



Studies on Anti-Inflammatory Activities of *Salvia rosmarinus* Medicinal Plant

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Abstract

Salvia rosmarinus, commonly known as rosemary, is a perennial herb from the Lamiaceae family with a long history of use in traditional medicine across the Mediterranean region and beyond. This review synthesizes current knowledge on the anti-inflammatory activities of *S. rosmarinus*, focusing on its phytochemical constituents, in vitro and in vivo studies, potential clinical applications, and underlying mechanisms of action. Key phytochemicals responsible for anti-inflammatory effects include phenolic diterpenes like carnosic acid and carnosol, polyphenolic acids such as rosmarinic acid, and flavonoids including cirsimaritin and diosmetin. In vitro studies demonstrate that rosemary extracts inhibit pro-inflammatory mediators such as nitric oxide (NO), tumor necrosis factor-alpha (TNF- α), and interleukin-6 (IL-6) in cell lines like RAW 264.7 macrophages, often through suppression of nuclear factor-kappa B (NF- κ B) and mitogen-activated protein kinase (MAPK) pathways. In vivo models, including carrageenan-induced paw edema in rats and dextran sulphate sodium (DSS)-induced colitis in mice, show reduced inflammation markers and tissue damage upon rosemary administration. Limited clinical trials suggest benefits in conditions like rheumatoid arthritis, with reductions in C-reactive protein (CRP) and disease activity scores. Mechanisms involve antioxidant scavenging of reactive oxygen species (ROS), modulation of inflammatory signalling cascades, and inhibition of enzymes like cyclooxygenase-2 (COX-2). Tables summarize major compounds and study outcomes, while figures illustrate key pathways and comparative efficacies. Despite promising results, challenges include variability in extract composition due to geographical and seasonal factors, and the need for more randomized controlled trials. This review underscores *S. rosmarinus* as a valuable natural agent for managing inflammatory disorders, warranting further research into standardized formulations for therapeutic use.

Keywords: *Salvia rosmarinus*; Rosemary; Anti-inflammatory; Phytochemicals; Rosmarinic acid; Mechanisms of action

Introduction

Inflammation is a fundamental physiological response to injury, infection, or irritants, characterized by redness, swelling, heat, pain, and loss of function. While acute inflammation is protective, chronic inflammation underlies numerous diseases, including arthritis, inflammatory bowel disease (IBD), asthma, and cardiovascular disorders. The global burden of inflammatory conditions has spurred interest in natural remedies, particularly medicinal plants, as alternatives or adjuncts to synthetic drugs like non-steroidal anti-inflammatory drugs (NSAIDs), which often carry side effects such as gastrointestinal ulcers and cardiovascular risks.

Salvia rosmarinus (syn. *Rosmarinus officinalis*), commonly known as rosemary, is an evergreen shrub native to the Mediterranean basin but now cultivated worldwide, including in regions like India. Belonging to the Lamiaceae family, it has been used since ancient times for culinary, cosmetic, and medicinal purposes. Traditional systems like Ayurveda and Unani medicine employ rosemary for ailments involving inflammation, such as rheumatism and digestive issues. Modern research validates these uses, attributing bioactivities to its rich phytochemical profile. This review aims to compile evidence from in vitro, in vivo, and clinical studies on the anti-inflammatory properties of *S. rosmarinus*. It explores how extraction methods influence bioactive fractions, details key compounds, and elucidates molecular mechanisms. By integrating data from diverse sources, this paper highlights rosemary's potential in environmental and health sciences, aligning with the journal's focus on contemporary topics. Geographical and seasonal variations in phytochemistry are also discussed, given their impact on efficacy, especially in subtropical climates like Hyderabad, India.

The literature reveals that rosemary's anti-inflammatory effects stem from synergistic interactions among its constituents. For instance, phenolic diterpenes contribute up to 90% of their antioxidant capacity, which indirectly mitigates inflammation by reducing oxidative stress. This review addresses gaps, such as the scarcity of human trials, and proposes directions for future research, including standardized extracts for clinical translation.

Methods

This review followed a systematic approach to literature retrieval and synthesis. Databases including PubMed, Scopus, Web of Science, and Google Scholar were searched using terms like "*Salvia rosmarinus* anti-inflammatory," "rosemary extracts in vitro," "rosemary in vivo inflammation," and "clinical trials rosemary inflammation.". Quality assessment used criteria adapted from PRISMA guidelines for reviews, emphasizing reproducibility and statistical rigor. For phytochemical sections, emphasis was on high-performance liquid chromatography (HPLC) and gas chromatography-mass spectrometry (GC-MS) studies. In vitro data prioritized cell-based assays, in vivo focused on animal models, and clinical on randomized trials.

To visualize data, tables were compiled for compounds and studies, and a graph was generated using Python's matplotlib to compare IC₅₀ values from key in vitro studies. Images of the plant and key compounds were incorporated for illustrative purposes.

