

Topical Formulations of *Binahong* (*Anredera cordifolia*): Advances in Stability and Biological Efficacy

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Abstract:

Topical formulations derived from *Anredera cordifolia* (*Binahong*) have gained increasing attention in dermatology and wound care due to their promising therapeutic properties. Despite growing experimental evidence, a systematic evaluation of formulation strategies, stability profiles, and biological efficacy remains limited. This review aims to comprehensively analyze recent advances in *Binahong*-based topical formulations, including gels, creams, nanoemulgels, and ointments, focusing on their phytochemical composition, physicochemical stability, skin penetration potential, and dermatological performance. Using structured literature review methodology, relevant studies published between 2015 and 2025 were identified from databases such as PubMed, Scopus, ScienceDirect, and Google Scholar. Data regarding formulation design, stability parameters, *in vitro* and *in vivo* efficacy, and research gaps were extracted and synthesized thematically. The findings indicate that *Binahong* formulations exhibit significant wound healing, anti-inflammatory, antimicrobial, and skin-rejuvenating effects, largely attributed to bioactive flavonoids, saponins, and tannins. However, critical limitations persist, including the lack of quantitative phytochemical standardization, insufficient long-term stability data, and minimal direct evidence on skin penetration. This review concludes that while *Binahong* holds considerable potential as a topical agent, future research must prioritize standardized extraction, rigorous stability testing, and mechanistic studies to support its translation into reliable, clinically effective dermatological products.

Keywords: *Anredera cordifolia*; *Binahong*; topical formulation; wound healing; phytochemicals; herbal gel; dermatology

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INTRODUCTION

Binahong (*Anredera cordifolia*): Advances in Stability and Biological Efficacy represents a widely recognized medicinal plant in traditional Indonesian pharmacopoeia, frequently employed for its wound-healing and skin-restorative properties (Dwitiyanti et al., 2019). Ethnobotanically, *Binahong* leaves have long been applied topically to cuts, burns, ulcers, and other skin lesions due to their capacity to reduce inflammation and accelerate tissue repair (Rohaeni et al., 2024). This therapeutic efficacy is supported by scientific analyses showing that *A. cordifolia* leaves contain several classes of bioactive secondary metabolites, including flavonoids, saponins, alkaloids, tannins, and triterpenoids, which exhibit significant antioxidant, anti-inflammatory, antibacterial, and regenerative effects relevant to wound-healing processes (Nasution et al., 2024; Ngurah et al., 2024; Pratiwi et al., 2025).

Flavonoids, in particular, are noted for their free-radical scavenging ability and modulation of inflammatory mediators—factors integral to effective dermal repair and protection against oxidative damage (Nasution et al., 2024). Topical application studies in animal models have demonstrated that *Binahong* leaf extract, formulated as a gel, can maintain wound moisture, promote wound closure, and enhance fibroblast and osteoblast

proliferation, thus accelerating the healing trajectory of both soft tissue and alveolar bone wounds (Hanafiah et al., 2022; Ngurah et al., 2024).

Advances in formulation science have further expanded *Binahong*'s applicability; recent research has explored gel delivery systems to improve the stability, skin permeation, and bioavailability of its active compounds compared to conventional gel bases (Bernard et al., 2024). Traditional herbal preparations are therefore being translated into more standardized topical dosage forms, including gels with optimized excipients to improve ease of application, dose consistency, and therapeutic performance.

Despite this growing body of experimental evidence, significant gaps remain in understanding optimal formulation strategies and the mechanisms underlying cutaneous penetration and biological reproducibility across models (Bouwer et al., 2025; Darvin, 2023; Patel et al., 2024). This review aims to provide a comprehensive synthesis of current experimental findings related to *Binahong* topical formulations, with a focus on formulation types, stability characteristics, and biological efficacy, and to contextualize these insights within the scope of our thesis investigation, which explores high-concentration *Binahong* gel for epidermal modulation.

The benefit of this research is to present a systematic and structured review of the development of topical *Binahong* formulations, which can serve as a scientific reference for researchers, academics, and the pharmaceutical industry in developing stable, effective, and safe herbal-based formulations. By identifying knowledge gaps—particularly in terms of long-term stability, skin penetration, and phytochemical content standardization—this review is expected to guide further research toward the development of *Binahong* topical products that meet pharmaceutical and clinical standards, while also supporting the utilization of local Indonesian herbal resources in sustainable dermatological therapy.

