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State-of-the-art research progress and emerging strategies in digital light processing (DLP) bioprinting for skin regeneration

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Article ID: IJB026220217

Citation: Fahad FI, Ahn M, Kim BS. State-of-the-art research progress and emerging strategies in digital light processing (DLP) bioprinting for skin regeneration. *Int J Bioprint*. 2026. doi: 10.36922/IJB026220217

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AccScience Publishing

REVIEW ARTICLE

Volume X Issue X (2026)

doi: 10.36922/IJB026220217

State-of-the-art research progress and emerging strategies in digital light processing bioprinting for skin regeneration

Running title: DLP-based bioprinting for skin engineering

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Citation: Fahad FI, Ahn M, Kim BS. State-of-the-art research progress and emerging strategies in digital light processing (DLP) bioprinting for skin regeneration. *Int J Bioprint*. 2026. doi: 10.36922/IJB026220217

Received: May 26, 2026

Revised: June 24, 2026

Accepted: June 26, 2026

Published online: June 29, 2026

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Abstract

Skin injuries including burns, chronic wounds, and diabetic ulcers present significant clinical challenges due to impaired healing, high risk of infection, and limited efficacy of conventional transdermal patches. Owing to recent advances in biomaterials and regenerative medicine, skin-repair strategies are currently focused on engineered patches that better mimic the native tissue structure and function. Particularly, digital light processing (DLP)-based 3D printing is a powerful platform for fabricating high-resolution personalized skin patches with precise architectural control than other conventional approaches. The rapid layer-by-layer photopolymerization of hydrogel-based materials enables the creation of mechanically compliant biocompatible constructs that support cell proliferation, immunomodulation, angiogenesis, and extracellular matrix remodeling. Furthermore, DLP technology enables controlled therapeutic delivery by facilitating the integration of advanced functionalities such as microneedle arrays, vascularized architectures, and stimuli-responsive systems. This review systematically discusses the fundamental principles of DLP printing, key parameters that govern printing fidelity, recent progress in bioink development, and emerging applications of DLP-fabricated skin patches in wound healing and skin regeneration. Additionally, current challenges and future perspectives are highlighted to guide the continued development and clinical translation of DLP-based regenerative skin therapies.

Keywords: Digital light processing; 3D printing; Transdermal drug delivery; Personalized patches; Skin regeneration; Wound healing

1. Introduction

The skin is the largest organ of the body, and it functions as a highly organized and multifunctional biological system that directly interfaces with the external environment. It comprises a complex assembly of structural proteins (e.g., collagen and elastin), cells, various plasma proteins and polypeptide constituents, and a substantial fraction of water to form a matrix, within which is embedded an extensive network of nerve fibers, blood vessels, and lymphatic nodes that support physiological signaling, nutrient exchange, and immune cell infiltration.^{1,2} Critically, this matrix is not architecturally uniform but is organized into three hierarchically distinct layers — the epidermis, dermis, and subcutaneous tissue — each characterized by unique cell populations, extracellular matrix compositions, and mechanical properties that collectively enable the skin's integrated functions, including mechanical strength, elasticity, metabolic activity, sensory capability, and physiological activity, to sustain overall physiological homeostasis through barrier protection, thermoregulation, immunological defense, and the perception of environmental stimuli.³⁻⁵ However, injuries such as burns, chronic wounds, diabetic ulcers, and surgical trauma severely compromise this protective, multi-layered organ, causing delayed tissue repair, high risk of infection, and substantial socioeconomic impact.^{6,7} Traditional wound management strategies such as gauze dressings and topical ointments are limited in their ability to provide a moist environment, promote cellular migration, and precisely deliver bioactive agents, and critically, they are entirely incapable of reproducing the stratified, hierarchical organization of native skin. These limitations often result in prolonged healing times, scarring, and poor functional recovery.⁸⁻
¹⁰ Recent progress in biomedical engineering in the development of advanced biomaterials such as natural polymers, synthetic hydrogels, and decellularized extracellular matrix (dECM)-based bioinks that offer tunable mechanics, biocompatibility, and controlled release of bioactive agents has catalyzed a regenerative approach for skin repair.¹¹⁻¹⁴ Nevertheless, conventional scaffold fabrication techniques used to process these biomaterials, including solvent casting, freeze-drying, and electrospinning, typically yield compositionally uniform constructs with limited spatial resolution and control, rendering them insufficient to replicate the discrete mechanical and biochemical gradients present across the epidermal, dermal, and subcutaneous strata of native skin. Three-dimensional (3D) printing has emerged to overcome these structural limitations by enabling spatially defined, layer-by-layer material deposition, allowing independent engineering of

compositionally and mechanically distinct zones within a single construct that more faithfully mimic the native multi-layered skin architecture. Accordingly, these advanced biomaterials have been increasingly coupled with 3D printing technologies to advance therapeutic strategies by enabling precise, customizable fabrication of transdermal patches and skin substitutes that closely mimic the native ECM architecture for promoting tissue regeneration and improving the effectiveness of engineered skin patches.¹⁵⁻¹⁷

Among the available 3D printing modalities, digital light processing (DLP) is a vat photopolymerization-based technique currently gaining significant attention for the fabrication of advanced skin patches, owing to a distinct set of advantages over other conventional 3D printing approaches. Conventional bioprinting approaches possess several inherent limitations that restrict their ability to recapitulate the complex microstructure of native skin. For instance, extrusion-based bioprinting, the most widely used technique, is constrained by relatively low printing resolution (typically 200–500 μm), shear-induced stress on encapsulated cells and bioactive agents, and limited capability to reproduce fine microscale features. Similarly, inkjet bioprinting enables high-throughput deposition of low-viscosity bioinks but suffers from nozzle clogging, restricted material compatibility, and insufficient mechanical robustness of the resulting constructs. Although stereolithography (SLA) affords high fabrication precision, its point-wise laser scanning constrains throughput for large or complex constructs, while extended photopolymerization exposure can adversely affect cell viability and compromise the integrity of fragile biomolecules. In contrast, DLP uses a digital micromirror device (DMD) to simultaneously cure entire layers of photosensitive material.^{18,19} This approach accelerates the fabrication process (up to 1 mm^3/s) while reducing mechanical stresses on the material. This process results in smoother surfaces that minimize irritation and enhance cell viability and biochemical stability, which are essential for skin-contact applications. DLP-based patches are often infused with hydrogel networks to create a hydrated biocompatible microenvironment that promotes cell proliferation, angiogenesis, and ECM remodeling in skin tissue regeneration.²⁰⁻²² Moreover, DLP shows versatility in fabricating various products such as microneedle (MN) arrays, vascularized constructs, stimuli-responsive dressings and theragnostic biomedical patch which improve the efficiency and precision of drug delivery, and integrate functionalities that support the various stages of wound healing in skin patches for notably superior skin regeneration.²³⁻²⁵

2. Objective & Methodology

This review aims to provide a comprehensive analysis of DLP-based skin patches & drug delivery techniques for skin regenerative application. It systematically examines the fundamental printing mechanisms underlying DLP technology, with particular emphasis on light-mediated photopolymerization and factors influencing structural fidelity and resolution, summarizes recent innovations in bioink development, especially the advancement of bioactive and functionalized hydrogel systems designed for enhanced skin regeneration. In addition, emerging therapeutic delivery strategies integrated within DLP-fabricated constructs are evaluated, highlighting controlled drug release, immunomodulation, and multifunctional patch design for skin regeneration. The systematic literature search was performed using PubMed, Google Scholar & Cochrane library to identify peer-reviewed articles. The search included keywords such as transdermal patches, transdermal drug delivery, DLP bioprinting scaffolds, wound healing, diabetic wound healing, skin regeneration, bioinspired patches, DLP-based drug delivery and stimuli-responsive drug delivery. Boolean operators (AND, OR) were used to refine the search strategy. Studies were included if they (1) evaluated DLP-based transdermal patches fabrication & (2) DLP-based transdermal patches for skin regeneration (e.g., wound healing, diabetic wound healing, psoriasis, atopic dermatitis, acne vulgaris) applications.

3. Design requirements of regenerative skin patches

The development of regenerative skin patches requires a comprehensive understanding of the structural, mechanical, biological, and functional characteristics of native skin. Unlike conventional wound dressings that primarily provide physical protection, advanced regenerative patches are designed to actively participate in the healing process by recreating key features of the native tissue microenvironment. Given the hierarchical organization and multifunctional nature of skin, successful regenerative systems must integrate biomimetic architectures, appropriate mechanical properties, controlled biological signaling, and responsive functionalities to support tissue reconstruction and functional restoration.^{26,27}

3.1. Structural, mechanical and morphological requirements

As skin is highly organized multilayered organ consisting of the epidermis, dermis, and hypodermis, each characterized by distinct cellular compositions, extracellular matrix (ECM)

organizations, and physiological functions. Therefore, regenerative skin patches should be designed to mimic the hierarchical architecture and physicochemical gradients present within native skin.^{5,28}

A critical structural requirement is the incorporation of an interconnected porous network capable of facilitating cell infiltration, nutrient transport, oxygen diffusion, and metabolic waste removal. Scaffold porosity significantly influences cellular behavior and tissue regeneration. Previous studies have demonstrated that pore sizes ranging from 5–15 μm support fibroblast infiltration, and those between 20–125 μm facilitate dermal tissue regeneration. Furthermore, gradient pore architectures have attracted considerable attention because they more closely replicate the heterogeneous microenvironment of native skin and provide spatial cues that enhance cellular migration, tissue integration, and re-epithelialization. In another study, high scaffold porosity (greater than 60%) was shown to enhance skin regeneration by improving nutrient supply and oxygen diffusion. Moreover, maintaining a moist environment is essential for promoting cell infiltration and supporting nutrient transport between the skin bed and the scaffold, which is strongly influenced by pore size and porosity.²⁹⁻³²

The mechanical properties of regenerative skin patches play a fundamental role in determining their clinical performance and biological functionality. Native skin exhibits viscoelastic behavior, allowing it to undergo continuous deformation while maintaining structural integrity. Therefore, engineered skin substitutes should possess mechanical properties that closely match those of the surrounding tissue. The elastic modulus of healthy human skin typically ranges between 4.5 and 8 kPa, although considerable variation exists depending on anatomical location and age. Scaffolds exhibiting comparable mechanical characteristics are better able to withstand physiological stresses while maintaining intimate contact with the wound surface. Mechanical mismatch between implanted materials and host tissue can impair cellular integration, induce inflammation, and compromise healing outcomes. Beyond simple mechanical matching, increasing evidence suggests that cells actively respond to the stiffness of their surrounding microenvironment through mechanotransduction pathways. This phenomenon, known as durotaxis, describes the tendency of cells such as fibroblasts, keratinocytes, and endothelial cells to migrate along stiffness gradients. Moreover, several studies have shown that direct contact with the wound bed and the topographical cues of engineered patches can induce mechanobiological pathway activation, thereby promoting

skin regeneration more effectively than flat, film-like structures. Therefore, incorporating controlled mechanical gradients with balanced pore size and porosity into regenerative patches may therefore provide a powerful strategy for directing nutrients infiltration, cellular migration, tissue organization, and wound closure.³¹⁻³⁴

3.2. Biological and functional regulation

Beyond providing structural support, regenerative skin patches should actively regulate the biological processes associated with wound healing. Tissue regeneration is orchestrated through complex interactions among cells, growth factors, cytokines, and extracellular matrix components.^{35,36} Consequently, advanced biomaterials increasingly function as bioactive platforms capable of delivering biological signals by a controlled therapeutic delivery. Skin tissue regeneration involves a complex cascade of cellular and biochemical events, and chronic or impaired conditions may result from the dysregulation of these biological activities. Skin patches incorporating exogenous growth factors and cytokines can effectively guide cellular behavior and enhance tissue repair. Key growth factors, including vascular endothelial growth factor (VEGF), fibroblast growth factor (FGF), and platelet-derived growth factor (PDGF), play critical roles in angiogenesis, cell proliferation, and tissue remodeling during regeneration. However, successful therapeutic outcomes depend not only on the presence of these biomolecules but also on their precise spatial localization and temporal delivery. Therefore, engineered scaffolds capable of controlled and sustained release are essential to coordinate the complex sequence of events involved in skin tissue regeneration.^{29,32,35}

Also, skin tissue is highly susceptible to microbial invasion and pathogen infection, particularly during the early stages of injury. Therefore, effective elimination of pathogens during the inflammatory phase is essential. However, prolonged or excessive inflammation can impair the healing process and delay tissue regeneration.³⁷ Consequently, proper immunomodulation is crucial, particularly the transition of macrophages from the pro-inflammatory M1 phenotype to the anti-inflammatory M2 phenotype. Engineered scaffolds should be designed to support this phenotypic shift, thereby promoting a balanced immune response and facilitating efficient skin tissue regeneration. Moreover, damaged skin tissue is associated with a high level of reactive oxygen species (ROS) generation, which can hinder tissue regeneration and prolong the

inflammatory phase. Excessive ROS not only causes oxidative stress but is also closely interconnected with the regulation of inflammation and anti-inflammatory responses. Therefore, it is essential to consider these factors in scaffold design, ensuring effective ROS scavenging and balanced immunomodulation. Such strategies can help reduce oxidative damage, regulate inflammation, and ultimately enhance skin tissue regeneration.³⁸⁻⁴⁰ Another important factor to consider is hypoxia, which can significantly impair skin tissue regeneration. Oxygen deficiency is a major limitation in chronic and ischemic conditions, where inadequate vascularization compromises tissue survival and regenerative capacity. Therefore, it is crucial to incorporate strategies such as oxygen-releasing particles, hemoglobin-based carriers during the scaffold development for skin regeneration. These approaches can enhance cellular metabolism, promote angiogenesis, and ultimately accelerate tissue regeneration.⁴¹⁻⁴³

