Plant-Based Hydrogel Dressings in Burn Care: Biomolecular Mechanisms, Biofunctional Advantages, and Translational Challenges

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ABSTRACT

Introduction: Burn injuries remain a major clinical challenge, particularly in developing countries. Researchers have implemented various strategies to manage burn wounds, one of which involves the use of advanced wound dressings such as hydrogels. Plant-based hydrogels offer advantages due to their natural origin and their antibacterial, anti-inflammatory, and antioxidant properties. This review aims to analyze recent developments in burn wound care using plant-based hydrogels.

Methods: A structured literature review was conducted using PubMed, Scopus, and Google Scholar, focusing on studies addressing the biomolecular mechanisms, biofunctional properties, and translational potential of plant-based hydrogels in burn treatment.

Results and Discussion: Plant-based hydrogels consist of a variety of biopolymers that offer multiple benefits. Their bioactivity, biocompatibility, and biodegradability make them superior not only in wound care but also in terms of environmental sustainability. Researchers have developed various crosslinking methods and material combinations, which continue to expand the potential of these hydrogels in burn wound management. Although preclinical findings are promising, rigorous Phase I–III clinical trials are required to validate the therapeutic potential and ensure the clinical translation of plant-based hydrogels in burn wound management.

Keywords: Plant-based hydrogel, Burn wound healing, Biomolecular therapy, Biofunctional materials, Advanced wound dressing.

1. Introduction

Burn injuries are one of the most common types of skin damage, contributing significantly to high rates of morbidity and mortality[1,2]. According to the World Health Organization (WHO) in 2023, burn injuries cause an estimated 180,000 deaths annually, with the highest incidence in low- and middle-income countries, particularly in Africa and Southeast Asia[4]. Children in these regions have up to a sevenfold higher mortality risk from burns compared with those in high-income countries. In low-income countries such as Iran, burn injuries result in mortality rates of up to 35.75%, whereas in high-income countries such as Spain and Singapore, the rates range from 0.86% to 4.61%[5]. These disparities highlight the urgent need for effective therapeutic innovations, with wound dressings playing a central role in improving burn care outcomes globally.

Wound dressings serve to temporarily cover the wound, protect it from further injury, and promote the healing process. Conventional dressings such as gauze, cotton, and bandages remain widely used due to their affordability and exudate-absorbing capacity. However, they have significant drawbacks—they often adhere to the wound bed and can cause secondary trauma during removal[2,3]. Advanced wound dressings with superior moisture retention are increasingly replacing traditional options. These modern dressings include films, foams, hydrogels, and hydrocolloids. Among these, hydrogels have attracted particular attention because of their hydrophilic nature. Their high water-absorbing ability provides a moist environment that accelerates wound healing[2].

Hydrogels may be synthesized from either synthetic polymers or natural polymers such as collagen, chitosan, and alginate. Plant-derived natural polymers offer several advantages over synthetic ones due to their superior biocompatibility and biodegradability. In addition, they provide antibacterial, anti-inflammatory, and other bioactive effects that play key roles in the burn healing process[6]. Moreover, plant-based hydrogels align with the principles of precision and sustainable medicine, delivering dual advantages for patient outcomes and environmental health. This literature review aims to analyze the latest developments in the application of plant-based hydrogels in burn care and to identify existing research gaps in order to guide future, more targeted and applicable studies in burn wound therapy.

2. Methods

We systematically searched PubMed, Scopus, and Google Scholar for relevant studies. We used the following keywords: "plant-based hydrogel", "burn wound", "natural polymer", "biocompatibility", "wound healing". The inclusion criteria were: (1) accessible full-text articles; (2) English language publications released between 2020-2025; and (3) experimental, preclinical, or review studies that specifically addressed plant-based hydrogels for burn treatment, including their biofunctional and biomolecular aspects. Exclusion criteria were: studies unrelated to burn wounds, hydrogels not derived from plants, publications in language other than English, and articles without full-text availability. Two reviewers independently screened the titles and abstracts of all retrieved articles, and any disagreements were resolved through discussion and consensus. In total, 29 eligible articles—including experimental, preclinical, and review studies—were ultimately included and systematically analyzed.

