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PLANT-DERIVED BIOACTIVES IN ADVANCED WOUND DRESSINGS: HYDROGEL TECHNOLOGIES, ON-DEMAND DELIVERY SYSTEMS, AND TRANSLATIONAL CHALLENGES

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ABSTRACT

Wound management has progressed from conventional topical preparations to advanced dressings designed to maintain an appropriate moisture balance, manage exudate, protect the wound bed, and support tissue repair. Plant-derived bioactive compounds have attracted considerable research interest because of their reported antioxidant, anti-inflammatory, antimicrobial, and tissue-modulating properties. However, botanical ingredients exhibit substantial variability in composition, biological activity, and safety, making standardization and formulation-specific evaluation essential. This narrative review examines the biological processes involved in wound healing, hydrogel technology, plant-derived bioactives, natural polymer matrices, and emerging strategies for developing advanced wound dressings. Selected botanical ingredients, including Aloe vera, curcumin from Curcuma longa, Centella asiatica, green-tea polyphenols, and neem-derived constituents, are discussed in relation to their potential formulation applications and the limitations of the available evidence. Cellulose derivatives, pectin, starch, and alginate are considered as matrix-forming materials, with their botanical or marine origins clearly distinguished. Particular attention is given to an emerging research concept involving a dry, unit-dose tablet that can be dispersed and hydrated to produce a wound-contact hydrogel. Such a system could offer advantages in portability and on-demand preparation, but its feasibility depends on reproducible hydration, gel cohesion, dose uniformity, extract stability, microbiological control, and biological compatibility. The proposed tablet-activated system should be regarded as a developmental concept rather than an established clinical technology. Future research should prioritize standardized botanical materials, comparative formulation studies, validated analytical methods, risk-based biological evaluation, and clinically relevant performance outcomes. Translational progress will depend on demonstrating a meaningful advantage over conventional ready-to-use dressings.

KEYWORDS: Plant-derived bioactives; wound dressings; hydrogel technology; phytotherapy; natural polymers; on-demand delivery; tablet-activated hydrogel; wound healing; formulation development; biocompatibility.

1. INTRODUCTION

Skin is a dynamic protective organ that limits fluid loss, restricts microbial entry, and contributes to temperature regulation and sensory function. Injury disrupts this barrier and initiates a coordinated repair response involving haemostasis, inflammation, proliferation, and tissue remodelling. Wound healing may be delayed by infection, inadequate perfusion, diabetes, pressure, malnutrition, repeated trauma, ageing, and other underlying conditions. Although a dressing cannot correct every underlying cause, it can help protect the wound, manage moisture, and minimize further mechanical injury.

Traditional healthcare systems have used plant-derived gels, pastes, oils, and extracts for various skin conditions. Contemporary pharmaceutical research has investigated botanical ingredients in films, sponges, nanofibres, ointments, and hydrogel dressings. Hydrogels are particularly relevant because their hydrated polymer

networks can retain water, conform to irregular surfaces, and provide a matrix for local delivery of selected bioactive compounds.[1–4]

Nevertheless, traditional use and laboratory observations should not be interpreted as proof of clinical efficacy. Antioxidant activity in a chemical assay does not establish improved wound closure in humans, and antimicrobial activity in vitro does not demonstrate prevention or treatment of clinical infection. Botanical identity, extraction conditions, marker-compound content, contaminants, chemical stability, release characteristics, and skin-cell compatibility must all be considered.

This review critically discusses plant-derived bioactives and hydrogel technologies, with particular attention to a proposed tablet-activated hydrogel dressing. The concept is examined in terms of formulation feasibility, potential advantages, quality requirements, safety considerations, and the evidence needed before clinical application.

2. REVIEW METHODOLOGY AND SCOPE

This article is structured as a narrative review of selected published literature on wound-healing biology, natural polymers, plant-derived bioactives, hydrogel dressings, and formulation development. The discussion draws on peer-reviewed reviews and experimental studies addressing botanical films, hydrogels, polysaccharide-based systems, curcumin-containing formulations, and Aloe vera-based materials.

The evidence is interpreted qualitatively because the available studies differ in botanical source, extraction method, polymer composition, experimental model, analytical method, and outcome measurement. These differences limit direct comparisons and do not justify combining heterogeneous findings into a single quantitative estimate.

This article is not presented as a systematic review. A formal systematic review would require reproducible database searches, predefined eligibility criteria, duplicate screening, risk-of-bias assessment, and transparent reporting of study selection.

