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Article

A Low-Monoterpene Rosemary Diterpene Scalp-Care Oil for Modulating Cutaneous Inflammatory and Oxidative-Stress Pathways: Formulation Characterization and Translational Evidence

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Abstract: Background: Scalp discomfort, itch, scaling, and barrier instability arise from interacting inflammatory, redox, sebaceous, and microbial processes. Rosemary contains both volatile monoterpenes and nonvolatile phenolic diterpenes; separating these chemical domains may improve the suitability of a rosemary-derived oil for leave-on scalp care while preserving the diterpene fraction most relevant to redox and inflammatory signaling. Methods: A standardized low-monoterpene rosemary nonvolatile diterpene fraction was produced by segmented supercritical CO2 extraction, neutral-alumina cleanup, and thin-film refining, then incorporated at 10.00% into a squalane/caprylic-capric triglyceride/jojoba oil vehicle. Batch quality markers, forecut-separation performance, and formulation composition were analyzed together with a targeted evidence synthesis of human scalp studies and mechanistic literature indexed through September 2026. Results: The standardized fraction contained 28.6% carnosic acid and 5.8% carnosol, with camphor 0.13%, 1,8-cineole 0.14%, peroxide value 2.9 meq/kg, and chlorophyll a+b 0.01%. Omission of the volatile forecut increased camphor to 0.26% and 1,8-cineole to 0.31%, corresponding to calculated relative reductions of 50.0% and 54.8%, respectively, with segmented collection. Human randomized data for topical rosemary preparations show clinically relevant reductions in scalp pruritus in seborrheic dermatitis, while mechanistic studies of carnosic acid/carnosol support regulation of NF-κB, Nrf2/HO-1, Syk/Src, STAT1, and related redox-inflammatory pathways. Conclusion: The evaluated formulation combines a chemically defined diterpene-rich rosemary fraction with a lipid vehicle suited to leave-on scalp application. Its analytical profile and the wider clinical-mechanistic literature provide a coherent basis for studying scalp comfort, oxidative balance, and inflammatory signaling in formulation-specific human investigations.

Keywords: rosemary diterpenes; carnosic acid; carnosol; scalp care; inflammation; oxidative stress; seborrheic dermatitis; skin barrier.

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1. Introduction

Scalp condition is determined by more than the presence or absence of a single microorganism or inflammatory mediator. The follicular-rich scalp combines high sebaceous activity, a dense microbial ecosystem, frequent exposure to surfactants and styling products, and a keratinized barrier that is repeatedly challenged by washing, scratching, ultraviolet exposure, and oxidative processes. In seborrheic dermatitis and dandruff, clinical signs such as erythema, flaking, and pruritus are accompanied by shifts in fungal and bacterial communities and by changes in barrier-associated physiology [1-3]. This multidimensional biology favors topical strategies that address irritant load and redox-inflammatory tone while maintaining a cosmetically acceptable lipid environment.

Rosemary (Salvia rosmarinus, syn. Rosmarinus officinalis) is chemically heterogeneous. Its volatile fraction contains monoterpenes such as camphor and 1,8-cineole, whereas the less volatile fraction is enriched in phenolic diterpenes, notably carnosic acid and carnosol. The latter compounds have been repeatedly linked with antioxidant and anti-inflammatory signaling, including modulation of NF-κB, Nrf2, Syk/Src, STAT1, MAPK, and inflammasome-associated pathways [4-9]. For a leave-on scalp formulation, therefore, one scientifically relevant design question is whether the volatile load can be constrained while the nonvolatile diterpene fraction remains analytically defined.

The present work characterizes such a low-monoterpene rosemary diterpene oil and places its composition within the context of published human and mechanistic evidence. The study formulation, developed within the TIMEFLYS cosmetic research program, uses a 10% standardized rosemary nonvolatile diterpene fraction in a squalane-, caprylic/capric triglyceride-, and jojoba-based oil system. The central scientific question is whether the chemical profile of this formulation is aligned with a plausible scalp-soothing and redox-modulating research rationale, while keeping clinical claims proportional to the available evidence.

2. Materials and Methods

2.1. Rosemary fraction preparation and quality control

Dried rosemary leaves with moisture not exceeding 8.0% were milled and extracted with supercritical carbon dioxide at 25 MPa and 45°C, using a CO2 flow rate of 30 kg/h for 3 h. At a separator pressure of 8 MPa and 35°C, the first 30 min were removed as a volatile-oil forecut and the subsequent 150 min were collected as the nonvolatile diterpene fraction. The fraction was passed through a short column containing 100-200 mesh neutral alumina at 30-35% of fraction mass, followed by thin-film refining at 115°C under an absolute pressure below 30 Pa with an average material residence time not exceeding 90 s. Mixed tocopherols (0.03-0.08% of refined-material mass) were added before 0.2 μm filtration under nitrogen.

