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Review Article

Nigella sativa as a bioactive agent: A systematic review of its pharmacological attributes

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Abstract

Nigella sativa (NS) is a highly beneficial medicinal plant. This plant has its significance described in ancient texts and literature. It has its foothold in Unani and Ayurvedic forms of medicine. *Nigella* is valued mostly for its seeds which are a great source of phytochemicals which includes omega-6 fatty acid linoleic acid, organic acids, reducing sugars, thymol, thymoquinone, thymohydroquinone, dithymoquinone, resins, metarbin, poisonous glucoside, *p*-cymene, sabinene, carvacrol, 4-terpineol, kaempferol (glucoside) *t*-anethol, longifolene(sesquiterpene), *α*-pinene, *α*-hederin (pentacyclic triterpene), proteins, minerals, carbohydrates, lipids and vitamins. *Nigella* seed oil is rich source of fatty acids such as linoleic, linolenic, oleic, and palmitic acids along with generous amounts of arachidonic acid, eicosadienoic acid, stearic acid, and myristic acid. Roots and shoots of *Nigella* are rich source of carotene and vanillic acid. The presence of these highly potent phytochemicals imparts *Nigella* several medicinal properties that comprises antifungal, antibacterial, antiviral, antidiabetic, anti-inflammatory, antioxidant, anticancer, antiasthmatic, neuroprotective, gastroprotective, immunomodulatory, pro-metabolic effects. This review demonstrates how the essential phytochemicals found in the *Nigella* plant can profoundly benefit human health, offering powerful pharmacological effects that underscore its importance as a natural remedy.

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Introduction

Nigella sativa is also known as black cumin, black caraway or kalonji. (Abdulina, S.A. ,1999). *Nigella is an* annual flowering plant in the family *Ranunculaceae.* It is wildly cultivated in southern Europe, North Africa and Southwest Asia. The morphology of the plant comprises of shoot that grows to 20-90 cm tall, with finely divided leaves, the leaf segments narrowly linear to threadlike. The flowers are white, yellow, pink, pale blue or pale purple, with 5-10 petals. The fruit is a capsule composed of several united follicles, each containing numerous seeds. Seeds are usually three-cornered, with two sides flat and one convex, black or brown externally white and oleaginous, strong agreeable aromatic odour, like that of nutmegs, and a spicy, pungent taste (Varghese E, 1996). The fruit is a large and inflated capsule composed of 3–7 united follicles, each containing numerous seeds. It has a pungent bitter taste and a faint smell of strawberries (Dwivedi SN, 2003). Black cumin seeds and their oil are prominent in Ayurveda and traditional Islamic medicine as therapeutic agents for treating several ailments, including chronic illnesses (Yimer et al., 2019). Phytochemical analyses of *N. sativa* displayed the presence of over hundreds of phytoconstituents which include mainly alkaloids, saponins, sterols, and essential oil but the composition of many of these have not been chemically recognized nor have been biologically verified. The *N. sativa* seed contain 26-34% fixed oil of which the major fatty acids are linoleic acid (64.6%) and palmitic acid (20.4%). The seed oil is

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comprised of 0.4%–2.5% essential oil (Mamun et al., 2018) (Ghahramanloo K. H et al.,2017). Amongst different active constituents reported so far, thymoquinone found as major component of the essential oil is the most bioactive compound and exhibits wide ranging therapeutic benefits (Haseena. S et al., 2017).

Scientific Classification

Kingdom: Plantae
Division: Magnoliophyta
Order: Ranunculales
Family: Ranunculaceae
Genus: *Nigella*
Species: *sativa*

Methodology

Well defined search using keywords such as '*Nigella sativa*', 'pharmacological uses', 'clinical trial', 'thymoquinone', 'health benefits' was performed over various electronic databases such as PubMed, Scopus, and Google Scholar for relevant peer-reviewed articles, conference papers, and reviews published between (2002) and (2025). An attempt was made to document relevant literature that is only focused on *N. sativa*.

Antidiabetic property

Nigella sativa is rich in antidiabetic activity which leads to an increase in the overall production of insulin by the liver. It also decreases blood level gluconeogenesis and consequently diminishes the absorption of glucose by the intestine. SGOT (Serum Glutamic Oxaloacetic Transaminase) and SGPT (Serum Glutamic Pyruvic Transaminase) are also impacted by *Nigella* phytoconstituents. It is also reported that N. sativa seeds impact the concentration of lipoproteins and lower the level of cholesterol and triglycerides. The most important constituent of *Nigella* is regarded as thymoquinone which plays a role in promoting β-cell activity and β-cell protection from oxidative stress (Maideen N., 2021).

