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Review Article

Formulation And Evaluation Of A Herbal Wound Healing Cream Using Neem, Aloe Vera, Turmeric And Tulsi

Sadanand Patil[1], Dr. Ganesh Bansode[1], Joshi D.A.[2].,Parshuram Garad[3], Aditya Holkar[4], Sivraj Mundkar[5]

[1]*Department of Pharmaceutical Chemistry, Latur College of Pharmacy, Hasegaon*
[2]*Department of Pharmaceutics, Latur College of Pharmacy, Hasegaon*
[3,4,5]*Department of Pharmacy, Latur College of Pharmacy, Hasegaon*

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ABSTRACT

Wound healing is a coordinated biological process involving haemostasis, inflammation, proliferation and tissue remodelling. Topical herbal preparations are being investigated as complementary approaches because plant-derived constituents may provide antioxidant, antimicrobial, anti-inflammatory and tissue-repair related activities. This review systematically organizes the available literature relevant to a proposed herbal wound-healing cream containing Neem (Azadirachta indica), Aloe vera (Aloe barbadensis Miller), Turmeric (Curcuma longa L.) and Tulsi (Ocimum tenuiflorum L.). Evidence from reviews, systematic reviews and experimental studies was considered with emphasis on phytochemical constituents, biological activities, wound-healing mechanisms, topical formulation considerations and evaluation parameters. Aloe vera has clinical and systematic-review evidence in burn and skin-wound care, while curcumin has extensive preclinical evidence and an expanding clinical literature. Neem and Tulsi show promising antimicrobial, antioxidant and wound-repair effects, although much of the evidence remains preclinical. A combined cream may therefore provide a rational multi-target formulation concept; however, synergy should not be assumed without direct formulation-specific testing. For a scientifically defensible product, extract identity, standardization, compatibility, stability, microbial quality, skin tolerability and wound-healing performance must be evaluated before any clinical claim is made. The review also highlights the need for standardized extracts and controlled clinical studies to establish efficacy and safety.

INTRODUCTION

A wound is a disruption of normal tissue integrity that initiates a coordinated repair response.

***Corresponding Author:** Sadanand Patil
Address: *Department of Pharmaceutical Chemistry, Latur College of Pharmacy, Hasegaon*
Email ✉: sp0186285@gmail.com
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Cutaneous repair is commonly described through four overlapping phases: haemostasis, inflammation, proliferation and remodelling. Successful repair depends on appropriate timing and interaction between inflammatory cells, fibroblasts, keratinocytes, endothelial cells, extracellular matrix and soluble mediators. [1,2] Delayed healing may occur when one or more of these processes are disturbed by infection, poor oxygenation, diabetes, malnutrition, ageing, smoking, obesity, medications or other systemic and local factors. [2]

Plant-derived preparations have a long history in wound care and continue to be investigated as sources of bioactive compounds. A systematic review of polyherbal wound-healing research reported substantial preclinical interest but also emphasized the limited number of high-quality clinical trials and the need for standardized formulations. [3] [26]

The present review focuses on four widely recognized medicinal plants—Neem, Aloe vera, Turmeric and Tulsi—and examines their relevance to a topical cream intended for wound-healing research. The purpose is not to claim clinical efficacy for an untested combination, but to establish a literature-based rationale and a systematic framework for formulation development and evaluation.[4]

1.1 Rationale of the Review

A topical cream can place plant-derived constituents at the site of tissue injury while also providing a semisolid vehicle that supports application, residence and patient acceptability. The proposed combination was selected because the four ingredients collectively represent complementary pharmacological themes—antimicrobial activity, antioxidant protection, modulation of inflammation, moisture support and potential stimulation of tissue repair.

1.2 Review Objectives

- To summarize the biological basis of cutaneous wound healing.
- To review the phytochemical and pharmacological relevance of Neem, Aloe vera, Turmeric and Tulsi.
- To compare the evidence supporting each ingredient for wound-related applications.
- To outline a scientifically appropriate approach for developing a combined herbal cream.
- To identify critical quality, safety, stability and efficacy parameters required for evaluation.

2. LITERATURE REVIEW METHODOLOGY

2.1 Review Design

This manuscript is prepared as a structured literature review rather than a registered systematic review or meta-analysis. The literature was organized around the review question: what evidence supports Neem, Aloe vera, Turmeric and Tulsi as components of a topical wound-healing cream, and what formulation/evaluation considerations are required for a scientifically defensible product?