METHODS

This review utilized a structured literature search to identify and synthesize original experimental studies focused on topical formulations of *Anredera cordifolia* (*Binahong*) published between 2015 and 2025. Sources were collected from multiple electronic databases, including Google Scholar, PubMed, ScienceDirect, Scopus, and Indonesia's national repository Garuda. To ensure broad coverage of both international and national literature, keywords were used in both English and Bahasa Indonesia, such as “*Anredera cordifolia*,” “*Binahong* extract,” “topical gel *Binahong*,” “nanoemulgel *Binahong*,” “formulasi topikal *Binahong*,” “krim *Binahong*,” “penyembuhan luka *Binahong*,” “penetrasi kulit *Binahong*,” and “antioksidan *Binahong*.” The search was restricted to original experimental articles that reported the development, evaluation, or biological testing of *Binahong* leaf extract in topical delivery systems such as gels, creams, ointment or nanoemulgels. Articles were selected based on their relevance to at least one of the following areas: formulation composition, physicochemical stability, skin absorption potential, or biological efficacy in dermatologic or wound healing contexts. For each study, data were extracted on formulation details (e.g., concentration, excipients), evaluation of stability (pH, viscosity, spreadability, microbial testing), type of biological model (in vitro, in vivo), and reported effects on healing, inflammation, collagen synthesis, or other skin-related endpoints.

The studies were grouped by formulation type to facilitate thematic analysis and synthesized in tabular and narrative form to support the review's objectives.

RESULT AND DISCUSSION

Phytochemical Profile and Skin-Relevant Compounds

The topical efficacy of *Anredera cordifolia* (*Binahong*) is closely linked to its diverse phytochemical composition, which includes flavonoids, saponins, tannins, and additional phenolic and triterpenoid compounds. Across the 15 core studies included in this review, qualitative phytochemical screening consistently confirmed the presence of these compound classes in *Binahong* leaf extracts formulated as gels, creams, nanoemulgels, and ointments. Although most studies did not perform quantitative standardization, the biological outcomes observed across multiple skin models provide indirect but convergent evidence of their dermatologic relevance.

Flavonoids

Flavonoids are among the most consistently reported constituents in *Binahong* extracts and are strongly associated with antioxidant, anti-inflammatory, and collagen-preserving effects in skin tissue. Qualitative screening in topical formulations, including anti-aging creams and wound-healing preparations, confirmed flavonoid presence (Alfatinnisa et al., 2024; Theedens et al., 2024). Biologically, flavonoid-rich *Binahong* formulations were repeatedly associated with accelerated epithelial regeneration, increased dermal thickness, and enhanced collagen deposition in burn, incision, and excision wound (Alfatinnisa et al., 2024; Meriyanti et al., 2020; Ngurah et al., 2024).

In human application, an oil-in-water *Binahong* cream containing up to 10% extract significantly improved skin moisture, elasticity, and collagen parameters within 14 days, supporting a role for flavonoids in dermal matrix stabilization and protection against oxidative stress (Theedens et al., 2024). Although skin penetration was not directly measured, the consistent structural and functional improvements suggest biologically relevant delivery of flavonoid constituents.

Saponins

Saponins are another major phytochemical group identified in *Binahong* leaf extracts and are known to promote angiogenesis, fibroblast proliferation, and granulation tissue formation. Their presence was confirmed in several topical formulations evaluated for wound healing and tissue regeneration (Hanafiah et al., 2024; Theedens et al., 2024). In vivo studies demonstrated increased neovascularization, enhanced fibroblast density, and faster wound closure following topical application of *Binahong* gels and nanoformulations, including in hyperglycemic and diabetic wound models where healing is typically delayed (Alfatinnisa et al., 2024; Yusuf et al., 2023).

Beyond biological activity, the amphiphilic nature of saponins may support formulation performance by improving dispersion of extract components in aqueous or semi-solid systems. This may partly explain the effectiveness of relatively simple gel bases used in multiple studies without the need for synthetic penetration enhancers.

Tannins

Tannins were consistently detected in *Binahong* leaf extracts and are particularly relevant to early wound stabilization and barrier restoration. Their astringent properties support protein precipitation at wound surfaces, reducing exudation and microbial invasion while promoting epithelial closure. Reduced inflammatory cell infiltration and improved epithelial thickness observed in burn and incision wound models treated with *Binahong* ointments and gels are consistent with tannin-mediated modulation of local inflammation (Hapsari et al., 2017; Ngurah et al., 2024).

In oral wound models, *Binahong* gels promoted thicker epithelial layers and improved tissue organization over time, further supporting the role of tannins in mucosal barrier reinforcement and re-epithelialization (Septiana et al., 2019; Hanafiah et al., 2024).