Carnosic acid and carnosol were quantified by HPLC-DAD using a C18 column (4.6 × 250 mm, 5 μm), 0.1% aqueous phosphoric acid as mobile phase A and acetonitrile as mobile phase B, a 45%-85% B gradient, 1.0 mL/min flow, 30°C column temperature, 230 nm detection, and a 10 μL injection volume. Camphor and 1,8-cineole were measured by headspace GC-MS using a DB-5MS column with selected-ion monitoring. Peroxide value was measured iodometrically and chlorophyll a+b by HPLC-DAD.

2.2. Scalp-care oil composition

The finished oil contained 10.00% rosemary nonvolatile diterpene fraction, 40.00% squalane, 40.70% caprylic/capric triglyceride, 8.00% jojoba seed oil, 0.50% mixed tocopherols, and 0.80% silica dimethyl silylate. Under nitrogen protection, the carrier oils were mixed at 35-45°C; the rosemary fraction and mixed tocopherols were added, followed by silica dimethyl silylate with dispersion at 1000-2000 rpm for 10-20 min. The material was vacuum-deaerated at -0.08 to -0.06 MPa for 5-10 min and filled under nitrogen.

Table 1. Composition and Functional Roles of the Rosemary-Based Formulation

Component	Mass %	Scientific/formulation role
Rosemary nonvolatile diterpene fraction	10.00	Standardized diterpene-rich active fraction
Squalane	40.00	Emollient lipid vehicle
Caprylic/capric	40.70	Carrier oil and spreading

triglyceride		phase
Jojoba seed oil	8.00	Wax-ester-rich emollient/skin-feel modifier
Mixed tocopherols	0.50	Antioxidant support for lipid phase
Silica dimethyl silylate	0.80	Oil-gel structuring agent

2.3. Comparative processing assessment

A same-batch comparator was produced without separate removal of the volatile-oil forecut while the downstream alumina and thin-film steps were retained. Camphor and 1,8-cineole were compared between the segmented process and the no-forecut comparator. Relative reduction was calculated as (comparator − segmented process)/comparator × 100.

2.4. Literature evidence synthesis

A targeted literature search was conducted through September 2026 using PubMed-indexed records and publisher/PMC sources. Priority was given to randomized or controlled human scalp studies involving rosemary preparations; systematic reviews and microbiome studies relevant to seborrheic dermatitis; mechanistic studies of carnosic acid/carnosol in skin or redox-inflammatory signaling; and dermatologic literature relevant to squalane, jojoba, topical antioxidants, and skin-surface lipids. The synthesis was narrative and translational rather than a meta-analysis, because the formulations, endpoints, and experimental systems were heterogeneous.

3. Results

3.1. Standardized fraction and process selectivity

From 10.000 kg of dried rosemary leaves, 0.630 kg of finished low-monoterpene nonvolatile diterpene fraction was obtained, corresponding to a 6.30% mass yield. The fraction contained 28.6% carnosic acid and 5.8% carnosol. Residual camphor was 0.13% and 1,8-cineole was 0.14%; peroxide value was 2.9 meq/kg and chlorophyll a+b was 0.01%. Carnosic acid recovery was 83.8% relative to the 215.0 g measured in the starting rosemary batch. These results place the fraction within the predefined quality-release ranges while maintaining a high diterpene-to-monoterpene contrast.

The no-forecut comparator contained 0.26% camphor and 0.31% 1,8-cineole. Relative to that comparator, the segmented process reduced these two volatile markers by 50.0% and 54.8%, respectively. This process-level result is relevant to a leave-on scalp product because it demonstrates that the volatile burden can be materially decreased without requiring a claim that the diterpene fraction itself has changed into a different chemical class.