4. Conventional approach for skin patch development.

Conventional wound dressings, including gauze, cotton wool, and adhesive bandages, remain the most widely used materials for wound management due to their simplicity, low cost, and accessibility. Their primary function is to provide a physical barrier against microbial contamination while absorbing wound exudates and maintaining basic wound coverage. However, these materials are largely passive and lack the biological and structural functionalities required to actively support tissue regeneration. Furthermore, conventional dressings often exhibit poor conformability to irregular wound geometries and may adhere to newly formed tissue, resulting in pain and secondary tissue damage during removal. Consequently, their ability to facilitate complete skin regeneration remains limited.^{44,45} To overcome these limitations, advanced fabrication technologies have been developed to better mimic the native skin microenvironment. Electrospinning has attracted considerable attention because it produces nanofibrous scaffolds that closely resemble the architecture of the extracellular matrix (ECM), thereby supporting cell adhesion, migration, and proliferation. The high porosity and surface-area-to-volume ratio of electrospun matrices facilitate nutrient exchange and cellular interactions. Nevertheless, electrospinning is primarily suitable for producing thin membrane-like structures and remains limited in its ability to fabricate thick, complex three-dimensional constructs required for full-thickness skin regeneration.⁴⁶⁻⁴⁸

To address this, additive manufacturing technologies, extrusion-based bioprinting is the most widely utilized owing to its versatility and compatibility with a broad range of biomaterials and cell-laden bioinks. The technique enables the deposition of highly viscous materials and supports the fabrication of large-scale tissue constructs. Therefore, extrusion printing is generally constrained by relatively low resolution and slow fabrication speed. In addition, the shear stress generated during extrusion can adversely affect cell viability and biological functionality, while nozzle clogging may compromise printing accuracy and reproducibility.⁴⁹⁻⁵¹ Similarly, inkjet bioprinting offers rapid and cost-effective fabrication through droplet-based deposition of biomaterials. Although suitable for high-throughput applications, its dependence on low-viscosity bioinks limits material selection and often results in constructs with inadequate mechanical strength and structural complexity for advanced skin tissue engineering applications.^{52,53} Therefore, light-based fabrication techniques have emerged as promising alternatives for improving printing resolution and structural fidelity. Stereolithography (SLA) utilizes a focused laser beam to selectively photopolymerize photosensitive materials and can generate constructs with excellent surface quality and dimensional accuracy. However, because the laser must sequentially scan each point within a layer, the fabrication process is relatively slow, particularly for large or geometrically complex structures. This limitation reduces its practicality for rapid production of personalized skin substitutes. Moreover, the prolonged exposure to laser irradiation and photopolymerization conditions can negatively affect cell viability and compromise the stability of fragile biomolecules.^{54,55}

In contrast, digital light processing (DLP) bioprinting has emerged as one of the most promising technologies for skin regeneration owing to its ability to combine high resolution, rapid fabrication, and excellent structural fidelity. Unlike SLA, digital light processing (DLP) utilizes a digital micromirror device (DMD) to project patterned light and cure entire layers simultaneously, markedly enhancing fabrication speed (up to $1 \text{ mm}^3 \text{ s}^{-1}$) while preserving microscale precision, thereby offering advantages for cell-laden patches and the delivery of fragile biomolecules. Furthermore, the nozzle-free nature of DLP eliminates issues associated with shear-induced cell damage and nozzle clogging commonly observed in extrusion-based systems. The high spatial resolution of DLP enables the fabrication of sophisticated skin-relevant architectures, including multilayer skin constructs, microneedle arrays, vascularized microchannel networks, and patient-

specific wound dressings. Additionally, DLP is highly compatible with photocurable hydrogel-based bioinks, allowing precise control over construct geometry, mechanical properties, and biological functionality. Collectively, these advantages position DLP as a particularly attractive platform for the development of next-generation regenerative skin patches capable of addressing the structural, biological, and functional requirements of skin tissue regeneration.^{21,56,57} The comparison between several fabrication process of skin patch is summarized in **Table 1**.

5. Fundamentals of DLP Bioprinting for skin regeneration.

5.1. DLP printing setup & mechanism

DLP-printer Setup: DLP apparatus comprises several interdependent components engineered to facilitate precise photopolymerization. The core is a high-resolution light source, which is typically an ultraviolet (UV) or visible light-emitting diode (LED) projector integrated with a digital DMD chip that modulates light wavelengths between 365 and 460 nm, to initiate radical polymerization reactions. Next, it contains a photocurable bioink that is held in a resin vat fabricated from transparent oxygen-permeable materials such as polydimethylsiloxane (PDMS) or fluorinated ethylene propylene (FEP) to ensure uniform light exposure and prevent early curing at the interface. Additionally, a motorized build platform is immersed in the vat and incrementally raised (typically, 25–100 μm per layer) to enable sequential layer formation. The projected light is focused using optical components such as lenses and mirrors to enhance the resolution. Finally, a control software such as CAD-based slicers or custom algorithms are used to transform the 3D models into binary masks for each layer (**Fig 1a**).

For biofabrication applications, the DLP system is typically enclosed in a sterile environment to minimize contamination. Furthermore, the bioink is supplemented with photo-initiators (PIs) such as lithium phenyl(2,4,6-trimethylbenzoyl) phosphonate (LAP) and photo absorbers (PAs) such as tartrazine to precisely control the curing kinetics and light penetration depth.^{4,58}

Printing mechanism: The DLP printing mechanism is based on the controlled photopolymerization of bioinks. The incident light initiates free-radical chain reactions to form covalently cross-linked bioink networks (**Fig 1c**). The first step of the process begins by slicing a digital 3D model (e.g., an STL file of a wound dressing) into two-dimensional (2D) cross sections, where each section represents an individual layer. Then, the DMD projector illuminates the bioink

with a patterned light mask, which activates the PIs to generate radicals that react with polymer chains such as poly-ethylene glycol-diacrylate (PEGDA) (**Fig 1d**). This process solidifies the layer within seconds (typically, 1–10 s). The second step involves the printed layer remaining attached to the build platform. In the third step, the build platform rises after each layer is cured, which allows the uncured bioink to flow into the voids via capillary action or mechanical agitation. This ensures uniform layer formation, and it prevents defects such as delamination or voids. This cycle is repeated until the complete structure is formed (**Fig 1b**).^{58,59} The post-processing steps include solvent rinsing to remove residual monomers, and additional secondary UV curing applied to enhance crosslink density, and lyophilization to modulate porosity and further refine the construct.⁶⁰

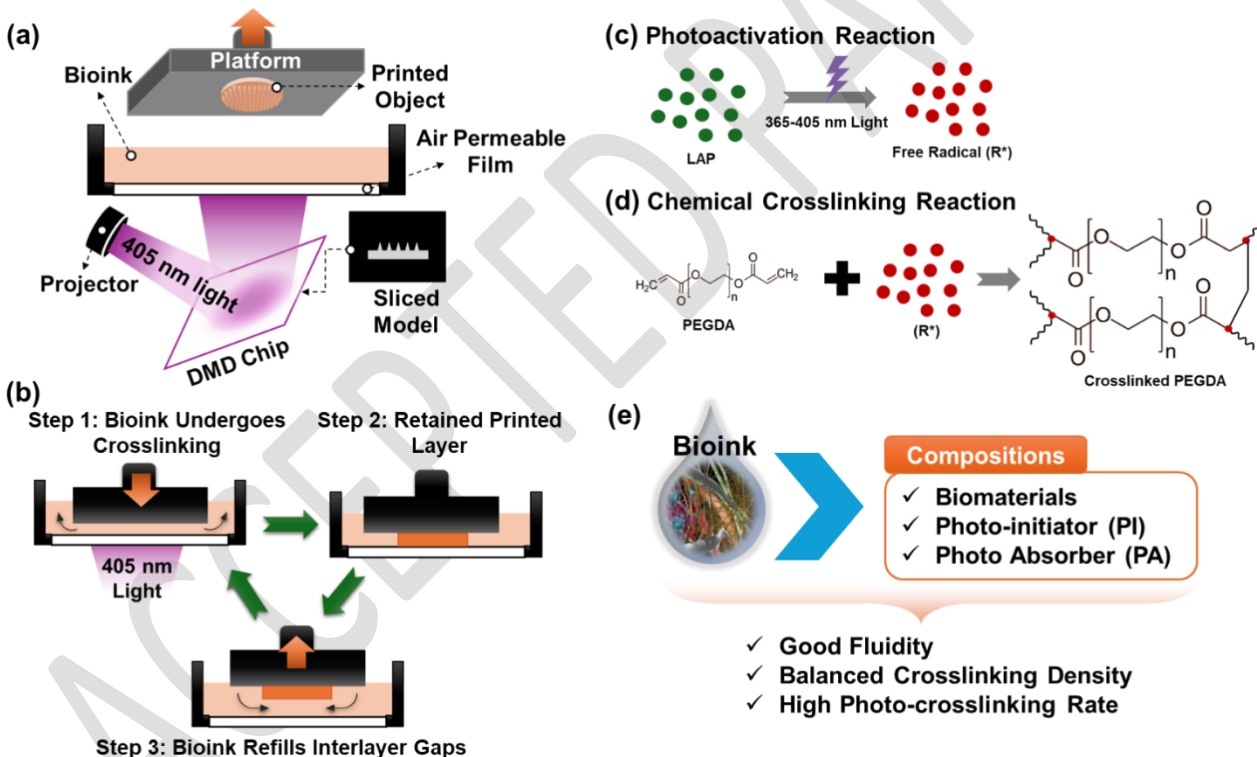


Figure 1. Overview of DLP bioprinting platform, photopolymerization, and bioink characteristics (a) DLP printer buildup; (b) Schematic representation of printing mechanism (arrow sign indicated the flow behavior of bioink); (c) Mechanism of photophysical reaction of photo-initiator; (d) Chemical crosslinking reaction mechanism; (e) Basic characteristics of bioink for DLP printing.

5.2. Design Strategies for High-Resolution DLP printing

5.2.1. Bioink criteria for High-fidelity DLP printing.

Bioink development is fundamental to the progress of DLP bioprinting. Particularly, the biocompatibility and functional performance of the bioink must be prioritized during early-stage formulation. Hydrogel-based bioinks are especially suitable for this purpose owing to their inherent biological compatibility and supportive interactions with cells. Therefore, bioinks must be photocurable bioactive materials that combine suitable physicochemical properties with strong biocompatibility to support accurate layer-by-layer polymerization while maintaining their intended biological function.⁶¹

An ideal photocurable bioink must satisfy several performance requirements to achieve high-fidelity printing. The bioink should exhibit sufficient fluidity to ensure its rapid flow at the uncured state into the gaps between the layers to enable efficient recoating and prevention of structural defects. Additionally, a high photo-crosslinking rate is essential during the initial curing step to solidify each layer within seconds and minimize printing time. Finally, a high cross-linking density must be maintained to achieve adequate stiffness and structural stability (**Fig 1e**). For example, PEGDA-based bioinks are widely recognized for their favorable printing characteristics—particularly because of their high fluidity, rapid photo-crosslinking rate, and ability to achieve a dense crosslinked network. Thus, PEGDA acts as an efficient photocurable matrix for DLP bioprinting. Yu et al. have shown that PEGDA exhibits both faster and higher crosslinking density compared with that of gelatin methacryloyl (GelMA) under DLP conditions, which results in improved printing fidelity and reliable structural formation. In addition to the choice of the base biomaterial, the concentration of PIs plays a critical role in determining DLP printability. Tong et al. have reported that increase in LAP concentration significantly accelerated the photo-crosslinking rate of silk methacrylate (SilMA) bioinks.^{58,62} Higher LAP levels reduce the curing time and enhance the polymerization efficiency, which improves layer formation during printing. Nevertheless, the use of higher PI concentrations necessitates careful consideration of biocompatibility because excessive LAP may induce cytotoxic effects. Therefore, optimizing LAP levels is essential to achieve a rapid curing performance balanced with cell viability and overall biological safety. Another important consideration in bioink design is the incorporation of PAs

such as tartrazine, orange G, and Maxgard® R1800. PAs function by competitively absorbing incident light and dissipating the energy as heat. This helps reduce light scattering in the X–Y plane and control curing depth along the Z axis.^{63,64} By lowering the intensity of scattered light below the polymerization threshold, PAs suppress unintended crosslinking outside the projected pattern, enabling the fabrication of fine features such as hollow channels and microscale pores (**Fig 2b & 2c**). For example, Huh et al.,⁶⁴ have shown that the inclusion of PAs significantly improved printing fidelity by reducing light scattering and enhancing spatial resolution during photopolymerization. **Fig 2b** shows the impact of PAs on printability. Bioinks without PAs exhibited pronounced over-curing; however, the incorporation of PAs effectively suppresses this over-curing behavior. Furthermore, PAs lowered the intensity of scattered light below the polymerization threshold to suppress unintended crosslinking outside the projected pattern, which enables the fabrication of fine features such as hollow channels and microscale pores by improving curing confinement and printing precision. However, the biocompatibility of PAs must be carefully evaluated because excessive PA concentrations could induce cytotoxic effects, which could adversely affect cell viability. In fact, optimal performance is typically achieved at PA concentrations of approximately 0.05–0.5%, which balances high printing resolution with adequate interlayer bonding and crosslinking density.⁶³

5.2.2. Relationships between rheological behavior and printability

Optimizing the printing parameters solely through experiments is both costly and time-consuming. Therefore, the printability of the bioink must be evaluated before printing. In this context, bioink must exhibit adequate flowability and rapid molecular diffusion for efficient photocuring because these enhance reaction kinetics and reduce the overall printing time.^{58,65–68} Among the formulation parameters, viscosity is particularly critical. DLP-printable bioinks typically require viscosities in the range of 0.2–10 Pa·s to ensure smooth processing. Resins with excessively high viscosity obstruct the recoating process and reduce printing resolution, whereas those with very low viscosity (<0.2 Pa·s) fail to properly wet the resin vat, which results in unstable and poorly controlled printing (**Fig 2d**).⁶⁵ Vazquez-Martel et al.,⁶⁶ assessed the suitability of functionalized vegetable oils for DLP printing by measuring the viscosity using a rotational viscometer. They found that olive and canola oils exhibited Newtonian behavior, whereas sunflower and soybean oils exhibit pronounced shear thinning. Nevertheless, all formulations exhibited a DLP-printable

viscosity range (0.2–10 Pa·s; shown in green color in **Fig 2e**). Furthermore, they noted that molecular diffusion reduced as viscosity increased, which slowed polymerization and increased the critical curing energy (E_c). This explains the higher E_c of soybean oil ink (18.49 $\text{mJ}\cdot\text{cm}^{-2}$) compared with those of sunflower- and canola-oil inks despite similar acrylate functionalization levels. Yu et al.,⁵⁸ found that fluidity improved as bioink viscosity decreased, which enabled rapid gap filling and prevented structural deformation during printing. Furthermore, 10% GelMA exhibited a viscosity comparable to that of commercial resins, which resulted in good flowability.

