UNVEILING THE POWER OF NIGELLA SATIVA: A COMPREHENSIVE REVIEW OF ITS PHYTOCHEMICAL ANTIOXIDANT AND ANTICANCER POTENTIAL

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Abstract

N. sativa or black seeds, has been utilized in traditional medicine across Asia, the Middle East, and the Far East to address ailments such as headaches, abdominal pain, rheumatism, and other conditions. The seeds of this plant have been the subject of extensive phytochemical and pharmacological research. The most significant active components in the plant include alkaloids, flavonoids, and phenolic compounds, which are used in various medicinal and culinary traditions. Thymoquinone is a principal component of black seeds essential oil, has been identified as the key compound responsible for many therapeutic benefits. A broad spectrum of pharmacological actions, including anti-inflammatory, antioxidant, anti-cancer, and anti-proliferative activities, has been revealed for *N. sativa*. This study aimed to extensively analyze published research on *Nigella sativa*. By reviewing the existing literature, it synthesized and evaluated findings on the species botanical characteristics, chemical composition, pharmacological properties, and applications in medicine. The review also identified key trends, knowledge gaps, and areas for further research, highlighting *N. sativa's* significance in traditional medicine and its growing role in modern pharmacology. This comprehensive analysis serves as a valuable resource for researchers and practitioners interested in this important species.

Key words: *Nigella sativa*, Thymoquinone, Pharmacological**,** Antimicrobial, Antioxidant Anticancer.

Introduction

Nigella sativa L., also known as Black Cumin and in India *nigella sativa* called *Kalonji* in Marathi is an annual herb from the Ranunculaceae family with a variety of medicinal applications (Jidnyasa *et al*., 2024)**.** *N. sativa* became well-known for its extensive medicinal uses, attributed to its seeds rich in phytoconstituents. Ongoing scientific studies on *N. sativa* seeds were essential to further comprehend their numerous medicinal benefits. This research also established a composition-based foundation that validated both old and new accounts of its advantageous properties (Shafodino et al., 2022). Plant-based foods have been vital for human diets, providing essential nutrition, maintaining health, and enhancing immunity to prevent various diseases. Recently, the idea of "nutraceuticals" or "functional foods" gained popularity, emphasizing the connection

between a healthy diet and longer life expectancy (Hannan *et al*., 2021). One of the primary benefits of using Nigella was that its seeds were abundant in the omega-6 fatty acid linoleic acid and offered an additional source of dietary phytochemicals.

Figure 1. Seeds of *Nigella sativa* plant

Morphology of Nigella sativa:

Nigella sativa was described as an annual flowering plant that typically grew to a height of 20-90 cm. It had finely divided leaves, with segments that were narrowly linear or threadlike. The flowers of the plant were delicate and usually appeared in colors such as white, yellow, pink, and pale blue or pale purple, with 5-10 petals. The fruit of the plant was a large, inflated capsule composed of 3-7 fused follicles, each containing numerous seeds (Ahmad *et al*., 2013). A detailed and comprehensive morphological and anatomical study was conducted on seeds from all 15 species currently recognized within the genus *Nigella* that also includes the related genera *Komaroffia* and *Garidella*. This analysis also extended to a selection of six intraspecific taxa, providing a broad perspective on the seed morphology within this group (Jidnyasa *et al*., 2024).

***Nigella sativa* Phytochemistry:**

Review has shown that since ancient times, the medicinally significant component of the Nigella sativa (NS) plant was recognized as its oil (NS oil). The effectiveness of NS oil was primarily attributed to its quinone constituents found in both the fixed and essential oils of the plant. Thymoquinone (TQ) being a particularly important bioactive component, comprising 30–48% of the total compounds. Other functional components of NS oil included p-cymene, carvacrol, thymohydroquinone (THQ), dihydrothymoquinone (DHTQ), α-thujene, thymol, t-anethole, β-pinene, α-pinene, and γ-terpinene (Sahak *et al*., 2016).

Table 1. Phytochemicals, plant part source, extract solvent used and therapeutic activity of *Nigella sativa*

