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Therapeutic Potential of *Nigella sativa* in Chronic Rhinosinusitis: A Narrative Review of Experimental and Clinical Evidence

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Abstract: Chronic rhinosinusitis (CRS) is a persistent inflammatory condition of the nasal and paranasal sinus mucosa that significantly impairs quality of life. Although topical and systemic corticosteroids and endoscopic sinus surgery remain the standard of care, many patients still experience relapse and require repeated courses of treatment. Biologic therapies have shown promising outcomes; however, limited availability and high costs pose major barriers, particularly in low- and middle-income countries. Therefore, there is a need for an effective, safe, and affordable adjuvant treatment option. Nigella sativa, commonly known as black seed (alhabahat alsawda), contains bioactive compounds, notably thymoquinone, with antioxidant, anti-inflammatory, and immunomodulatory properties.

This narrative review summarizes experimental and clinical evidence on Nigella sativa in CRS. Relevant peer-reviewed studies were identified through major biomedical databases, including PubMed, Scopus, and Google Scholar, and were selected based on their clinical or mechanistic relevance to chronic rhinosinusitis. In vitro studies suggest thymoquinone attenuates pro-inflammatory signaling, reduces fibroblast proliferation, and modulates epithelial barrier–related markers. In animal rhinosinusitis models, thymoquinone improves histopathology and decreases inflammatory cell infiltration. Limited clinical studies using nasal spray or oral extracts report improvements in validated symptom scores and quality-of-life measures with acceptable tolerability. Overall, Nigella sativa shows potential as an adjunctive therapeutic option in CRS, but the current evidence base is heterogeneous and small. Well-designed, adequately powered randomized controlled trials using standardized formulations, dosing regimens, and long-term follow-up are needed to confirm efficacy, safety, and clinical applicability.

Keywords: Adjuvant therapy; Black seed; Chronic rhinosinusitis; Nigella sativa; Thymoquinone.

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Introduction

Chronic rhinosinusitis (CRS) is a persistent inflammatory disorder of the nasal and paranasal sinus mucosa characterized by nasal obstruction, rhinorrhea, facial pressure, and olfactory dysfunction lasting at least 12 weeks. The condition imposes substantial healthcare and socioeconomic burdens and significantly affects quality of life. Contemporary understanding recognizes

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CRS as a multifactorial inflammatory disease involving epithelial barrier dysfunction, immune dysregulation, microbial interactions, and tissue remodelling processes (Grayson et al., 2020). Distinct inflammatory endotypes, particularly those differentiating CRS with nasal polyps from CRS without nasal polyps, further highlight the complexity of its pathophysiology (Cao et al., 2019).

Although intranasal corticosteroids, saline irrigation, antibiotics, and endoscopic sinus surgery constitute standard therapeutic approaches, recurrence and incomplete symptom control remain frequent, especially in patients with Type 2 inflammatory phenotype. These limitations have prompted exploration of adjunctive therapies targeting inflammatory signalling pathways and oxidative stress mechanisms that sustain mucosal inflammation.

In recent years, CRS has been increasingly framed through distinct inflammatory patterns, broadly grouped into Type 2 and non–Type 2 inflammation. Type 2 inflammation is typically associated with eosinophil-predominant mucosal inflammation and a higher tendency toward nasal polyp formation, which together contribute to greater disease burden and relapse risk. By contrast, non–Type 2 CRS is often described as Type 1 and Type 3 patterns: Type 1 is more commonly linked to cellular immune–dominant inflammation and may present with less prominent eosinophilia, whereas Type 3 is frequently characterized by a more neutrophil-leaning inflammatory profile and persistent mucosal inflammation that can be less responsive to conventional anti-inflammatory regimens. While mixed or overlapping patterns also occur, recognizing these inflammatory profiles is clinically relevant because the dominant inflammatory milieu can influence treatment responsiveness and underscores the rationale for adjuvant therapies that modulate both inflammation and oxidative stress.