Furthermore, the smooth separation of the cured layer from the uncured bioink is essential to ensure accurate and reliable printing during the recoating process. In fact, after each layer is cured, the uncured bioink is required to readily refill the gap to enable the formation of the subsequent layer (**Fig 2f**). Hence, photorheological analysis is widely performed to evaluate the photo-crosslinking behavior of bioinks to predict their curing kinetics and mechanical evolution under light exposure.^{21,58,69-71} The storage modulus (G') represents the ability of the material to store elastic deformation energy, and it is indicative of its elastic stiffness; the loss modulus (G'') reflects energy dissipation during viscous deformation, and it corresponds to the viscous behavior of the material. During photo-crosslinking analysis, G' and G'' are continuously monitored as the bioink undergoes light-induced crosslinking. The point at which G' and G'' intersect is defined as the gel point (GP), and the time required to reach this point is referred to as the gelation time (GT). In DLP bioprinting, high printing resolution requires the efficient separation of the cured structure from the uncured bioink. This occurs when the crosslinked construct possesses high stiffness and uncured ink shows low viscosity. The parameter ΔG is defined as the difference in G' between the cured and uncured states, and it reflects the rheological contrast between the solidified structure and remaining hydrogel.⁵⁸ For example, Tong et al.,⁶² found that silk fibroin methacrylate (SilMA) showed improved printing fidelity at higher ΔG values than at lower ΔG values. Moreover, increase in bioink concentration increased the difference between G' and G'' , following the initiation of photopolymerization (**Fig 2h & 2i**). Typically, complete crosslinking is impractical, and experimental evidence indicates that optimal crosslinking density is achieved at approximately 80% of the maximum $\log_{10}(G')$. Therefore, this level is considered the ideal exposure condition (printable windows) for DLP printing (shown in gray in **Fig 2g**).^{58,62} Similarly, Yu et al.,⁵⁸ have reported that increasing the GelMA bioink concentration increased the ΔG values, which indicates

a high degree of contrast between the solidified and uncrosslinked states. This behavior may be attributed to the increased probability of C=C double-bond interactions within the GelMA molecules during photopolymerization, which enhances the crosslinking density and overall reaction efficiency. Thus, higher GelMA concentrations promoted faster crosslinking kinetics and improved printing-based bioprinting (PBP) performance, which yielded constructs with superior structural fidelity. Additionally, they evaluated the effect of PAs and found that increasing PA concentration reduced the ΔG value, which indicates a reduction in the stiffness of the printed constructs. These results highlight the importance of optimizing the PA concentration prior to printing to achieve balanced mechanical properties and printing performance.

In contrast, the elastic behavior of the printed construct needs to dominate the viscous behavior for stable shape retention. A large difference between G' and G'' corresponds to improved shape fidelity. This behavior is quantified through the ΔM parameter, which is defined as the logarithmic difference between G' and G'' after full light exposure during PBP (**Fig 2g**). Tong et al.,⁶² have shown that ΔM increases from the gel point onward, which indicates progressive crosslinking and network reinforcement in SilMA under continuous illumination. Higher ΔM values correspond to increased elasticity, which improves printing resolution and structural fidelity (**Fig 2h & 2i**).

Another important factor in the DLP printing process is the viscoelastic dynamic of bioink—particularly under the mechanical stresses induced during recoating. The storage modulus (G') remained consistently higher than the loss modulus (G''), indicating that bioinks have as an elastic solid across a wide range of strains. This demonstrated the material can absorb mechanical stress without substantial deformation, while maintaining structural stability (**Fig 2j & 2k**). The frequency-dependent rheological behavior of the bioink also demonstrated the suitability for dynamic applications. As shown in **Fig 2l**, both the storage modulus (G') and loss modulus (G'') increased with frequency, while the phase angle decreased, indicating enhanced elastic dominance at higher frequencies. This behavior suggests improved structural stability, rapid recovery after deformation, and strong resistance to repetitive or fluctuating mechanical stresses.⁷¹⁻⁷⁵ Yang et al.,⁷⁶ have reported that as frequency increased, the GelMA & ColMA bioinks exhibited stable viscoelastic behavior with G' consistently exceeding G'' across the tested range. In the linear viscoelastic region, the G' of ColMA-S was 4.67-fold higher than that of GelMA-S, which indicates superior scaffold stiffness. Furthermore, frequency-dependent oscillatory shear

measurements confirmed the predominantly elastic gel behavior of both scaffolds. Additionally, the strain-dependent oscillatory rheology showed that G' of 0.5% ColMA and 5% GelMA DLP-printed scaffolds remained constant within the LVR, which confirmed their viscoelastic solid-like behavior.

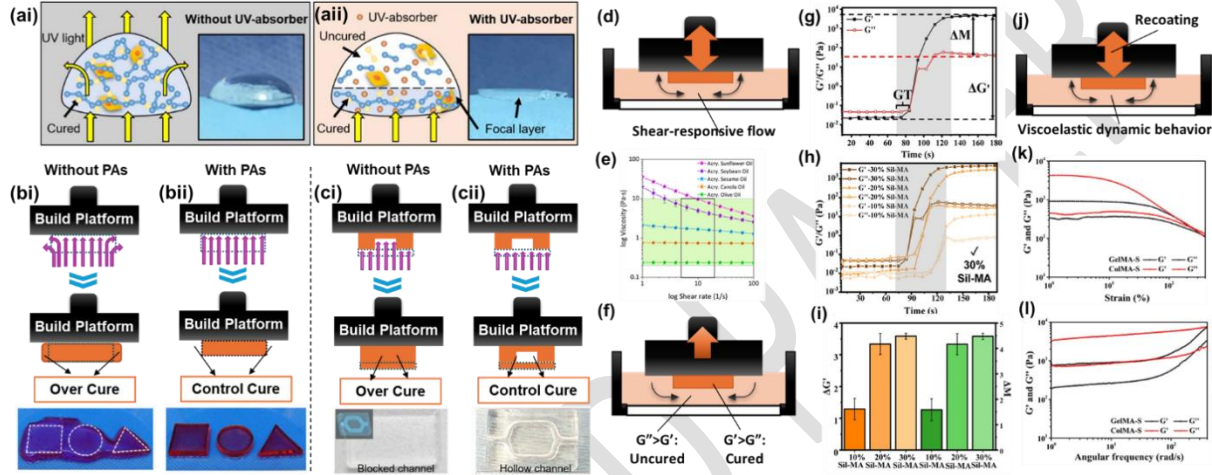


Figure 2. Key photophysical and rheological properties governing DLP printability. (a) Efficacy of light penetration depth mechanism on bioink (Modified and reprinted with permission from Huh et al.⁶⁴ Copyright © 2021 IOP Publishing Ltd.); (b & c) Efficacy of photo-absorber for control cure depth (Modified and reprinted with permission from Huh et al.⁶⁴ Copyright © 2021 IOP Publishing Ltd.); (d) Schematic representation of flowable properties mechanism during printing (arrow sign indicated the flow behavior of bioink); (e) Viscosity analysis of bioink (Modified and reprinted with permission from Vazquez-Martel et al.⁶⁶ Copyright © 2021 American Chemical Society); (f) Schematic representation of phase-separation mechanism of cured and uncured bioink during printing (arrow sign indicated the flow behavior of bioink); (g) ΔG value and ΔM value analysis of UV curable printing ink (Modified and reprinted with permission from Tong et al.⁶² Copyright © 2025 American Chemical Society); (h & i) Photo-rheological characterization of a UV-curable printing ink under varying exposure times (Modified and reprinted with permission from Tong et al.⁶² Copyright © 2025 American Chemical Society); (j) Schematic representation of dynamic viscoelastic behavior of bioink during printing (arrow sign indicated the flow behavior of bioink); (k) Shear strain evaluation of bioink for DLP printing (Modified and reprinted with permission

form Yang et al.⁷⁶ Copyright © 2024 Elsevier B.V.). (l) Angular frequency analysis of bioink for DLP printing (Modified and reprinted with permission form Yang et al.⁷⁶ Copyright © 2024 Elsevier B.V.).

5.2.3. Jacob's working curve and application in printability analysis

Jacob's working curve is a fundamental analytical model in vat polymerization techniques such as DLP, because it defines the relationship between absorbed light energy and the resulting cured thickness of a material. This model has been derived from the Beer–Lambert law, which describes the exponential attenuation of light intensity as it propagates through the bioink owing to absorption by PIs and other light-absorbing components.⁷⁷⁻⁸⁰ This relationship is mathematically expressed by the Jacobs working curve equation:

$$C_d = D_p \ln\left(\frac{E_0}{E_c}\right) \dots \dots \dots (1)$$

where C_d indicates the cure depth (thickness of solidified bioink); D_p indicates light penetration depth; E_0 indicates incident radiant exposure (energy per unit area); and E_c indicates critical exposure (minimum energy required to initiate gelation of bioink).

Typically, layer thickness is selected as 50–100% of the calculated cure depth, and Jacob's working curve helps predict the suitable layer thicknesses to ensure sufficient interlayer overlap and strong bonding between successive layers. The definition of exposure energy $E_0 = I_0 \times t$ indicates that the total radiant dose delivered to the bioink is determined by the applied light intensity (I_0) and exposure time (t). Exposure time may be precisely controlled by rearranging the governing equation (**Eq. 1**) to identify the desired cure depth without requiring excessive energy input. Bioinks with lower critical exposure require shorter exposure times, which enhances vertical resolution and mitigates over curing-related effects such as dimensional distortion and surface fidelity loss. Overall, Jacob's working curve provides a systematic framework for balancing cure depth, resolution, and printing speed.^{78,81-84} For instance, Vazquez-Martel et al.,⁶⁶ applied the Jacob's working curve model to predict the optimal exposure time and layer thickness for DLP printing. The cure depth was evaluated by exposing the inks to a fixed light intensity of 25 mW cm⁻² at varying exposure times and plotting the penetration depth (D_p) as a function of exposure energy using Jacob's working curve. They analyzed six vegetable oil-based inks and found that

canola ($Cd = 103 \pm 3.5 \mu\text{m}$) and sunflower oil ($Cd = 104 \pm 3.5 \mu\text{m}$) based inks exhibited the highest curing depth (**Fig 3a**).

This analysis helped determine the optimal exposure time (1.15–1.20 s) and layer thickness (100 μm), based on which canola and sunflower oil-based inks were used to print a plant and helical sculpture, respectively (**Fig 3b**). In another study, Li et al.,⁸⁰ have developed a theoretical framework for predicting DLP printing conditions based on Jacob's working curve. They constructed a model to evaluate both the solid and liquid-phase absorbances, and systematically evaluated solid-phase absorbance, liquid-phase absorbance, and gelation time to derive a modified predictive equation to determine the optimal printing parameters (**Fig 3c**).

Within this framework, the curing of DLP printing process comprised two main phases. In the initial phase, the photocurable solution is exposed to UV light for a predefined duration known as the threshold time (t_T), which results in a partially cured or pre-cured state. Subsequently, 3D structures were fabricated through a layer-by-layer curing process, during which the pre-cured material was further irradiated for an additional exposure time (Δt). This led to complete curing over a defined thickness in accordance with Jacob's working curve. Notably, the absorbance of the photocurable material was tuned by adjusting the concentration of the photo absorber (PIs) to exert precise control over t_T and Δt for a given material system. Subsequently, after the recoating time (t_R) has elapsed, the next-layer printing occurred according to this mechanism until the full model was printed (**Fig 3d**). Additionally, the gelation time (GT) was experimentally determined using a rheometer and was incorporated into the developed predictive equation:

$$t_H = t_T \cdot \left[\frac{A_s - A_l}{A_s} + \frac{A_l}{A_s} \cdot \exp(-A_s \cdot H) \right] \dots \dots \dots (2)$$

where t_H indicates the exposure time for curing thickness H ; t_T indicates threshold time; A_s indicates solid absorbance of bioink; A_l indicates liquid absorbance of bioink; and H indicates layer thickness.

They used this model to validate their theoretical predictions through experiments conducted with 20% PEGDA hydrogels. After experimentally determining the A_l , A_s , and t_T in Eq. 2, Jacob's working curve for PEGDA hydrogels could be theoretically predicted (black lines, L_t) and compared with the experimentally measured cured thicknesses at different exposure times (red

points) and their fitted curves (red dashed lines, L_e). The intersection of L_e with the exposure-time axis is defined as t_e (experimental exposure time). Although L_t and L_e were nearly parallel, the difference between t_r and t_e , which is defined as the threshold time deviation ($\Delta t_r = t_r - t_e$), varied with the PAs concentration (C_{uv}). This deviation acted as a quantitative indicator of the accuracy of the theoretical prediction, and it increased from -0.4 s to 0.8 s as C_{uv} increased (**Fig 3e**). The variation Δt_r is divided into three distinct regions based on the UV-absorber concentration (**Fig 3e**). When C_{uv} is $0-0.15\%$ (yellow region), Δt_r is negative, which indicates that the actual critical energy required to pre-cure PEGDA hydrogels exceeds the theoretically predicted value. In contrast, when C_{uv} is $>0.2\%$ (blue region), Δt_r becomes positive, which suggests that experimental pre-curing occurs faster than that predicted by the theoretical model. Notably, when C_{uv} is in the $0.15-0.2\%$ range (green region), Δt_r approaches zero, which implies a close agreement between the theoretical predicted Jacob's working curve and experimental data. Consequently, the UV absorber concentration within this green region was identified as the optimal range for PEGDA hydrogels because it yielded the most accurate theoretical prediction of Jacob's working curve. Using this plot, they determine the exposure time as 2.79 s for $10\text{-}\mu\text{m}$ layer thickness and printed three periodic surface contract and MNs with high resolution (**Fig 3f & 3g**). Overall, Jacob's working curve aids in determining the optimal exposure time and appropriate cure thickness while significantly reducing experimental effort and material waste.