3. Results and discussions

3.1. Botanical sources and hydrogel formation

Plant-based hydrogels form three-dimensional networks primarily composed of natural polysaccharides, which possess significant water absorption and retention capacities. These polysaccharides—including cellulose, alginate, pectin, dextran, tuber starches, and seed gums—are extracted from plants via photosynthetic and biochemical processes. Researchers source these polymers from a wide range of botanical origins, such as cotton, seaweed, algae, tubers, wood, wood fibers, and legume seeds[7]. As illustrated in **Figure 1**, each polymer displays unique functional properties, underscoring the broad potential of plant-derived polymers for hydrogel fabrication beyond conventional wound coverage.

Figure 1 Plant-based hydrogel polymers

Despite their inherent biocompatibility and biodegradability, many plant-derived polymers display limited mechanical integrity and structural stability, necessitating the application of chemical or physical crosslinking strategies to establish robust three-dimensional networks[7]. Chemical crosslinking methods such as photo-crosslinking and click chemistry provide stable covalent networks, while physical methods including ionic interactions, temperature shifts, and pH changes offer tunable and biocompatible alternatives. For instance, ionic interactions such as calcium chloride crosslinking in alginate result in denser and more stable polymer networks[8]. As depicted in **Figure 2**, chemical and physical crosslinking serve as key mechanisms for controlling the structural and functional performance of hydrogels.

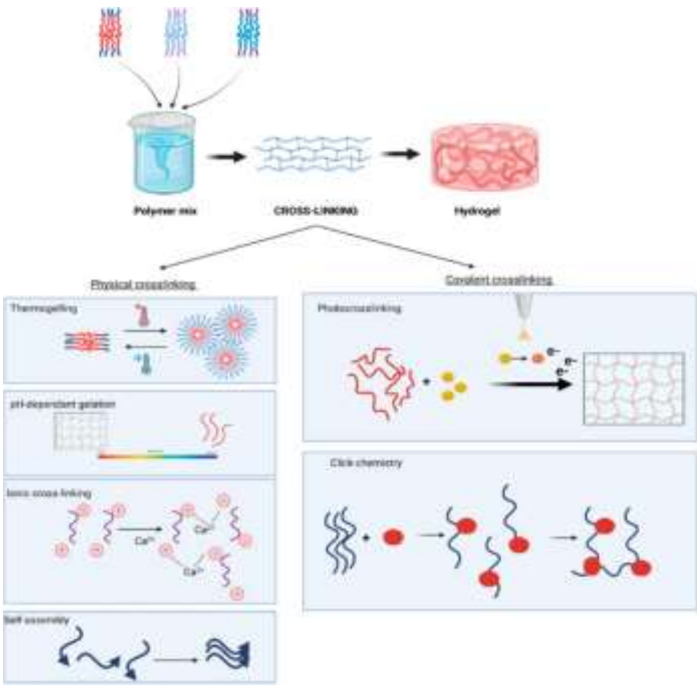

Figure 2 Chemical and physical crosslinking

Currently, researchers are exploring less-studied plant species as novel sources of polymers for hydrogel fabrication. Cactus mucilage (Opuntia spp.) and okra seeds (Abelmoschus esculentus) provide abundant pectin, while taro (Colocasia esculenta) offers high-amylose starch for thermally induced gels[9,10,11]. Southeast Asian plants such as Jatropha curcas and Cassia alata exhibit strong gelling capacity due to rich polysaccharide content, whereas porang (Amorphophallus muelleri) supplies glucomannan and starch with stable hydroxyl groups[12,13,14]. Exploring endemic plant species offers cost-effective, locally sourced, and eco-friendly alternatives for hydrogel development.

