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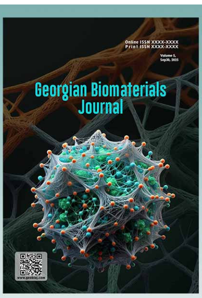

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Review Article

Plant-derived biomaterials as sustainable platforms for controlled release dressings in drug-resistant wounds

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A B S T R A C T

The rising incidence of drug-resistant wound infections poses a major problem for modern healthcare, demanding innovative and sustainable solutions in wound care. Plant-based biomaterials have become promising alternatives for creating advanced wound dressings because of their natural biocompatibility, biodegradability, and rich supply of bioactive compounds with antimicrobial, antioxidant, and anti-inflammatory effects. These natural materials, like cellulose, lignin, and various plant extracts, can be engineered into hydrogels, films, and nanofiber scaffolds that resemble the extracellular matrix and keep a moist environment that promotes tissue regeneration. Additionally, embedding controlled release systems into plant-based dressings allows for the continuous and localized delivery of therapeutic agents, specifically targeting drug-resistant bacteria while reducing systemic side effects. This strategy not only improves wound healing outcomes but also addresses the urgent demand for eco-friendly, multifunctional dressings capable of overcoming the limitations of traditional antibiotics. This review showcases recent progress in plant-based biomaterials as sustainable platforms for controlled release dressings, and applications in Wound Healing.

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1. Introduction

Plant-based biomaterials are increasingly seen as a promising, eco-friendly option for advanced wound dressings, especially for difficult-to-treat, drug-resistant wounds [1, 2]. The rising incidence of chronic wounds complicated by antimicrobial resistance presents a significant clinical challenge, necessitating innovative solutions that effectively control infections while being biocompatible and environmentally sustainable [3-5]. Natural plant polymers provide key benefits like biodegradability, compatibility with the body, and the ability to deliver drugs in a controlled manner, making them well-suited for the development of next-generation wound care products [6].

The move to sustainable wound dressings supports broader environmental and healthcare goals, focusing on renewable resources and green chemistry in material production [7-9]. Plant-derived biomaterials like cellulose, alginate, and other polysaccharides are processed using eco-friendly methods, including enzymatic crosslinking and green solvents [10]. These approaches reduce environmental impacts while maintaining or improving therapeutic effectiveness. Embracing these sustainable practices not only decreases the carbon footprint of wound care products but also encourages cost-effective manufacturing suitable for large-scale production [7].

Besides their sustainability, plant-based biomaterials can be engineered to have multiple functions essential for wound healing [11]. These functions include maintaining wound moisture, facilitating gas exchange, absorbing fluids, and providing mechanical protection [12]. They can also be designed as controlled release systems that deliver antimicrobial agents, growth factors, or other bioactive substances directly to the wound, helping to combat drug resistance and biofilm development [13, 14]. These dressings enhance healing by providing localized, continuous drug delivery and minimizing systemic side effects [15]. Recent progress in biomaterial science has facilitated the integration of plant-based polymers with nanotechnology and bioactive

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molecules, boosting antimicrobial activity and aiding tissue regeneration [16, 17]. For instance, composites that combine plant cellulose with natural antibacterial agents or nanoparticles show great promise in eliminating resistant bacterial strains and speeding up wound healing [3, 6]. These developments underscore the active interaction between natural biomaterials and advanced drug delivery systems, opening the path to smarter, more efficient wound dressings [18]. This review discusses the current state of plant-derived biomaterials as eco-friendly platforms for controlled release dressings. It covers their composition, fabrication techniques, antimicrobial approaches, and clinical significance in treating drug-resistant wounds. By reviewing recent advances and future prospects, the aim is to offer a thorough understanding of how plant-based materials can transform wound care with sustainable, biocompatible, and effective therapeutic options.

2. Plant-Derived Biomaterials

Plant-derived biomaterials are natural substances obtained from plants, including cellulose, lignin, pectin, alginate, and nanocellulose [19, 20]. They are increasingly valued for their biocompatibility, biodegradability, renewability, and environmentally friendly properties [21, 22]. These features make them well-suited for various uses in biomedical engineering, tissue regeneration, wound care, drug delivery, food technology, cosmetics, environmental health, and energy fields [23].

The advantages of Plant-derived biomaterials are shown in Fig. 1. Also, Table 1 provide a concise overview of the main types, their biomedical relevance, and properties of Plant-Derived Biomaterials.