Antifungal property

The essential biological active compounds found in *Nigella* include thymoquionone, thymol and thymohydroquinone. Several studies concluded the antifungal properties of ethanolic extract of *Nigella* essential oil containing thymohydroquinone against the growth of several species of Candida (O. Zaiyirch, 2022). Inhibition of many skin pathogens has also been reported (Aliyale et al., 2005). These skin pathogens also known as dermatophytes are Trichophyton, Microsporum and Epidermophyton. The main mode of inhibitory action shown by *Nigella* bioactive extract comprises- introduction of oxidative stress, membrane degeneration, decrease in the expression of genes involved in adhesion or biofilm formation (Almshurri H et al., 2016). Reviews also emphasized that TQ found in *Nigella* has aspects for beneficial use in clinical combination therapy and improved formulation designs by applying nanoparticle carriers (Hannan et al., 2001).

Antibacterial property

Antibacterial effects of *Nigella sativa* proved to be effective against several human pathogenic strains such as *S. aureus, E. coli, P. aeruginosa* (Chaieb et al., 2011). Inhibitory action against MRSA (Methicillin Resistant Staphylococcus aureus) has been recorded (Randhawa et al., 2008). These inhibitory effects are largely mediated through mechanisms against pathogens by means of several biochemical changes that cause membrane degeneration.

Anticancer property

Recent studies demonstrates that its major bioactive constituent, thymoquinone (TQ), exerts potent antiproliferative, pro-apoptotic, anti-inflammatory, and anti-metastatic effects across multiple cancer cell lines and animal models (Mostofa et al., 2017; Khan et al., 2017). TQ has been shown to induce apoptosis through both intrinsic and extrinsic pathways, including modulation of Bax/Bcl-2 ratios, activation of caspases, and generation of reactive oxygen species (Majdalawieh et al., 2024). Additionally, it inhibits key oncogenic signaling pathways such as PI3K/AKT, NF-κB, STAT3, and MAPK, thereby reducing proliferation, angiogenesis, and metastasis (Sheikhnia et al., 2023). In breast, colorectal, pancreatic, and oral squamous carcinoma models, TQ not only suppressed tumor growth but also enhanced the sensitivity of cancer cells to conventional chemotherapeutic agents (Chu et al., 2014; Ravi et al., 2025). Although these findings are predominantly preclinical, they provide a strong mechanistic basis for the potential integration of *N. sativa* or TQ into anticancer strategies. Clinical investigations remain limited, highlighting the need for well-designed trials to evaluate efficacy, safety, and bioavailability in humans (Tavakkoli et al., 20).

Antiasthmatic property

Preclinical and clinical evidence indicates *Nigella sativa* (and its major constituent thymoquinone, TQ) reduce airway hyperresponsiveness, eosinophilic inflammation, Th2 cytokines and leukotriene