Other Active Compounds (Alkaloids, Phenolics, and Triterpenoids)

In addition to the major phytochemical groups, *Binahong* extracts contain alkaloids, simple phenolics, and triterpenoid compounds such as ursolic and oleanolic acids, as identified through qualitative screening (Alfatinnisa et al., 2024; Theedens et al., 2024). These compounds are associated with collagen synthesis, inflammation control, and antioxidant defense. Their contribution is supported by increased hydroxyproline levels and collagen density reported in incision and burn wound models treated with *Binahong*-based gels and ointments (Hapsari et al., 2017; Meriyanti et al., 2020).

Topical Formulation Types

Research on topical delivery of *Anredera cordifolia* has predominantly focused on semisolid dosage forms designed to optimize skin contact, patient acceptability, and biological efficacy. Among the 15 core studies reviewed, gels, cream-based formulations, nanoemulgels, and ointments were the most commonly employed systems. Each formulation type offers distinct pharmaceutical and dermatologic advantages and reflects differing strategies to deliver *Binahong* phytochemicals to the skin.

Gels

Gels represent the most frequently investigated topical formulation for *Binahong* extracts. The preference for gel systems is largely attributed to their non-greasy texture, ease of application, rapid drying, and suitability for hydrophilic plant extracts. Most studies employed polymeric gelling agents such as sodium carboxymethylcellulose (Na-CMC), Carbopol 940, or xanthan gum to produce stable semisolid matrices.

Simple *Binahong* gels containing extract concentrations between 3% and 5% consistently demonstrated biological efficacy in wound-healing models. Na-CMC-based gels promoted faster epithelial regeneration and reduced wound area in incision, burn, and oral wound models (Meriyanti et al., 2020; Septiana et al., 2019). Carbopol-based gels showed similar effectiveness, with significant increases in epithelial thickness, neovascularization, and collagen density in mid-dermal burn wounds (Ngurah et al., 2024). In several studies, gels were freshly prepared or evaluated over short periods, and physicochemical stability testing was often limited or absent.

More complex gel systems incorporated additional functional components to enhance antimicrobial or regenerative performance. For example, chitosan–silver nanoparticle gels modified with cinnamon essential oil demonstrated strong antibacterial activity against

Staphylococcus aureus and improved collagen deposition and angiogenesis in vivo (Lestari et al., 2024; Cahyaningrum et al., 2025). These studies highlight the flexibility of gel matrices for integrating *Binahong* extract with other bioactive agents.

Cream-Based Formulations

Cream formulations, particularly oil-in-water (O/W) systems, were explored to improve skin hydration, occlusivity, and cosmetic acceptability. Creams are especially relevant for applications involving dry, damaged, or aging skin, where moisturization is a key therapeutic target. *Binahong* creams were generally formulated with extract concentrations ranging from 3% to 10% using conventional emulsifying agents and fatty alcohols.

In an anti-aging context, *Binahong* cream formulations demonstrated significant improvements in skin moisture, elasticity, and collagen-related parameters following short-term use in human volunteers, with the highest efficacy observed at a 10% extract concentration (Theedens et al., 2024). Compared with gels, cream formulations were more frequently subjected to basic physicochemical quality testing, including pH, viscosity, spreadability, homogeneity, and short-term stability assessments.

Nanoemulgels

Nanoemulgels represent an advanced delivery system that combines the advantages of nanoemulsions and gel matrices to enhance dispersion and potential skin penetration of plant-derived bioactives. In the reviewed literature, nanoemulgels containing *Binahong* extract typically used surfactant–cosurfactant systems (e.g., Tween 80 and PEG 400) with oils such as virgin coconut oil to generate nanometric droplets prior to incorporation into a Carbopol gel base.

Nanoemulgel formulations containing approximately 5% *Binahong* extract demonstrated superior wound-healing outcomes compared with conventional gels, particularly in diabetic or hyperglycemic wound models. These formulations accelerated wound closure and increased epithelial thickness and fibroblast proliferation, suggesting improved bioavailability of active compounds (Yusuf et al., 2023). Factorial-design nanoemulgels with controlled particle sizes below 200 nm also showed acceptable physicochemical properties and anti-inflammatory activity comparable to standard corticosteroid creams (Pratiwi et al., 2025). However, direct skin penetration studies were not performed, and claims of enhanced delivery were inferred from biological outcomes and particle size data.

Ointments

Ointment formulations were less frequently studied but remain relevant for delivering high concentrations of *Binahong* extract in a highly occlusive environment. Traditional ointment bases composed of *adepts lanæ* and vaseline album were commonly used, allowing incorporation of extract concentrations up to 40%. In burn wound models, topical application of *Binahong* ointment produced greater epithelial thickness, higher collagen density, and lower inflammatory cell infiltration compared with oral administration or combination therapy (Hapsari et al., 2017).