The tablet-activated hydrogel discussed in this article is a proposed research concept. Its inclusion does not imply that a particular tablet-based wound dressing has been validated or established for clinical use.

3. SKIN STRUCTURE AND THE PHYSIOLOGY OF WOUND HEALING

The epidermis forms the outer protective barrier, while the dermis contains collagen, elastin, blood vessels, nerves, fibroblasts, and immune cells. The subcutaneous tissue provides cushioning and structural support. Damage to these layers initiates a coordinated sequence of biological events.

Haemostasis begins with vascular responses, platelet activation, and fibrin-clot formation. The inflammatory phase involves immune-cell recruitment and removal of damaged tissue and microbial contaminants. During proliferation, fibroblasts produce extracellular matrix, keratinocytes migrate across the wound surface, angiogenesis supports tissue development, and granulation tissue forms. During remodelling, collagen is reorganized and the repaired tissue gradually gains mechanical strength.[5,6]

These phases overlap rather than occurring as completely separate events. Excessive or persistent inflammation, impaired circulation, infection, and metabolic disturbances can interfere with repair.

A suitable dressing should maintain an appropriate moisture balance, protect fragile tissue, and manage wound exudate without causing maceration. Chronic wounds may require additional interventions, including pressure relief, debridement, infection management, and treatment of underlying vascular or metabolic conditions. Consequently, the suitability of a hydrogel must be assessed for the intended wound type rather than assumed from its general material properties.

4. HYDROGEL TECHNOLOGY IN WOUND MANAGEMENT

Hydrogels are three-dimensional polymer networks capable of absorbing and retaining water while maintaining a network structure. Their swelling behaviour depends on polymer chemistry, crosslink density, pH, ionic strength, temperature, and the surrounding fluid.

Physical crosslinking may involve ionic interactions, hydrogen bonding, crystallites, or polymer-chain entanglement. Chemical crosslinking involves covalent bonds and requires careful assessment of residual reagents and degradation products.

Potential advantages of hydrogels include high water content, conformability, reduced adherence in suitable formulations, and the ability to incorporate selected therapeutic agents. Depending on their composition, they may provide moisture to relatively dry wounds or support local delivery of bioactive compounds.

Important limitations include inadequate mechanical strength, dehydration, excessive swelling, uncontrolled release, and the difficulty of maintaining product stability during storage. Sterilization can also alter polymer properties or degrade sensitive botanical constituents.

Hydrogels are not inherently antimicrobial. Claims of antimicrobial action, infection prevention, or accelerated wound closure require appropriate experimental or clinical evidence. Material performance must be

evaluated together with biological safety and the intended clinical application.[1–4]

5. NATURAL AND PLANT-DERIVED POLYMER MATRICES

Natural polymers offer different combinations of hydration, gel formation, film-forming ability, biodegradability, and mechanical performance. Their suitability depends on material grade, molecular characteristics, processing conditions, and the intended dressing design.

Table 1: Comparison of selected polymeric materials for hydrogel dressing development.

Material	Typical source	Potential formulation role	Main limitations
Cellulose derivatives	Plant cellulose or other specified sources	Water retention, viscosity control, film formation	Mechanical properties depend on grade and blending
Pectin	Plant cell walls	Gel formation and matrix development	Sensitive to pH, ions, and formulation conditions
Starch and modified starch	Cereals and tubers	Hydrophilic, potentially economical matrix	Water sensitivity and variable wet strength
Alginate	Brown seaweed	Ionic gel formation and exudate management	Marine rather than land-plant origin; may require a secondary dressing
Chitosan	Commonly crustacean or fungal chitin	Film formation and potential biological interactions	Not inherently plant-derived; source and purity require documentation
Gelatin and collagen	Usually animal-derived	Matrix formation and cell-interactive properties	Source-dependent characteristics and potential biological variability
Hyaluronic acid	Animal-derived or fermentation-produced	Hydration and extracellular-matrix-related applications	Properties depend on molecular weight and manufacturing source

Alginate deserves particular consideration because it forms gels in the presence of suitable divalent ions. Cellulose derivatives and pectin may provide useful hydration and matrix-forming properties, whereas starch-based systems require careful evaluation of wet strength and stability.

The term “natural polymer” should not be used interchangeably with plant-derived polymer. Material origin, processing, purity, and grade should be stated explicitly. Combining polymers may improve handling and gel integrity, but it can also introduce compatibility problems and additional variability.[5,13–15]

For a tablet-activated system, the dry matrix must withstand manufacturing, transport, and storage while remaining capable of reproducible hydration. The final hydrated material must retain adequate cohesion and be compatible with the intended wound-contact application.