3. Mechanisms of Controlled Release

Controlled release from plant-derived biomaterials typically relies on the physicochemical and structural properties of the biopolymer matrix, enabling the regulated and sustained delivery of encapsulated bioactive agents such as nutrients, drugs, or agrochemicals [41, 42]. One of the primary mechanisms involves diffusion-controlled release, where the encapsulated compound migrates through the biopolymer matrix as a result of a concentration gradient. The rate of this diffusion can be modified by manipulating the polymer's composition, molecular arrangement, and internal porosity, allowing the release profile to be tailored from rapid to sustained over prolonged periods [8, 41]. Another common mechanism is matrix swelling, found in hydrogels and other plant-based polymer systems [8, 43]. When exposed to aqueous environments, these materials absorb water and swell, thereby enabling the contained agents to gradually escape as the hydrogel network loosens. This process is influenced by the hydrophilicity and crosslink density of the polymer network, both of which can be engineered to achieve the desired release kinetics [44].

Degradative release is also important, especially for applications that require release triggered by environmental or biological stimuli [45, 46]. Plant-derived biomaterials, such as lignin or modified cellulose, can be designed to undergo controlled degradation, either through hydrolysis or enzymatic action [47]. As the polymer structure erodes, it releases the encapsulated bioactive compound, with the release rate determined by the rate of matrix breakdown [46, 48].

Stimuli-responsive or smart release systems offer advanced control using external or environmental triggers [49, 50]. These systems respond to changes such as pH, temperature, or the presence of specific enzymes by altering the polymer's properties to facilitate the release of the active ingredient. For example, incorporating enzyme-sensitive linkers or crosslinks into plant-derived matrices allows for selective release in the presence of particular biological signals, which is particularly valuable for targeted drug delivery or precision agriculture [51]. The versatility in tuning these mechanisms, by varying the plant biopolymer type, structural modification, or environmental responsiveness, makes plant-derived biomaterials highly attractive for developing safe, effective, and sustainable controlled release systems for applications across biomedicine, agriculture, and food technology [52].

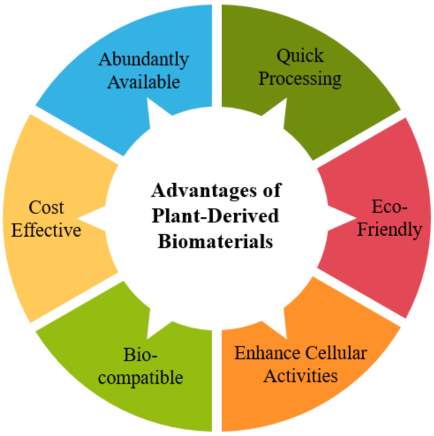

Fig. 1. Advantages of Plant-Derived Biomaterials

Table 1. Types and Characteristics of Plant-Derived Biomaterials

Type	Description	Source	Characteristics	References
Nanocellulose	Natural biopolymer with hierarchical fibrillar structure	Wood, hemp, cotton, potato tuber, algae	High mechanical strength, biocompatible, biodegradable, forms nanocrystals	[24, 25]
Alginate	Polysaccharide from brown seaweed	Marine algae (brown algae)	Biocompatible, biodegradable, hydrogel-forming, low-cost, moderate cell adhesion	[24, 26]
Pectin	Polysaccharides typical of plant cell walls	Land plants	Used as a gelling agent, biocompatible and biodegradable	[27, 28]
Starch	Polysaccharide storage molecule	Plants like potato, corn	Polysaccharide, biodegradable, widely available	[24, 29, 30]
Agarose	Polysaccharide from red algae	Red algae	Thermoreversible gel, biocompatible, structurally supportive	[31]
Fucoidan	Sulfated polysaccharide from brown algae	Brown algae	Anti-inflammatory, anticoagulant properties; biomedical applications	[32]
Carrageenan	Sulfated polysaccharide from red seaweed	Red algae	Gel-forming and bioactive	[31, 33]
Protein-based Polymers	Plant-derived proteins	Plants	Biocompatible, biodegradable, useful in scaffolds	[34]
Extracellular Vesicles	Nano-sized vesicles released by plant cells	Plant cells	Used in drug delivery, signaling	[35]
Mucilage	Polysaccharide-rich gel-like substances from plants	Plants (seeds, leaves)	Biocompatible, biodegradable	[36-38]
Decellularized Scaffolds	Plant tissues processed to remove cells but retain structure	Whole plants (after cell removal)	Natural structural framework, biocompatible	[39]
Whole Plant-Based Biomass	Bulk plant material used for composite biomaterials	Plants	Renewable, eco-friendly scaffold materials	[23, 40]

4. Applications in Wound Healing

Applications of plant-derived biomaterials in wound healing have gained significant attention due to their natural properties, biocompatibility, biodegradability, and ability to mimic the extracellular matrix (ECM), which supports tissue regeneration and repair [53, 54]. These biomaterials are used to create wound dressings and formulations that enhance the healing process, especially by promoting cell adhesion, proliferation, moisture retention, and antimicrobial activity [55].

