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Therapeutic Potential of *Nigella sativa* in Asthma Management: A Review of Mechanistic Insights and Emerging Clinical Evidence

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ABSTRACT

Asthma is a serious global health concern that is characterized by persistent airway inflammation, oxidative stress, and immunological dysfunction. While conventional medications are effective, they can cause negative effects and fail to entirely treat symptoms in some patients. *Nigella sativa* (NS), often known as black seed, has emerged as a promising phytotherapeutic agent with anti-inflammatory, antioxidant, immunomodulatory, bronchodilatory, and anti-allergic properties that are relevant to asthma pathophysiology. This review covers current molecular, preclinical, and clinical evidence (2020-2025) that show NS's potential as an adjuvant in asthma treatment. Thymoquinone, the key bioactive element, modulates Th2 cytokines (IL-4, IL-5, and IL-13), decreases IgE production, and improves antioxidant defense systems, all while boosting airway smooth muscle relaxation and decreasing eosinophilic infiltration. Preclinical studies show improvements in airway inflammation and remodeling markers, but limited clinical trials reveal increased lung function (FEV_1), Asthma Control Test scores, and lower FeNO and IgE levels. However, translational problems remain due to methodological heterogeneity, a lack of standardized formulations, and a scarcity of large-scale randomized controlled trials. To confirm the therapeutic role of NS in asthma, future research should focus on standardized extract characterisation, dose optimization, biomarker-integrated clinical trials, and long-term safety evaluation. Collectively, *Nigella sativa* shows great promise as a safe, cost-effective asthma supplemental therapy, necessitating rigorous mechanistic and clinical testing.

Keywords: *Nigella sativa*; Thymoquinone; Asthma; Airway inflammation; Oxidative stress; Immunomodulation; Bronchodilation

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Introduction

Asthma is a widespread noncommunicable disease (NCD) that affects both children and adults. It is also the most prevalent chronic condition among children. Asthma symptoms are produced by inflammation and obstruction of the lungs' small airways, which may include cough, wheeze, shortness of breath, and chest tightness [1]. Asthma is a chronic respiratory condition that affects over 339 million people globally, including around 25 million in the United States, with 5.5 million children [2]. According to estimations, an additional 100 million people worldwide could be affected by 2025 [3]. Asthma has two phases: early and late. During the early phase, IgE-mediated mast cell activation produces histamine, prostaglandins, and leukotrienes, which cause airway constriction. During the late phase, eosinophils and T-cells produce inflammation. Persistent inflammation causes airway hyperresponsiveness and remodeling, including collagen production and basement membrane thickening, resulting in persistent airflow blockage [4].

The N. sativa supplement enhanced respiratory symptoms, PFT levels, and asthma control tests. In asthmatic individuals, the plant also increased anti-inflammatory cytokines while decreasing pro-inflammatory cytokines. Eventually, N. sativa supplements may give a cost-effective and clinically established useful therapeutic option for asthmatic patients with fewer side effects [5].

Botanical Overview of *Nigella sativa*

Nigella sativa L. (Ranunculaceae), often known as black cumin or black seeds, is a spicy, medicinal herb that has long been used in cuisine and traditional medicine to treat a variety of diseases and conditions, including asthma, bronchitis, rheumatism, headache, back pain, back pain, anorexia, amenorrhea, paralysis, inflammation, mental debility, eczema, and hypertension. Black cumin is native to the eastern Mediterranean, northern Africa, the Indian subcontinent, and Southwest Asia, and it is grown in many countries, including Egypt, Iran, Greece, Syria, Albania, Turkey, Saudi Arabia, India, and Pakistan [6].

N. sativa contains alpha-hedrein, carvacrol, nigellimine, N-oxide, nigellicine, p-cymene, carvacrol, 4-terpineol, t-anethole, sesquiterpene, α-pinene, thymol, TQ, and alkaloids, including pyrazole alkaloids and uncommon indazole ring alkaloids with remarkable biological activities [7]. Furthermore, the distribution of bioactive compounds in *N. sativa* has been comprehensively studied, with a focus on composition variation (Figure 1).