Nigella sativa (black seed; alhabahat alsawda) has long been used in traditional medicine and has gained scientific attention due to its bioactive constituent, thymoquinone. Preclinical investigations demonstrate that thymoquinone modulates inflammatory mediators and oxidative stress pathways, including inhibition of nuclear factor kappa B signalling and reduction of pro-inflammatory cytokines (Fatima Shad et al., 2021; Gholamnezhad et al., 2016; Liu et al., 2022; Tavakkoli et al., 2017). A systematic review and meta-analysis further indicate that *Nigella sativa* supplementation may reduce circulating inflammatory biomarkers in human subjects (Montazeri et al., 2021).

Experimental models of inflammatory lung injury provide additional mechanistic insights. In a lipopolysaccharide-induced inflammatory model, thymoquinone administration reduced histopathological injury, attenuated interstitial edema, decreased inflammatory cell infiltration, and suppressed serum levels of interleukin-1 beta and tumor necrosis factor alpha, alongside reduced nuclear factor kappa B expression (Al-Gabri et al., 2017). These findings suggest that thymoquinone can reduce key inflammatory processes involved in chronic airway diseases.

Emerging evidence has extended investigation into sinonasal conditions. In vitro studies using nasal polyp–derived fibroblasts demonstrate modulation of cellular viability and remodelling-related mediators following thymoquinone exposure (Sofyan et al., 2022). Animal models of chronic rhinosinusitis with nasal polyps indicate regulation of epithelial and remodelling markers, including p63, claudins, and periostin, after thymoquinone administration (Ulfa et al., 2025). Clinical investigations further report symptomatic improvement in patients with chronic rhinosinusitis treated with *Nigella sativa* in various formulations, including nasal spray and oral extract preparations (Karaarslan et al., 2024; Mahboubi, 2018; Nemati et al., 2021; Rezaeian & Amoushahi Khouzani, 2018). A recent systematic review specifically addressing rhinosinusitis underscores increasing research interest in this domain (Muhamad Najemudin et al., 2025).

Safety considerations are critical when evaluating adjunctive therapeutic strategies. A phase I clinical trial assessing thymoquinone-rich black cumin oil in healthy subjects demonstrated favourable tolerability (Thomas et al., 2022). Broader safety and pharmacological reviews further support its acceptable safety profile and potential nutraceutical application (Alu'datt et al., 2024; Burdock, 2022; Hannan et al., 2021; Mashayekhi-Sardoo et al., 2020) .

Despite growing interest in *Nigella sativa* across experimental, translational, and clinical settings, evidence that is specifically relevant to chronic rhinosinusitis remains scattered and is often discussed without a clear CRS-focused clinical context. This gap matters because CRS is a heterogeneous inflammatory disease in which relapse and treatment response are closely linked to underlying inflammatory pathways, making the evaluation of affordable adjunctive options particularly timely. Accordingly, consolidating and critically appraising the existing CRS-specific evidence is necessary to clarify what is currently supported, what remains uncertain, and where future studies should be directed. The objective of this narrative review is to critically examine the therapeutic potential of *Nigella sativa* in CRS by integrating mechanistic rationale, preclinical findings, available clinical outcomes, and safety data, while identifying key limitations and priorities for future investigation.

Materials and Methods

This manuscript was prepared as a narrative review intended to synthesize experimental and clinical findings concerning the therapeutic potential of *Nigella sativa* in chronic rhinosinusitis. Unlike a systematic review, the present work does not aim to perform quantitative pooling of outcomes or structured risk-of-bias assessment. Instead, the objective was to integrate mechanistic insights and clinical observations into a coherent translational perspective relevant to sinonasal disease.

A literature search was conducted using major biomedical databases, including PubMed, Scopus, and Google Scholar. The search strategy combined keywords related to the intervention and disease of interest, including "Nigella sativa", "thymoquinone", "chronic rhinosinusitis", "sinusitis", and "nasal polyps". Articles published in English between 2016 and 2025 were considered. Relevant studies were screened based on their clinical or mechanistic relevance to chronic rhinosinusitis and the biological effects of Nigella sativa or thymoquinone.

The analysis was conducted using a preselected set of peer-reviewed publications that included in vitro experiments, animal studies, randomized clinical trials, systematic reviews, pharmacological analyses, and safety evaluations. Studies were considered relevant if they examined *Nigella sativa* or its principal bioactive compound, thymoquinone, in relation to inflammatory mechanisms, airway pathology, sinonasal disease, or human safety outcomes.