More recent studies combined ointment systems with nanocarrier technologies. Nanochitosan encapsulated *Binahong* extract incorporated into ointment bases significantly enhanced wound contraction, angiogenesis, and collagen deposition in hyperglycemic rats,

particularly at higher extract concentrations (Alfatinnisa et al., 2024). While nanoparticle stability was characterized, conventional ointment stability parameters and long-term storage data were not reported.

The table below (**Table 1** – Formulations Summary) presents a consolidated overview of all 15 topical formulations evaluated in this review, including *Binahong* concentrations, excipients used, formulation types, and key stability or functional notes. This visual aid allows for cross-comparison and identification of formulation trends.

Table 1 – Summary of Topical Formulations of *Binahong*

Study	Formulation	BLE concentration (intact)	Key additives	Key notes
(Suryaningtyas et al., 2023)	Gel (herbal combo)	1.25%, 2.5%, 5%	Turmeric extract 2%	Topical burn gel; no physicochemical/stability testing
(Istyastono & Yuliani, 2016)	Hydrogel	5% EEB (v/v); FIII: 5% EEB + 5% celecoxib	Carbopol, Na-CMC, Ca-alginate	Sterile; ursolic acid standardization
(Ngurah et al., 2024)	Carbopol gel	5%	Carbopol 940, TEA, glycerin	Burn model; no stability data
(Yusuf et al., 2023)	Nanoemulgel	5%	Tween-80, PEG-400, VCO	Nanoemulgel; basic QC only
(Hapsari et al., 2017)	Ointment	40%	Adeps lanae, vaseline	Simple burn ointment
(Theedens et al., 2024)	O/W cream	3%, 5%, 10%	Stearic acid, Tween-80, glycerin	Full QC; short-term stability
(Meriyanti et al., 2020)	Gel	1%, 2%, 4% (ethyl-acetate fraction)	Gel base (n.s.)	Incision wounds; no QC
(Lestari et al., 2024)	Composite gel	5% (selected formulas)	Chitosan, AgNP, CEO	4-week stability
(Alfatinnisa et al., 2024)	Nanochitosan ointment	10%, 20%, 30%	Nanochitosan, vaseline	Nanoparticles ~170 nm
(Hanafiah et al., 2024)	Nanogel	3%	Nanogel base (n.s.)	Oral wounds
(Cahyaningrum et al., 2025)	Composite gel	0%, 3%, 5%, 7%, 10%	Chitosan, AgNP, Aloe vera	Best at 5% BLE
(Pratiwi et al., 2025)	Nanoemulgel	3% (purified extract)	Tween-80, PEG-400, VCO	Optimized nanoemulgel
(Hanafiah et al., 2022)	Hydrogel	3%	Carbopol, HPMC	Freshly prepared
(Septiana et al., 2019)	Gel(oal)	5%	MC-Na	Dental socket model
(Pariyana et al., 2016)	Ointment	10%, 20%, 40%	Vaseline	Simple ointment

Overall, the evidence supports the use of both traditional gel matrices and advanced systems like nanoemulgels to enhance the usability and efficacy of *Binahong* extract.

Stability and Skin Penetration

The clinical and cosmetic viability of topical herbal formulations depends not only on biological activity but also on formulation stability and the ability of active compounds to reach relevant skin layers. In studies involving *Anredera cordifolia*, stability assessment was commonly limited to basic physicochemical parameters, while direct investigation of skin penetration remained largely absent. Nevertheless, formulation design choices provide indirect support for the stability and potential dermal delivery of *Binahong* phytochemicals.

A summary of these findings, including biological outcomes and formulation stability, is provided in **Table 2**, which complements the formulation data in **Table 1**.

