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REVIEW ARTICLE ON A MIRACULOUS *BLACK CUMIN* SEED

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ABSTRACT: Black cumin (*Nigella sativa L.*, family: Ranunculaceae) is an annual herb known for its extensive medicinal properties, in addition to its commercial significance as a spice-producing plant. The seeds of black cumin are widely used in traditional herbal medicine across the globe for the treatment and prevention of various diseases. They contain a variety of medicinally important chemical compounds, including thymoquinone, thymohydroquinone, thymol, carvacrol, nigellidine and α-hederin. Black cumin exhibits numerous therapeutic effects, such as diuretic, antiurolithic, anti-inflammatory, antioxidant, anticancer, anthelmintic, antidiabetic, gastrointestinal disease relief, asthma management, antihistamine, antihypertensive, hypoglycemic, antifungal, hair health, fertility enhancement, antibacterial, and bronchitis treatment.

INTRODUCTION: *Nigella sativa L.* (Family: Ranunculaceae), also known as Black Cumin, is an annual herb recognized for its wide range of medicinal properties and its significant commercial importance as a spice [1]. The *Nigella* genus includes approximately 14 species, including *N. arvensis, N. ciliaris, N. damascena, N. hispanica, N. integrifolia, N. nigellastrum, N. orientalis* and *N. sativa*. While other species have shown therapeutic potential, *N. sativa* is the most extensively studied and utilized. Black cumin is predominantly cultivated in Southern Europe, the Middle Eastern Mediterranean, Saudi Arabia, Pakistan, Northern India, Turkey, Syria, and Iran. Since the early Arabian and Indian civilizations, *N. sativa* seeds have been used for both culinary and medicinal purposes.

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This plant grows to a height of 20-90 cm and is characterized by long peduncles with solitary flowers **Fig. 1A** that develop into an inflated fruit capsule containing multiple black seeds **Fig. 1B**. Despite their pungent and bitter aroma, *Nigella seeds* are widely used as a spice in Middle Eastern and Indian cuisines, where they flavor vegetables, bread, curries, pickles, and pulses. Additionally, these seeds are a key ingredient in the PanchPhoron spice mixture, essential to Bengali cuisine, and are also used independently. Topical application of black cumin seed oil has been associated with treating dermatitis, and various crude or purified extracts have demonstrated antihistamine, antihypertensive, hypoglycemic, antifungal, anti-inflammatory, and anti-neoplastic activities.

Collectively, these findings highlight the significant potential of black cumin seeds in modern medicine [2]. The seeds of *N. sativa* have long been used in traditional medicine throughout the Middle East and various Asian countries, including Unani, Ayurveda, Chinese, and Arabic Medicine. They are employed to promote overall health and treat a

range of conditions such as fever, the common cold, headaches, asthma, rheumatic diseases, microbial infections, intestinal worms, and even cancer. The Islamic Prophet Mohammad praised the therapeutic properties of black seeds, asserting that they could cure all diseases except death. For over 2000 years, *N. sativa* seeds have been a staple in Middle Eastern folk medicine for addressing numerous ailments [3-6]. They contain a range of bioactive compounds, including thymoquinone, nigellidine, nigellimine, dithymoquinone, thymohydroquinone, and thymol. Among these, thymoquinone, present in the essential oil, is the primary active component driving its pharmacological effects. With a low toxicity profile, the plant is utilized across the food, pharmaceutical, and cosmetic industries [7].

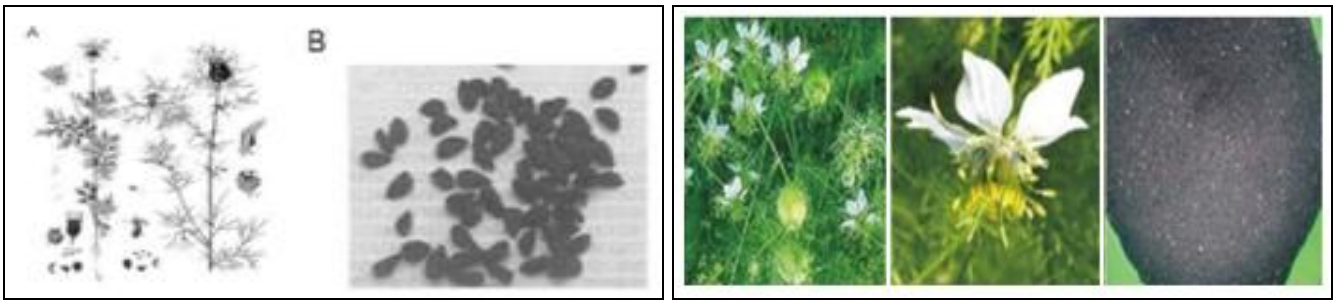


FIG. 1: (A) MORPHOLOGICAL FEATURES OF *N. SATIVA PLANT*, AND (B) BLACK CUMIN SEEDS CONTAINING OIL HAVING THYMOQUINONE (TQ) AS THE ACTIVE PRINCIPLE

Pharmacognostical Characteristics:

Morphology of *Nigella sativa*: *N. sativa* **Fig. 2** is an annual flowering plant grows between 20 and 90 cm in height. It features narrow, threadlike leaf segments and finely divided foliage. The plant produces flowers with 5-10 petals, which can be white, yellow, pink, pale blue or pale purple. The fruit develops into a large, inflated capsule with 3-7 fused follicles, each filled with numerous seeds [8-9].