From each article, the following elements were extracted: study design, experimental model or patient population, formulation and route of administration, primary biological targets, clinical endpoints where applicable, and safety outcomes. Because of methodological heterogeneity among the included studies, findings were synthesized qualitatively. The evidence was subsequently organized into thematic domains: (1) biological and pharmacological mechanisms, (2) experimental evidence in airway inflammation, (3) clinical studies in chronic rhinosinusitis, and (4) safety considerations.

Biological and Pharmacological Basis of Nigella sativa

Phytochemical Profile and Bioactive Constituents

Nigella sativa contains a complex mixture of fixed oils, volatile oils, alkaloids, saponins, and phenolic compounds. Among these constituents, thymoquinone has been identified as the principal bioactive molecule responsible for many of the plant's anti-inflammatory and antioxidant effects (Burdock, 2022; Hannan et al., 2021). Comprehensive phytochemical analyses have characterized additional compounds such as dithymoquinone, thymohydroquinone, nigellidine, and alpha-hederin, each potentially contributing to biological activity (Alu'datt et al., 2024).

Pharmacological reviews have emphasized that the therapeutic properties of *Nigella sativa* are not attributable to a single pathway but rather to pleiotropic interactions affecting oxidative stress regulation, cytokine production, and cellular signalling cascades (Gholamnezhad et al., 2016; Tavakkoli et al., 2017). This multi-target profile is particularly relevant in chronic inflammatory diseases, where redundant inflammatory networks often limit the efficacy of single-pathway interventions.

Anti-inflammatory and Antioxidant Mechanisms

At the molecular level, thymoquinone has been shown to modulate nuclear factor kappa B signaling, suppress pro-inflammatory cytokines, and attenuate oxidative stress–related damage (Fatima Shad et al., 2021; Liu et al., 2022). These mechanisms are central to chronic airway inflammation, including CRS, where persistent cytokine production and epithelial barrier dysfunction sustain mucosal edema and remodelling.

A systematic review and meta-analysis of randomized controlled trials demonstrated that *Nigella sativa* supplementation is associated with reductions in circulating inflammatory biomarkers and oxidative stress parameters in human subjects (Montazeri et al., 2021). Although these studies were not limited to sinonasal disease, the findings support a broader anti-inflammatory profile that may be applicable to chronic mucosal inflammation. Taken together, available pharmacological evidence suggests that *Nigella sativa* exerts biologically plausible effects on pathways implicated in CRS pathogenesis, including cytokine modulation, oxidative stress attenuation, and epithelial barrier stabilization.

Experimental Evidence in Airway Inflammation

Inflammatory Models and Mechanistic Insights

Experimental models provide mechanistic support for the anti-inflammatory properties of thymoquinone in airway-related inflammation. In a lipopolysaccharide-induced model of acute lung injury, thymoquinone administration resulted in reduced histopathological damage, diminished inflammatory cell infiltration, and suppression of pro-inflammatory mediators including interleukin-1 beta and tumor necrosis factor alpha (Al-Gabri et al., 2017). Nuclear factor kappa B expression was also attenuated, indicating modulation of a central inflammatory signalling pathway. Although this model represents

pulmonary rather than sinonasal inflammation, the underlying inflammatory cascades are shared across airway mucosa, making these findings mechanistically relevant to CRS.

Sinonasal Cellular and Polyp-Related Studies

More directly relevant to CRS, in vitro investigations using nasal polyp–derived fibroblasts have shown that thymoquinone influences cellular viability and pathways associated with tissue remodelling (Sofyan et al., 2022). Fibroblast activity plays a critical role in polyp formation and extracellular matrix deposition, suggesting that thymoquinone may exert modulatory effects beyond simple cytokine suppression.

In a chronic rhinosinusitis with nasal polyps animal model, thymoquinone administration was associated with altered expression of epithelial and remodelling-related markers, including p63, claudins, and periostin (Ulfa et al., 2025). These markers are linked to epithelial integrity and structural remodelling, processes that contribute to disease persistence and recurrence. Key experimental findings are summarized in **Table 1**.