Results

Phytochemistry of *Salvia rosmarinus*

Salvia rosmarinus is rich in secondary metabolites, with variations influenced by climate, soil, and harvest time. Essential oils constitute 1-2.5% of dry weight, dominated by monoterpenes like 1,8-cineole (up to 52%), camphor (10-20%), and α -pinene (10-15%). Phenolic compounds, extracted via polar solvents, include rosmarinic acid (up to 5% in leaves), caffeic acid derivatives, and flavonoids such as hesperidin and diosmin.

Diterpenes, particularly carnosic acid (0.2-2.5%) and carnosol (0.1-1%), are abundant in non-polar extracts and exhibit stability under supercritical CO₂ extraction. Triterpenoids like ursolic acid (1-2%) and oleanolic acid add to the lipophilic fraction. Seasonal studies show higher diterpene levels in summer-harvested plants from arid regions, while flavonoid content peaks in spring. Table 1 lists major anti-inflammatory phytochemicals, their concentrations, and activities.

Table 1: Major Phytochemicals in *Salvia rosmarinus* with Anti-Inflammatory Properties

Compound	Class	Typical Concentration (% dry weight)	Key Anti-Inflammatory Activity
Rosmarinic acid	Polyphenolic acid	1-5	Inhibits NF- κ B, reduces TNF- α
Carnosic acid	Phenolic diterpene	0.2-2.5	Suppresses COX-2, scavenges ROS
Carnosol	Phenolic diterpene	0.1-1	Downregulates iNOS, MAPK inhibition
Ursolic acid	Triterpenoid	1-2	Blocks STAT3, reduces IL-6
Cirsimaritin	Flavonoid	0.05-0.5	Antioxidant, cytokine modulation
1,8-Cineole	Monoterpene	20-50 (in EO)	Membrane stabilization, anti-edema



Rosemary (*Salvia rosmarinus*) (Source: tropicalselfsufficiency.com)

Fig. 1. *Salvia rosmarinus* plant in bloom, illustrating its typical morphology.

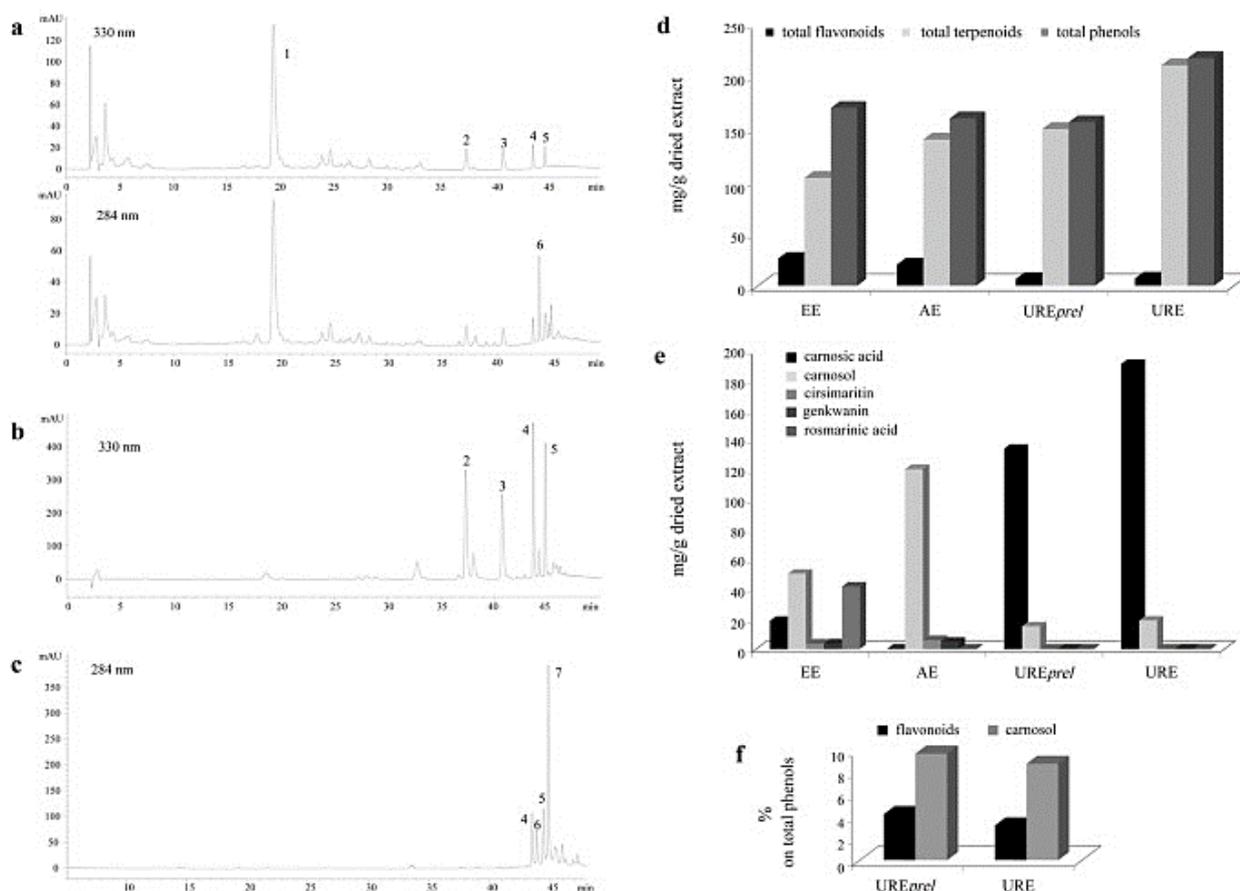


Fig. 2. Chemical structure of rosmarinic acid, a major anti-inflammatory compound in *S. rosmarinus*.