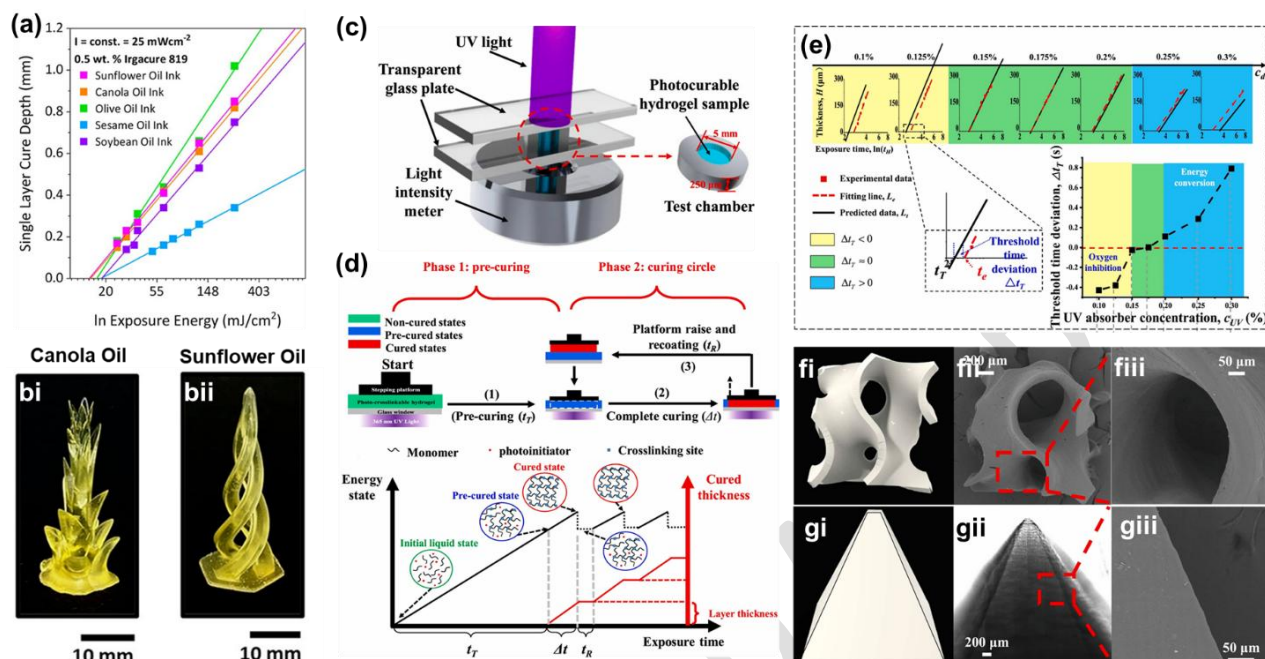


Figure 3. Influence of optical properties on photopolymerization and printing fidelity in DLP bioprinting. (a) Jacob's working curve plot of six vegetable oils bioink (Modified and reprinted with permission from Vazquez-Martel et al.⁶⁶ Copyright © 2021 American chemical Society); (b) Printed object of cannola oil and sunflower oil bioinks bioink (Modified and reprinted with permission from Vazquez-Martel et al.⁶⁶ Copyright © 2021 American chemical Society) (Scale bar = 10 mm); (c) Designed model for collection of the absorbance of bioink (adapted with permission from Li et al.⁸⁰ Copyright © 2021 Elsevier B.V.); (d) Schematic representation of mechanism of photopolymerization during DLP printing (Modified and reprinted with permission from Li et al.⁸⁰ Copyright © 2021 Elsevier B.V.); (e) Jacob working curve plot by varying photo-absorber concentrations (Modified and reprinted with permission from Li et al.⁸⁰ Copyright © 2021 Elsevier B.V.); (f & g) Printed helical structure PEGDA bioink (Modified and reprinted with permission from Li et al.⁸⁰ Copyright © 2021 Elsevier B.V.) (Scale bar = (fii) 200 μm & (fiii) 50 μm); (g) Printed microneedle of PEGDA bioink (Modified and reprinted with permission from Li et al.⁸⁰ Copyright © 2021 Elsevier B.V.) (Scale bar = (gii) 200 μm & (giii) 50 μm).

5.2.4. Analysis of printing defects

Theoretical models such as the Jacob's working curve are widely used in DLP printing to estimate curing depth, exposure time, and layer thickness; however, these models are based on ideal

assumptions such as uniform light propagation and homogeneous material properties. In practice, deviations from these assumptions result in discrepancies between the theoretical predictions and experimental outcomes that manifest as printing defects. These errors are defined as the differences between the fabricated construct and intended digital design. They are inherent to DLP printing and primarily arise from light scattering and excessive curing in the depth direction. Owing to the layer-by-layer nature of vat polymerization, printing errors are systematically categorized into 2D errors that occur within individual layers and 3D errors that occur along the vertical (Z) direction between successive layers.^{58,73,75,80,82,85}

2D printing errors occur because of lateral light scattering, which causes unintended crosslinking beyond the projected exposure area and reduces the in-plane (XY) resolution. The extent of this scattering is determined by material properties such as polymer concentration, molecular heterogeneity, and phase behavior. Although light scattering cannot be completely eliminated, its influence may be mitigated by incorporating light absorbers that attenuate the scattered photons below the polymerization threshold. However, this mitigation strategy reduces the effective incident light intensity, which slows the polymerization kinetics and limits the crosslinking density. Consequently, theoretical predictions must be experimentally adjusted to balance lateral resolution and curing efficiency.⁸⁶⁻⁸⁸ Yu et al.,⁵⁸ showed that patterned light was projected onto the bottom of the resin vat and underwent lateral scattering owing to the optical inhomogeneity of the partially cured GelMA during printing with unintended crosslinking beyond the designed exposure region, resulting in 2D printing errors. Optimal balance of PAs, bioink concentrations, light intensity and exposure time could be beneficial for overcome 2D printing error.

In contrast, 3D printing errors occur because of excessive curing depth in vertical (Z-axis) direction. Curing depth is required to slightly exceed the nominal layer thickness to ensure sufficient interlayer bonding; however, excessive overcuring leads to surface roughness, loss of vertical resolution, and dimensional distortion. In contrast, insufficient curing results in weak interlayer adhesion and structural instability—particularly in low-solid-content hydrogel bioinks. Curing depth is highly sensitive to exposure time, light intensity, bioink concentration, and light absorber content, which highlights the limitations of using theoretical models in isolation.^{58,89,90} Yu et al.,⁵⁸ have reported that decreasing light intensity reduced the crosslinking density of GelMA, whereas a sufficiently high interlayer crosslinking density was required to ensure reliable bonding between

successive layers. Furthermore, inadequate crosslinking leads to structural deformation or collapse owing to the low solid content of the hydrogel bioinks. Although increasing bioink concentration or exposure conditions may enhance crosslinking, these strategies additionally increase the curing depth and may be led to reduce printing precision. Therefore, optimal balance of PAs, bioink concentrations, light intensity and exposure time could be beneficial for controlling the curing depth and minimizing printing errors.⁹¹

5.3. Optimizing printing parameters for skin patch design

The key parameters optimization includes exposure time, light intensity, layer thickness and physio-chemical compatibility (temperature, pH) of bioink for regenerative skin patch; these directly influence polymerization kinetics and curing behavior of photocurable materials. Improper parameter selection leads to insufficient curing, cell cytotoxicity, weak interlayer adhesion, or over curing-induced dimensional inaccuracies. Therefore, parameter optimization must be systematically validated through a combination of theoretical modeling (such as Jacob's working curve) and experimental verification to ensure reliable and reproducible printing performance.^{21,72,92}

In this context, both the lateral (XY axis) and vertical (Z axis) resolutions are essential metrics for evaluating printing fidelity because they determine feature accuracy of individual layers and precision of interlayer stacking, respectively.^{59,67,90,93-95} For example, Choi et al.,⁷³ have designed a composite bioink composed of GelMA and SilMA to fabricate a full-thickness skin model. Before printing the final skin construct, they evaluated printing fidelity by performing 3D square lumen printing tests in both the XY and Z directions. They found that the lumen width and height in the XY plane increased as silk-GMA concentration increased. Notably, the width-to-height ratios were close to unity for most lumens fabricated using the 10G10S (10% GelMA and 10% SilMA) formulations, which indicated a high lateral printing accuracy. In contrast, well-defined lumens were not observed along the Z direction for the 20G (20% GelMA) and 17.5G2.5S (17.5% GelMA and 2.5% SilMA) formulations, which suggested compromised vertical resolution. Moreover, the lumen dimensions in the Z direction increased proportionally with pore size for both the 10G10S and 15G5S formulations, which indicated comparable vertical fidelity between these two compositions. In another study, He et al.,⁷⁵ evaluated the printing fidelity in both the XY and

Z directions after selecting an appropriate printing window based on exposure time (10-30s) and light intensity (6 mW/cm^2) for wound patch development. Their results showed that reducing per-layer thickness significantly improved printing accuracy at both the lateral (XY) and vertical (Z) resolutions. Therefore, evaluating experimentally optimized printing parameters such as layer thickness, exposure time, and light intensity, through a systematic assessment of both the lateral (XY) and vertical (Z) resolutions, is crucial following theoretical validation.

For fabrication of skin patches, the biocompatibility is one of the most critical considerations because the photopolymerization process relies on PIs, PAs, and light irradiation, all of which can influence cellular viability and the stability of biomolecules. Therefore, successful DLP fabrication requires careful optimization of photopolymerization parameters to achieve rapid curing and high structural fidelity while maintaining a cytocompatibility microenvironment.^{21,63,72} For instance, Tong et al.,⁶² fabricated a DLP-printed microneedle (MN) patch by optimizing the concentrations of PIs and PAs. By balancing biocompatibility and rheological properties, they established optimal printing conditions using 0.3% LAP and 0.05% tartrazine, with minimal light intensity (15 mW/cm^2) and exposure time (60 s). The fabricated MN patch demonstrated high cell viability and enhanced cell proliferation compared to the control. Similarly, Fu et al.,⁶³ reported that a formulation containing 0.25% LAP and 0.05% tartrazine concentration enabled the fabrication of high-fidelity, cell-laden constructs with sustained fibroblast viability and well-organized cytoskeletal architecture using DLP printing technology. This strategy highlights the versatility to fabricate vascular architectures to help angiogenesis in skin tissue regeneration. Moreover, several studies have identified optimized LAP (0.03–0.3% w/v) and tartrazine (0.04–0.05% w/v) concentrations as an “optimal window” for achieving rapid fabrication while maintaining cell viability above 90%, which is essential for clinical translation. DLP-printed should be consider as based on light wave-length. Several DLP-based printed developed with visible blue light (405-450 nm), which are beneficial for fabrication of cell laden or light sensitive biomolecules skin patches.²¹

Another considerable factor is temperature, which is required to fabricate skin patches for several biomaterials like GelMA. It is crucial to optimized temperature during printing process.^{76,96} Yang et al.,⁷⁶ demonstrated the influence of temperature on printability varies considerably among different bioink systems. While GelMA benefits from elevated temperatures that improve fluidity

and processability, collagen-based bioinks require lower processing temperatures to preserve their native triple-helical structure and biological functionality. Excessive heating may induce collagen denaturation, leading to the loss of bioactivity and mechanical performance.

6. Advances in bioink development for DLP-based printing on basis of tissue specificity

Vat photopolymerization techniques such as DLP widely use commercial resins owing to their high printing efficiency, resolution, and capacity to fabricate complex geometries. However, these resins show drawbacks such as cytotoxicity and biodegradability; hence, pure nonfunctionalized photocurable inks are being used instead. Recently, PEGDA is commonly used because of its biocompatibility, tunable mechanical properties, and rapid photopolymerization, which enable the fabrication of hydrated hydrogel scaffolds that are suitable for skin tissue engineering. Additionally, other acrylate-based polymers and hybrid composite formulations have been developed on basis of biological functionality and investigated to optimize printability, mechanical integrity, and biological performance in biomedical applications.^{60,97-101} However, researcher focus on advancements of bioink from natural sources which possesses biological and biochemical function that help skin tissue regeneration. Therefore, current advancements in bioinks and their properties are summarized in **Table 2**.