3.2. Biocompatibility and safety profile

Plant-based hydrogels consist of natural polymers that exhibit good biocompatibility with human tissue[7]. Researchers have evaluated their safety profiles through comprehensive in vitro and in vivo tests[3]. For example, gelatin-based hydrogels showed no cytotoxicity and successfully promoted the healing of second-degree burns in rat models[15]. Alginate hydrogels combined with zeolite nanocomposites were also well tolerated in third-degree burn models and modestly enhanced healing compared to controls[16]. In addition, essential oil-based hydrogels demonstrated safety in L929 fibroblast cultures, while also exhibiting antimicrobial activity against Staphylococcus aureus and Escherichia coli, along with anti-inflammatory effects through reduced IL-6 and TNF-α and increased VEGF and EGF[17]. Collectively, these findings indicate that plant-based hydrogels are generally safe and unlikely to trigger allergic or immune responses. Nevertheless, certain risks remain, as variability in polymer purity, extraction methods, and crosslinking agents can still influence immunogenicity and cytotoxicity. Thus, the establishment of standardized preparation protocols and rigorous preclinical testing is critical before these materials can be adopted in routine clinical practice.

3.3. Bioactivity and healing promotion

Researchers initially developed hydrogels solely as wound coverings to maintain moisture. However, recent advancements have expanded their therapeutic functions. Plant-based hydrogels not only protect wounds but also contain phytochemicals such as flavonoids, tannins, saponins, glycosides, phenolic acids, terpenoids, and alkaloids. These bioactive compounds exhibit anti-inflammatory, antioxidant, antimicrobial, and angiogenic properties, which actively contribute to tissue regeneration[18].

3.3.1. Antimicrobial activity

Phytochemicals including flavonoids, saponins, tannic acid, alkaloids, and berberine inhibit the growth of bacteria such as Pseudomonas aeruginosa and Staphylococcus aureus by disrupting cell membrane integrity and inhibiting bacterial enzymes. Essential oil–based hydrogels further enhance antimicrobial activity against pathogenic bacteria[17].

3.3.2. Antioxidant effects

Many plant-derived compounds act as antioxidants by reducing reactive oxygen species (ROS) and preserving cellular integrity during healing. Curcumin and chlorogenic acid decrease ROS level and enhance fibroblast viability[41,42]. Curcumin also downregulates pro-inflammatory mediators such as TNF-α, matrix metalloproteinases (MMPs), and inducible nitric oxide synthase (iNOS), thereby reducing oxidative stress[43].

3.3.3. Angiogenic regulation and tissue regeneration

Flavonoid derivatives such as quercetin stimulate wound healing by upregulating VEGF, TGF-β1, and IL-10, while inhibiting TNF-α and MAPK signaling pathways[19]. Hesperidin induces the expression of TGF-β, Smad2/3, and VEGF-C, activating angiogenic signaling pathways that promote angiogenesis and collagen synthesis[20]. Similarly, tannic acid and kebulagic acid enhance keratinocyte and fibroblast proliferation and facilitate angiogenesis through the overexpression of VEGF[18].

3.3.4. Emerging bioactive sources

Some underutilized plant species also provide unique wound-healing phytochemicals. Brown seaweed (Sargassum polycystum) extract contains flavonoids and phenolic compounds that promote fibroblast proliferation, migration, and upregulation of COL1A1 and COL3A1, supporting extracellular matrix remodeling[21]. Likewise, Hsian-tsao polysaccharides from Mesona procumbens enhance VEGF and IL-8 expression while inhibiting matrix-degrading enzymes such as MMP-2 and MMP-9[22].

Collectively, these studies confirm that plant-derived phytochemicals exert multi-targeted effects by modulating oxidative stress, inflammatory cascades, and angiogenesis.

3.4. Structural and functional optimization

Several factors determine the quality of a hydrogel, with physical properties being the most critical. These include porosity, swelling rate, and degradation rate. Hydrogels with high porosity facilitate wound healing by improving nutrient transport, exudate absorption, and oxygen exchange. These features enhance fibroblast migration and proliferation, facilitating faster wound closure in preclinical models. High porosity also increases swelling capacity, which is essential for fluid absorption and rapid exudate removal. The degradation rate further affects healing outcomes. Hydrogels that degrade rapidly can minimize secondary skin damage during dressing changes, promote cell migration and proliferation, and enhance angiogenesis. Importantly, the degradation by products must be non-toxic to support wound recovery[8,23].