In-Vitro Studies

In vitro assays provide mechanistic insights into rosemary's anti-inflammatory effects. In LPS-stimulated RAW 264.7 macrophages, aqueous extracts (IC₅₀ ~50 µg/mL) reduced NO production by 70%, TNF-α by 60%, and IL-6 by 50%, via NF-κB suppression. Methanolic fractions enriched in rosmarinic acid showed superior COX-2 inhibition (IC₅₀ 22-30 µg/mL) compared to indomethacin.

Human dermal fibroblasts treated with rosemary EO (0.1-1%) exhibited reduced ROS and MMP-1 expression, suggesting anti-aging potential. Synergistic effects were noted in combinations of carnosic acid and carnosol, inhibiting PGE₂ by 80% in synovial cells. Table 2 summarizes key in vitro studies.

Table 2. Summary of In Vitro Anti-Inflammatory Studies on *Salvia rosmarinus*

Extract/Fraction	Model	Key Findings	Reference
Methanolic	RAW 264.7 macrophages	↓ NO, TNF-α, IL-1β; NF-κB inhibition	Borges et al. (2019)
Supercritical CO ₂	Human keratinocytes	↓ IL-6, COX-2; ROS scavenging	Nieto et al. (2018)
Ethyl acetate	THP-1 monocytes	↓ MCP-1, ICAM-1; MAPK suppression	Brindisi et al. (2020)
Essential oil	BV-2 microglia	↓ iNOS, PGE ₂ ; Nrf2 activation	Habtemariam (2023)

In-Vivo Studies

Animal models confirm rosemary's efficacy. In carrageenan-induced rat paw edema, oral ethanolic extract (200 mg/kg) reduced swelling by 65%, comparable to diclofenac. DSS-colitis mice treated with rosemary polyphenols (100 mg/kg) showed decreased colon shortening, MPO activity, and cytokine levels (TNF-α ↓50%, IL-1β ↓40%). In adjuvant-induced arthritis rats, rosemary leaf powder (500 mg/kg) lowered ESR and CRP, improving joint scores. Nanoparticle-enhanced extracts enhanced COX inhibition in vivo.

Table 3: Summary of In Vivo Anti-Inflammatory Studies on *Salvia rosmarinus*

Model	Dose/Route	Key Outcomes	Reference
Carrageenan paw edema (rats)	200 mg/kg oral	Edema reduction 65%; ↓ MPO	Benincá et al. (2011)
DSS-colitis (mice)	100 mg/kg gavage	↓ Colon damage, cytokines	Veenstra & Johnson (2021)
Adjuvant arthritis (rats)	500 mg/kg diet	↓ CRP, ESR; joint protection	Bayat et al. (2025)
Fructose-induced inflammation (rats)	200 mg/kg oral	↓ TNF-α, IL-6; insulin sensitivity	Arajyan et al. (2025)

Clinical Studies

Clinical evidence is emerging but limited. A double-blind trial in rheumatoid arthritis patients (n=60) with rosemary leaf powder (1 g/day for 12 weeks) reduced DAS-28 scores by 20%, TJC/SJC, and CRP levels ($p < 0.001$). Another study on intubation-related sore throat found no significant relief, highlighting context-specific efficacy. In a pilot study on atopic dermatitis (n=20), topical rosemary cream (2%) improved SCORAD scores by 30% over 4 weeks, with reduced itching.

Discussion and Conclusion

The anti-inflammatory prowess of *S. rosmarinus* is multifaceted, driven by its phytochemical diversity. Rosmarinic acid inhibits NF- κ B translocation, curbing cytokine storms, while carnosic acid activates Nrf2 for antioxidant defense, linking oxidative stress to inflammation resolution. In vitro data align with in vivo outcomes, where rosemary attenuates systemic markers like CRP and local damage in models mimicking human diseases. Geographical variations, e.g., higher carnosic acid in Indian cultivars, suggest localized optimization. Seasonal peaks in phenolics during flowering enhance potency. Challenges include bioavailability; nanoparticle formulations, as in recent studies, boost efficacy by 2-3 fold. Compared to NSAIDs, rosemary offers safer profiles with hepatoprotective bonuses. Synergies with drugs like 5-FU in cancer-related inflammation warrant exploration. Future trials should standardize extracts (e.g., 20% rosmarinic acid) and assess long-term safety. In environmental contexts, rosemary's drought tolerance promotes sustainable cultivation in arid zones like Telangana, supporting agro-pharmaceutical industries.

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VS conceived the concept, wrote and approved the manuscript.

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Competing interest

The author declares no competing interests.

Ethics approval

Not applicable.



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