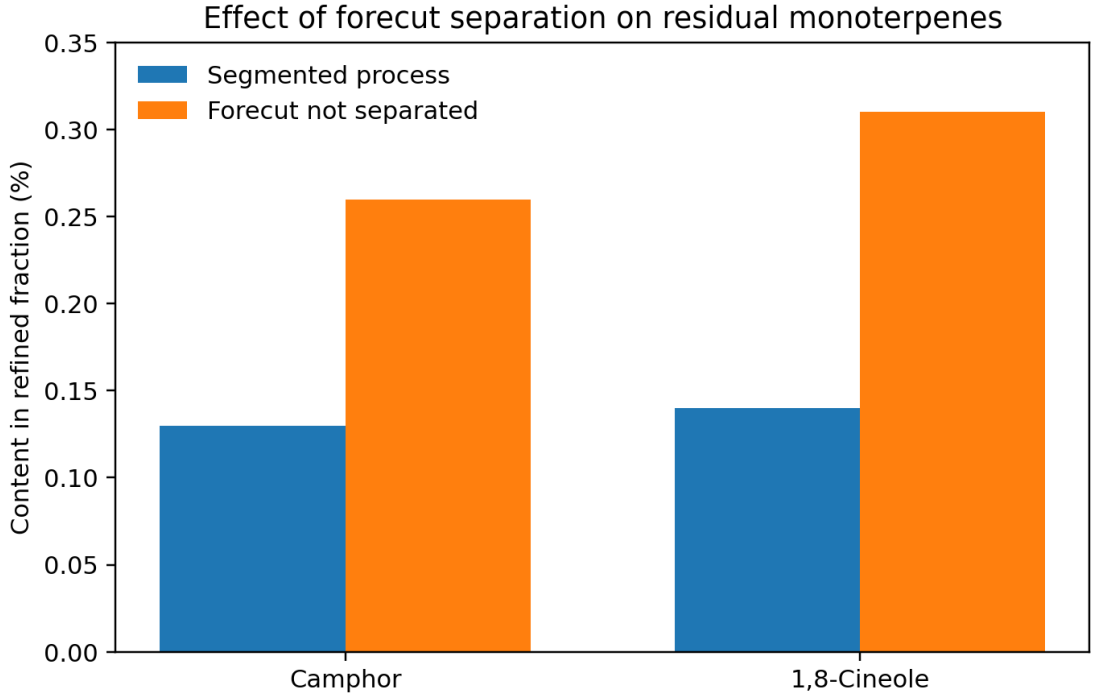


Figure 1. Residual camphor and 1,8-cineole after the segmented process versus the same-batch comparator in which forecut separation was omitted. Values are measured batch data; calculated relative

reductions were 50.0% and 54.8%, respectively.

3.2. Clinical context for scalp comfort

The strongest directly relevant human evidence identified was a double-blind randomized controlled trial in 42 patients with scalp seborrheic dermatitis comparing a 5% rosemary extract lotion with 2% ketoconazole lotion for two months [10]. Thirty-nine participants completed the study. Both groups showed large reductions in flaking and itch. Ketoconazole produced a greater reduction in ASFS than rosemary (between-group P=0.011 in the crude analysis), whereas the rosemary group showed a greater reduction in itching at month 1 (P<0.001) and remained lower at month 2. Quality-of-life scores improved in both groups without a significant between-group difference [10]. The trial is clinically informative because pruritus is a central scalp-comfort endpoint and because it evaluates a topical rosemary preparation rather than oral exposure.