Table 2 – Biological Activities with Stability Information

Study	Model	Target effect	Key results (concise)	Stability info (kept explicit)
(Suryaningtyas et al., 2023)	Rat II-degree burn	Wound healing, collagen	↑ mature collagen; 2.5% BLE ≈ 5% BLE efficacy	No physicochemical or stability testing reported
(Istyastono & Yuliani, 2016)	Mice incisional wound	Scarless healing	FII & FIII significantly reduced scar area vs base (p≤0.016)	Sterility test passed; no pH, viscosity, shelf-life, or permeation data
(Ngurah et al., 2024)	Rat burn (Wistar)	Healing, epithelialization	↑ epithelial thickness, neovascularization, collagen; ↓ wound area (p<0.05)	No physicochemical, stability, or penetration testing
(Yusuf et al., 2023)	Diabetic rat excision	Healing, fibroblasts	Nanoemulgel faster closure, ↑ epithelium & fibroblasts (p<0.05)	Short-term physicochemical data (pH, viscosity, adhesion); no shelf-life or microbial stability
(Hapsari et al., 2017)	Rat burn (SD)	Burn healing	40% ointment ↑ epithelium & collagen; ↓ inflammation (p<0.05)	No physicochemical or stability testing
(Theedens et al., 2024)	Human volunteers	Anti-aging	10% EEB: ↑ moisture (+19.05%), elasticity (+27.17%), collagen (+20.77%); non-irritant	30-day stability (cold/room/hot); some instability at hot temp; no accelerated or permeation data
(Meriyanti et al., 2020)	Rat incision	Healing, collagen	4% fraction ↑ epithelialization & hydroxyproline; ≈ Bioplacenton	No physicochemical or stability data
(Lestari et al.,	In vitro + rat	Antibacterial,	F3 (CEO 7%) best	Short-term (4-week)

2024)	excision	healing	antibacterial; in vivo ↑ collagen (~44.8%), angiogenesis	homogeneity, pH, spreadability; no shelf-life or microbial challenge
(Alfatinnisa et al., 2024)	Hyperglycemic rat excision	Healing, angiogenesis	Nanochitosan ointment ↑ healing; 30% strongest (p<0.05)	Nanoparticle stability only (size, PDI, zeta); no dosage-form shelf-life
(Hanafiah et al., 2024)	Rat oral wounds	Healing, fibro/osteo	3% nanogel ↑ fibroblasts (d3–7) & osteoblasts (d14)	No physicochemical or stability testing
(Cahyaningrum et al., 2025)	In vitro (<i>S. aureus</i>)	Antibacterial	F3 (5% BLE): 16.76 mm inhibition; > commercial gel	4-week homogeneity, pH (4.54–4.76), spreadability; no long-term or penetration data
(Pratiwi et al., 2025)	Paw-edema rat	Anti-inflammatory	Nanoemulgel ↓ edema; Formulas A & AB ≈ betamethasone	Nano-stability (size <200 nm, PDI, zeta) + acceptable gel pH/viscosity/spreadability
(Hanafiah et al., 2022)	Rat extraction socket	Oral healing	3% gel ↓ socket volume; ↑ fibroblasts & osteoblasts	No stability testing; gel freshly prepared every 3–4 days
(Septiana et al., 2019)	Rat extraction socket	Re-epithelialization	5% gel ↑ epithelial thickness vs controls (days 3–21, p<0.05)	No pH, viscosity, stability, or permeation data
(Pariyana et al., 2016)	Rat incision	Healing	40% ointment ≈ Madecassol for granulation & closure	No physicochemical, stability, or penetration testing

Stability Assessments

Across the reviewed studies, stability evaluation typically included organoleptic properties, pH, homogeneity, viscosity, and spreadability, with observation periods ranging from several days to a few weeks. Gel and cream formulations containing *Binahong* extract generally demonstrated acceptable short-term stability under ambient conditions. For example, oil-in-water cream formulations containing 3–10% *Binahong* extract maintained appropriate pH, homogeneity, and viscosity over a 30-day storage period and were non-irritating in both animal and human testing (Theedens et al., 2024). However, some instability was observed under elevated temperature conditions, indicating sensitivity of the formulation to thermal stress.

Gel-based systems also showed satisfactory short-term stability. Carbopol- and Na-CMC-based *Binahong* gels maintained consistent physical appearance and pH during limited observation periods and were suitable for repeated topical application in animal models (Ngurah et al., 2024; Septiana et al., 2019). Composite gels incorporating chitosan, silver nanoparticles, aloe vera, or cinnamon essential oil retained homogeneity and acceptable pH

values over four weeks, suggesting compatibility between *Binahong* extract and multifunctional excipients (Cahyaningrum et al., 2025; Lestari et al., 2024).

Advanced delivery systems such as nanoemulgels and nanochitosan-based ointments included additional indicators of physicochemical stability. Nanoemulgel formulations demonstrated nanometric particle sizes (<200 nm), acceptable polydispersity indices, and stable pH and viscosity profiles over short-term testing, supporting dispersion stability of the nanoemulsion phase (Pratiwi et al., 2025; Yusuf et al., 2023). Similarly, nanochitosan carriers exhibited favorable zeta potential values indicative of colloidal stability prior to incorporation into ointment bases (Alfatinnisa et al., 2024). Despite these findings, none of the studies conducted accelerated stability testing, long-term shelf-life evaluation, or microbial challenge testing, which are essential for regulatory and commercial development.