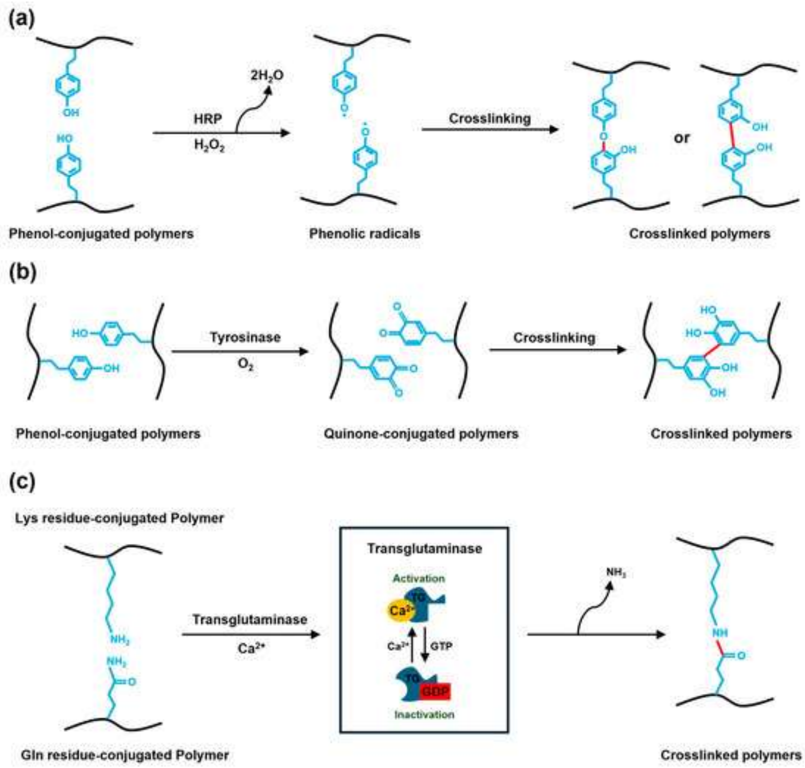

Figure 3 Enzymatic crosslinking

To optimize functional performance, researchers have applied diverse crosslinking strategies aimed at enhancing porosity, swelling behavior, degradation rate, and mechanical strength. Traditional hydrogels typically rely on chemical or physical crosslinking, while modern approaches introduce innovative methods to enhance wound-healing properties[8]. One of the promising approaches currently under development involves enzymatic crosslinking. This strategy, as illustrated in **Figure 3**, offers a highly specific and biocompatible approach to hydrogel formation. This method employs enzymes such as horseradish peroxidase, transglutaminase, and tyrosinase, which react with H_2O_2 to convert phenolic compounds into phenol radicals. These radicals subsequently interact with pectin, alginate, or gelatin to form dense, structured hydrogels[24]. Another strategy to produce more stable hydrogels involves creating composite or hybrid hydrogels by combining plant-based hydrogels with other materials. In one study, researchers combined chitosan with silver nanoparticles (AgNPs) to develop a hybrid hydrogel, which significantly improved the healing stages of burn wounds[44]. Other studies on composite hydrogels revealed that combining polyethylene glycol diacrylate with sodium alginate-based nanoparticles enhanced VEGF expression and stimulated rapid granulation tissue formation[44]. Moreover, combining gelatin-based hydrogels with Manuka honey has emerged as an attractive approach due to the mixture's excellent biocompatibility with human fibroblasts, suggesting its potential use in medical applications[25].

A particularly promising yet underexplored approach involves developing layered hydrogel systems that mimic the natural dermal-epidermal architecture. A recent study reported the potential of a bilayer hydrogel model composed of PLLA thermoplastic membranes, nanofibrous fibrin, human dermal fibroblasts, collagen hydrogels, and keratinocytes. These systems strengthened the skin structure in experimental settings and supported epidermal cell proliferation[26]. Another study using gelatin methacrylamide (GelMA) and poly-L-lactide (PLLA) indicated that bilayered hydrogels may enhance wound healing by promoting angiogenesis and collagen fiber regeneration[27]. This strategy provides a framework for achieving differentiated skin regeneration across multiple layers, although further studies are required to clarify its long-term safety and clinical applicability.