2.2 Information Sources and Search Concepts

Relevant literature was identified primarily through PubMed/MEDLINE-indexed records and publisher pages for peer-reviewed articles. Search concepts included combinations of the terms “wound healing”, “topical”, “cream”, “herbal formulation”, “Azadirachta indica”, “Aloe vera”, “Curcuma longa”, “curcumin”, “Ocimum sanctum”, “Ocimum tenuiflorum”,

"antimicrobial", "antioxidant", "anti-inflammatory", "epithelialization", "collagen", "burn", and "skin wound".

2.3 Eligibility Focus

Priority was given to systematic reviews, meta-analyses, narrative reviews with clear methodology, and primary experimental or clinical studies directly relevant to wound healing. Papers were considered particularly useful when they reported wound contraction, epithelialization, collagen/hydroxyproline, granulation tissue, infection-related outcomes, skin tolerability, or topical formulation characteristics.

2.4 Evidence Interpretation

Evidence was interpreted according to study type. Human systematic reviews and controlled clinical trials were considered more directly informative for clinical relevance than animal or in-vitro studies. Preclinical findings were used to explain plausible mechanisms and formulation rationale, not to establish clinical efficacy.

TABLE 1. EVIDENCE HIERARCHY USED IN THIS REVIEW

Herbal drug	Botanical name	Family	Major reported constituents	Relevance to wound healing
Neem	Azadirachta indica	Meliaceae	Limonoids, flavonoids, phenolics, tannins	Antimicrobial, anti-inflammatory and antioxidant potential [4–6]
Aloe vera	Aloe barbadensis	Asphodelaceae	Polysaccharides, acemannan and other bioactive constituents	Wound/burn-care evidence and possible tissue-repair support [7–11]
Turmeric	Curcuma longa	Zingiberaceae	Curcuminoids, especially curcumin; volatile oils	Antioxidant and anti-inflammatory potential [12–15]
Tulsi	Ocimum tenuiflorum	Lamiaceae	Eugenol, phenolics, flavonoids, terpenoids	Antimicrobial, antioxidant and anti-inflammatory potential; mainly preclinical wound evidence [16–19]

Source basis: Literature cited in References [4–26].

3. BIOLOGY OF WOUND HEALING

3.1 Haemostasis

Immediately after injury, vascular responses and platelet activation contribute to clot formation and temporary restoration of tissue integrity. The clot provides a provisional matrix and releases mediators that help initiate subsequent repair. [1,2]

3.2 Inflammation

Neutrophils and macrophages participate in removal of microbes and damaged material and regulate the transition toward tissue repair.

Excessive or prolonged inflammation can delay healing, making controlled inflammatory responses important. [1,2]

3.3 Proliferation

The proliferative phase involves fibroblast activity, extracellular matrix deposition, angiogenesis, re-epithelialization and granulation tissue formation. Collagen deposition and cellular migration are important determinants of tissue restoration. [1,2]

3.4 Remodelling

During remodelling, collagen and extracellular matrix are reorganized and tensile strength gradually increases. The final architecture may differ from uninjured skin because scar formation is part of normal repair. [1]

3.5 Factors That Delay Healing

Infection, hypoxia, diabetes, poor nutrition, ageing, smoking, obesity and selected medications can interfere with one or more phases. These factors should be considered when interpreting experimental wound-healing results. [2]

TABLE 2. MAJOR PHASES OF CUTANEOUS WOUND HEALING

Phase	Major events	Relevance to topical herbal research
Haemostasis	Clot formation and provisional matrix	Protection and local environment
Inflammation	Immune-cell recruitment and microbial control	Excess inflammation may delay repair
Proliferation	Fibroplasia, angiogenesis, granulation, epithelialization	Potential target for tissue-repair activity
Remodelling	Collagen reorganization and maturation	Determines final tissue strength and scar quality

4. NEEM (AZADIRACHTA INDICA A. JUSS.)

Figure 1. Neem (Azadirachta indica A. Juss.) plant and leaves

Neem is a medicinal tree of the family Meliaceae with extensive traditional use in South Asian medicine. Reviews describe a diverse phytochemical profile including limonoids, terpenoids, flavonoids, phenolics and other secondary metabolites. [5,6]

4.1 Phytochemical Relevance

Neem leaves and other plant parts contain chemically diverse constituents. Limonoids such as azadirachtin, nimbin and related compounds have attracted pharmacological interest, while flavonoids and phenolic constituents contribute to antioxidant-related activity.