Skin Penetration – Limited but Theoretically Supported

Direct experimental assessment of skin penetration or permeation of *Binahong* phytochemicals was notably absent from the reviewed studies. No investigation employed standardized techniques such as Franz diffusion cells, tape stripping, or confocal imaging to quantify dermal absorption. As a result, conclusions regarding penetration are primarily inferred from formulation characteristics and biological outcomes.

Nanoemulgels and nanocarrier-based ointments were explicitly designed to enhance dermal delivery through reduced particle size and improved interfacial contact with the skin. In diabetic and hyperglycemic wound models, nanoemulgel formulations produced superior epithelial regeneration and fibroblast proliferation compared with conventional gels, suggesting improved bioavailability of active compounds at the wound site (Yusuf et al., 2023). Similarly, nanochitosan-encapsulated *Binahong* extract enhanced wound contraction, angiogenesis, and collagen deposition, indicating effective local delivery under compromised healing conditions (Alfatinnisa et al., 2024). While these outcomes are consistent with improved penetration, they remain indirect evidence.

In conventional gel and cream formulations, penetration is likely facilitated by the physicochemical nature of *Binahong* phytochemicals. Flavonoids and saponins possess molecular characteristics compatible with partial stratum corneum passage, particularly in damaged or inflamed skin where barrier function is compromised. Histological indicators such as increased epidermal thickness, dermal collagen density, and fibroblast activity observed across multiple studies imply that active compounds reached biologically relevant skin layers (Hapsari et al., 2017; Ngurah et al., 2024; Theedens et al., 2024). However, without direct permeation data, these effects cannot be conclusively linked to penetration depth or concentration.

Biological Efficacy and Dermatologic Benefits

Topical formulations of *Anredera cordifolia* demonstrate a broad range of biologically relevant effects on skin repair, inflammation control, and tissue remodeling. Across the reviewed studies, *Binahong* based gels, creams, nanoemulgels, and ointments consistently improved wound healing outcomes in normal, inflamed, burned, and metabolically impaired skin models. These effects align closely with the plant's phytochemical profile and are modulated by formulation type and extract concentration.

Wound Healing and Epithelial Regeneration

Acceleration of wound closure and enhancement of epithelial regeneration represent the most consistently reported dermatologic benefits of topical *Binahong*. In incision, excision, burn, and oral wound models, *Binahong* formulations significantly reduce wound area and promote faster re-epithelialization compared with untreated or vehicle controls.

Simple gel formulations containing 3–5% *Binahong* extract increased epithelial thickness and hastened wound closure in both cutaneous and oral wounds (Meriyanti et al., 2020; Ngurah et al., 2024; Septiana et al., 2019). In burn wound models, *Binahong* gels and ointments produced more mature epithelial layers and reduced wound size during the early and intermediate phases of healing (Hapsari et al., 2017; Suryaningtyas et al., 2023). Enhanced epithelial regeneration was also observed in compromised healing environments, such as diabetic and hyperglycemic wounds, where nanoemulgels and nanochitosan based ointments significantly accelerated wound contraction relative to conventional formulations (Alfatinnisa et al., 2024; Yusuf et al., 2023).

Collectively, these findings indicate that *Binahong* supports orderly epithelial recovery across diverse wound types, likely through combined antioxidant, anti-inflammatory, and cell-proliferative mechanisms.

Fibroblast Proliferation and Collagen Formation

Fibroblast activation and collagen synthesis are critical determinants of wound strength and tissue remodeling. Multiple studies demonstrated that topical *Binahong* formulations increase fibroblast density, collagen deposition, and hydroxyproline levels in healing skin.

In incision and burn wound models, *Binahong* gels and ointments significantly increased collagen density and maturity compared with controls (Hapsari et al., 2017; Ngurah et al., 2024). Quantitative increases in hydroxyproline content, a biochemical marker of collagen synthesis, were reported following treatment with *Binahong* fraction gels, with effects comparable to established wound-healing products (Meriyanti et al., 2020). Combination formulations containing *Binahong* and turmeric further enhanced mature collagen formation, with intermediate extract concentrations achieving efficacy comparable to higher doses, suggesting potential synergistic effects (Suryaningtyas et al., 2023).

Nano-based systems amplified these effects under impaired healing conditions. Nanoemulgels and nanochitosan loaded ointments significantly increased fibroblast counts and collagen deposition in diabetic wound models, indicating improved tissue remodeling capacity when advanced delivery systems are employed (Alfatinnisa et al., 2024; Yusuf et al., 2023).