6. PLANT-DERIVED BIOACTIVES FOR WOUND DRESSINGS

6.1. Aloe vera

Aloe vera contains polysaccharides and other constituents whose composition depends on plant material and processing. Its inner-leaf gel has been investigated in hydrogel formulations because of its hydration properties and potential biological activity.[2]

Reported research has explored antioxidant effects, inflammatory responses, fibroblast behaviour, and epithelial repair. However, outcomes depend on the formulation, concentration, preparation method, and experimental model.

The inner-leaf gel must be distinguished from the latex layer, which contains anthraquinone-related constituents and may introduce unwanted effects. Botanical identity, plant part, extraction procedure, chemical characteristics, microbial quality, and stability should be specified.

A standardized Aloe vera ingredient may serve as a bioactive component, a hydrophilic ingredient, or both. Its inclusion should not be assumed to improve gel performance automatically. Extract loading can influence pH, viscosity, colour, mechanical strength, and microbial stability. The finished formulation therefore requires physicochemical characterization and biological evaluation.

6.2. Curcumin from Curcuma longa

Curcumin is a polyphenolic constituent of Curcuma longa that has been investigated for antioxidant and anti-inflammatory properties. Its limited aqueous solubility and sensitivity to environmental conditions create formulation challenges.

Hydrogel systems may support local delivery, but the extent of release depends on the drug's physical state, the polymer network, and the surrounding medium. Dispersions, complexation strategies, or carrier systems may improve formulation performance, although each approach introduces additional variables that require testing.

Curcumin-containing hydrogel studies provide a basis for further investigation, but experimental findings should not be generalized to every curcumin formulation.[3,4,11,12] A suitable analytical method should

establish marker content and stability during manufacture, storage, hydration, and release.

Purified curcumin, turmeric powder, and crude turmeric extract are not equivalent materials. The identity of the ingredient used must match the biological and formulation claims made in the article.

6.3. Centella asiatica

Centella asiatica contains triterpenoids, including asiaticoside, madecassoside, asiatic acid, and madecassic acid. These constituents have been investigated in relation to extracellular-matrix biology, inflammation, and tissue repair.

The chemical composition of an extract may vary with plant source, plant part, cultivation, and extraction conditions. Standardized extracts and defined marker specifications may improve reproducibility.

For hydrogel development, the extract should be assessed for marker content, compatibility with the polymer matrix, chemical stability, release behaviour, and cell compatibility. Mechanistic findings should be described according to the actual evidence available for the particular preparation.

6.4. Other botanical candidates

Additional candidates include green-tea polyphenols from Camellia sinensis, neem-derived constituents from Azadirachta indica, calendula preparations, chamomile extracts, and selected plant-derived flavonoids.

These materials may have different chemical profiles and biological effects. Their suitability depends on evidence quality, potential irritation or sensitization, extract reproducibility, availability, sustainability, and compatibility with the polymer system.[3,4,8,9]

Polyherbal combinations can broaden the range of constituents in a formulation but complicate standardization and interpretation. Early formulation studies may therefore benefit from evaluating a single standardized extract before investigating combinations.

7. PHYTOCHEMICALS AND THEIR POTENTIAL FUNCTIONS

Plant-derived constituents include polyphenols, flavonoids, terpenoids, saponins, and polysaccharides. Certain compounds have been investigated for antioxidant activity, inflammatory modulation, antimicrobial effects, or interactions with cells involved in tissue repair.

However, a broad chemical category does not guarantee a consistent biological response. Compounds within the same category may differ in potency, solubility, stability, toxicity, and interactions with other formulation components.

A decrease in reactive oxygen species in a chemical assay does not establish a clinical antioxidant effect. Similarly, bacterial growth inhibition in vitro does not demonstrate effectiveness against a wound infection or biofilm.

A practical formulation strategy should identify suitable chemical markers and use validated methods to assess their identity, quantity, and stability. Total phenolic content may provide supplementary information but cannot replace marker identification or a suitable chemical fingerprint.

The effects of the polymer alone must also be distinguished from those of the botanical ingredient. Appropriate blank formulations, extract-only controls, and suitable comparators are essential when interpreting experimental findings.

8. PROPOSED MECHANISMS OF PLANT-LOADED HYDROGELS

Plant-loaded hydrogel dressings may combine the physical functions of a dressing with the local delivery of selected bioactive compounds.