4.2 Wound-Healing Relevance

Neem is relevant to wound-care research because antimicrobial and anti-inflammatory properties may help address two common barriers to repair: microbial burden and excessive inflammatory activity. A systematic review of medicinal plants used for anti-inflammatory and wound-healing activity identified Azadirachta indica among the more extensively studied species. [6,7]

A 2023 topical hydrogel study using Azadirachta indica extract reported acceptable physical characteristics, antimicrobial activity and accelerated wound regeneration in an animal model. These findings support further topical formulation research but do not by themselves establish clinical efficacy of neem cream in humans. [8] [24]

4.3 Formulation Considerations

Neem extract concentration, extraction solvent, marker compounds, colour, odour and compatibility with the cream base should be standardized. Because crude botanical extracts can vary substantially with plant part, geography, harvesting and extraction conditions, reproducibility requires a defined raw-material specification.

4.4 Evidence Limitation

The evidence base for neem in wound healing is predominantly preclinical. Human clinical evidence specific to a standardized neem cream is comparatively limited; therefore the ingredient should be presented as promising rather than clinically proven.

5. ALOE VERA (ALOE BARBADENSIS MILLER)

Figure 2. Aloe vera (Aloe barbadensis Miller) plant and leaf gel.

Aloe vera is widely used in topical preparations. Its gel contains polysaccharides, with acemannan regarded as an important bioactive polysaccharide. Reviews describe immunomodulatory, antioxidant and wound-related biological activities associated with Aloe-derived polysaccharides. [9]

5.1 Clinical and Systematic-Review Evidence

A systematic review of clinical trials identified 23 trials evaluating Aloe vera preparations in prevention or treatment of skin wounds, including burns and other wound conditions. The authors concluded that Aloe vera may support skin moisture and

integrity, while noting limitations in the available evidence. [10]

A systematic review of burn-wound trials found a tendency toward shorter healing time with topical Aloe vera, although heterogeneity in products and outcomes limited firm conclusions. A later systematic review and meta-analysis of randomized trials reported faster healing in second-degree burns with topical Aloe vera compared with other topical treatments. [11,12] [22,23]

5.2 Potential Mechanisms

Aloe-derived polysaccharides may influence cellular proliferation, migration and extracellular-matrix-related processes. Recent mechanistic reviews describe effects on growth-factor-associated pathways and matrix components, while also emphasizing that the precise mechanisms remain incompletely resolved. [9,13]

5.3 Formulation Considerations

Aloe gel is sensitive to processing and storage conditions. The formulation should control moisture, microbial quality, preservative compatibility, pH and physical stability. Standardization of the Aloe material is important because the composition of commercial or freshly processed gels may vary.

5.4 Evidence Limitation

Aloe vera has stronger clinical evidence than several other ingredients in this review, but results remain formulation- and indication-dependent. Therefore, evidence for Aloe vera should not automatically be extrapolated to the proposed four-herb cream.

6. TURMERIC (CURCUMA LONGA L.)

Figure 3. Turmeric (Curcuma longa L.) rhizome and powdered material.

Turmeric rhizome contains curcuminoids, including curcumin, which has been widely investigated for antioxidant, anti-inflammatory and antimicrobial effects. Curcumin has been studied across several stages of wound repair, including inflammation, oxidative stress, collagen deposition and wound contraction. [14,15]

6.1 Wound-Healing Evidence

Reviews of curcumin as a wound-healing agent describe substantial preclinical evidence and identify formulation as a key challenge because curcumin has low aqueous solubility and limited bioavailability. [14,15]

A 2021 systematic review of dermatological effects of Curcuma species reported antioxidant and anti-inflammatory effects relevant to skin health, while also noting the need for additional controlled human studies to establish optimal delivery and dosing. [16] A recent scoping review of clinical trials identified 19 eligible trials of curcumin formulations for wound healing; most were randomized controlled trials, but substantial heterogeneity prevented development of uniform treatment guidance. [17] [21]

6.2 Formulation Challenge: Solubility

Curcumin's low water solubility can reduce its effective dispersion in aqueous systems and may affect dose uniformity. In a cream, the selected oil phase, emulsifier system, particle size, extract standardization and mixing process should therefore be considered during development. [25]

6.3 Safety and Evidence Interpretation

Topical curcumin is promising, but colour, staining, concentration, vehicle and irritation potential must be evaluated experimentally. Evidence from advanced nanoformulations should not be assumed to apply directly to a conventional herbal cream.