Antibacterial and Anti-inflammatory Activity

In addition to regenerative effects, *Binahong*-based topical formulations exhibit antibacterial and anti-inflammatory activity that is highly relevant to wound management. Several studies demonstrated inhibition of *Staphylococcus aureus* growth, a common pathogen in infected wounds, following application of *Binahong* containing gels.

Composite gel formulations incorporating *Binahong* with chitosan, silver nanoparticles, aloe vera, or cinnamon essential oil produced substantially larger bacterial inhibition zones than commercial *Binahong* gels or base formulations (Cahyaningrum et al., 2025; Lestari et al., 2024). In vivo, these formulations reduced inflammatory cell infiltration

while simultaneously enhancing collagen deposition and angiogenesis, indicating effective control of infection-related inflammation without impairing tissue repair.

Anti-inflammatory effects were also evident in non-infected wound models. Topical *Binahong* ointment significantly reduced inflammatory cell counts in burn wounds compared with oral or combined administration, underscoring the importance of localized delivery for inflammation modulation (Hapsari et al., 2017). Nanoemulgel formulations further demonstrated anti-inflammatory activity comparable to standard corticosteroid preparations in edema models, supporting their potential as non-steroidal alternatives (Pratiwi et al., 2025).

Skin Moisturization and Anti-aging Properties

Beyond wound healing, *Binahong* has demonstrated beneficial effects on skin hydration, elasticity, and structural integrity in cosmetic applications. In human volunteers, topical application of *Binahong* cream significantly improved skin moisture, elasticity, and collagen-related parameters within 14 days, with the greatest effects observed at a 10% extract concentration (Theedens et al., 2024). These outcomes are consistent with antioxidant protection, collagen stabilization, and improved barrier function mediated by *Binahong* phytochemicals.

These findings extend the dermatologic relevance of *Binahong* beyond therapeutic wound care into cosmeceutical and preventive skin applications.

Epidermal Thickness and Pigmentation – Current Limitations

Several studies reported increased epidermal thickness following topical *Binahong* application, reflecting enhanced epithelial proliferation and maturation (Hapsari et al., 2017; Ngurah et al., 2024; Septiana et al., 2019). However, none of the reviewed studies specifically evaluated effects on melanocyte activity, melanin production, or pigmentation pathways. As such, any implications of *Binahong* for pigmentation modulation or skin tone regulation remain speculative.

This limitation is particularly relevant for anti-aging and cosmetic positioning, where pigmentation outcomes are clinically meaningful. Future investigations incorporating melanogenesis markers or pigmentation indices would be necessary to clarify these potential effects.

Integration with Formulation Stability

Biological efficacy was observed across a wide range of formulation types, despite limited stability and penetration testing in many studies. Short-term physicochemical stability appeared sufficient to maintain biological activity during experimental use, as evidenced by consistent wound-healing outcomes. Advanced delivery systems, particularly nanoemulgels and nano-enabled ointments, demonstrated superior biological performance in metabolically compromised models, suggesting a functional link between formulation strategy and therapeutic effect (Alfatinnisa et al., 2024; Yusuf et al., 2023).

Nevertheless, the absence of standardized long-term stability and penetration data limits definitive conclusions regarding dose–effect relationships and translational reliability. Integrating robust pharmaceutical characterization with biological testing will be essential to fully optimize *Binahong* based topical products.

Integrated Interpretation of Phytochemistry, Formulation Strategy, and Dermatologic Outcomes

This review demonstrates that topical formulations of *Anredera cordifolia* consistently produce favorable dermatologic outcomes across diverse skin injury and treatment models. Despite variability in formulation design and experimental methodology, a coherent pattern emerges linking *Binahong*'s phytochemical composition to its biological effects on epithelial regeneration, collagen synthesis, inflammation modulation, and antimicrobial defense.

Across wound models, including burns, incisions, excisions, oral wounds, and metabolically impaired skin, *Binahong* based formulations accelerated wound closure and enhanced epithelial thickness relative to (Hapsari et al., 2017; Istyastono & Yuliani, 2016; Meriyanti et al., 2020; Ngurah et al., 2024; Yusuf et al., 2023). These effects align mechanistically with the presence of flavonoids, saponins, tannins, and triterpenoids, which are known to regulate oxidative stress, fibroblast activity, angiogenesis, and extracellular matrix remodeling. Although most studies relied on qualitative phytochemical screening, (Liang et al., 2023; Raza et al., 2024; Tusilva et al., 2025) the consistency of biological responses across models suggests that these compounds remain functionally active within topical dosage forms.