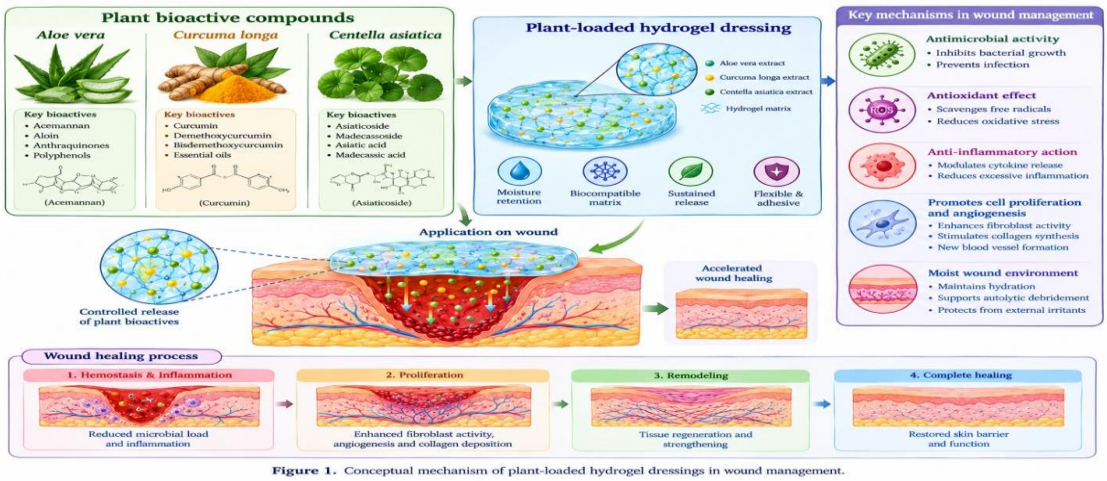


Figure 1: Conceptual mechanism of plant-loaded hydrogel dressings in wound management.

Figure 1: Conceptual mechanism of plant-loaded hydrogel dressings in wound management.

The physical and biological functions must be evaluated separately. Moisture retention and fluid uptake are material properties, whereas changes in cell viability, inflammatory markers, bacterial burden, or wound closure are biological outcomes.

Antioxidant assays, antimicrobial tests, cell-migration studies, and histological analyses provide different types of evidence. No single assay establishes the overall clinical effectiveness of a dressing. The conclusions should reflect the strength and limitations of the evidence available for each formulation.[4,9–12]

9. PROPOSED TABLET-ACTIVATED HYDROGEL DRESSING

9.1. Concept and rationale

A tablet-activated hydrogel dressing is proposed as a dry, unit-dose formulation that is dispersed and hydrated before application. The intended advantages include portability, reduced water content during storage, defined unit-dose handling, and the possibility of separating moisture-sensitive ingredients from the hydration medium.

The concept remains a research proposal. The established literature on hydrogels does not, by itself, establish the safety, effectiveness, or clinical availability of this particular tablet-based approach.

A possible system could contain

1. A dry compact containing selected swellable polymers and a standardized botanical ingredient.
2. A separately packaged hydration medium, where required.
3. A suitable single-use mixing or application component.
4. A compatible sterile backing or secondary dressing, where appropriate.

The hydrated product would need to form a reproducible, cohesive material suitable for the intended wound-contact application.

9.2. Technical challenges

Crushing may introduce powder loss, uneven dispersion, contamination, and variation in the final gel. Tablet compression may also affect polymer hydration or the stability of sensitive botanical constituents.

Important development questions include

- Can the tablet be dispersed reproducibly?
- Does hydration produce a uniform gel without persistent particles?
- Can the formulation achieve suitable pH, cohesion, and spreadability?
- Does the botanical marker remain stable during processing and storage?
- Can microbiological quality be maintained throughout preparation and use?
- Does the proposed design offer a meaningful advantage over a ready-to-use hydrogel?

An alternative design that disperses without crushing may reduce preparation variability. The final design should be selected on the basis of performance, usability, and risk assessment rather than novelty alone.

The proposed system must not be recommended for direct clinical use until its preparation method, biological safety, microbiological controls, and performance have been adequately validated.

10. FORMULATION DEVELOPMENT STRATEGY

Formulation development should proceed through predefined stages rather than selecting ingredients solely on the basis of their reported biological properties.

Table 2: Proposed development and evaluation framework.