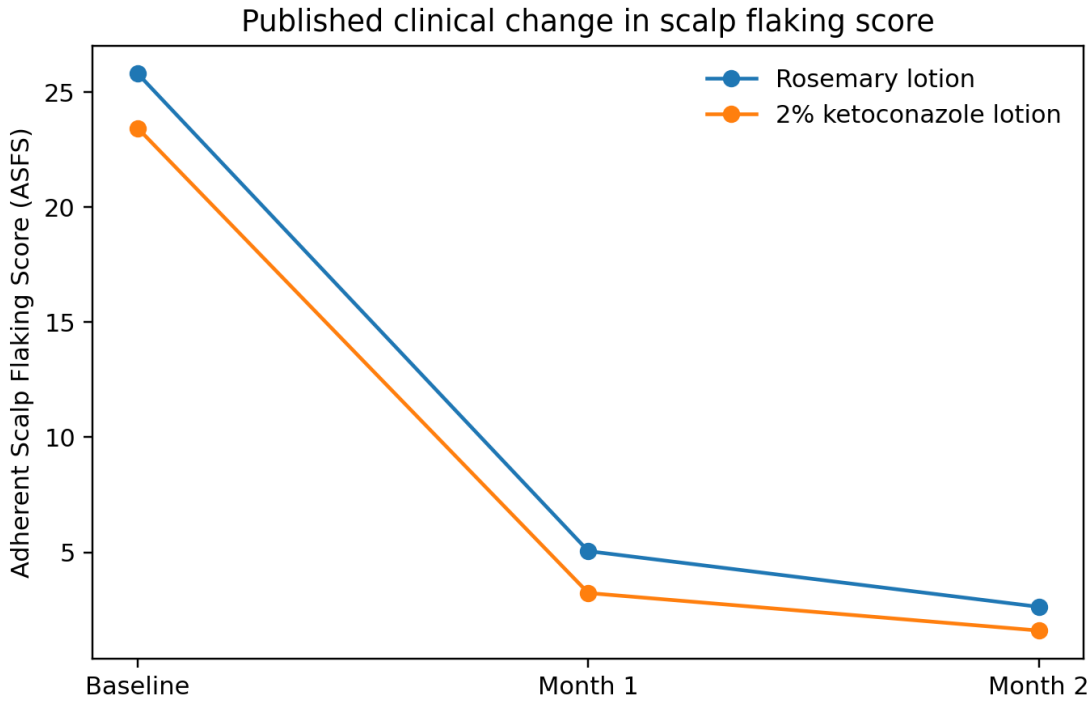


Figure 2. Published mean Adherent Scalp Flaking Score (ASFS) values from the two-month randomized trial of topical rosemary lotion versus 2% ketoconazole lotion [10]. The figure is a redrawing of reported numerical data and is not a result of the present formulation study.

3.3. Mechanistic evidence for inflammatory and redox modulation

Carnosic acid has repeatedly shown activity at signaling nodes relevant to cutaneous inflammatory stress. In keratinocytes, carnosic acid suppressed stimulus-induced IL-6, IL-8, and MCP-1 and inhibited upstream Syk/Src-PI3K-Akt signaling associated with NF-κB activation [5]. A 2025 study further identified direct targeting of STAT1 in experimental psoriasis- and rosacea-like inflammation, with reduced STAT1 phosphorylation and downstream inflammatory mediators [6]. Separately, topical rosemary extract enriched in carnosic acid accelerated wound repair and reduced fibrosis in murine models through TRPA1-dependent sensory-neuronal signaling [7]. These models address different dermatologic contexts, but collectively they demonstrate that carnosic acid can engage multiple cutaneous signaling systems rather than acting solely as a chemical radical scavenger.

Redox regulation provides a complementary mechanistic axis. Carnosic acid can activate Nrf2/HO-1 signaling while attenuating NF-κB-linked inflammatory output [8], and carnosol has been shown to increase nuclear Nrf2 and induce the stress-response protein sestrin-2 [9]. The broader rosemary-diterpene literature likewise describes convergent effects on NF-κB, MAPK, Nrf2, SIRT1, STAT3, and NLRP3-related pathways [4]. For scalp biology, this is relevant because oxidative stress, barrier disturbance, and inflammatory signaling can amplify one another, particularly in sebaceous regions repeatedly exposed to environmental and microbial oxidants.

3.4. Vehicle relevance to the scalp barrier and surface-lipid environment

The carrier phase is not inert from a biophysical perspective. Squalane is a saturated emollient related to squalene, a major component of human sebum, and is widely used for skin hydration and spreading properties [11-13]. Jojoba oil is rich in long-chain wax esters and has a long history in

dermatologic formulations; experimental human-skin organ culture work has reported reductions in LPS-induced IL-6, IL-8, and TNF-α after topical jojoba wax exposure [14,15]. Mixed tocopherols add lipid-phase antioxidant capacity, while the stratum corneum itself relies on an endogenous antioxidant network in which α-tocopherol is a prominent surface antioxidant [16,17]. These characteristics support the rationale for evaluating the formulation as a barrier-compatible leave-on oil rather than considering the rosemary fraction in isolation.

Table 2. Summary of Scientific Evidence Supporting the Therapeutic Potential of Rosemary-Based Formulation for Scalp Health

Evidence layer	Model / population	Key observation	Relevance
Human RCT	42 patients with scalp seborrheic dermatitis	Rosemary lotion improved flaking and itch; itch reduction exceeded ketoconazole at assessed time points [10]	Direct scalp clinical context
Skin-cell signaling	Stimulated keratinocytes and immune cells	Carnosic acid reduced IL-6/IL-8/MCP-1 and NF-κB-linked signaling [5]	Mechanistic support for inflammatory modulation
Experimental inflammatory skin	Psoriasis-/rosacea-like models	Carnosic acid targeted STAT1 and reduced inflammatory signaling [6]	Additional cutaneous pathway evidence
Skin repair model	Topical rosemary extract/carnosic acid	TRPA1-dependent acceleration of repair in mice [7]	Topical skin relevance
Redox signaling	Cellular Nrf2/HO-1 studies	Carnosic acid and carnosol activated antioxidant-response pathways [8,9]	Biological plausibility for redox balance
Scalp microbiome literature	Systematic review and clinical scalp studies	SD/dandruff associated with altered Malassezia/Staphylococcus patterns and barrier features [1-3]	Context for multifactorial scalp care