6.1. Functionalization of biomaterials for DLP-based skin patch development

Bioink functionalization is essential for the use of biologically relevant materials in DLP, which requires rapid light-induced polymerization to achieve high-resolution fabrication. Chemical modifications allow natural and synthetic polymers to acquire photo-crosslinkable properties while maintaining their biological functionality.^{56,102,103} For instance, methacrylation is the most widely used approach to make polymers photopolymerizable.⁶² This is achieved by grafting methacryloyl groups onto functional side chains of natural biomaterials. For example, lysine residues are grafted in gelatin to form GelMA or hydroxyl groups in hyaluronic acid to form hyaluronic acid methacrylate (HAMA).^{62,104} Additionally, synthetic polymers such as PEGDA act as standard photocurable backbones owing to their tunable mechanical properties despite frequently requiring blending with natural polymers to introduce cell-adhesive motifs.⁵⁶ Controlling the degree of substitution (DS) achieves sufficient crosslinking density while preserving the biological function. For example, collagen methacrylate (ColMA) synthesized under alkaline conditions

(approximately pH 9) exhibited a high DS (approximately 68%) while maintaining its native triple-helical structure, which is essential for its mechanical stability, ECM like activity and bioactivity.¹⁰⁵ The mechanical properties bioink for skin patch fabrication is crucial.¹⁰⁶ Tong et al.,⁶² developed a silk based bioink by optimized methacrylation of silk fibroin using glycidyl methacrylate. This strategy enhanced the mechanical properties of Silk-based bioink and functionalized enable high-fidelity DLP printing. In addition, decellularized extracellular matrix (dECM) are characterized as emerging biomaterials in regenerative field, as it has ability to closely mimic the native tissue microenvironment. Derived from natural tissues, dECM retains essential structural proteins, such as collagen, elastin, and glycosaminoglycans, along with inherent bioactive cues that regulate cell behavior. This biomimetic composition promotes cell adhesion, proliferation, and differentiation, while also supporting angiogenesis and tissue remodeling.^{107,108} Therefore, Hewawasam et al.,¹⁰⁹ developed functionalized dECM via thiolation-based functionalization for photo-crosslinkable ability. In this strategy, dECM participates in thiol–ene Michael addition reactions after the primary amines are converted into thiol groups using Traut's reagent. This enables its integration into hybrid hydrogel networks, which highlights the development of microarchitecture via DLP. Typically, these systems use PEG-based methacrylate backbones and undergo a two-stage crosslinking process: an initial Michael addition to form a soft tissue-mimetic hydrogel, followed by secondary photopolymerization to increase stiffness. The high molecular weight of thiolated dECM reduces the number of elastically inactive chain segments, which improves network integrity and mechanical performance. Rapid gelation and faster fabrication processes can significantly enhance the clinical acceptability of fabrication patches, which is beneficial for fabrication light sensitive therapeutic and cell laden scaffolds.¹¹⁰ For example, Zhu et al.,¹¹¹ developed a phenol mediated functionalization strategy that utilizes endogenous tyrosine residues present in proteins such as collagen and casein. Under visible light irradiation, these tyrosine residues form stable dityrosine bonds in the presence of ruthenium-based photoredox catalysts, eliminating the need for extensive chemical modification. This approach is particularly effective for developing bio-adhesive and hemostatic sealants, as covalent bonding occurs both within the hydrogel network and at the tissue interface, resulting in enhanced mechanical stability and tissue adhesion. Such systems exhibit rapid gelation and strong adhesion under physiological conditions and are ideal for supporting applications in wound sealing and

tissue repair while simultaneously promoting regenerative responses such as angiogenesis and immune modulation.^{102,103,111,112}

6.2. Hybrid and composite biomaterials composition for DLP-based skin patch development.

Hybrid and composite biomaterial compositions are advantageous for integrating complementary mechanical, biological, and physicochemical properties, which enables the precise optimization of printability, structural integrity, and bioactivity to suitably match the functional requirements of target tissues.^{113,114} Mechanical strength is a key requirement for hybrid and composite bioinks. In DLP, this property is commonly enhanced by incorporating mechanically robust reinforcements into the bioactive hydrogel matrices, is beneficial to fabricate MNs patch and vascular skin model with high resolution.¹⁰³ For example, Li et al.,¹¹⁵ developed a patch where bacterial nanocellulose (BNC) was incorporated into GelMA bioinks to create a denser polymer network that improved the compressive modulus from 16.4 kPa to 73.0 kPa, which provided the necessary stiffness to support confluent cell monolayers. Similarly, Choi et al.,⁷³ developed a silk fibroin (SF) bioink that was used as a mechanical dopant owing to its high β -sheet folding content. This conferred superior tensile strength and resilience to SF-based hydrogels to withstand the dynamic mechanical stresses associated with tissues such as skin, cartilage or bone.

For better wound healing, swelling and water uptake properties is most necessary. It facilitates high number of cellular infiltration and nutrients supports, lead to faster tissue regeneration.^{116,117} For example, Zhang et al.,¹¹⁸ developed an microneedles (MNs) patch for extracting interstitial skin fluid (ISF) with an optimized HAMA-to-GelMA ratio of 8:2 achieved swelling rates that exceeded 1200%. This facilitated rapid biomarker recovery. In another study showed that the incorporation of dECM into synthetic networks increased the average molecular weight between crosslinks. This modification increased the mesh size, which improved nutrient diffusion and the equilibrium swelling ratio because of strong hydrogen bonding between water molecules and protein fragments, thereby facilitating wound-healing applications.^{109,118} In addition, the swelling behavior and degradability of skin patches are critical factors, as they directly influence the release profile of therapeutic agents. The drug delivery timeline should be carefully selected based on the condition of the tissue. For instance, rapid therapeutic delivery is essential for antimicrobial agents, as it enables effective elimination of pathogens in damaged skin and facilitates faster

immunomodulation. In contrast, therapies involving antioxidants and angiogenic factors require sustained and controlled release to support prolonged tissue regeneration. Therefore, the design of composite materials enables the tuning of both rapid and sustained release profiles, allowing them to be matched to specific clinical timelines. HAMA-based structures are typically chosen for short-term drug delivery because they degrade in ≤ 1 week. In contrast, silk-based constructs provide sustained structural support lasting from a few weeks.^{56,119}

The adhesive properties of patches are critical for ensuring stable and intimate bonding with the surrounding skin in wound beds. This is often achieved through biomimetic designs inspired by mollusks that use catechol-rich moieties or polyphenols such as tannic acid (TA).^{103,120,121} For example, Lu et al.,¹²² reported that dopamine-functionalized PEGDA hydrogels formed robust wet-tissue adhesion, which facilitate the patch attached well during bending and curvature condition. In another study, Silva et al.,¹⁰⁴ reported that surface functionalization with gallic acid (GA) has been shown to improve adhesive strength by over 100%, an effect further amplified by the addition of Fe^{3+} ions which facilitate coordination-based bonding. Moreover, applications involving self-healing and tissue mimicking have advanced through the bioprinting of heterogeneous models that replicate the stratified architecture of natural organs.^{123,124} For example, Li et al.,¹¹⁵ designed heterogeneous skin model incorporating a “dermal bioink” (10%GelMA/0.3%BNC) with large pores for fibroblast migration and a “basal bioink” (10%GelMA/1.5%BNC) with a dense network to support epidermal stratification. These scaffolds provide biochemical cues (growth factors and cytokines) found in native dECM, which guide lineage-specific cellular maturation. In another study, self-healing hydrogel scaffolds such as the PTLA system designed by Wu et al.¹⁰³ By comprising MTA, hyperbranched polylysine, and acrylic acid use dynamic physical interactions such as hydrogen bonding and ionic attraction to restore their integrity. These materials achieve rapid in situ healing, which enables the construct to recover its original stretch-ability and modulus after mechanical failure.

7. DLP printing transdermal patches for skin tissue regeneration

Wounds caused by trauma, surgery, and burns present significant clinical challenges that require timely intervention to promote healing, prevent infection, and minimize scarring. Skin

regeneration proceeds through four overlapping phases—hemostasis, inflammation, proliferation, and remodeling—each requiring distinct cellular, molecular, and microenvironmental cues.^{125,126} However, wound characteristics vary considerably among patients due to differences in wound type, anatomical location, and underlying health conditions. Consequently, conventional wound dressings often fail to provide the dynamic and stage-specific support necessary for optimal tissue repair. These limitations have driven the development of advanced regenerative skin patches capable of delivering tailored structural, mechanical, and biological functions according to the evolving needs of the wound microenvironment. In this regard, DLP bioprinting offers a promising platform for fabricating patient-specific skin patches with customized architectures and therapeutic functionalities.^{127,128} Therefore, recent DLP-based skin regeneration strategies and their corresponding applications are summarized in **Table 3**.

7.1. Antimicrobial and Anti-Infective Skin Patches

Infected wounds represent a major barrier to successful skin regeneration because bacterial colonization, biofilm formation, and toxin secretion can prolong inflammation, delay re-epithelialization, and increase the risk of systemic infection. Therefore, regenerative skin patches should not only provide a protective physical barrier and maintain a moist wound environment but also possess active antimicrobial and anti-biofilm capabilities. Several DLP-fabricated skin patches have demonstrated effective infection control through different mechanisms.^{129,130} For instance, Park and colleagues,¹³¹ developed a DLP-fabricated patch for treating acne vulgaris using a dual-phase therapeutic strategy. In the initial phase, self-locking MN arrays deliver antibacterial agents such as salicylic acid and *Cannabis sativa* extract to disrupt *Cutibacterium acnes* biofilms and regulate excess sebum production. In the following maintenance phase, MNs loaded with anti-inflammatory and antioxidant compounds such as chamomile, glutathione, and niacinamide suppress inflammation and promote lesion resolution. Therapeutic evaluation indicated a rapid clinical response with 81.4% decrease in acne lesions in ≤ 3 days and pronounced decrease in sebum secretion. In another study, Chen et al.,¹³² reported a piezocatalytic bioink composed of silk fibroin methacrylate (SF-MA), polyethylene glycol diacrylate (PEGDA), and Ag@BaTiO₃ (BT) nanoparticles. Under ultrasonic stimulation, the piezoelectric BT nanoparticles generate piezoelectric polarization, leading to ROS generation, which exhibit strong antibacterial activity,

achieving a 99.96% reduction against *S. aureus*. This effective bacterial elimination creates a favorable microenvironment for skin tissue repair, leading to complete wound closure within 12 days. Beyond killing bacteria, clearing the bacterial secreted cytotoxic proteins (pore-forming toxins or PFTs) is essential to protect host cells from membrane damage and secondary poisoning. For example, Tao et al.,¹³³ developed a bioink combines GelMA with self-assembled polydiacetylene (PDA) nanoparticles, which are engineered to function as toxin “decoys.” These PDA nanoparticles mimic the structural and chemical features of cellular membranes, enabling them to selectively bind pore-forming toxins (PFTs) produced by bacteria. By capturing and neutralizing these toxins before they interact with host cells, the nanoparticles effectively prevent toxin-induced membrane damage, thereby protecting surrounding tissues and supporting skin regeneration. This system, achieved nearly 100% neutralization of toxins in vitro. Moreover, phototherapy has also been widely applied to suppress bacterial growth while providing additional biological functionalities. Liu et al.,¹²⁹ developed a therapeutic patch incorporating near-infrared (NIR)-assisted phototherapy, which induces reactive oxygen species (ROS) generation upon irradiation (**Fig 4a**). This process facilitates the release of MXene from the microneedle (MN) patch, conferring additional anti-inflammatory and antioxidant effects that accelerate wound healing. Notably, by day 7, the NIR-triggered patch group exhibited the significant antibacterial efficacy, achieving a 68% reduction in bacterial viability (*S. aureus*: 32.59%; *E. coli*: 48.17%) under NIR irradiation than control group (**Fig 4d**).

7.2. Immunomodulatory Skin Regeneration

The management of chronic wounds, particularly diabetic ulcers, represents a significant clinical challenge due to a persistent hyperglycemic microenvironment that traps the wound in a state of prolonged inflammation and high oxidative stress.^{63,103,134} The primary goal of immunotherapeutic scaffolds in skin regeneration is the precise modulation of the local immune microenvironment through the regulation of macrophage polarization from the pro-inflammatory M1 state to the pro-regenerative M2 state. The prolonged dominance of M1 macrophages is a hallmark of chronic wounds and inflammatory skin disorders in which the sustained secretion of ROS and pro-inflammatory cytokines impairs tissue repair.¹³⁵⁻¹³⁸ To address this, Fu et al.,⁶³ developed a high-resolution digital light processing (DLP) bioprinting platform capable of fabricating cell-laden collagen constructs that conform precisely to diabetic wound beds, ensuring intimate contact for

efficient therapeutic delivery. The bioink was based on methacrylated collagen (CMA) integrated with dihydromyricetin (DHM), a flavonoid with potent anti-inflammatory and antioxidant properties, and further enhanced using a multi-crosslinking strategy to improve mechanical stability in dynamic wound environments. The resulting CMA-DHM hydrogel demonstrated effective reactive oxygen species (ROS) scavenging and successfully promoted macrophage polarization from the M1 to M2 phenotype. In vivo studies revealed a significant reduction in iNOS⁺ (M1) cells and an increase in CD163⁺ (M2) cells, leading to enhanced re-epithelialization and collagen deposition in full-thickness diabetic wounds. Concurrently, this immunoregulatory shift suppresses the expression of key inflammatory mediators such as interleukin-6 (IL-6), Interleukin-1 beta (IL-1 β), and tumor necrosis factor- α (TNF- α) and so on, the levels of which are typically elevated in chronic and non-healing wound condition.^{63,112,139} Collectively, this macrophage reprogramming strategy mitigates inflammatory tissue damage and promotes a timely transition from the inflammatory phase to the proliferative and remodeling phases of wound healing, thereby enhancing overall regenerative outcomes.

7.3. Vascularization-Promoting Skin patches

Vascularization is a fundamental requirement for successful skin regeneration because newly formed tissue depends on a functional blood vessel network to sustain cellular survival and tissue remodeling. Following injury, disruption of the native vasculature creates a hypoxic and nutrient-deficient microenvironment that impairs cellular function and delays wound healing. Therefore, a patch which promotes angiogenesis from pre-existing vasculature, is crucial for faster skin regeneration.^{140,141} Precise positioning and self-organization of vascular cells represent a key strategy in vascular tissue engineering, where co-printing heterogeneous cell populations is used to guide natural vessel formation.¹⁴¹ For instance, Zhou et al.¹⁴² developed a biomimetic functional living skin (FLS) using a GelMA/HA-NB/LAP bioink that closely replicates the native extracellular matrix. The construct featured a dense epidermis-like upper layer and a porous dermis-like lower layer containing interconnected microchannels (~200 μ m) and cantilever beam structures, which enhanced nutrient transport and reduced flow resistance. By precisely positioning human umbilical vein endothelial cells (HUVECs) and human skin fibroblasts (HSFs), the system supported spontaneous self-organization into stable microvascular networks that persisted for over 30 days, while in vivo studies further confirmed enhanced neovascularization and the formation

of skin appendages. Similarly, Mazari-Arrighi et al.¹⁴³ utilized DLP bioprinting to encapsulate endothelial progenitor cells (EPCs) within a multi-component GelMA bioink, enabling them to guide cellular organization into predefined vascular geometries. Within days, EPCs proliferated and self-assembled into branched tubular networks (10–100 μm in diameter) with lumen-like structures and tight cellular junctions, demonstrating functional connectivity through successful dye perfusion. In another approach, Choi et al.⁷³ employed a print–pause–print strategy to fabricate a full-thickness stratified skin model using methacrylated silk fibroin and gelatin. This method allowed sequential deposition of a pre-vascularized dermal layer, additional stromal support layers, and an epidermal layer, while maintaining high cell viability (>95%). The resulting constructs exhibited enhanced CD31 expression, confirming vascular differentiation and providing adequate support for the development of upper skin layers. Collectively, these studies highlight how the integration of biomimetic architecture, precise cell positioning, and advanced fabrication strategies enables the formation of functional vascular networks in promoting effective skin tissue regeneration.