Stage	Main activity	Important evaluation parameters
I	Polymer screening	Flow, compactability, moisture sensitivity and hydration
II	Botanical incorporation	Marker content, compatibility and chemical stability
III	Tablet and gel optimization	Crushing strength, friability, dispersion time, gel cohesion and spreadability
IV	Performance evaluation	Swelling, fluid uptake, pH, erosion and marker release
V	Biological evaluation	Cell compatibility and justified antimicrobial testing
VI	Packaging and stability	Moisture protection, seal integrity, marker stability and microbiological quality
VII	Further translational assessment	Risk evaluation, relevant preclinical evidence and justified clinical investigation

Experimental designs, including factorial or response-surface approaches, may help evaluate the effects of polymer ratio, compression force, particle size, and hydration volume. Responses should be selected before experimentation and assessed using appropriate replication and statistical analysis.

No particular composition or concentration should be described as optimal without supporting experimental data. The formulation should be selected using predefined acceptance criteria and comparison with appropriate controls.

11. PHYSICOCHEMICAL CHARACTERIZATION AND RELEASE

The physical performance of a tablet-activated hydrogel depends on the dry compact and the hydrated matrix. Tablet evaluation may include mass variation, dimensions, crushing strength, friability, moisture content, and dispersion time.

Hydrated-gel evaluation may include swelling ratio, fluid uptake, pH, spreadability, gel cohesion, erosion, mechanical properties, and water-vapour transmission where relevant to the intended use.

The swelling ratio can be expressed as

Swelling ratio = (Wet mass − Dry mass) / Dry mass

The test method, hydration medium, temperature, and sampling time should be specified to ensure reproducibility.

Release may involve diffusion, polymer relaxation, swelling, erosion, or combinations of these processes. The behaviour of a complex botanical extract may not be represented adequately by a single marker compound. Where possible, release studies should therefore use a justified analytical marker and acknowledge this limitation.

Release conditions must be appropriate for the ingredient and formulation. A good mathematical fit to a release model does not, by itself, establish the underlying mechanism or demonstrate clinical benefit.

A suitable comparison should include a polymer-only control, a botanical-loaded formulation, and an appropriate comparator. Analytical interference from extract colour, turbidity, or polymer components must be considered during method development.[13, 14]

12. MANUFACTURING, QUALITY CONTROL, AND STABILITY

A potential manufacturing sequence includes botanical authentication, extract preparation and standardization, polymer qualification, particle-size control, blending, tablet compression, finished-product testing, packaging, and stability evaluation.

Botanical raw materials require suitable controls for identity, contaminants, microbial quality, and marker content. Manufacturing records should document the plant species, plant part, supplier or collection source, extraction conditions, marker assay, polymer grade, processing parameters, and packaging materials.

A low-moisture product is not necessarily sterile. The appropriate microbiological control strategy must be established according to the product's intended use and applicable requirements. Any sterilization or aseptic-processing approach must be assessed for its effects on polymer properties, botanical stability, and final product performance.

Quality control should cover the attributes of both the dry compact and the hydrated material. Chemical testing should address marker identity, content, degradation, and release. Microbiological testing should be justified by the intended product and include sterility testing if the product is labelled sterile.

Packaging should protect the formulation from moisture, light, and other relevant environmental factors. Stability studies should use justified storage conditions and predefined acceptance criteria.

13. BIOLOGICAL SAFETY AND RISK MANAGEMENT

Botanical origin does not guarantee safety. Potential concerns include irritation, allergic sensitization, cytotoxicity, contaminants, residual solvents, microbial contamination, and harmful degradation products.

Biological evaluation should consider the nature and duration of contact, the intended wound type, the quantity applied, and the characteristics of the final formulation. Testing may include cytotoxicity, irritation, sensitization, and other endpoints justified by the product's risk profile.

The complete formulation must be evaluated because polymer–extract interactions and processing can change its properties. Individual ingredients that appear acceptable cannot automatically establish the safety of the finished dressing.

Microbiological control is particularly important for hydrated products. The manufacturing and packaging strategy should minimize contamination and preserve product quality throughout the intended period of use.

The proposed tablet-activated dressing should not be described as clinically safe or effective until appropriate biological and performance evidence is available. Regulatory and biological evaluation should be conducted by qualified personnel using applicable standards and requirements.[2,3]

14. COMPARISON WITH CONVENTIONAL WOUND DRESSINGS

Conventional dressings differ in their ability to manage moisture, absorb exudate, protect tissue, and accommodate different wound types.