Table 1. Summary of Experimental Studies Investigating Nigella sativa or Thymoquinone in Airway-Related Inflammation

Study	Model	Intervention	Key Outcomes	Main Implication
(Al-Gabri et al., 2017)	Lipopolysaccharide-induced inflammatory rat model	Thymoquinone	↓ IL-1β, ↓ TNF-α, ↓ NF-κB, improved histopathology	Suppression of pro-inflammatory signaling pathways
(Sofyan et al., 2022)	Nasal polyp–derived fibroblast culture	Thymoquinone ± TGF-β1	Modulation of fibroblast viability	Potential regulation of remodeling-related cellular activity
(Ulfa et al., 2025)	Chronic rhinosinusitis with nasal polyps animal model	Thymoquinone	Regulation of p63, claudin, periostin expression	Influence on epithelial integrity and structural remodeling

Clinical Evidence in Chronic Rhinosinusitis

CRS Without Nasal Polyps

Clinical studies investigating *Nigella sativa* in CRS without nasal polyps have reported improvements in symptom severity and clinical scores. In a randomized study evaluating a *Nigella sativa* nasal spray, patients demonstrated significant reductions in symptom scores compared with baseline measurements (Rezaeian & Amoushahi Khouzani, 2018). In this randomized clinical trial, 65 patients with chronic rhinosinusitis without nasal polyps were allocated to receive either *Nigella sativa* nasal spray (1 g/day) or placebo for 8 weeks. The intervention group showed significantly greater reductions in Lund–McKay, Modified Lund–Kennedy, and Sino-Nasal Outcome Test-22 (SNOT-22) scores compared with the placebo group ($P < 0.0001$).

Similarly, administration of *Nigella sativa* extract in patients with CRS was associated with improvement in validated symptom measures (Nemati et al., 2021). In a randomized double-blind study, patients receiving *Nigella sativa* extract demonstrated a significant reduction in SNOT-22 scores after treatment compared with the placebo group, indicating improvement in CRS-related symptoms and quality of life. These findings suggest that topical or systemic formulations may provide symptomatic benefit, although study sizes and follow-up durations remain limited.

Adjunctive Use in Sinusitis

Earlier clinical observations have proposed *Nigella sativa* oil as an adjunctive therapy in sinusitis management, particularly in combination with conventional treatment (Mahboubi, 2018). While these reports are exploratory in nature, they contribute to the rationale for further controlled trials in CRS populations.

Upper Airway Infection and Translational Relevance

In pediatric populations, *Nigella sativa* oil has been evaluated for prophylaxis and treatment of upper respiratory tract infections, demonstrating potential reductions in infection frequency (Karaarslan et al., 2024). Although not specific to CRS, recurrent upper airway infections are recognized contributors to sinonasal inflammation, providing indirect translational relevance.

A recent systematic review focusing specifically on rhinosinusitis further indicates emerging but still limited clinical evidence in this area (Muhamad Najemudin et al., 2025). Clinical studies are summarized in **Table 2**. Overall, available clinical data suggest consistent symptomatic improvement across different formulations of *Nigella sativa*, although study sizes, duration, and methodological rigor vary considerably.

Table 2. Clinical Studies Evaluating Nigella sativa in Chronic Rhinosinusitis and Upper Airway Conditions

Study	Study Design	Population	Formulation	Primary Outcome	Clinical Relevance
(Rezaeian & Amoushahi Khouzani, 2018)	Randomized Clinical Trial	CRS without nasal polyps	Nasal spray	Improvement in symptom scores	Symptomatic benefit in CRSsNP
(Nemati et al., 2021)	Randomized Double-Blind Clinical Trial	Chronic rhinosinusitis	Extract	Reduction in validated symptom severity	Potential adjunctive therapy
(Mahboubi, 2018)	Narrative Review	Sinusitis patients	Oil (adjunct)	Clinical symptom improvement	Supportive role with standard therapy
(Karaarslan et al., 2024)	Clinical Observational Study	Pediatric upper airway infection	Oil	Reduced infection frequency	Possible impact on upper airway inflammation
(Muhammad Najemudin et al., 2025)	Systematic Review	Rhinosinusitis subjects	Various	Review of clinical outcomes	Emerging but limited clinical evidence

Safety and Translational Considerations

Evaluation of adjunctive therapies in chronic inflammatory diseases requires careful consideration of safety, tolerability, and feasibility for clinical use. Although *Nigella sativa* has been widely used in traditional medicine, modern therapeutic adoption necessitates evidence derived from controlled human studies and toxicological assessment.