7.4. Controlled & stimuli-responsive drug delivery system for skin regeneration

A transformative approach in advanced wound care and skin regeneration is the fabrication of smart, stimuli-responsive and controlled drug delivery systems that surpass conventional passive diffusion to achieve precisely regulated on-demand therapeutic release tailored to the dynamic physiology of the wound microenvironment.¹⁴⁴ The high spatial precision and layer-by-layer fabrication capabilities of DLP bioprinting enables the strategic incorporation of bioactive components (e.g., growth factors and proteins) into hydrogel matrices with a defined spatial distribution to achieve localized responsiveness to specific internal or external cues.^{73,122,145} For example, Li et al.,¹⁴⁶ fabricated hydrogel microneedle (HMN) patches using DLP bioprinting and loaded them with PRP. On activation, the controlled release of PRP — a cascade of growth factors including TGF- β , PDGF, FGF, HGF, and VEGF, which play key roles in regulating cell proliferation and migration. In vivo, these HMN patches significantly accelerated wound healing, as evidenced by enhanced re-epithelialization and collagen deposition on day 14.

In contrast, heparin conjugation is a stimuli-responsive wound-healing strategy. Owing to its high density of negative charges, heparin functions as a molecular sequestration reservoir that

selectively binds to and retains positively charged endogenous growth factors from the wound microenvironment.¹⁴⁷⁻¹⁵⁰ This activates intrinsic healing processes without requiring exogenous growth factor supplementation. For example, Joshi et al.,¹⁴⁸ developed personalized micropyr amid wound dressings designed to sequester growth factors via heparin incorporation to regulate tissue regeneration. In vivo evaluation validated the efficacy of these dressings, as evidenced by the significant improvement of wound healing outcomes by day 14. In another study, Sun et al.,¹⁵¹ developed a succulent-inspired MN patch with controllable long-term drug release by integrating thiolated heparin (Hep-SH), which promotes sustained growth factor sequestration and release and graphene oxide (GO) nanosheets, which promote on-demand drug release under near-infrared (NIR) laser irradiation. These MN patches exhibited good biocompatibility and effectively promoted endothelial cell proliferation, migration, and angiogenesis; additionally, these effects were validated in vivo.

Furthermore, the integration of functional nanomaterials into DLP-printed constructs has substantially enhanced the efficacy of controlled therapeutic delivery and accelerated skin tissue regeneration.¹⁵² Nanomaterials such as MXene, graphene oxide, or metal–organic frameworks impart stimuli-responsiveness, which enables temperature, pH or light-triggered release of bioactive agents. Simultaneously, they provide antibacterial activity, antioxidant effects, or pro-angiogenic signaling.^{129,149,153} For instance, Yang et al.,¹⁵⁴ developed a glucose-responsive MN system for diabetic and metabolically active wounds. This system uses glucose oxidase (GOx) to enzymatically convert excess glucose into hydrogen peroxide and gluconic acid. This induced localized acidification, which triggered hydrogel degradation and facilitated the controlled release of the therapeutics encapsulated within carriers such as metal–organic frameworks (MOFs). The GOx/MoS₂ MN platform has shown high antibacterial efficacy by achieving a 91.1% inhibition zone in vitro. Furthermore, both accelerated wound healing and antibacterial performance were confirmed in vivo, with MN-treated wounds exhibiting a 19% higher healing rate than that of untreated controls after 7 days. Liu et al.,¹²⁹ developed an NIR-responsive personalized MN patch for diabetic wound management. This MXene-based eutectogel MN system (MF-MXene@MN) integrates photothermal responsiveness, antioxidant activity, and temperature-triggered drug release to enable efficient photothermal conversion and ROS scavenging (**Fig 4a & 4b**). A gradient-height design inspired by crocodile teeth has shown potential in enhancing tissue

adhesion; additionally, DLP 3D printing enabled the fabrication of patient-specific wound dressings with resolutions of <50 μm . In vitro and in vivo evaluations showed 94.88% wound closure rate within 10 days (**Fig 4c**), 3.2-fold increase in angiogenesis, 68% reduction in bacterial viability (*S. aureus*: 32.59%; *E. coli*: 48.17% under NIR irradiation) than control group. Also, pH and temperature-responsive mangiferin release (88.3% cumulative release) was achieved by over five NIR cycles. These multifunctional properties synergistically accelerated wound healing, enhanced antibacterial activity, and controlled therapeutic delivery to surpass the performance of conventional wound dressings and standard MN systems. Furthermore, controlled therapeutic delivery is essential for effective wound healing. Lu et al.,¹²² developed a curcumin-loaded micellar system (C-PNPD) that enabled sustained release (~80% over 4–5 days), ensuring prolonged therapeutic activity for infection-associated diabetic wounds. The incorporation of PF-127 micelles within a PNIPAm-based, thermo-responsive matrix further facilitated on-demand drug release and tissue contraction, thereby enhancing treatment efficacy compared to conventional wound dressings (**Fig 4e – 4g**). In vivo studies demonstrated that the C-PNPD group achieved the highest wound healing efficacy within 14 days (**Fig 4h**), highlighting the advantage of controlled and sustained drug delivery. Similarly, Li et al.¹⁴⁶ developed patient-specific GelMA–SFMA-MN patches designed for localized delivery of platelet-rich protein (PRP) to accelerate wound healing. They integrated high-resolution 3D scanning and DLP-based printing with fabricated customized MN patches that precisely conformed to the unique sizes, shapes, and depths of individual wounds. These GelMA–SFMA patches exhibited appropriate mechanical strength, puncture resistance, and sustained-release profile of growth factors, which ensured both structural stability and therapeutic efficacy. In vivo, these patient-specific noses within seconds to minutes per layer. This ability highlights the potential of DLP for personalized regenerative medicine applications.^{71,154,155}

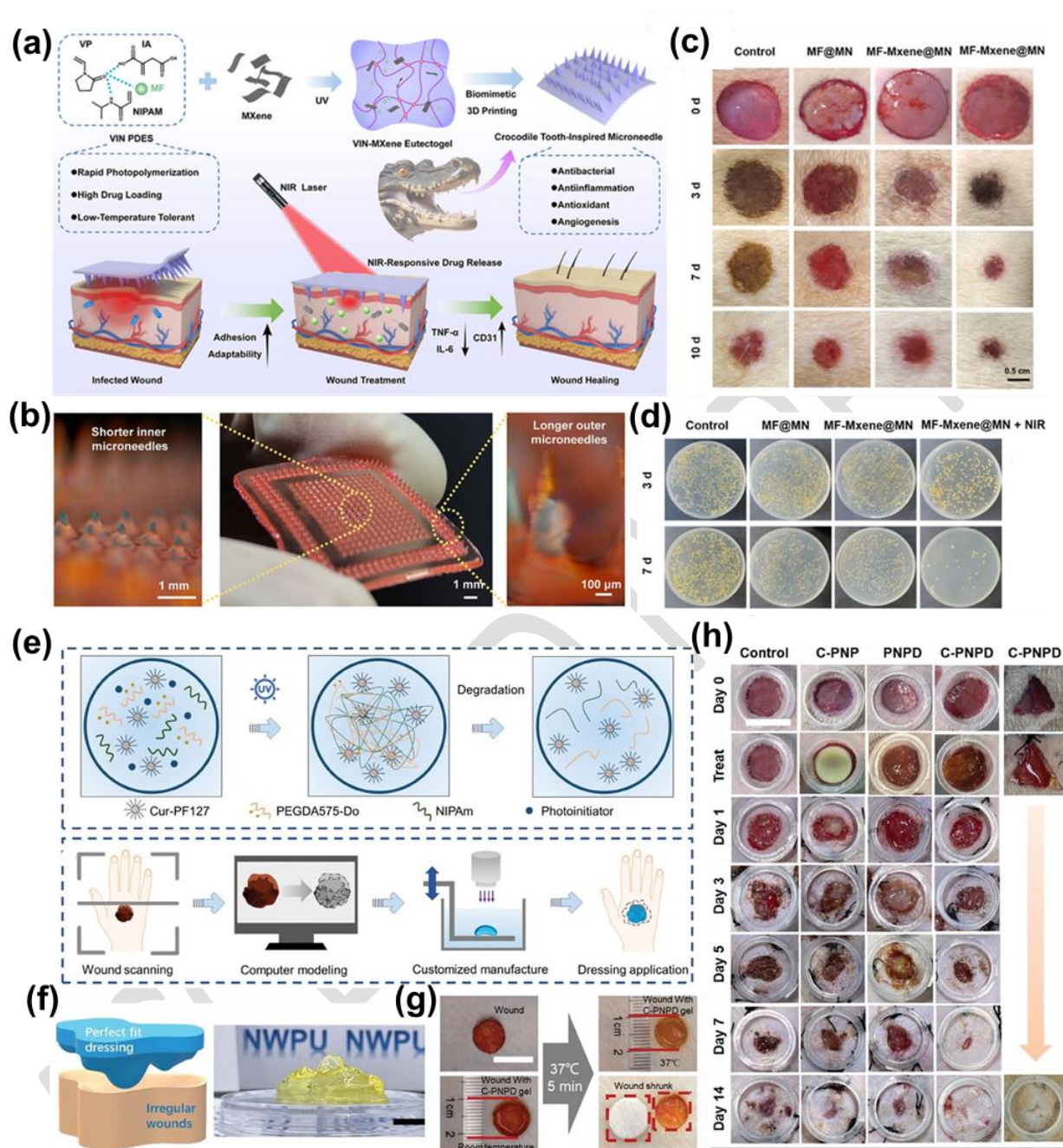


Figure 4. DLP-bioprinted smart wound healing patches. (a) Schematic representation of NIR-responsive bioinspired MNs patches fabrication and application (Modified and reprinted with permission from Liu et al.¹²⁹ Copyright © 2025 Wiley-VCH GmbH); (b) Fabricated MNs patches with shorter and longer microneedles (Modified and reprinted with permission from Liu et al.¹²⁹ Copyright © 2026 2025 Wiley-VCH GmbH); (c) In-vivo digital images and outlines of the wounds closer rate of MNs patches (Modified and reprinted with permission from Liu et al.¹²⁹ Copyright

© 2025 Wiley-VCH GmbH) (Scale bar = 0.5 cm); (h) (Scale bar = left to right, 1 mm, 1mm & 100 μ m, respectively); (d) In-vitro digital image of anti-microbial efficacy of MNs patches (Modified and reprinted with permission from Liu et al.¹²⁹ Copyright © 2025 Wiley-VCH GmbH); (e) Schematic representation of personalized adhesive patch fabrication strategies for wound healing (Modified and reprinted with permission form Lu et al.¹²² Copyright © 2023 Wiley-VCH GmbH); (f) Patch model & printed patch with C-PNPD bioink (Modified and reprinted with permission form Lu et al.¹²² Copyright © 2023 Wiley-VCH GmbH) (Scale bar = 1cm); (g) Temperature responsive contractibility efficacy of C-PNPD bioink (Modified and reprinted with permission form Lu et al.¹²² Copyright © 2023 Wiley-VCH GmbH) (Scale bar = 1 cm); (h) In-vivo schematic diagram of wound closure rate of C-PNPD patches (Modified and reprinted with permission form Lu et al.¹²² Copyright © 2023 Wiley-VCH GmbH) (Scale bar = 1 cm).

In addition to chemical delivery, DLP-fabricated MN arrays function as mechanical stimulators that bypass the stratum corneum or epidermal layer and modulate skin regeneration through physical cues. Epidermal penetration activates peripheral sensory neurons and associated mechano-transduction pathways, which induces the upregulation of repair-related markers such as Ki67 and CK14 and enhances keratinocyte proliferation. Simultaneously, surface micro- and nano-topography play decisive roles in regulating cellular behaviors such as adhesion and migration, which are essential for tissue regeneration.^{62,156} Joshi et al.,¹⁴⁸ have reported that micropyramidal surface architectures significantly promote cell migration than flat wound patches. Particularly, cells showed upward movement along the pyramidal features within 12h of seeding, and they reached the apex by 48h. Furthermore, quantitative analysis confirmed the time-dependent increases in migration distance. Collectively, these findings indicate that mechanically and topographically engineered wound dressing architectures actively regulate cellular responses and accelerate wound healing through physical stimulation.