Characteristic of Seed Powder: Macroscopically, seeds are small, dicotyledonous, trigonus, angular, and regulose-tubercular, measuring 2-3.5 mm in length and 1-2 mm in width. They are black externally and white internally, with a slightly aromatic odor and a bitter taste. Microscopically, a transverse section of the seed reveals a single-layered epidermis composed of elliptical, thick-walled cells, covered externally by a papillose cuticle and filled with dark brown contents. The epidermis is followed by 2-4 layers of thick-walled, tangentially elongated parenchymatous cells, which provide structural support. This is succeeded by a reddish-brown pigmented layer consisting of thick-walled, rectangular, elongated cells, which contributes to the seed's distinctive color. Inner to this pigment layer is another layer of thick-walled, rectangular, elongated, or nearly columnar cells, providing additional reinforcement. The endosperm is composed of thin-walled, rectangular or polygonal cells that are mostly filled with oil globules, which serve as a nutrient reserve for the developing embryo. In powder form, the seed exhibits a brownish-black color, with microscopic analysis revealing parenchymatous cells and abundant oil globules. The presence of these oil globules, along with the distinctive cell structures, can aid in the identification and authentication of the seed material. Additionally, the seed's characteristic odor and bitter taste are important sensory markers, further contributing to its identification in both raw and processed forms. These features, combined with its microscopic and macroscopic characteristics, make the seed easily distinguishable from similar plant materials [10-11].

Ayurvedic View:

Drug Name: Kalonji Seeds

Latin Name: *Nigella sativa. Linn*

Family: Ranunculaceae

Asa: Katu, Tikta

Virya: Ushna

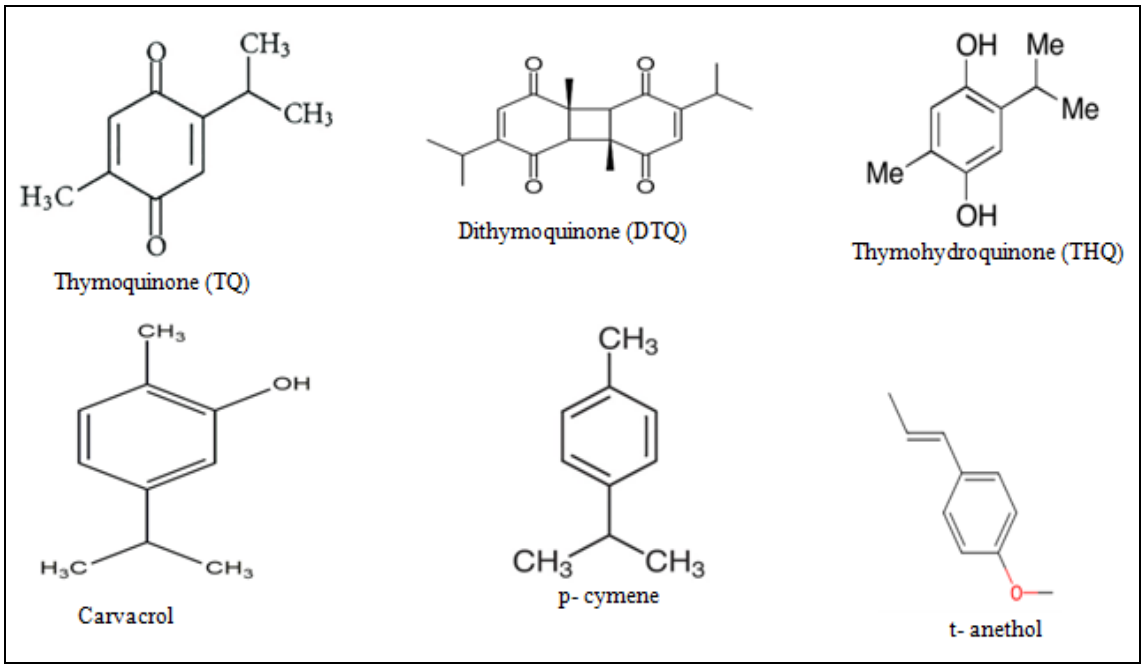
Vipaka: Katu

Guna: Laghu, Ruksha, Tikshna

Synonym(s): *Nigella indica Roxb. ex Flem.*, *Nigella truncata* Viv.5 [12].