3.5. Clinical evidence and translational potential

While structural and functional optimization has significantly improved hydrogel properties, their ultimate validation requires rigorous clinical evaluation to ensure safety and efficacy in real-world burn care. To date, no registered Phase I-III clinical trials have specifically assessed plant-based hydrogels for burn care. Existing studies have only evaluated these hydrogels in animal models and cell cultures. Clinical research involving plant-based hydrogels has largely focused on chronic wounds, such as diabetic ulcers. The current lack of clinical trials specifically addressing burns underscores an urgent research priority, as findings from diabetic ulcers or chronic wounds may not directly translate to acute thermal injuries. For example, alginate-based hydrogels enriched with vitamins A and E have been shown to reduce inflammatory infiltration. This gap highlights the need for further translational research to validate extensive preclinical findings. Future clinical research should prioritize multicenter Phase I safety trials, followed by randomized controlled studies comparing plant-based with synthetic hydrogels[28].

Translational studies may encounter numerous challenges. Hydrogel stability is a major concern. These hydrogels must maintain their structural integrity within a complex microenvironment and resist premature degradation from hydrolytic mechanisms. Achieving this requires a combination of crosslinking strategies to ensure long-term stability. Another issue is scalability. Not all plant-based hydrogels can be mass-produced due to variations in polymer composition. Hydrogels that employ click chemistry or are thermosensitive may be easier to produce at scale because of their rapid gelation, whereas natural-based hydrogels may show more variability. Product standardization is also challenging, given the inherent variability in plant-derived materials, complicating quality control and consistent validation.

Regulatory hurdles persist as well, especially for hydrogels containing bioactive agents such as growth factors (e.g., VEGF), which must comply with both pharmaceutical and medical device standards[29].

Beyond biofunctional and biomolecular properties, hydrogel development must consider environmental and economic factors. From an environmental perspective, the biodegradability of plant-based hydrogels is particularly important in regions with limited waste management infrastructure. Unlike synthetic hydrogels, natural hydrogels degrade more readily. Moreover, chemical catalysts, solvents, and ionic liquids used in synthesis should align with eco-friendly principles. From an economic standpoint, production must be cost-effective, for example, by utilizing agricultural waste. Ethnobotanical knowledge also provides a valuable foundation for hydrogel development. Traditional herbal wound treatments can guide the selection of promising plant species and enhance community acceptance, as the materials are culturally familiar[30]. While clinical evidence is still scarce, innovative strategies are emerging to expand the therapeutic functions of plant-based hydrogels, particularly as drug delivery platforms.

3.6. Synergistic therapies and combination platforms

Plant-based hydrogels hold significant potential as drug delivery systems. They can encapsulate bioactive molecules, release them in a controlled manner, and extend the therapeutic duration of drugs at targeted sites[31]. Research has shown that pectin-based polymer hydrogels combined with antibiotics such as carbenicillin, chloramphenicol, and kanamycin exhibit significant antibacterial activity. These formulations also support protein stability, making them suitable for dermatological wound care[32]. Hydrogels formulated from starch, gelatin, and polyacrylamide have also demonstrated effective amoxicillin delivery[33]. Beyond antibiotics, plant-based hydrogels can support cell therapy and growth factor delivery. Hydrogels composed of hyaluronan, gelatin, and polylactic acid (PLA) effectively carry mesenchymal stem cell secretomes. They provide sustained release of paracrine proteins and extracellular vesicles, supporting cell proliferation and angiogenesis[34]. GelMA hydrogels loaded with mesenchymal stem cell secretomes regulate fibroblast migration in vitro, promote endothelial tubulogenesis, and enable controlled release of VEGF and TGF-β[35]. Together, these findings show that plant-based hydrogels can serve as active and responsive platforms to support a therapeutic microenvironment.