A phase I clinical trial evaluating thymoquinone-rich black cumin oil in healthy volunteers demonstrated favourable tolerability without serious adverse events (Thomas et al., 2022). The study reported acceptable safety parameters across hematologic and biochemical indices, supporting the short-term safety of standardized formulations. While conducted in healthy subjects rather than patients with chronic rhinosinusitis, these findings provide an important foundation for further clinical investigation.

Broader safety evaluations have characterized the toxicological profile of *Nigella sativa* and its constituents. A comprehensive safety overview reported low toxicity in both experimental and human studies when administered within therapeutic ranges (Mashayekhi-Sardoo et al., 2020). Similarly, pharmacological analyses emphasize that adverse effects are generally mild and dose-dependent, with gastrointestinal discomfort being the most commonly described complaint (Burdock, 2022; Hannan et al., 2021). Reviews focusing on functional and nutraceutical applications further highlight the relative safety of black seed–derived preparations, particularly when standardized and quality-controlled (Alu'datt et al., 2024).

Nevertheless, translational challenges remain. Formulation variability, differences in thymoquinone concentration, and lack of standardized dosing regimens complicate comparison across studies. Clinical trials in chronic rhinosinusitis have used different preparations, including nasal sprays, oil-based formulations, and extracts, limiting direct generalization (Nemati et al., 2021; Rezaeian & Amoushahi Khouzani, 2018). Additionally, long-term safety data in CRS populations, particularly in patients with comorbid inflammatory conditions, remain limited.

Taken together, available evidence suggests that *Nigella sativa* possesses an acceptable safety profile when administered within studied dosage ranges. However, rigorous standardization of formulation and further long-term clinical evaluation are necessary before routine integration into CRS management algorithms.

Clinical Implications and Future Directions

The heterogeneity of chronic rhinosinusitis underscores the importance of targeted therapeutic strategies. Given its anti-inflammatory and antioxidant properties, *Nigella sativa* may be particularly relevant in inflammatory endotypes characterized by persistent cytokine activation and oxidative stress.

Current evidence suggests that *Nigella sativa* is best considered as an adjunctive therapy rather than a replacement for established treatments. Clinical studies to date have demonstrated symptomatic improvement, but sample sizes remain modest and follow-up durations are limited (Nemati et al., 2021; Rezaeian & Amoushahi Khouzani, 2018). Future trials should incorporate standardized outcome measures, including validated symptom scores, endoscopic grading, and objective inflammatory biomarkers.

From a translational perspective, future work should focus on defining the most effective dose, route, and treatment duration. In CRS, head-to-head comparisons between topical and systemic formulations could be particularly valuable given the predominantly localized mucosal inflammation. Linking observed molecular effects to measurable clinical improvement would also help strengthen causal interpretation.

Emerging experimental findings suggest that thymoquinone may influence epithelial barrier markers and remodelling pathways (Sofyan et al., 2022; Ulfa et al., 2025). Whether these molecular effects translate into reduced recurrence rates or improved surgical outcomes remains to be determined. Large-scale randomized controlled trials with longer follow-up periods are therefore required to establish definitive clinical benefit and determine patient subgroups most likely to respond.

Conclusion

Nigella sativa demonstrates biologically plausible anti-inflammatory and antioxidant effects that align with key mechanisms implicated in chronic rhinosinusitis. Experimental models indicate modulation of inflammatory signalling and remodelling pathways, while early clinical studies suggest symptomatic improvement in selected patient populations. Safety data from controlled human trials and pharmacological evaluations support its tolerability within studied dosage ranges.

Although current findings are encouraging, the evidence base remains limited by small sample sizes, heterogeneity in formulations, and short follow-up durations. At present, *Nigella sativa* may be considered a potential adjunctive option in CRS management, pending confirmation through larger, well-designed clinical trials.

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