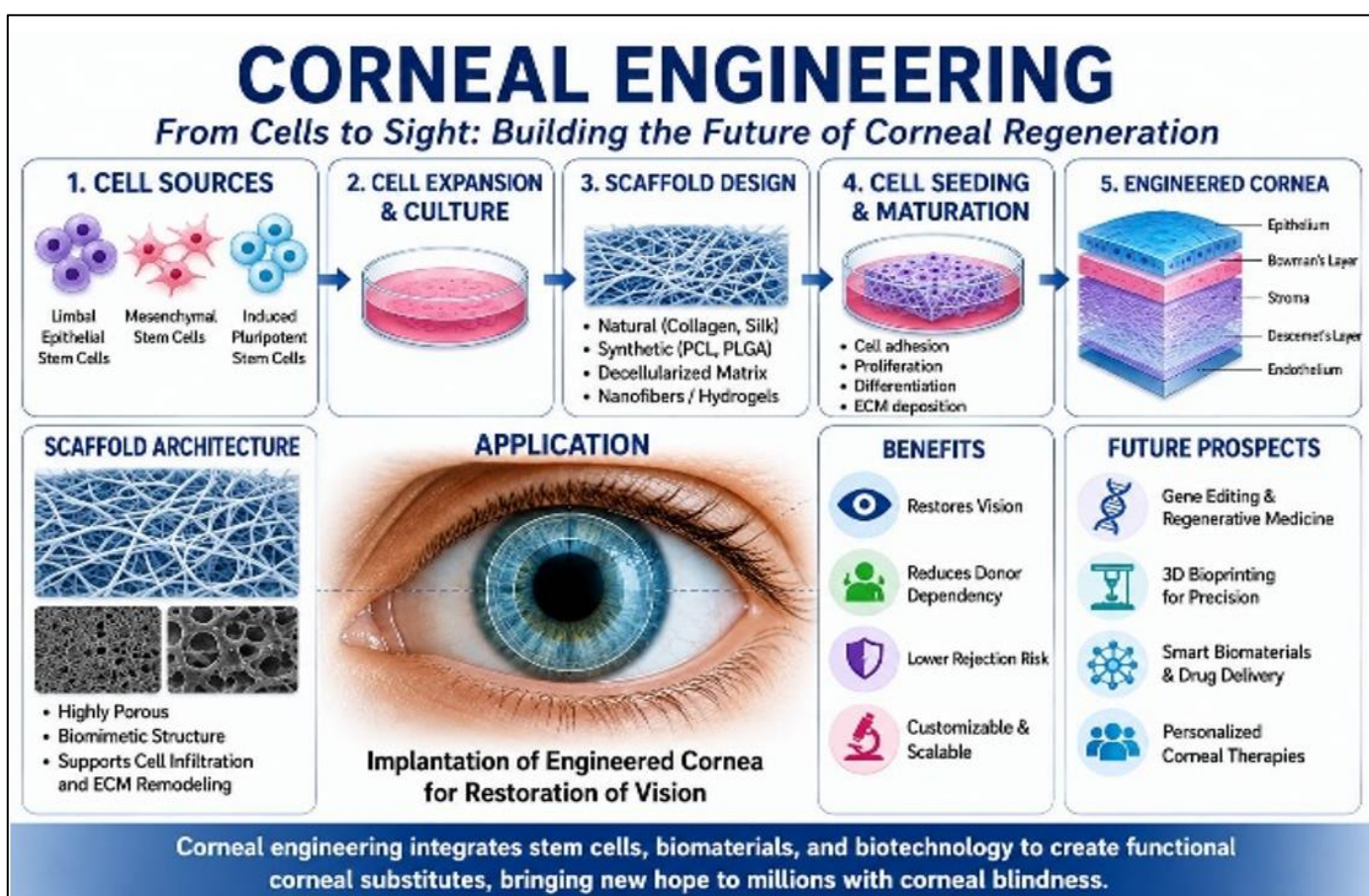


Fig 2 Corneal Tissue Engineering Strategy for Corneal Regeneration and Repair

In corneal tissue engineering, this technology is used to produce corneal stromal equivalents, which are structures that replicate the middle layer of the human cornea responsible for maintaining its transparency and mechanical strength [35]. To fabricate these structures, special printable biomaterials known as bioinks are used. Commonly used bioinks include collagen, alginate, gelatine, chitosan, and polyvinyl alcohol

(PVA). These biomaterials are selected because they possess important characteristics such as biocompatibility, transparency, mechanical stability, and the ability to support cell growth. Collagen is particularly important because it is the major structural protein present in the natural corneal stroma [36,37].