4. Discussion

The principal analytical finding is that the production strategy achieves a chemically distinct balance: carnosic acid and carnosol remain at high concentrations while two representative volatile monoterpenes are kept below 0.15% in the characterized batch. The same-batch comparison supports the contribution of the 30-min forecut step to this selectivity. This matters because the term "rosemary extract" covers preparations with very different chemical profiles. An essential-oil-dominant material and a nonvolatile diterpene-rich fraction should not be expected to have identical sensory behavior, irritancy potential, stability characteristics, or mechanistic emphasis.

The clinical literature provides a useful, but formulation-dependent, bridge to scalp outcomes. In the seborrheic dermatitis trial, topical rosemary was associated with substantial improvement in itch and flaking over two months [10]. The stronger ketoconazole effect on ASFS and the stronger rosemary effect on itch illustrate that different endpoint domains can respond differently. This pattern is compatible with a research model in which antifungal activity, barrier behavior, sensory-neuronal signaling, and inflammatory modulation are partially separable. It also argues for future formulation-specific trials that measure pruritus, erythema, flaking, transepidermal water loss, sebum, and microbiome endpoints together rather than relying on a single global score.

The diterpene chemistry of the present oil is particularly relevant to inflammatory and oxidative pathways. Carnosic acid and carnosol are redox-active phenolic diterpenes with both direct antioxidant chemistry and signaling effects [4]. The Syk/Src-NF-κB findings in keratinocytes [5], STAT1

targeting in inflammatory skin models [6], and Nrf2/HO-1 observations [8,9] provide mutually reinforcing mechanistic routes through which a diterpene-rich system may influence the local response to irritants or oxidative challenge. The TIMEFLYS formulation therefore offers a defined matrix in which these pathways can be examined under controlled topical-use conditions, while the published evidence guides endpoint selection and biological interpretation.

The oil vehicle may also shape the user-relevant outcome. Squalane and caprylic/capric triglyceride provide a low-water lipid phase with efficient spreadability; jojoba wax esters contribute emolliency and may support a favorable barrier environment; mixed tocopherols help protect the lipid system from oxidation [11-18]. In a scalp context, maintaining a stable formulation and minimizing excessive volatile load are practical variables because stinging, odor, oxidation products, and barrier disruption can influence adherence and subjective comfort independently of the primary botanical actives.

5. Current Scope and Future Directions

The current study was designed to integrate chemical standardization and translational evidence rather than to duplicate a finished-formulation efficacy trial. The analytical dataset establishes composition, process selectivity, peroxide control, and marker levels, while the human literature provides clinically relevant context for rosemary-containing topical preparations. Building on these findings, a prospective scalp study could evaluate the complete oil with predefined endpoints such as itch numeric rating, erythema, ASFS, corneometry, transepidermal water loss, sebum output, and microbiome composition. Stratification by baseline dandruff severity and scalp sensitivity would further clarify which users derive the greatest cosmetic benefit.

Future work could also measure local biomarkers linked to the mechanistic pathways identified here, including Nrf2-responsive genes, NF-κB-related cytokines, lipid-peroxidation markers, and selected barrier proteins. Such studies would extend the present analytical and mechanistic framework from formulation chemistry to direct human scalp physiology while preserving the distinction between cosmetic scalp care and disease-directed therapy.

6. Conclusion

A segmented supercritical-thin-film process produced a rosemary fraction rich in carnosic acid and carnosol while maintaining low residual camphor and 1,8-cineole. Incorporation of 10% of this standardized fraction into a squalane/CCT/jojoba/tocopherol oil created a chemically defined leave-on scalp-care system. Published human evidence demonstrates that topical rosemary preparations can improve clinically relevant scalp symptoms, especially pruritus, and mechanistic studies provide convergent support for modulation of inflammatory and oxidative-stress pathways. Together, the formulation data and literature establish a focused scientific basis for subsequent human evaluation of scalp comfort, redox balance, and barrier-associated outcomes.

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