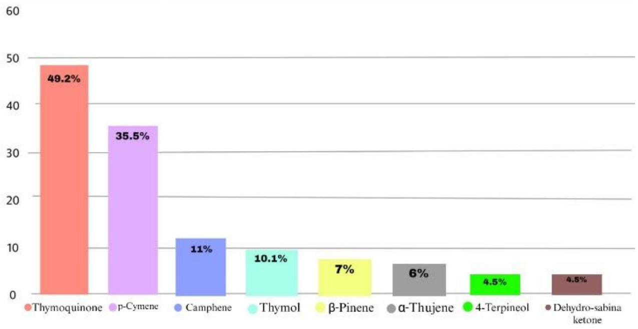

Figure 1: Composition variation *N. sativa*

When taken orally, thymoquinone is slowly absorbed but rapidly excreted. To overcome this issue, nanoparticle-based drug delivery systems have been designed to improve the pharmacokinetic profile. These nanoformulations enhance solubility, bioavailability, targeted distribution, and prolonged release, resulting in lower doses and fewer side effects than standard formulations [8].

Mechanistic Insights into *Nigella sativa's* Anti-Asthmatic Action

Anti-Inflammatory Actions

Nigella sativa (NS) and its key constituents (e.g., thymoquinone, α-hederin) have significant anti-inflammatory effects in asthma models by down-regulating Th2-cytokines (IL-4, IL-5, IL-13), reducing IgE levels, and attenuating eosinophilic infiltration in ovalbumin-induced asthma. A recent meta-analysis of preclinical models shown that NS dramatically lowered IL-4, IL-5, IL-13, and IgE levels in animal asthma models [9]. These data indicate that NS may disrupt the persistent airway inflammation that is important to asthma pathogenesis.

Antioxidant and Free-Radical Scavenging

In asthma, oxidative stress, caused by reactive oxygen species (ROS), leads to airway inflammation, smooth muscle dysfunction, and remodeling. In airway smooth muscle (ASM) cell tests, NS oil fractions demonstrated effective radical-scavenging capacity (against $O_2^{\bullet -}$, OH•, H_2O_2) and reduced GC-insensitive chemokine production (CCL5, CXCL-10, CXCL-8) generated by TNF-α/IFN-γ in human ASM cells [10]. These antioxidant and chemokine-modulating activities contribute to NS's mechanistic potential for lowering oxidative damage and pro-remodeling signals in asthma.

Immunomodulatory Properties

Aside from direct anti-inflammatory and antioxidant activities, NS also has immunomodulatory properties. A 2024 review found that NS can modify immunological responses in allergic disorders by balancing Th1/Th2 activity, boosting regulatory T-cell responses, and reducing IgE-mediated pathways [11]. In experimental models, NS therapy reduced Th2-type responses while increasing IFN-γ and regulatory cytokine production, indicating a potential role in rectifying the dysregulated immunological milieu of asthma.

Bronchodilatory and Smooth Muscle Relaxation Effects

The most common causes of asthma symptoms are airway smooth muscle spasm and hyperresponsiveness. In vitro studies have found that NS oil and its components diminish ASM-derived chemokines and oxidative signals, implying a modulatory effect on ASM behavior [10]. Clinical studies have previously revealed that NS extracts have bronchodilatory properties in asthmatic patients [12].

Preclinical Evidence

In-Vitro Studies

In human airway smooth muscle (ASM) cell models, *N. sativa* oil fractions, including neutral lipids, glycolipids, phospholipids, and unsaponifiable lipids, were shown to significantly inhibit the production of glucocorticoid-insensitive chemokines (CCL5, CXCL-10, CXCL-8) following stimulation with TNF-α/IFN-γ, and simultaneously exhibited potent reactive oxygen species (ROS) scavenging activity ($O_2^{\bullet-}$, $OH^{\bullet}$, H_2O_2) at concentrations of 25-50 µg. These findings imply that N. sativa may affect essential airway structure cell functions related to asthma pathogenesis (inflammation, oxidative stress, and ASM signaling) in vitro [10].

Animal Studies

In animal models of ovalbumin-induced asthma and other allergic airway inflammation, *N. sativa* and its chief bioactive constituent Thymoquinone produced robust improvements: a 2025 meta-analysis of 18 studies in 502 animals found significant reductions in IL-4, IL-5, IL-13, and IgE following *N. sativa* intervention in OVA-sensitized rodents (Ghobadi *et al*, 2025). Furthermore, albeit slightly earlier, research such as the 2022 experimental animal study of *N. sativa* oil in a rat allergic rhinitis model demonstrated significant decreases in eosinophil infiltration and goblet cell hyperplasia, which are mechanistically important to airway allergies [13]. These preclinical in-vivo studies support *N. sativa's* ability to reduce airway inflammation, eosinophilia, and allergic remodeling in asthma-like diseases.