Recently, interest has grown in “smart” hydrogels capable of responding pH and temperature changes. These systems exploit physiological changes in pH and temperature at injury sites, delivering therapeutic agents within specific ranges suited to intracellular compartments. This responsiveness is achieved through compositional modifications and crosslinking systems that endow hydrogels with environmental sensitivity. Commonly used plant-based components in such systems include chitosan, alginate, hyaluronic acid, guar gum, and dextran[36]. Plant-based hydrogels are often engineered to degrade under acidic conditions ($pH < 5–6$), as prolonged inflammation typically lowers wound pH. In addition to pH and temperature responsiveness, some hydrogels are microenvironment-sensitive, relying on the release of basic fibroblast growth factor (bFGF) and excessive expression of matrix metalloproteinases (MMPs) at the wound site. Although these smart hydrogels show promising results, variability in individual wound microenvironments presents a significant challenge, necessitating further strategy development to create effective, tailored hydrogels for burn treatment[31].

3.7. Sustainability and ethical consideration

Currently, there is increasing attention to the ecological implications of hydrogel production, especially regarding sustainability and waste disposal. It is essential to select hydrogel compositions that reduce toxic byproducts and promote environmentally friendly manufacturing[37]. Plant-based hydrogels are composed of natural polysaccharides, which are biodegradable and part of living organisms. These polysaccharides can be continually sourced from renewable resources, ensuring that their production is not limited by finite materials. Their versatility, natural abundance, and biological functionality make them highly attractive for continued development[38]. This eco-friendly advantage positions plant-based hydrogels not only as therapeutic innovations but also as contributors to the circular bioeconomy.

The sourcing, cultivation, and extraction of raw materials should also minimize environmental impact. The use of plant waste as raw materials has gained significant interest in recent years. For instance, citrus peels contain pectin capable of forming viscoelastic and bioadhesive hydrogels, although further evaluation is needed regarding their wound-healing and antimicrobial activities[46]. Other plant wastes, such as banana stems, contain cellulose suitable for hydrogel formation[39]. These waste materials offer a promising opportunity to reduce agricultural waste and support the development of sustainable green hydrogels. Furthermore, polymer extraction from plant sources should prioritize eco-friendly solvents, such as natural deep eutectic solvents (NADES), to reduce environmental toxicity[40].

From an ethical standpoint, fair trade practices and transparent benefit-sharing are essential to ensure that local farmers and indigenous communities receive equitable recognition and protection of their contributions. These measures, aligned with the Convention on Biological Diversity (CBD) and the Nagoya Protocol, help prevent biopiracy and global economic disparities. Moreover, traditional knowledge of medicinal plants must be acknowledged and safeguarded from exploitation or monopolization[41].

3.8. Research gaps and future directions

In the field of plant-based hydrogel research, promising natural materials from tropical regions, such as porang (Amorphophallus muelleri), cactus (Opuntia spp.), and taro (Colocasia esculenta), remain underexplored. Investigating plant species adapted to diverse climates could broaden the diversity of hydrogel raw materials and uncover novel biofunctional properties. However, the clinical application of plant-based hydrogels in burn wound care remains limited. Translating preclinical evidence into clinical practice is essential to confirm safety and efficacy in human subjects. Most available studies are preclinical and vary widely in terms of polymer source, fabrication methods, and outcome assessment. This heterogeneity limits direct comparison and makes meta-analysis currently unfeasible.

Looking ahead, future research should emphasize customized hydrogel systems designed to interact with the wound microbiome and tailored to individual patient profiles, thereby advancing sustainable personalized therapies. To achieve this, Phase I safety trials in specialized burn centers, randomized comparative studies between plant-based and synthetic hydrogels, and precision approaches incorporating microbiome profiling should be prioritized. Such strategies could establish a new generation of targeted hydrogel treatments that bridge precision medicine with bio-based innovation. Bridging these gaps will enable the translation of promising preclinical findings into real-world burn care solutions.

4. Conclusion

Plant-based hydrogels hold substantial promise for burn wound therapy by combining biocompatibility, multifunctional bioactivity, and eco-sustainability. However, their clinical translation will require rigorous Phase I–III trials, standardized fabrication protocols, and cross-disciplinary collaboration to transform preclinical promise into global burn care impact.

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