Table 3: General comparison of wound-dressing approaches.

Dressing type	Principal function	Important limitation
Gauze	Basic coverage and fluid absorption	Dry gauze may adhere to the wound bed
Film dressing	Protective barrier and visual inspection	Limited fluid absorption
Foam dressing	Absorption and cushioning	May not be appropriate for every wound
Alginate dressing	Fluid uptake and gel formation	Often requires a secondary dressing
Hydrocolloid dressing	Occlusive protection and interaction with exudate	Suitability depends on wound condition
Ready-to-use hydrogel	Moisture donation and local contact	May require additional coverage
Proposed tablet-activated hydrogel	Potential portability and on-demand preparation	Preparation variability, hydration, sterility and usability require validation

A botanical-loaded hydrogel may add local delivery of selected plant-derived compounds to the physical functions of a dressing. However, this additional complexity increases requirements for standardization, chemical stability, release testing, and biological evaluation.

A tablet-based approach should be compared with ready-to-use alternatives to determine whether its potential advantages justify the added preparation steps. Dressing selection must depend on wound characteristics, exudate, tissue condition, patient comfort, and appropriate clinical assessment.[1,5,7]

15. CLINICAL TRANSLATION AND REGULATORY CONSIDERATIONS

Translating a laboratory formulation into a clinical product requires reproducible manufacturing, validated analytical methods, appropriate biological evaluation, and evidence of performance in the intended application.

Favourable swelling or antioxidant results do not establish that a dressing will improve clinical outcomes. Application difficulty, pain during removal, instability, contamination, or inadequate performance may limit its usefulness.

The regulatory pathway depends on the intended purpose, composition, mechanism of action, and applicable jurisdiction. A dressing containing botanical ingredients may require a different regulatory assessment depending on its claims and characteristics. In India, the applicable classification and requirements should be confirmed with qualified regulatory professionals and the relevant authority.

Clinical investigations should specify the wound type, inclusion criteria, comparator, background standard of care, endpoints, adverse-event monitoring, and follow-up. Potential outcomes include wound-area reduction, time to complete closure, pain during dressing changes, exudate management, infection-related outcomes, and quality of life.

Any clinical investigation must follow applicable ethical and regulatory requirements. Established wound care should not be withheld in order to test an experimental dressing.

16. RESEARCH GAPS AND FUTURE DIRECTIONS

Several challenges remain in the development of plant-loaded hydrogel dressings. These include inconsistent botanical standardization, incomplete reporting of marker compounds, variability in experimental methods, limited long-term stability data, and insufficient clinical evidence for many formulations.

Research should distinguish the contribution of the polymer from that of the botanical ingredient and use appropriate controls. Negative findings should also be reported to improve the reliability of the evidence base.

For tablet-activated systems, priorities include determining whether compression affects botanical stability, whether hydration is uniform, whether the resulting gel remains cohesive, and whether preparation introduces unacceptable contamination or dose variability.

Future studies should compare the proposed system with a ready-to-use hydrogel and a polymer-only control. The evaluation should consider manufacturing feasibility, packaging, user handling, reproducibility, and the intended clinical application from the beginning of development.

Sustainable sourcing is another consideration. Plant-derived materials may vary in availability, quality, and environmental impact. Traceable supply chains and suitable extraction methods may improve reproducibility, but the terms “natural” and “sustainable” should not be treated as automatic evidence of safety or environmental superiority.

17. CONCLUSION

Plant-derived bioactives incorporated into hydrogel dressings represent a research approach that combines moisture management with the potential for local delivery of selected botanical constituents. Aloe vera, curcumin, Centella asiatica, and other plant-derived materials have been investigated in experimental wound-care formulations, while cellulose derivatives, pectin, starch, and alginate offer different matrix-forming properties.

Their potential should be assessed individually because botanical composition, polymer structure, release behaviour, and biological effects vary between formulations. Laboratory activity alone cannot establish clinical effectiveness.

The proposed tablet-activated hydrogel dressing offers a concept for portable, on-demand preparation, but its advantages remain to be demonstrated. Reproducible hydration, gel integrity, dose uniformity, chemical stability, microbiological quality, usability, and biological compatibility are essential development requirements.

Further progress requires standardized ingredients, appropriate controls, validated characterization methods, staged biological evaluation, and clinically relevant comparative studies. Traditional phytotherapy can provide inspiration for formulation research, but the development of a reliable wound dressing must be guided by reproducible evidence, appropriate quality standards, and demonstrated benefit.

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