7.5. Bioinspired smart transdermal patches for skin regeneration

Biological systems exhibit highly optimized structural and functional features that support mechanical robustness, adhesion, and efficient mass transport. Currently, biomimetic design strategies that have been inspired by these natural architectures are being widely adopted for

developing transdermal patches in the field of skin regeneration.^{4,157,158} For example, Ma et al.,¹⁵⁹ developed an octopus-inspired skin–electronic interface to enhance skin adhesion for theragnostic applications. They used DLP-based bioprinting to fabricate a multifunctional patch named PAMS that integrates both diagnostic and therapeutic functions (**Fig 5a & 5b**). This bioinspired design exhibited moderate swelling behavior, notable mechanical deformability (up to 460% strain), high sensing sensitivity (gauge factor = 4.73), and robust controllable bioadhesion with a 109.29% increased shear strength. Additionally, the patch exhibited reliable performance under extreme conditions such as resistance to freezing at -20°C . Functionally, the skin–electronic interface enabled sensitive monitoring of physiological signals such as temperature, motion, and electrocardiogram activity. In a rat frostbite model, the patch was effective in accelerating wound healing when applied as a wound dressing (**Fig 5c**). Collectively, this study has highlighted the potential of bioinspired DLP-fabricated skin–electronic interfaces to improve adhesion, sensing performance, and therapeutic efficacy. Thus, it provides a promising strategy for next-generation bioelectronic devices, personalized diagnostics, and integrated wound care. Liu et al.,¹⁴⁵ developed a coral-inspired biomimetic MN patch designed for the real-time sensing and treatment of wound infections. This design was inspired by the adaptive behavior of soft coral polyps, which extend from porous coral reefs for feeding and retract into the reef structure for protection (**Fig 5d**). DLP printing was performed to fabricate polycaprolactone methacrylate (PCLMA) MNs that featured uniformly porous outer shell and internal cavity loaded with a heparin-based functional hydrogel incorporating therapeutic agents (e.g., monocycline) (**Fig 5e**). This architecture mimicked coral polyps embedded within a rigid reef, with the heparin hydrogel acting as the soft absorbent component. After penetrating the wound scab (**Fig 5f**), the MNs absorbed the wound exudate through surface-guiding grooves and interconnected porous networks. Exudate collection enabled real-time infection sensing through a pH-responsive colorimetric reaction that used phenol red and adsorption of the inflammatory proteins by the heparin hydrogel (**Fig 5i-5k**). Upon detection of the infection, the system autonomously triggered rapid drug release, which was facilitated by the reversible drying–wetting behavior of the hydrogel. Once the infection was controlled, the exudate levels decreased, which led to a corresponding slow down or stoppage of drug release. Thus, a closed-loop self-regulating therapeutic response was established. For fabrication, polycaprolactone (PCL) was first methacrylated and precisely structured into a mechanically robust porous architecture using DLP printing. Subsequently, a drug-loaded heparin/HAMA

hydrogel was incorporated into the scaffold via vacuum-assisted infusion, yielding the composite HepMi-PCL system (**Fig 5g & 5h**). This intelligent MN platform significantly accelerated the healing of infected wound by achieving >200% increase in healing rate. This result highlights the potential of integrating diagnostic sensing and responsive drug delivery within a single biomimetic MN system for advanced chronic wound management. Overall, this approach provides a promising strategy for advanced management of chronic and infected wounds.

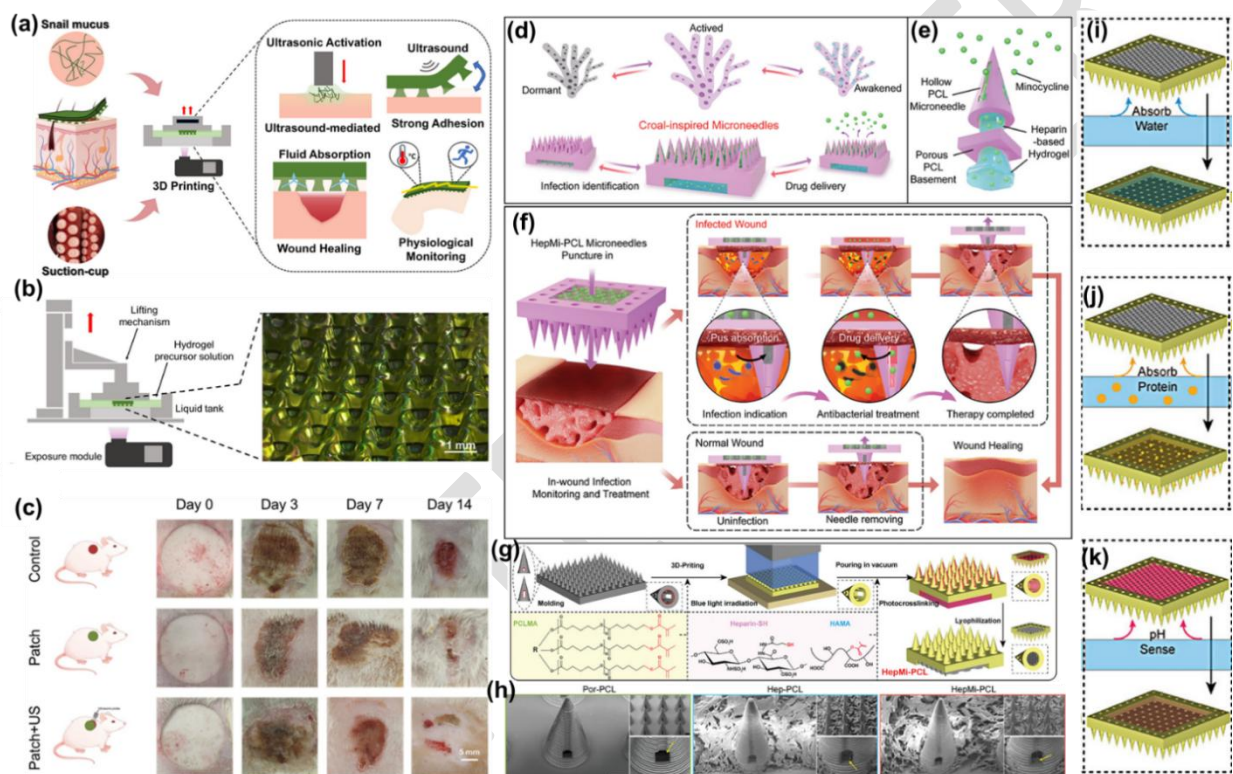


Figure 5. DLP-bioprinted multifunctional theranostic wound healing patches. (a) Schematic representation of octopus & snail inspired bio-adhesive suction patches and its therapeutic application process (Modified and reprinted with permission from Ma et al.¹⁵⁹ Copyright © 2024 Acta Materialia Inc.); (b) DLP printed bioinspired suction patches (Modified and reprinted with permission from Ma et al.¹⁵⁹ Copyright © 2024 Acta Materialia Inc.); (scale bar = 1 mm, right) (c) In-vivo digital images of wound healing efficacy of bioinspired suction patches (Modified and reprinted with permission from Ma et al.¹⁵⁹ Copyright © 2024 Acta Materialia Inc.) (Scale bar = 5 mm); (d-f) Schematic representation of coral inspired multifunctional hollow MNs patches and its therapeutic scheme for wound healing (Modified and reprinted with permission from Liu et al.¹⁴⁵

Copyright © 2024 Wiley-VCH GmbH); (g) Fabrication strategies of coral inspired hollow MNs patches (Modified and reprinted with permission from Liu et al.¹⁴⁵ Copyright © 2024 Wiley-VCH GmbH); (h) fabricated Por-PCL, Hep-PCL & HepMi-PCL Hollow MNs patch (Modified and reprinted with permission from Liu et al.¹⁴⁵ Copyright © 2024 Wiley-VCH GmbH); (i-k) Functional schematic diagram of Hollow MNs patch under water, protein and acidic condition (Modified and reprinted with permission from Liu et al.¹⁴⁵ Copyright © 2024 Wiley-VCH GmbH).

7.6. Personalized customization and wound conformity

Effective contact between the wound bed and the patch is critical for efficient fluid uptake and nutrient transport. Several studies have demonstrated that personalized, conformal scaffolds that closely match the wound geometry significantly enhance therapeutic outcomes compared to conventional flat patches. Therefore, personalized wound patches are particularly advantageous as they conform to the unique geometry, size, and depth of each patient's wound; furthermore, these patches aid in maintaining an optimal microenvironment that supports rapid and effective healing. DLP-based bioprinting is an effective platform for fabricating customized dressings. It integrates high-resolution 3D scanning with digital CAD modeling to produce patient-specific patches that match the wound bed with notable precision—often with resolutions of $<50\text{ }\mu\text{m}$. This intimate “perfect fit” eliminates gaps where bacteria might proliferate and enhances local healing efficiency. Moreover, the rapid layer-by-layer fabrication capability of DLP enables the on-demand creation of complex anatomical structures such as asymmetric multilayer hydrogels or individualized grafts for ears and force induced wound contraction.^{45,148,160} For example, Lu et al.,¹²² have addressed diabetic wound healing by developing personalized wound-conforming patches. They captured high-resolution images of the wound bed and generated corresponding digital models, followed by fabrication of the dressings directly at the point-of-care (**Fig 4e & 4f**). The engineered patch has been termed as C-PNPD, and it comprised a multifunctional composite of degradable crosslinkers such as N-isopropylacrylamide (NIPAm), curcumin-loaded Pluronic F127 micelles (Cur-PF127), and poly (ethylene glycol) diacrylate-dopamine (PEGDA575-Do). In this system, PEGDA575-Do provided robust tissue adhesion and controlled biodegradability, whereas Cur-PF127 imparted an antibacterial functionality (**Fig 4c**). Furthermore, the use of poly(N-

isopropylacrylamide) (PNIPAm) enabled thermo-responsive contractility by undergoing a phase transition at its lower critical solution temperature (approximately, 32–34 °C). Below this temperature, the hydrogel remained swollen, whereas above this temperature, hydrophobic interactions caused water expulsion and network shrinkage, which generated a contraction force. In combination with strong tissue adhesion, this MN patches significantly enhanced wound healing by promoting rapid re-epithelialization, collagen deposition, and overall tissue regeneration in ≤ 14 days.

8. Current challenges and future outlook

Despite the significant promise of DLP bioprinting for skin regeneration, its clinical translation remains constrained by several critical challenges that necessitate targeted strategies. A primary limitation lies in the restricted availability of photocurable bioinks that can simultaneously achieve high printability, biocompatibility, biodegradability, and long-term mechanical stability. Current systems often require trade-offs between biological functionality and structural integrity. To address this, future efforts should prioritize the development of biomimetic hybrid bioinks that integrate naturally derived polymers (e.g., GelMA, collagen, hyaluronic acid) with synthetic networks to enhance mechanical robustness while preserving bioactivity. The incorporation of decellularized extracellular matrix (dECM), dynamic or reversible crosslinking chemistries, and stimuli-responsive elements may further enable improved cell–material interactions, tunable degradation, and functional adaptability. Another major bottleneck in clinical translation is insufficient vascularization within engineered constructs, which limits nutrient diffusion and long-term tissue integration. Advanced strategies, including pre-vascularized bioinks, angiogenic factor delivery, and microfluidic-assisted vascular patterning, should be further explored to promote rapid neovascularization and functional tissue regeneration.

Manufacturing scalability and regulatory compliance also present substantial barriers. Current DLP systems are largely confined to laboratory-scale production, with unresolved issues in batch-to-batch consistency, sterilization, and storage. Notably, conventional sterilization and storage methods, such as autoclaving, gamma irradiation, refrigeration (4 °C), freezing (−20 °C/−80 °C), and lyophilization, may compromise hydrogel integrity and bioactivity, particularly in cell-laden

or drug-loaded systems. To overcome these limitations, the establishment of standardized fabrication protocols, automated quality-control systems, GMP-compliant workflows, and non-destructive sterilization techniques will be essential for ensuring reproducibility and regulatory approval.

Looking forward, several emerging technologies offer promising solutions to these challenges. Artificial intelligence and machine learning can facilitate the optimization of printing parameters, predict material performance, and enable real-time process monitoring. Hybrid manufacturing approaches that combine DLP with complementary techniques such as electrospinning, extrusion bioprinting, or microfluidics may further enhance mechanical performance, biological functionality, and structural complexity. Moreover, advances in patient-specific imaging, computer-aided design, and digital manufacturing are expected to enable the fabrication of highly customized skin patches that precisely conform to irregular wound geometries and individual therapeutic requirements. The integration of biosensing platforms, wireless monitoring systems, and stimuli-responsive drug delivery mechanisms may further transform DLP-fabricated patches into intelligent therapeutic systems capable of dynamically responding to changes in the wound microenvironment.

9. Conclusion

DLP-based bioprinting is a powerful platform for fabricating high-resolution customizable transdermal patches and skin-regenerative constructs with precise control over their geometry, composition, and therapeutic function. Despite challenges related to material limitations, mechanical stability, and clinical translation, advances in bioink design, nanomaterial integration, and intelligent manufacturing strategies are steadily addressing the issues that hinder DLP bioprinting in clinical applications. Overall, combining DLP bioprinting with stimuli-responsive systems, immunomodulatory therapies, and real-time sensing technologies could lead to the advent of next-generation smart patches with enhanced healing efficacy and high clinical applicability, which would transform wound care from a passive treatment to an active personalized intervention.

Acknowledgments

None.

Funding

This work was supported by a two-year Research Grant of Pusan National University.

Conflict of interest

The authors declare they have no competing interests.

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Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Availability of data

Not applicable.

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Tables

Table 1. Comparison of Skin Patch Fabrication Technologies

Printing Technology	Resolution	Printing Speed	Cell Viability	Bioink Compatibility	Structural Complexity	Application Area
DLP	High (micron-level, down to 10 μm)	Highest (layer-wide projection)	High (nozzle-less system reduces stress)	Photopolymer-based bioinks (GelMA, Sil-MA, ColMA)	High (complex 3D architectures and micro-features possible)	Soft tissues, micro-structures, vascular constructs, skin patches
Extrusion-based	Low–Medium (~150–400 μm)	Low–medium (point-by-point path)	Medium to high (though risk of cell lysis due to nozzle pressure)	Widest range of bioinks and viscosities	Limited (higher risk of structural sagging/collapse)	Cartilage, bone, skin tissue
Inkjet-based	Medium–High	High	Medium (potential thermal or mechanical stress)	Low-viscosity inks only (typically 3.5–12 mPa·s)	Limited (due to low viscosity of materials)	Skin, neural tissue
Electrospinning	Sub-micron (fiber level) to micron-scale	Medium (slow accumulation of fiber layers)	High (often acellular; cells usually seeded post-fabrication)	Synthetic and natural polymers (PCL, Silk, Gelatin)	Limited (primarily 2D mats or thin fibrous films) ¹⁴	ECM mimicry, thin fibrous dressings, unidirectional fluid transport
Wound Dressings	N/A	N/A	Generally acellular passive materials.	Traditional fibers, gauze, and non-printed polymers	Low (uniform films, meshes, or foam sheets)	Physical barrier, superficial wounds, exudate absorption

Table 2. Advancements in Bioinks for DLP-printing transdermal patch fabrication.