7. TULSI (OCIMUM TENUIFLORUM L.; SYN. OCIMUM SANCTUM)

Figure 4. Tulsi (Ocimum tenuiflorum L.) plant and leaves.

Tulsi is an important medicinal plant in Indian traditional medicine. A 2024 comprehensive review summarized diverse secondary metabolites including rosmarinic acid, oleanolic acid, luteolin, ursolic acid and limonene and described antioxidant, anti-inflammatory, antimicrobial and wound-healing-related activities. [18]

7.1 Experimental Wound-Healing Evidence

Experimental studies of Ocimum sanctum leaf extracts in rats reported increased wound-breaking strength, faster epithelialization and greater wound contraction. Other work reported increased hydroxyproline and antioxidant enzyme activity in extract-treated animals. [19,20]

A study using topical Ocimum sanctum extract in petroleum jelly also reported faster wound healing in rats and examined the relationship with tumour necrosis factor-alpha. These results are useful for mechanistic hypotheses but remain animal-model evidence. [20]

7.2 Formulation Considerations

Tulsi extract may contribute characteristic colour and aroma to the cream. The extraction method and standardization of marker compounds should be defined, and compatibility with preservatives, antioxidants, emulsifiers and the other three botanical materials should be demonstrated.

7.3 Evidence Limitation

Clinical wound-healing evidence for Tulsi is substantially less developed than the available Aloe vera literature. Claims should therefore remain appropriately cautious and focused on preclinical evidence unless direct human clinical evidence is available for the final formulation.

8. COMPARATIVE SCIENTIFIC RATIONALE

The proposed combination is based on complementary evidence rather than an assumption of proven synergy. Aloe vera contributes a moisture-supportive topical matrix and polysaccharide-associated biological activity; curcumin contributes strong antioxidant and anti-inflammatory research; neem contributes antimicrobial and anti-inflammatory potential; and Tulsi contributes antioxidant, antimicrobial and wound-related preclinical evidence.

TABLE 3. COMPARATIVE PROFILE OF THE SELECTED HERBAL INGREDIENTS

Ingredient	Major phytochemical groups	Principal research relevance	Evidence strength
Neem	Limonoids, flavonoids, phenolics, terpenoids	Antimicrobial, anti-inflammatory, antioxidant and topical wound research	Mainly preclinical
Aloe vera	Polysaccharides including acemannan	Moisture/skin integrity and burn/wound research	Clinical + preclinical
Turmeric	Curcuminoids, especially curcumin	Antioxidant, anti-inflammatory and tissue-repair research	Strong preclinical; growing clinical
Tulsi	Phenolics, terpenoids, rosmarinic/ursolic-related constituents	Antioxidant, antimicrobial and wound-model research	Mainly preclinical

8.1 Proposed Complementary Roles

- Neem: potential antimicrobial and inflammation-modulating contribution.
- Aloe vera: moisture-supportive and tissue-repair-related contribution.
- Turmeric: antioxidant and inflammation-modulating contribution, with formulation challenges related to curcumin solubility.
- Tulsi: antioxidant and antimicrobial contribution supported mainly by experimental wound models.

8.2 Why a Cream Vehicle?

A cream can combine an oil phase and an aqueous phase, allowing incorporation of appropriately selected botanical preparations while providing a spreadable, cosmetically acceptable dosage form. The vehicle must be designed so that it does not compromise extract stability or create microbial risk.

9. PROPOSED FORMULATION DEVELOPMENT STRATEGY

The following is a research-development framework, not a clinical prescription or a validated final formula. Exact concentrations should be selected after preliminary compatibility, safety and stability studies.