Chemical Constituents: *N. sativa*, commonly known as black cumin, contains major chemical components such as fats, proteins, carbohydrates, crude fiber, and ash in the proportions of 28.5%, 26.7%, 24.9%, 8.4%, and 4.8%, respectively. The plant also has various minor components including vitamins, copper (Cu), phosphorus (P), zinc (Zn), and iron (Fe). Notably, several bioactive compounds are present in black cumin, with the most significant being thymoquinone (TQ), dithymoquinone (nigellone), thymohydroquinone, carvacrol, p-cymene, sesquiterpene, thymol, 4-terpineol, longifolene, t-anethole, and α-pinene [13, 14]. TQ is the most abundant active compound, attributing to the pharmacological properties of black cumin. Additionally, limonene, carvone, and trace amounts of citronellol are found. Isoquinoline alkaloids like nigellicimine and nigellicimine-N-oxide, pyrazole alkaloids such as nigellidine and nigellicine and α-hederin have also been identified [15, 16]. Fatty oils from black cumin seeds are rich in both saturated and unsaturated fatty acids. Unsaturated fatty acids include oleicacid, linoleic acid, dihomolinoleic acid, and eicosadienoic acid, whereas saturated fatty acids comprise palmitic acid and stearic acid. Sterols, primarily α-sitosterol and stigmasterol, are other constituents of *N. Sativa* [17, 18]. Bitter cumin (Shahi jeera) seeds contain calcium, Vitamin A, potassium, sodium, iron, magnesium, and phosphorus, with low levels of essential oils mainly composed of carvone, limonene, and p-cymene, yielding a brownish to yellowish green oleoresin. Due to the limited scientific evidence on bitter cumin's health benefits, this review focuses on *N. sativa* (black seeds or black cumin). There is a resemblance between the seeds of *N. sativa* and *N. damascena*, which are also used in ethnotherapy. However, *N. damascena* differs in sesquiterpenoid content and lacks thymoquinone [19, 20].

Sesquiterpenoids contain anthranilic acid derivatives and 15-carbon compounds, with the most abundant being germacrene A and β-elemene, [21] while anthranilic acid derivatives like damascenine and damascinine are considered toxic. In contrast, *N. sativa seeds* have minimal reported toxicity [22]. Therapeutic evaluations of *N. sativa* are primarily conducted on seed extracts. For example, the anticancer effectiveness has been studied using ethanolic extracts of *N. sativa* seeds [23]. Microwave extraction is an environmentally friendly method that reduces extraction time and increases the yield's quality and quantity [24]. Chemically, *N. sativa* seeds contain proteins, amino acids, carbohydrates, alkaloids, volatile oils and saponins. The four main active compounds in *N. sativa* oil t-anethole, thymoquinone, carvacrol, and 4-terpineol exhibit 2,2′-diphenyl-p-picrylhydrazyl (DPPH) antiradical scavenging activities [25].



Taxonomical Classification:
Kingdom: Plantae

Subkingdom: Tracheobionta

Phylum: Magnoliophyta

Class: Magnoliopsida

Order: Ranunculales

Family: Ranunculaceae

Genus: *Nigel*

Species: *N. sativa* [26]

Common Names:
English: Fennel flower, Nutmeg flower, Black sesam, Roman coriander, Blackseed

Assamese: Kaljeera or kolajeera

Bengali: Kalo jeeray

Kannada: Krishna Jeerige

Tamil: Karumjeerakam

Hindi/Urdu: Kalaunji/mangrail

Russian: Chernushka

Hebrew: Ketzakh

Turkish: Corek out

Arabic: Habbat al-barakah

Persian: Siyahdane

Indonesian: Jintanhitam [27]

Medicinal Uses: In various traditional medicinal practices such as Arabian medicine, Ayurveda, and traditional Chinese medicine, *Nigella sativa seeds*, known as "Habbat-ul-barakah" or "seeds of blessing," are used to treat respiratory issues like asthma, gastrointestinal problems, menstrual disorders, and skin infections. The oil from the seeds is recognized for its anti-inflammatory, antibacterial, antioxidant, and immunomodulatory properties.

Culinary and Other Uses: With their pungent and bitter taste, *Nigella sativa seeds* are used to flavor bread, pickles, curries, and beverages like tea and coffee. They are also sprinkled on salads or mixed with honey. Additionally, the seeds serve as an insect repellent and their essential oil is used in various beauty products.