Chemical Constituent	Part of plant	Activity	Extract	Reference
Thymoquinone	Seeds	Anti-inflammatory, antifungal, anticancer	Methanol	(Sahak et al., 2016; Salehi *et al*., 2021; Heiss et al., 2011; Tiji *et al*., 2021)
Carvacrol	Seeds	Anti-inflammatory, antioxidant	Ethanol	(Tiji *et al*., 2021)
α-Pinene	Seeds	Anti-inflammatory	Ethanol	(Sahak *et al*., 2016)
P-Cymene	Seeds	Antioxidant, anti-inflammatory, anti-parasitic, antidiabetic,	Ethanol	(Heiss et al., 2011; Tiji *et al*., 2021)
Thymol	Seeds	Anti-inflammatory	Methanol	(Sahak *et al*., 2016)
4-terpinoel	Seeds	Anti-inflammatory, antioxidant	Ethanol	(Tiji *et al*., 2021)
Sesquiterpene longifolene	Seeds	Antibactrial, Anti-inflammatory	Ethanol	(Rahman *et al*., 2024; Alshwyeh *et al*., 2022)
Nigellidine	Seeds	Anti-inflammatory	Aqueous	(Thakur *et al*., 2021)
Nigellicine	Seeds	Anti-inflammatory	Aqueous	(Thakur *et al*., 2021)
Nigellicimine-N-Oxide	Seeds	Antifungal	Methanol	(Thakur et al., 2021)
Alpha-hederin	Seeds	Antibacterial, Anti-inflammatory	Aqueous	(Tiji *et al*., 2021)
Nigellicimine	Seeds	Antifungal	Methanol	(Tiji *et al*., 2021)
Thujene	Seeds/ Leaves	Antibacterial, Anti-inflammatory	Aqueous	(Sahak *et al*., 2016)
Sabinene	Seeds/ Leaves	Antibacterial, Anti-inflammatory	Aqueous	(Rahman *et al*., 2024; Alshwyeh *et al*., 2022).
Beta-sitosterol	Seeds/ Leaves	Antibacterial, Anti-inflammatory	Aqueous	(Rahman *et al*., 2024; Alshwyeh *et al*., 2022).
Phellandrene	Seeds/ Leaves	Antibacterial, Anti-inflammatory	Aqueous	(Rahman *et al*., 2024; Alshwyeh *et al*., 2022).
Carvone	Seeds/ Leaves	Antibacterial, Anti-inflammatory	Aqueous	(Khan *et al*., 2011)
Limonene	Seeds/ Leaves	Antibacterial, Anti-inflammatory	Aqueous	(Rahman *et al*., 2024; Alshwyeh *et al*., 2022).
B Pinene	Seeds/ Leaves	Antibacterial, Anti-inflammatory	Aqueous	(Sahak *et al*., 2016)
d -citronellol	Seeds/ Leaves	Antibacterial, Anti-inflammatory	Aqueous	(Rahman *et al*., 2024; Alshwyeh *et al*., 2022).
Saponin	Seeds/ Leaves	Antibacterial, Anti-inflammatory	Aqueous	(Salehi *et al*., 2021)

Antimicrobial activity:

Antimicrobial activity against pathogenic bacterial strains, including *E. coli, P. aeruginosa, S. aureus*, and *B. subtilis*, was evaluated using the disc diffusion method with various preparations of *N. sativa* seeds (Shafodino *et al*., 2022). *Nigella sativa* demonstrated significant activity against *Pseudomonas aeruginosa*, at a concentration of 100 mg/ml for both extracts (Usman *et al*., 2018). Antimicrobial assays showed strong antifungal activity against *Aspergillus niger, Penicillium*, and *Candida albicans*, as well as notable inhibition zones against broad spectra of bacteria, including *Salmonella typhi*, *Pseudomonas aeruginos*a, *Escherichia coli*, *Staphylococcus aureus*, *Enterobacte*r, and *Bacillus subtilis*. The minimum inhibitory concentration (MIC) of *Nigella sativa* essential oil was determined for *Staphylococcus aureus*, *Bacillus cereus*, *Escherichia coli*, and *Candida albicans*. The results demonstrated that the hexane extract had been effective against both types of bacteria (Tiji *et al*., 2021; (Kmail et al., 2023).

Antioxidant activity:

Oxidative stress play a vital role in the life of all organisms, and its long-term effects on the human body has implicated in the development of various chronic diseases, including cancer. Chronic oxidative stress led to the oxidation of biomolecules such as nucleic acids, lipids, and proteins, or trigger the activation of inflammatory signalling pathways. This, in turn, result in the activation of several transcription factors or the disregulation of gene and protein expression, which subsequently lead to tumor initiation or the survival of cancer cells. Additionally, it was well established that chronic intestinal diseases, such as inflammatory bowel disease (IBD), were associated with an increased risk of cancer, with a link between oxidative stress and the initiation and progression of IBD being reported.

The essential oil of *Nigella sativa* has been evaluated for its potential antioxidant activity using the diphenylpicrylhydrazyl (DPPH) assay (Dalli *et al*., 2021). The impact of *Nigella sativa* oil on the antioxidant enzyme levels and heart tissue in rats treated with cyclosporine A Pre-treatment with *Nigella sativa* oil lessened the heart damage caused by cyclosporine A, as evidenced by normalized cardiac histology, reduced lipid peroxidation, enhanced antioxidant enzyme activity, and decreased cellular protein oxidation, indicating that its protective effect may be due to its antioxidant properties (Abedi *et al*., 2017).

Anticancer activity:

Cancers result from abnormal cell growth due to genetic alterations. Therefore, any agent with anti-cancer properties either protect genetic material from alterations or destroy the genetically altered cancer cells. The active compounds, particularly thymoquinone (TQ), found in *Nigella sativa*, acted on cancer cells by targeting and killing them through various molecular pathways (Khan *et al*., 2011). A literature search identified that a lot of studies have lately been done out on the cancer-fighting properties of *N. sativa* and some of its active components, such as thymoquinone (Randhawa & Alghamdi, 2011). Though its anticancer action's molecular mechanisms are still unclear, certain research has proven that TQ boosts the body's defences, and promotes apoptosis, and regulates the AKT

pathway in addition to its antioxidant characteristics. Even though the cancer-fighting effects of *N. sativa* components have been recognized for thousands of years, substantial scientific study with this significant traditional medicine has been carried out in the past two to three decades (Khan *et al*., 2011).