One example is a study by Buzzi et al [56] on the therapeutic use of Calendula officinalis extract in diabetic foot ulcers (DFUs), where clinical studies have shown that topical application of its hydroethanolic extract, combined with appropriate dressing, results in significant wound closure rates (up to 78% within 30 weeks), reduces exudate, and diminishes necrotic tissue without adverse effects.

The current use of plant-derived dressings in wound care reflects significant advances leveraging natural compounds for enhanced healing properties [57-59]. Various biopolymeric formulations incorporating herbal bioactives such as Aloe vera (AV), plant extracts, and polysaccharides are being developed into modern wound dressings like hydrogels, films, creams, and nanofiber scaffolds [60]. These dressings not only provide traditional protection but actively promote wound healing through antimicrobial, antioxidant, and tissue-regenerating effects [61, 62].

Hydrogels containing natural polymers and plant extracts maintain a moist wound environment that accelerates epidermal regeneration, reduces infection, and stimulates autolytic debridement [63]. For example, AV-loaded hydrogels combined with polymers like sodium hyaluronate and chitosan have demonstrated efficacy in skin tissue regeneration within days [64].

Film dressings infused with extracts from plants like Plantago lanceolata, Calendula officinalis, Lawsonia inermis, and Moringa oleifera have been optimized for properties such as antioxidant and anti-inflammatory activity, enhancing wound closure and tissue repair [65]. These polymer-based films show promising in vitro and in vivo results in accelerating healing processes [66].

Cutting-edge research also focuses on plant-based materials for transdermal delivery, exploiting biocompatible gums, mucilages, and secondary metabolites with versatile pharmacological benefits [4]. Secondary plant metabolites with antimicrobial and bioactive properties are integrated into dressings to improve therapeutic effects while leveraging the natural biodegradability and cost-effectiveness of plant-derived components [58].

Innovations include soy protein isolate-based dressings, such as NeuEsse Inc.'s OmegaSkin™, which degrade into beneficial amino acids that support cellular repair at the wound site [67]. Such bioactive, biodegradable dressings are particularly valuable for chronic and burn wounds, reducing pain and infection risk through minimal dressing changes [68, 69].

5. Future Perspectives and Challenges

Advances in materials science have enabled the design of modern wound dressings incorporating natural polymers with intrinsic antimicrobial, anti-inflammatory, and regenerative properties that align well with the complex biology of wound healing [70, 71]. These natural biomaterials, provide biocompatible matrices that facilitate cell adhesion, proliferation, moisture retention, and protection against infection, all critical for treating chronic and drug-resistant wounds [3]. An important future direction involves integrating these plant-derived materials with smart bioactive components, such as antimicrobial phytochemicals, growth factors, and regenerative agents, to enhance therapeutic efficacy while reducing dependence on conventional antibiotics amid rising antimicrobial resistance [58, 72].

However, significant challenges remain before widespread clinical translation. Many bioactive dressings still lack rigorous clinical validation, with most studies conducted in vitro or in animal models [72]. There is also a need to better understand the mechanisms of action of these natural compounds and their interactions within complex wound microenvironments. Regulatory approval processes, production scalability, cost-effectiveness, and integration into patient care protocols must also be addressed [73]. Furthermore, the development of plant-derived dressings capable of real-time monitoring and responsive action to dynamic wound conditions such as smart dressings responsive to infection or inflammation biomarkers represents an emerging area with great potential but technical complexity [74].

6. Conclusion

Plant-derived biomaterials provide a sustainable and promising platform for controlled release dressings aimed at drug-resistant wounds. Their inherent biocompatibility, biodegradability, and bioactivity, such as antimicrobial and anti-inflammatory properties, make them ideal candidates for advanced wound care applications. These natural polymers can facilitate targeted drug delivery, maintain a moist healing environment, and promote faster tissue regeneration while reducing side effects and resistance issues associated with synthetic materials. Additionally, innovations that incorporate plant-derived components with other biomaterials have shown improved mechanical strength and enhanced therapeutic effectiveness in wound healing models. Therefore, utilizing plant-derived biomaterials aligns with the growing demand for eco-friendly, effective, and controllable wound dressings, especially for managing difficult infections and drug-resistant wounds.

Author Contributions

Mahsa Borzouyan: Conceptualization, Writing – original draft, Writing – review & editing; **Mehrasa Nikandish:** Writing – original draft, Writing – review & editing. All authors read and approved the final version of manuscript.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data Availability

No data is available.

Ethical issues

The authors confirm full adherence to all ethical guidelines, including the prevention of plagiarism, data fabrication, and double publication.

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