Bioink Types	Bioink composition	Additives & Wave length	Advancements	Advantages	References
Photo-functionalized bioink composite	Casein-based bioink (Milk Protein)	RU-SPS, 450 nm	Exploiting intrinsic tyrosine residues to induce stable di-tyrosine bond formation via white-light-mediated photochemical activation using ruthenium-based catalysts	Ultrafast gelation (2 to 10s); provides robust covalent adhesion that can withstand pressures exceeding 180 mmHg without peeling force from tissue.	111
	dECM (decellularized ECM) based bioink	RU-SPS, 450 nm	The di-tyrosine bonds are formed through the coupling of tyrosyl free radicals, thereby facilitating the preservation of native bioactivity for regenerative medicine applications	This strategy effectively mimics tissue-specific microenvironments and provides biochemical cues for lineage-specific differentiation, while Ru-SPS PIs systems further reduce cytotoxicity.	161
	ColMA (Collagen Methacryloyl)	LAP, 405 nm	Low-temperature DLP fabrication under acidic conditions (pH 3) enables a high degree of substitution (up to 98%) while preserving the triple-helical protein structure.	Maintains structural integrity with enhanced mechanical properties and resistance to enzymatic degradation compared to GelMA alone.	76
	Silk-GMA (Methacrylated Silk Fibroin)	LAP & Tartrazine, 405 nm	Methacryloyl modification enhances the mechanical stability and photo-crosslinking capability of the biomaterial, facilitating the formation of stable porous 3D structures suitable for cell encapsulation.	The material exhibits enhanced tensile strength and flexibility, closely mimicking the elastic properties of native skin while providing a stable architecture for cell growth.	73
	GelMA-KerMA (Gelatin-Keratin methacrylate)	LAP, 405 nm	Integrating methacrylated gelatin & keratin improves structural integrity and photo-crosslinking capability, enabling the fabrication of thin, high-precision patch constructs	Enhanced crosslinking density increases bioactive binding sites, promoting cell adhesion and proliferation through cysteine-rich fragments.	162

	HAMA / GelMA (Hyaluronic Acid / Gelatin Methacryloyl)	Tartrazine & LAP, 405 nm	Fine-tuning the bioink composition (HAMA-GelMA = 8:2 ratio) enables uniform microneedle geometry with swelling behavior exceeding 1200%.	HAMA/GelMA composite exhibits high water retention and mechanical resilience, enabling rapid biomarker recovery while maintaining minimal invasiveness.	118
	LdECM-MA (liver dECM-methacrylate) & GelMA composite	Eosin Y (EY) & TEOA, 400-700 nm	The LdECM–GelMA composite exhibits rapid crosslinking kinetics, excellent printability, and preserved native bioactivity, while demonstrating low cytotoxicity within the 400–700 nm light.	The hybrid composite demonstrated enhanced mechanical properties and excellent cell friendly printability.	163
Multifunctional bioink composite	AMPS-Na / CMC / PEGDMA	TPO-L & LAP, 450 nm	A dual photoinitiator system (TPO-L/LAP) under 450 nm enabled fabrication through synergistic reinforcement mechanisms, including nanofiber strengthening and hydrogen/coordination bonding	Non-UV photopolymerization minimizes cytotoxicity, while the material's high-water uptake and retention capacity significantly improve hemostatic performance.	75
	NIPAM, PEGDA-Dopamine bioink composites (C-PNPD)	Li-TMPP & LI-LAP, 405 nm	Incorporation of thermo-responsive NIPAM enables 4D printing of dynamic constructs with temperature-triggered shape transformation, while dopamine enhances adhesiveness and PEGDA improves mechanical robustness.	Thermally induced contraction (~52% shrinkage) at physiological temperature promotes wound closure, inflammatory regulation, and stable adhesive wound contact.	122
	NIPAM, MXene-based Eutectogel (VIN-MXene-eutectogel)	TPO-L, 405 nm	Eutectogel incorporation provides bioinspired adhesiveness, while NIR-triggered MXene nanosheets exhibit efficient photothermal conversion and strong antioxidant activity.	This strategy exhibits multi-stimuli responsiveness (NIR, pH, and temperature), enhances tissue anchoring through bioinspired adhesion, and enables precise on-demand drug release.	129
	Zingerol-OH-based bioink	TPO, 385 nm	Zingerol modification via ether, ester, or urethane backbones enables tunable mechanical and biodegradation properties.	The zingerol-based composite exhibits intrinsic anti-biofilm and immunomodulatory activity without exogenous antibiotics.	164
	PTLA bioinks composite (TA/HPL/AA)	TPO, 395 nm	3D printing of catechol-rich modified tannic acid with hyperbranched polylysine enables rapid self-healing.	The material exhibits strong wet-tissue adhesion, outperforming commercial adhesives in blood-rich environments while maintaining structural integrity at –90 °C	103

ColMA-PA (Collagen with Procyanidins)	LAP, 405 nm	Procyanidin incorporation enhances ColMA network stability and oxidative resistance through bio-derived crosslinking and ROS scavenging.	Procyanidins enhance mechanical properties and cell proliferation while scavenging residual free radicals generated during printing.	105
GelMA & MCCA (Allyl Cellulose)	Tartrazine & LAP, 405 nm	The combination of GelMA with photopolymerizable allyl cellulose enhances gel fraction and degradation resistance.	Cellulose derivatives enhance the absorption and retention of wound exudates, maintaining a moist healing environment conducive to repair.	104

Table 3. DLP-printed therapeutic patches for drug delivery & skin tissue regeneration.

Bioink Composition	Delivered Therapeutics	Therapeutic Class	Molecular target	References
SF-MA & PEGDA	Ag@BT (Silver-Barium Titanate) NPs	Piezocatalytic induced antibacterial therapy & tissue regeneration	Piezocatalytic properties enable ultrasound-induced piezoelectric polarization, leading to ROS generation for the inhibition of bacterial infection	132
GelMA & SFMA	Platelet-rich proteins (PRP)	Personalized MNs patches for sustained PRP delivery to accelerate tissue regeneration	Sustained delivery of TGF- β , PDGF, FGF, HGF, and VEGF from the GSPMNs patch significantly upregulates CD31 and α -SMA expression at day 7, facilitating neovascularization and enhancing the wound healing process.	146
CMA & Zins ions (Zn ²⁺)	AHP-8 (Anti-wrinkle peptide)	AHP-8 loaded anti-aging collagenase eye patches	Upon AHP-8 release, the HYP (hydroxyproline), COL (Collagen deposition) and SOD (superoxide dismutase) were increased and MDA (malondialdehyde) was decreased – enhanced skin regeneration.	165
GelMA & PEGDA	Doxycycline, GOx & MoS ₂ (Molybdenum disulfide)	Glucose-responsive Antibacterial therapy & diabetic wound healing	Upon glucose stimulation, GOx catalyzes the conversion of glucose into gluconic acid and H ₂ O ₂ . The resulting gluconic acid decreases hyperglycemia and acidifies the local microenvironment, which is beneficial for wound healing. Simultaneously, H ₂ O ₂ undergoes catalytic activation by MoS ₂ , generating bactericidal ROS that eradicate infection and support subsequent tissue regeneration.	154
AMPS-Na, PEGDAMA & CMC	N/A	Hemostatic & Antibacterial properties to wound repair	The hemostatic and antimicrobial properties of CMC reduced blood clotting time and inhibited microbial infections caused by <i>S. aureus</i> , <i>E. coli</i> & MRSA microbial infection- thereby supporting tissue repair.	75
ColMA	N/A	Biomimetic personalized scaffold for skin tissue regeneration.	The unique triple-helical structure of ColMA, characterized by high proline and hydroxyproline content, significantly enhanced the expression of vimentin, α -SMA, and collagen I compared to GelMA on day 7, thereby promoting skin tissue regeneration.	76
Silk-GMA & Gel-GMA	Epidermal Growth Factor (EGF)	An artificial skin model for skin wound healing	he EGF-loaded skin model significantly increased the gene expression of cytokeratin 13, FGF, and CD31 within two weeks, demonstrating strong potential for skin tissue regeneration.	73

AM & PEGDA	MXene nanosheets	Bioinspired theragnostic patches with antibacterial application in wound healing	The adhesive capacity, ultrasound-mediated interfacial toughening mechanism, and antibacterial properties of MXene nanosheets collectively support wound healing within 14 days.	159
CMA & DHM	HDF cells	Porous cell-laden hydrogel constructs for diabetic tissue regeneration	Prolonged antioxidant activity effectively scavenged ROS, induced macrophage phenotypic transition from pro-inflammatory M1 to pro-regenerative M2 states, and increased collagen deposition at day 18, collectively contributing to improved tissue remodeling.	63
GelMA & ACA	CNPs & MSCs-EVs	Auxetic, elastic & sticky (AuxES) patches for tissue regeneration	AuxES patches upregulated Ccr4, Ackr4, Cd7, Il-17b, and Il-2 gene expression, promoting the transition from an inflammatory to a proliferative microenvironment and thereby supporting wound healing.	166
PCLMA & Heparin Hydrogel	Minocycline hydrochloride (Mi)	Bioinspired porous theragnostic hollow MNs patches for wound infection	HepMi-PCL microneedle (MN) patches inhibited bacterial infection and downregulated pro-inflammatory cytokines, including TNF- α , IL-6, and IL-1 β , thereby promoting tissue regeneration.	145
PEG-DPA, BAPO & NVP	N/A	Bioinspired adhesive, Flexible wound dressings (PD-NVP)	The antioxidant activity of PC-NVP downregulated pro-inflammatory cytokines (TNF- α , IL-6, and IL-1 β) and scavenged reactive oxygen species (ROS), thereby promoting wound healing by day 12.	167
NIPAm & PEGDA575-Do	Curcumin-loaded micelles	Wound specific thermo-contractile, adhesive hydrogel scaffold (C-PNPD) for diabetic tissue regeneration	C-PNPD inhibited MRSA-induced diabetic wound infection and promoted wound healing by modulating inflammation (downregulating IL-6) and enhancing angiogenesis (upregulating VEGF).	122
Vinyl pyrrolidone, Itaconic acid, NIPAM (PDES)	Mangiferin (MF), MXene nanosheets	Bioinspired NIR responsive MF-Mxene@MNs patches for infected wound regeneration.	MF-Mxene@MNs patches inhibited <i>S. aureus</i> associated infection, downregulated pro-inflammatory cytokines via anti-oxidant potential-supports infected tissue regeneration.	129
SG (SilkMA & GelMA) & TA-Fe ³⁺	W ₁₈ O _{49-x} @Au	NIR responsive phototherapeutic (STFWA) for wound regeneration	NIR-triggered ROS production exerted potent antibacterial effects, and protein-protein interaction analysis revealed CDKN1A as a central regulatory node governing cell cycle control, cellular proliferation, and immunomodulatory responses, thereby contributing to enhanced wound repair.	168
HAMA & PEGDA	Growth Factors (VEGF), Graphene Oxide (GO)	Bioinspired, NIR-responsive, personalized MNs patches (GO/VEGF@MNs) for control drug release in tissue regeneration	GO/VEGF@MNs patches promoted enhanced cell proliferation, migration, and angiogenesis, as evidenced by tube formation in HUVECs <i>in-vitro</i> .	151

SFMA, GelMA & HAMA	HaCaT cells, Cu-EGCG (Copper-polyphenol)	Personalized Cu-EGCG loaded hydrogel scaffold for infectious wound healing and scar treatment.	The hydrogel scaffold exhibited potent antimicrobial and anti-inflammatory effects and enhanced angiogenesis within 10 days via activation of the HIF-1 α /VEGF signaling pathway.	112
HEMA & PEGDA	Silver nanoparticles (AgNPs)	Anti-bacterial wearable hydrogel wound patch.	AgNPs disrupted bacterial protein synthesis and inhibit bacterial growth at the wound site, thereby supporting infection control and promoting tissue regeneration.	169
CMA & BDDE	Retinol (VA)	Retinol loaded personalized eyes patches for antiaging therapy.	Upon VA release, the HYP (hydroxyproline), COL (Collagen deposition) and SOD (superoxide dismutase) were increased and MDA (malondialdehyde) was decreased – enhanced skin regeneration.	170
Sil-MA	Ferulic Acid, MTX, Minoxidil	MNs transdermal delivery & skin regeneration	MN treatment resulted in a higher density of positively stained cells for Ki67, CK14, TGM-1, and TGF- β compared to the control group, indicating enhanced skin microwound repair.	62
HA (Hyaluronic Acid)	Salicylic Acid, Niacinamide	Self-locking MNs patches with anti-bacterial and anti-inflammatory effect for acne vulgaris	Sequential MNs patches (anti-bacterial than anti-inflammatory) implications repaired acne lesion and decreased sebum secretion by day 7.	131
GelMA	HDF cells & Graphene	Electrical stimulates induce skin regeneration	Electrical stimulation of GelMA scaffolds seeded with HDF cells upregulated FGF2, collagen I (Col-I), and MMP9 expression, thereby promoting wound regeneration by day 7	171
GelMA & PEGDA	Heparin	Biomimetic sequestration of growth factors for tissue regeneration.	Upon heparin release, exogenous growth factors such as VEGF are sequestered, promoting tissue regeneration by day 14.	148
Casein (Milk Protein), Ru-SPSS	N/A	Adhesive, Hemostatic therapy for wound repair	The hemostatic properties of tyrosine-rich proteins reduced the blood clotting index (BCI%), thereby supporting tissue repair.	111
HA, PVP & Dihydromyricetin	Lidocaine	MNs patches drug delivery for psoriasis treatment.	The DMY-LD MN patch demonstrated the ability to attenuate immune-inflammatory responses in psoriasis by inhibiting the TLR4/NF- κ B signaling pathway.	134