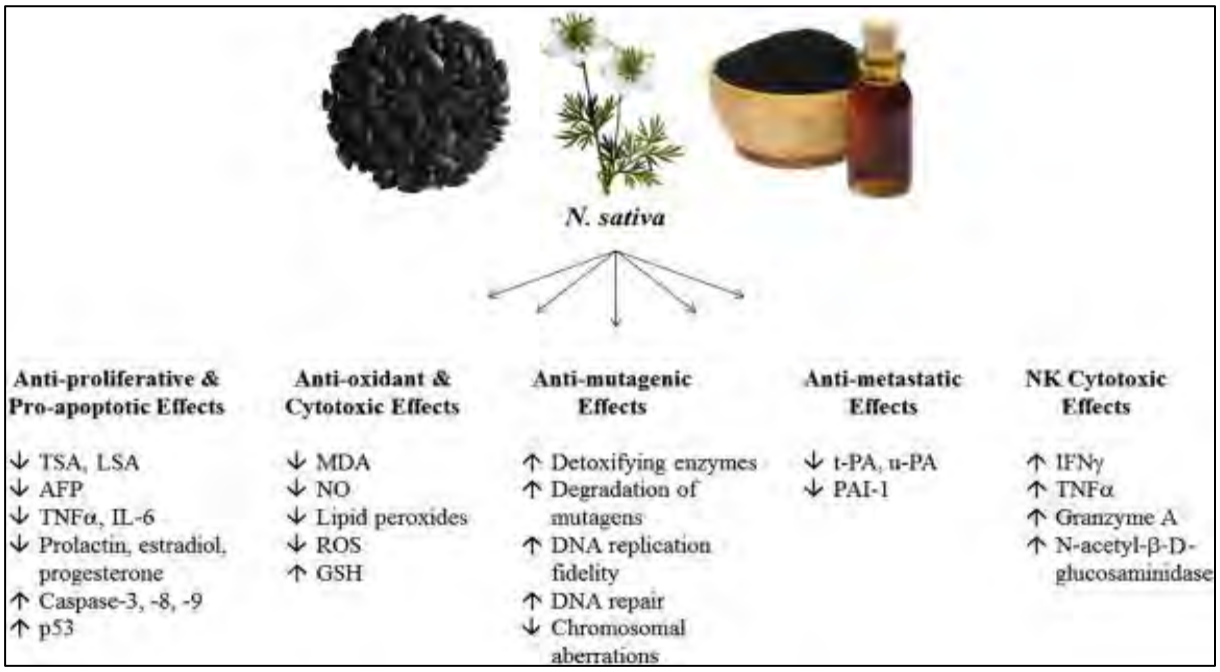

Figure 1. A brief summary of the known molecular and cellular mechanisms underlying the anti-proliferative, pro-apoptotic, anti-oxidant, cytotoxic, anti-mutagenic, anti-metastatic, and NK-mediated cytotoxic effects of *N. sativa*. (TSA: total sialic acid, LSA: lipid-bound sialic acid, AFP: α-fetoprotein, TNFα: tumor necrosis factor α, IL-6: interleukin-6, MDA: malondialdehyde, NO: nitric oxide, ROS, reactive oxygen species, GSH: glutathione, t-PA: tissue-type plasminogen activator, u-PA: urokinase-type plasminogen activator, PAI-1: plasminogen activator inhibitor type 1, IFNγ: interferon γ. [Hannan, M. A., et al. (2021)]

production, improve pulmonary function and asthma control scores, and show bronchodilator and anti-inflammatory effects in animal models and small human trials. Key randomized clinical evidence shows improved asthma control and normalization of blood eosinophilia after NS supplementation. *Nigella sativa* L. (black seed) has long been used in traditional medicine for respiratory disorders, and modern research provides scientific support for its antiasthmatic potential. The primary bioactive constituent, thymoquinone (TQ), exhibits strong anti-inflammatory, bronchodilatory and immunomodulatory effects, which contribute to improved airway function (Koshak et al., 2017; Boskabady et al., 2011). Experimental studies have shown that *N. sativa* extract significantly reduces airway hyperresponsiveness, inhibits leukotriene and histamine release, and suppresses inflammatory cell infiltration in animal models of asthma (Boskabady et al., 2007; Keyhanmanesh et al., 2010). Clinical evidence also supports these findings—administration of *N. sativa* oil or capsules improved pulmonary function parameters such as FEV1 and PEF, and reduced asthma symptoms in human subjects (Koshak et al., 2017). Moreover, *N. sativa* modulates Th2 immune responses, decreases eosinophil counts, and lowers serum IgE levels, suggesting a role in targeting the immunopathogenesis of asthma (Keyhanmanesh et al., 2010). These results indicate that *N. sativa* may serve as a promising adjunctive therapy for asthma management, although further large-scale, placebo-controlled clinical trials are needed to establish standardized doses and formulations for clinical use (Boskabady et al., 2011).

Neuroprotective property

Nigella exerts many neuroprotective roles for humans mainly due to its active bio-constituents like thymoquinone (TQ). Neural disorders which include Alzheimer's disease, Parkinson's disease, epilepsy, stroke, and cognitive impairment are major concerns. Thymoquinone reduces lipid peroxidation and stimulates the production of antioxidant enzymes such as SOD, GSH, and catalase, and activates the Nrf2-ARE pathway to promote cytoprotection (Farkhondeh et al., 2018). Reduced oxidative stress, inflammatory response, and apoptosis are triggered by TQ during specific studies in a 6-OHDA Parkinson's model. Anti-apoptotic function is controlled by the regulation of Bcl-Bax, caspase, and cytochrome c release (R. Sedaghat et al., 2014). Prevention of the response to dopamine in neural networks during Parkinson studies is also reported. The main factor associated with neurodegenerative diseases is encountered in memory-related regions of the brain. TQ has potential to alleviate oxidative stress, cut off the accumulation of Amyloid beta(Aβ) toxicity in Alzheimer models (Zlong et al., 2021).