Clinical Evidence in Asthma

Several randomized trials and meta-analyses suggest that *Nigella sativa* (NS) can enhance asthma control and lung function when administered in conjunction with standard medication. In a Saudi Arabian single-blind, placebo-controlled RCT, patients with partly controlled asthma received 1 g or 2 g/day NS plus inhaled therapy for 12 weeks. The 2 g group showed significant increases in FEV_1 and $FEF_{(25-75)}$, improved PEF variability in both NS groups, and reductions in FeNO, serum IgE, and fewer exacerbations [14]. A 2020 meta-analysis of four RCTs (pre-June 2019) indicated that NS supplementation significantly raised Asthma Control Test (ACT) scores and FEV_1 compared to control, despite the small and heterogeneous trials (Han and Shi, 2021). More recent evaluations indicate that, while clinical trials of NS in asthma have been limited since 2020, NS's molecular profile (anti-inflammatory, antioxidant, immunomodulatory) demands additional large-scale human research [15].

Limitations and Gaps in Clinical Data

Despite encouraging preclinical and preliminary clinical findings for *Nigella sativa* in asthma, several significant limitations and gaps need to be addressed. Existing clinical trials had small sample sizes, short durations, and restricted biomarker analysis; for example, one RCT indicated improved lung function but did not include bronchoalveolar lavage or induced sputum assessments [14]. Furthermore, formulations of *Nigella sativa* are inadequately characterized in many research, leaving dose-response, standardization, and pharmacokinetic features unknown [16]. In terms of mechanistic research, there is a significant scarcity of late-phase human trials, particularly big, multicenter RCTs in asthma, as well as insufficient investigation of long-term outcomes, airway remodeling, and subtype-specific responses. Another gap is the translation of comprehensive in vitro/animal mechanistic findings (such as ASM cell chemokine regulation) onto clinical endpoints in human asthma populations. As stated in a recent meta-analysis of preclinical asthma models, more research is needed to advance from OVA-induced animal studies to clinical efficacy and safety in people [9].

Challenges and Future Research Directions

Limited Clinical Evidence and Heterogeneous Study Designs

While several clinical investigations using *Nigella sativa* (NS) in asthma and respiratory illnesses indicate improved lung function and symptoms, the data is limited due to small sample sizes, short durations, and variable endpoints. A 2018-19 randomized study in partially controlled asthma showed better FEV_1 and ACT scores, but lacked sputum or bronchoalveolar lavage indicators for mechanistic insight [14]. An analysis of meta-analyses showed that the majority of NS research have "critically low" methodological quality and so require careful interpretation.

Lack of Standardization in Formulations and Bioactive Content

Variations in NS seed genotype, extraction processes, oil composition, and active ingredient (such as thymoquinone) content impede translational development. A 2024 study found substantial differences in thymoquinone and total phenolic content among NS genotypes and sowing conditions [17]. Without standardized products and unambiguous dose-response relationships, data from different research are difficult to interpret and duplicate.

Translational Gap Between Mechanistic Preclinical Findings and Human Outcome Data

Extensive preclinical research demonstrates that NS and its contents lower IL-4, IL-5, IL-13, IgE, and oxidative markers in OVA-induced asthma models [9].

However, clinical trials seldom detect these mechanistic biomarkers or differentiate asthma subtypes, limiting our understanding of which individuals may benefit and how. Future research will need to bridge this gap by including biomarker endpoints and phenotype-specific designs.

Future Research Priorities

To advance NS from promising adjunct to clinically adopted therapy in asthma, future research should incorporate (i) large, well-powered, multicenter randomized controlled trials using phytochemically defined NS preparations; (ii) pharmacokinetic and dose-finding to establish optimal dosing; (iii) inclusion of mechanistic biomarkers (such as FeNO, sputum eosinophils, cytokine panels); (iv) stratification by asthma endotypes (e.g., eosinophilic vs non-eosinophilic) to id A 2024 review stated that "more clinical trials are needed to establish the optimal dose and fully explore its action mechanisms" [15].

Conclusion

Nigella sativa has a high therapeutic promise for asthma control due to its multimodal pharmacological profile, which includes anti-inflammatory, antioxidant, immunomodulatory, and bronchodilatory activities. Evidence from animal models and limited human trials suggests that adding NS to standard therapy improves respiratory function, inflammatory markers, and overall asthma management. Despite these encouraging results, current clinical data are hampered by small sample sizes, diverse formulations, and short research periods. Addressing these deficiencies requires well-designed, large-scale, biomarker-driven clinical trials to establish NS's efficacy, safety, and optimal dosage. Furthermore, future research should prioritize formulation standardization, pharmacokinetic profiling, and mechanistic validation to make it easier to integrate into evidence-based asthma therapy. In conclusion, while *Nigella sativa* is not yet suitable for widespread clinical use, increasing mechanistic and rising clinical data points to its potential as a helpful supplemental therapy in asthma care.

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