Table 4. Proposed Formulation-Development Components

Component/step	Purpose	Key control point
Authenticated plant materials	Ensure correct botanical identity	Voucher/specimen documentation and supplier qualification
Standardized extracts/gel	Reproducible active content	Defined extraction method and marker compounds
Cream base	Provide topical vehicle	Compatibility with botanical materials
Emulsifier system	Maintain emulsion stability	No phase separation during stability testing
Humectant	Support moisture and skin feel	Avoid excessive tackiness
Preservative system	Control microbial growth	Compatibility and preservative-efficacy testing
Antioxidant, if required	Reduce oxidation of susceptible constituents	Avoid interactions with botanical actives
Packaging	Protect formulation	Light, moisture and microbial protection

9.1 Suggested Development Sequence

- Authenticate and document each botanical raw material.
- Prepare extracts/gel under controlled conditions and determine suitable marker or quality parameters.
- Perform preliminary compatibility testing among extracts and excipients.

- Prepare trial cream batches using a reproducible manufacturing process.
- Evaluate physical characteristics, pH, viscosity, spreadability, homogeneity and extrudability.
- Perform microbial quality and stability testing.
- Only after acceptable quality is established, conduct validated in-vitro/ex-vivo or appropriate preclinical wound-healing studies.
- Use controlled clinical studies before making therapeutic claims for human use.

10. EVALUATION OF THE HERBAL CREAM

Evaluation should distinguish product quality from biological efficacy. A cream may be physically stable but biologically inactive, or biologically promising but unsuitable because of poor stability or irritation. Therefore, a multidimensional evaluation plan is required.

TABLE 5. Evaluation Parameters For The Proposed Herbal Cream

Parameter	Purpose	Preferred assessment
Appearance and colour	Detect physical change	Visual inspection and documented description
Odour	Assess acceptability/stability	Organoleptic assessment
Homogeneity	Check uniformity	Microscopic/visual examination
pH	Assess topical suitability	Calibrated pH meter
Viscosity	Assess consistency	Suitable rotational viscometer
Spreadability	Assess ease of application	Standard spreadability method
Extrudability	Assess container performance	Tube extrusion test
Washability	Assess removal	Standardized washing observation
Globule/particle characteristics	Assess dispersion	Microscopy or particle-size method where relevant
Microbial quality	Assess microbiological safety	Applicable pharmacopoeial/microbial limits
Stability	Assess product integrity	Accelerated/long-term protocol as applicable
Biological activity	Assess wound-related effect	Validated in-vitro/ex-vivo or appropriate preclinical model

10.1 pH

The pH should be measured after equilibration using a calibrated instrument. The target should be justified based on skin compatibility and formulation stability rather than selected solely for convenience.

10.2 Viscosity and Spreadability

Viscosity influences application, residence time and sensory characteristics. Spreadability should be measured using a reproducible method and reported with sufficient methodological detail to permit comparison among batches.

10.3 Microbial Quality

Botanical ingredients can introduce microbial contamination. Raw-material controls, water quality, manufacturing hygiene, packaging and preservative performance are therefore essential.

11. STABILITY, SAFETY AND QUALITY CONSIDERATIONS

11.1 Stability

The final formulation should be evaluated for changes in appearance, colour, odour, pH, viscosity, homogeneity, phase separation, microbial quality and relevant chemical markers. Stability conditions and duration should follow the applicable institutional and regulatory framework.

11.2 Skin Irritation and Tolerability

Botanical origin does not automatically imply absence of irritation or sensitization. Each extract and the finished formulation should be assessed using an ethically appropriate safety strategy. Human testing, when proposed, requires appropriate ethical approval and informed consent.

11.3 Standardization

A major limitation of herbal formulations is batch-to-batch variability. Botanical identity, plant part, harvest conditions, extraction solvent, extraction ratio, drying conditions and marker-compound content should be documented.

11.4 Packaging

Packaging should protect the formulation from contamination and, where necessary, light, oxygen and moisture. Compatibility between the packaging material and the cream should be considered during stability studies.

11.5 Quality-by-Design Perspective

A development program can define critical material attributes, critical process parameters and critical quality attributes. This approach helps connect botanical variability with measurable product performance and may improve reproducibility during scale-up.