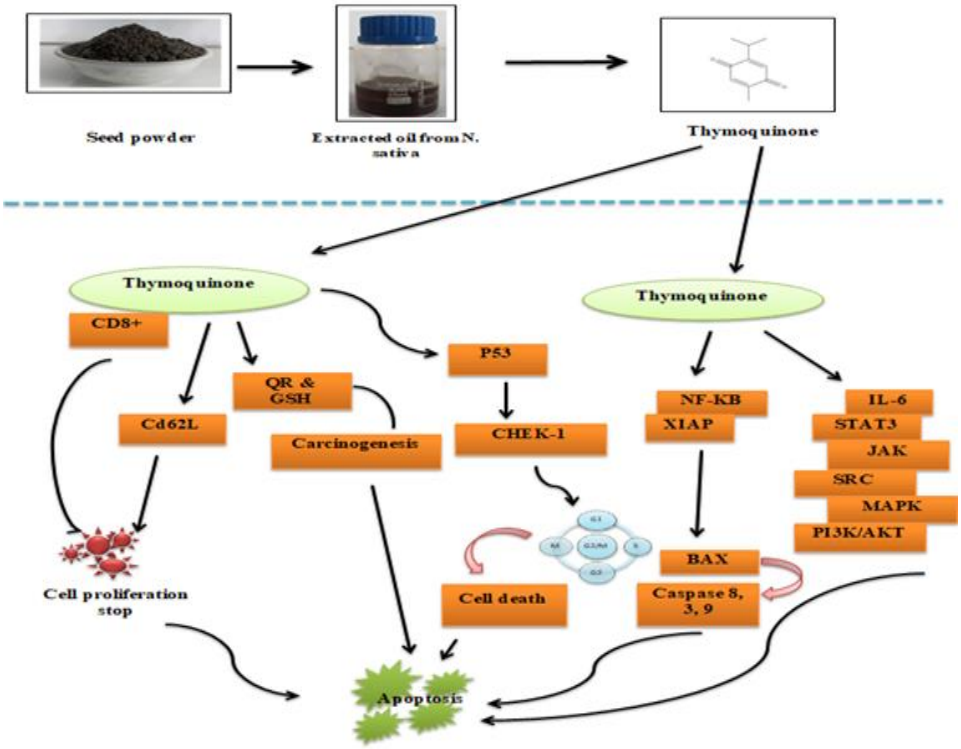

Figure 2. Molecular mechanism of Thymoquinone: CD8+T: immune system cells which kill, L-selectin, or cd62L Quinone reductase, or QR glutathione **(GSH),** tumor protein **p53,** NF-KB: Nuclear factor kappa light chain enhancer of activated B cells, **CHEK-1:** checkpoint kinase-1, The protein known as X-linked inhibitor of apoptosis **(XIAP) Bax: X** protein associated with **Bcl-2**, **Interleukin-6,** or **IL-6 STAT3**: transcription activator and signal transducer 3. SRC: oncogene, JAK: Janus kinase, Mitogen-activated protein kinase, and **MAPK PI3K/Akt** stands for protein kinase B and phosphoinositide 3-kinase

***Nigella sativa* as Gastroprotective agent:**

N. sativa oil enhances gastric mucin and glutathione levels while reducing the histamine content in the gastric mucosa, which can significantly contribute to treating gastric ulcers caused by indomethacin and ethanol. The pepsinogen proenzyme, released by stomach cells, interacts with hydrochloric acid in the gastric juice to convert into pepsin. TQ promotes the activation of pepsinogen into pepsin within the gastric juice, offering a protective effect against gastric ulcers. The antioxidant properties and free radical scavenging activities of TQ are crucial in its beneficial impact on gastrointestinal disorders (El-Dakhakhny et al., 2000; Magdy et al., 2012).

Conclusion:

Building on this evidence, black seed, black seed oil, and their active components continue to demonstrate remarkable therapeutic potential across a broad spectrum of conditions affecting both humans and animals. Their potent antimicrobial, antiparasitic, antiviral, antifungal, anti-inflammatory, and antidiabetic properties are particularly noteworthy, offering promising avenues for addressing various health challenges. Given its long-standing use in traditional medicine and its relative safety, black seed could serve as a cornerstone in developing new therapeutic agents. The pharmaceutical and nutraceutical industries are encouraged to explore the potential of black seed more thoroughly, recognizing its ability to serve as a natural alternative or complement to conventional treatments. The development of a new drug derived from *Nigella sativa* active ingredients represents a promising area of innovation. This endeavor would benefit greatly from the application of cutting-edge technologies and methodologies that could optimize the extraction, characterization, and synthesis of these bioactive compounds. Furthermore, robust experimental and clinical research is crucial to validate and expand our understanding of black seed's effects on the body.

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