VII. RETINAL ENGINEERING

Retinal degeneration is a major cause of irreversible vision loss worldwide. Retinal cells, especially photoreceptors and retinal pigment epithelial (RPE) cells, are harmed by conditions such as retinitis pigmentosa, diabetic retinopathy, and age-related macular degeneration. The primary goal of current treatments is to delay the progression of the disease, but they are unable to restore lost vision. In order to create fake retinal tissues, 3D bioprinting is being investigated as a regenerative technique [38].

In one study, researchers developed a hybrid retinal model using 3D bioprinting. The structure included ARPE-19 cells, a polycaprolactone ultrathin film, and Y79 cells mixed with alginate/Pluronic bioink. A drop-by-drop printing method was used to place the cells in layers. The Y79 cells were seeded above the ARPE-19 cell layer to achieve uniform distribution [39].

For two weeks, the printed cells were examined under a microscope. Scanning electron microscopy and the live/dead assay were used to assess cell morphology and survival. The findings demonstrated that ARPE-19 cells spread, proliferated, and created a monolayer on the membrane [39]. The finished structure closely resembled the human retina and demonstrated good compatibility with cells, indicating that 3D bioprinting may eventually aid in the treatment of retinal ailments.

➤ *Spritam®: The First 3D Printed Drug*

In 2015, the U.S. Food and Drug Administration (FDA) approved Spritam® (Levetiracetam) [40], manufactured by Aprelia Pharmaceuticals. This drug is used for the treatment of epilepsy and seizures.

Spritam tablets have a porous structure that allows them to disintegrate rapidly with a small amount of liquid, making them suitable for patients [41] who experience swallowing difficulties. Spritam was the first demonstration that 3D printing technology can be successfully applied in pharmaceutical manufacturing [42].



Fig 3 Spritam®: The First 3D Printed Drug

➤ *Concept of Multi-Drug Pills (Polypills)*

One of the major advantages of 3D printing in pharmaceuticals is the possibility of producing **polypills** [43], which are tablets containing multiple drugs in different compartments.

This approach is particularly useful for patients with chronic diseases who require several medications daily.

Using 3D printing, scientists can design tablets where each drug has:

- A different dose
- A different release profile
- Separate layers or compartments

This technology allows the production of personalized medicines and simplifies complex treatment regimens [44].

Ongoing Research on 3D Printed Polypill for Cardiovascular Diseases

Researchers at the University College London (UCL) developed a 3D-printed polypill containing five different cardiovascular drugs [45]. These include:

- Aspirin
- Atenolol
- Ramipril
- Pravastatin
- Hydrochlorothiazide

Each drug in the tablet can be programmed to release at different times. This approach can significantly improve medication adherence in patients suffering from cardiovascular diseases. However, such multi-drug 3D-printed polypills [43] are currently in the research and development stage and have not yet been widely commercialized.

VIII. CONCLUSION

3D printing has revolutionized pharmaceutical sciences by enabling the development of personalized and patient-centric drug delivery systems. The technology offers precise control over drug dosage, formulation design, and release characteristics, thereby improving therapeutic effectiveness and patient compliance. Various printing techniques have been successfully applied to fabricate tablets, implants, transdermal systems, and targeted drug delivery platforms [43]. Despite significant progress, challenges related to regulatory approval, manufacturing scalability, material selection, and quality control still need to be addressed. Advances in biomaterials, digital technologies, and artificial intelligence are expected to further enhance the capabilities of pharmaceutical 3D printing. Overall, 3D printing represents a promising and innovative approach that is transforming drug development and manufacturing, with the potential to play a crucial role in the future of precision medicine and advanced healthcare.

➤ *Conflict of Interest:*

It is hereby declared that there is no conflict of interest among authors.

➤ *Acknowledgement:*

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