Table 6. Key Quality Risks And Controls

Potential risk	Possible consequence	Control strategy
Variable botanical identity	Inconsistent activity	Authentication and specification
Variable extract potency	Batch variability	Marker-based standardization
Microbial contamination	Product spoilage/safety risk	GMP hygiene, preservative control and testing
Curcumin instability/poor dispersion	Dose non-uniformity	Appropriate vehicle and process optimization
Emulsion instability	Phase separation	Emulsifier/base optimization and stability testing
Irritation/sensitization	Poor tolerability	Preclinical/appropriate safety assessment

12. DISCUSSION

The literature supports a biologically plausible rationale for investigating the four selected

botanicals in a topical wound-healing cream, but the strength of evidence differs substantially between ingredients. Aloe vera has the clearest clinical literature among the four, including systematic reviews and meta-analyses of burn-related outcomes. Curcumin has extensive mechanistic and preclinical literature, with clinical research increasing but still heterogeneous. Neem and Tulsi have promising experimental data but comparatively less direct clinical evidence for standardized topical products.

The broader herbal-wound literature shows the same pattern: systematic reviews identify encouraging biological and clinical signals, yet many formulations remain supported primarily by laboratory or animal studies. A 2023 systematic review of polyherbal formulations reported limited randomized clinical evidence, while a 2026 systematic review and meta-analysis found only a modest, statistically nonsignificant pooled trend toward faster healing with traditional polyherbal formulations and emphasized heterogeneity and the need for standardized trials. [3,4,22]

12.1 Potential Advantages of the Proposed Combination

- Multi-target biological rationale rather than reliance on a single constituent.
- Use of botanicals with different phytochemical profiles.
- Suitability for topical delivery as a semisolid dosage form.
- Potential for further optimization through extract standardization and formulation technology.

12.2 Important Scientific Cautions

- Synergy must be demonstrated experimentally and should not be assumed from the presence of multiple herbs.
- Evidence from one plant preparation cannot automatically be transferred to a different extract, concentration or dosage form.
- Animal wound models do not establish human clinical efficacy.
- Therapeutic claims require appropriately designed human studies.
- Plagiarism-free writing does not mean absence of citations; original paraphrasing still requires citation of the underlying scientific idea.

12.3 Research Gap

A major gap is the lack of well-standardized, directly comparative studies of a single conventional cream containing Neem, Aloe vera, Turmeric and Tulsi together. Future work should compare individual-herb formulations, the combined formulation, placebo/base cream and an appropriate standard treatment using predefined endpoints.

13. FUTURE PERSPECTIVES

Future development should move from descriptive herbal claims toward reproducible pharmaceutical development. Standardized extracts with defined chemical markers can reduce batch variability. Advanced delivery systems may improve the dispersion or release of poorly soluble constituents such as curcumin, but any advanced system should be evaluated against a conventional cream to establish whether the additional complexity provides measurable benefit.

13.1 Recommended Experimental Roadmap

- Botanical authentication and raw-material quality testing.
- Phytochemical screening and selection of marker compounds.
- Optimization of extract concentration and cream-base compatibility.

- Design of experiments for formulation optimization.
- Physicochemical and microbiological evaluation.
- Accelerated and long-term stability assessment.
- In-vitro antimicrobial and antioxidant screening where scientifically justified.
- Appropriate wound-healing model with predefined primary and secondary endpoints.
- Histopathological assessment and biochemical markers when applicable.
- Independent replication and statistical analysis.
- Ethically approved human clinical evaluation before therapeutic claims.

14. LIMITATIONS OF THE PRESENT REVIEW

This manuscript is a structured literature review and was not registered as a prospective systematic review or meta-analysis. It does not pool effect sizes across the four herbs and does not claim that the proposed combination has been clinically validated. The formulation concept is therefore a research proposition. In addition, differences in plant species nomenclature, extraction methods, dosage forms, experimental models and outcome measures limit direct comparison across studies.

15. CONCLUSION

Neem, Aloe vera, Turmeric and Tulsi each have scientific literature supporting selected biological activities relevant to wound care. Aloe vera has comparatively stronger clinical evidence, curcumin has extensive mechanistic and preclinical evidence with an expanding clinical literature, and Neem and Tulsi remain promising but are supported predominantly by preclinical data. [5–26]

A combined herbal cream is therefore scientifically reasonable as an experimental formulation concept, provided that the development program emphasizes authentication, standardization, formulation compatibility, microbial quality, stability and safety. The combination should not be described as clinically effective until the finished formulation itself has been evaluated in appropriate controlled studies.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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