Table 1. Pharmacological benefits of *Nigella sativa*

Pharmacological Activity	Description	Evidence/Studies	Key Compounds Responsible
Anti-inflammatory	Reduces inflammation, beneficial in conditions like rheumatoid arthritis	Clinical trials and systematic reviews demonstrate significant reduction in inflammatory markers	Thymoquinone, Nigellone
Antioxidant	Scavenges free radicals, protects against oxidative stress	Numerous studies show high antioxidant activity, especially due to phenolic compounds like thymoquinone	Thymoquinone, phenols
Anticancer	Exhibits anti-proliferative, pro-apoptotic effects against various cancer cell lines	Research indicates potential in breast, lung, cervical cancers; induces apoptosis in vitro and in vivo	Thymoquinone, alkaloids
Antidiabetic	Lowers blood glucose, improves insulin sensitivity	Clinical trials show hypoglycemic effects and improved lipid profiles in diabetic patients	Thymoquinone, flavonoids
Cardiovascular	Reduces risk factors like high blood pressure and lipid levels	Clinical studies demonstrate cardioprotective effects and lipid-lowering properties	Thymoquinone, fatty acids
Antimicrobia and Antifungal	Inhibits growth of bacteria and fungi	Studies report antimicrobial effects, useful in infections	Thymoquinone, nigellidine
Neuroprotective & Cognitive	Potential in managing neurological disorders, neuroprotection	Preliminary studies show neuroprotective effects, potential in Alzheimer's and depression	Thymoquinone
Hepatoprotective & Renal	Protects liver and kidney tissues against toxic damage	Experimental models demonstrate reductions in organ toxicity	Thymoquinone
Respiratory & Bronchodilator	Relief in asthma, bronchitis	Clinical evidence supports bronchodilatory effects	Thymoquinone
Immune Modulation	Enhances immune response, useful in infections and immune disorders	Studies show immune system boosting effects	Thymoquinone

Synaptic signals and their specific markers (PSD-95), protection and improvised (BDNF) brain-derived neurotrophic factor leads to improved neural signalling and cognitive response (E. Andreucci et al, 2021).

Gastroprotective property

Nigella sativa has been scientifically proven to protect the stomach lining and reduce ulcer formation in several animal studies. The seed extract protects against damage caused by drugs such as

indomethacin by lowering oxidative stress and increasing the stomach's natural protective factors. In a study published in 2020, *Nigella sativa* seed extract notably decreased ulcer formation in rats with drug-induced ulcers. It reduced malondialdehyde (a compound indicating oxidative stress) and total protein, while increasing protective substances such as thiols, hexose, and mucus in the gastric lining. Importantly, it did not change gastric acid secretion, meaning the protective effect was due to antioxidant and mucus-enhancing activities rather than reduced acidity. (Paseban M. et al.,2019). Another experiment in 2023 demonstrated that *Nigella sativa* oil protected rats from experimentally induced ulcers by up to 73%, a result comparable to the standard anti-ulcer medication ranitidine. The oil worked by improving the mucus barrier and maintaining cellular integrity in the stomach lining (Khan SZ. et al.,2023) These protective effects are largely attributed to thymoquinone — a potent antioxidant compound in *Nigella sativa*. Thymoquinone helps by scavenging free radicals, increasing the secretion of protective mucin, limiting leukotriene activity, and enhancing the formation of cytoprotective prostaglandins. These combined actions strengthen the stomach's defense mechanisms and promote healing (Jarmakiewicz-Czaja S. et al., 2023). In summary, *Nigella sativa* protects the stomach through its antioxidant, anti-inflammatory, and mucus-enhancing properties. These features make it a promising natural alternative or supplement to conventional ulcer therapy.

with their biological compound such as thymoquinone and beta-caryophyllene, which contribute to its antioxidant, anti-inflammatory, anticancer, antimicrobial, antidiabetic, gastroprotective, hepatoprotective, and immunomodulatory properties. Current Pharmacological benefits of *Nigella sativa* are extensively recognized for its potent antioxidant activity, protecting cells from oxidative stress and its associated conditions such as cardiovascular disease, cancer, and neurodegenerative disorders. It exhibits notable anti-inflammatory and immunomodulatory effects, aiding in the management and prevention of chronic inflammation, autoimmune diseases such as rheumatoid arthritis, and allergic reactions. Clinical and preclinical studies support its role in managing diabetes, improving lipid profiles, reducing blood pressure, and promoting overall metabolic health. Black seed has shown efficacy against microbial infections, including bacteria, viruses, and fungi, making it a candidate for antimicrobial therapies. Its use as a supportive agent in cancer therapy and prevention is promising, with activity reported against various cancers due to thymoquinone. There is a need for rigorous, large-scale clinical trials establishing standardized protocols for *Nigella sativa's* dosage, safety, and efficacy, especially in diverse populations and chronic conditions. Mechanistic research to clarify the molecular pathways responsible for its therapeutic effects must be expanded, enabling targeted applications for specific diseases. Novel formulation strategies to improve the bioavailability and systemic delivery of its active compounds (e.g., through nanoparticles, liposomes) are necessary to maximize efficacy.

Conclusions

Nigella sativa (commonly known as black seed) demonstrates wide-ranging pharmacological benefits, particularly due to its bioactive compounds

Studies should investigate drug interactions and the long-term safety profile of black seed, particularly with chronic use and in combination therapies. Standardization of cultivation, extraction, and quality control remains a challenge, requiring clear regulatory policies to ensure consistency and safety of black seed products in the market**.**

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