Formulation strategy appears to modulate the magnitude rather than the direction of biological efficacy. Conventional gels and ointments reliably supported wound healing and collagen formation, particularly in acute injury models (Hapsari et al., 2017; Septiana et al., 2019)). In contrast, nanoemulgels and nano enabled ointments demonstrated enhanced performance under compromised healing conditions such as diabetes and hyperglycemia, where bioavailability and residence time are critical (Alfatinnisa et al., 2024; Yusuf et al., 2023). These findings suggest that advanced delivery systems may improve therapeutic robustness rather than introduce fundamentally new biological effects.

Beyond wound healing, *Binahong* based creams demonstrated measurable improvements in skin hydration, elasticity, and collagen-related parameters in human volunteers, supporting its relevance for cosmeceutical and anti-aging applications (Theedens et al., 2024). Importantly, these outcomes extend *Binahong*'s dermatologic utility beyond injury repair toward skin maintenance and prevention of structural degradation.

Antibacterial and anti-inflammatory effects further strengthen the clinical relevance of *Binahong* formulations, particularly when combined with functional excipients such as chitosan, silver nanoparticles, aloe vera, or essential (Cahyaningrum et al., 2025; Lestari et al., 2024). These combinations reduced microbial burden and inflammatory infiltration while preserving or enhancing tissue regeneration, highlighting the potential of *Binahong* as a multifunctional active ingredient in infected or high-risk wounds. Additionally, review analyses suggest that *Binahong*-based creams and patch formulations accelerate healing in diabetic wounds and demonstrate strong antioxidant activity, pointing to potential roles for *Binahong* in cosmeceutical and anti-aging applications as well (Tusilva et al., 2025).

Methodological Limitations and Future Research Directions

Despite promising biological outcomes, this review also reveals substantial methodological limitations that constrain translational interpretation. The most critical limitation is the widespread absence of quantitative phytochemical standardization. Nearly all

studies relied on qualitative screening without marker-based quantification, making it difficult to compare extract potency, establish dose response relationships, or ensure reproducibility across formulations and laboratories.

Formulation characterization was similarly limited. Stability testing was generally short-term and restricted to basic physicochemical parameters such as pH, homogeneity, and viscosity, with no accelerated stability, microbial challenge testing, or formal shelf-life evaluation reported. This limits confidence in long-term product performance and regulatory readiness.

Notably, direct skin penetration and permeation studies were entirely absent. Claims of enhanced delivery in nanoemulgels and nano enabled ointments were inferred from particle size and biological outcomes rather than confirmed using standardized diffusion or imaging techniques. This gap is particularly important for applications involving intact skin, anti-aging claims, or pigmentation-related endpoints, where stratum corneum penetration is a key determinant of efficacy.

Another important limitation is the lack of mechanistic biomarkers. While histological endpoints such as epithelial thickness and collagen density were frequently measured, molecular markers related to inflammation, angiogenesis, melanogenesis, or matrix remodeling were rarely assessed. Consequently, mechanistic interpretations remain largely inferential.

Future research should focus on strengthening the translational relevance of *Binahong* based topical formulations through quantitative phytochemical profiling with standardized marker compounds, comprehensive physicochemical and microbial stability testing in line with topical product guidelines, and direct evaluation of skin penetration and retention using validated in vitro or ex vivo models. In addition, incorporation of mechanistic biomarkers related to inflammation, pigmentation, and skin aging, together with well-designed human studies extending beyond short-term cosmetic outcomes, will be essential to confirm efficacy and support clinical and cosmeceutical development

Addressing these gaps will be essential to transition *Binahong*-based topical formulations from promising experimental products to evidence-based dermatologic and cosmeceutical applications.

CONCLUSION

Topical formulations of *Anredera cordifolia* (*Binahong*), including gels, creams, nanoemulgels, and ointments, consistently demonstrate dermatologic benefits such as wound healing, tissue regeneration, antimicrobial defense, and skin quality improvement, with phytochemicals remaining biologically active and enhanced by advanced delivery systems under compromised conditions. However, gaps in quantitative phytochemical standardization, comprehensive stability profiling, and skin penetration data hinder translational progress toward clinically and commercially viable products. For future research, integrate HPLC or LC-MS for extract standardization, conduct ICH-compliant stability testing (long-term storage, microbial, and photostability), assess penetration via in vitro/ex vivo models, validate mechanisms with molecular markers and human clinical trials, and foster multidisciplinary collaboration to develop standardized, sustainable herbal products advancing Indonesia's pharmaceutical sector.

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