Use of *Nigella sativa* in Modern Medicine: Recent scientific research, particularly in regions like the Middle East and South Asia, has focused on the health benefits of *Nigella sativa*, particularly its bioactive compounds such as thymoquinone. Studies highlight its potential in antioxidant, anti-inflammatory, anti-cancer, hypoglycemic, anti-microbial, anti-nephrotoxic, anti-hepatotoxic, and immunostimulating applications, as well as its protective effects against diabetes, kidney, skin, cardiac, liver, and brain disorders, dyslipidemia [28].

Pharmacological Activities: *Nigella sativa* has been widely researched for its biological effects and has demonstrated a broad range of activities, including diuretic, antihypertensive, bronch-odilator, gastroprotective, hepatoprotective, antidiabetic, anticancer, immunomodulatory, antimicrobial, analgesic, anti-inflammatory, spasmolytic, renal protective, and antioxidant properties.

Anti diabetic Activity: This study investigated the impact of crude ethanol extract from NS seeds on insulin secretion in INS832/13 and βTC-tet pancreatic β-cell lines, as well as on glucose uptake in C2C12 skeletal muscle cells and 3T3-L1 adipocytes. After an 18-hour treatment, NS extract enhanced glucose-stimulated insulin secretion by over 35%, without altering glucose sensitivity, and promoted β-cell proliferation.

The treatment also increased basal glucose uptake by 55% in muscle cells, which is roughly twice the effect of 100 nM insulin and by approximately 400% in adipocytes, equating to the effect of 100 nM insulin; the effect in adipocytes was fully additive with insulin. Furthermore, NS treatment of differentiating pre-adipocytes boosted triglyceride accumulation similarly to treatment with 10 μM rosiglitazone. These findings suggest that the well-established antihyperglycemic effects of NS seed extract *in-vivo* can be attributed to its combination of insulinotropic and insulin-mimetic properties [29].

Antioxident Activity: In this study, the antioxidant activity of methanolic extracts from black cumin *(Nigella sativa L.)* seeds collected and evaluated using three different methods: the β-carotene-linoleic acid system, 1,1-diphenyl-2-picrylhydrazyl (DPPH) radical scavenging activity, and reducing power assays. Among the six black cumin samples from different origins, the seeds from Konya exhibited the most potent radical scavenging activity across all assays, with 94.59% inhibition at 1 mg/mL in the β-carotene bleaching method and 44.44% inhibition at 0.5 mg/mL in the DPPH radical scavenging method. A positive correlation was observed between the total phenolic content of the black cumin extracts and their antioxidant activities. The antioxidant activity values were comparable to or exceeded those of standard BHA and BHT controls. These promising results suggest the potential of black cumin seeds as health-promoting ingredients, including dietary supplements and nutraceuticals [30].

Anthelmintic Activity: Increasing resistance to traditional anthelmintic drugs highlights the importance of discovering new anthelmintic compounds from natural plants. *Nigella sativa* (*N. sativa*) is widely recognized for its medicinal properties, including its anthelmintic activity. *Caenorhabditis elegans* (*C. elegans*), a commonly used and cost-effective model organism, is valuable for evaluating the anthelmintic potential of compounds derived from natural sources.

In our study, we aimed to assess the nematocidal activity of *N. sativa* on *C. elegans* during both its larval and adult stages using toxicity assays. Various concentrations of *N. sativa* oil (900, 450, and 270 mg/mL) were tested, and the number of surviving nematodes was counted under a stereomicroscope to evaluate toxicity. The study demonstrated that *N. sativa* essential oil significantly reduced the survival of *C. elegans* at both larval and adult stages, with the highest concentration of 900 mg/mL showing the most pronounced effect. Larval-stage worms were more susceptible to the oil than adults. We recommend further studies to explore other effects of *N. sativa* on *C. elegans* after isolating and removing the toxic compound(s) from the extract. Identifying the specific compounds responsible for the anthelmintic activity and understanding their mechanisms of toxicity could lead to the development of new therapeutic agents [31].

Anticonvulsent Activity: Curcumin, valproate, and *Nigella sativa* oil (NSO) have been studied for their antioxidant effectiveness in chronic epilepsy, focusing on their impact on levels of reduced glutathione, nitric oxide, and malondialdehyde, as well as the activities of catalase (CAT), Na+, K+-ATPase, and acetylcholinesterase enzymes [32]. Treatment with NSO, curcumin and valproate was found to alleviate pilocarpine-induced physiological changes and normalize Na+, K+-ATPase activity. These findings suggest that curcumin and NSO possess both anticonvulsant and antioxidant properties, which help to reduce oxidative stress, excitability, and seizure onset in epileptic animals, while also counteracting the harmful effects of antiepileptic drugs [33].

N. sativa seed aqueous extracts, volatile oils, and major components such as α-pinene, thymoquinone (TQ), and p-cymene have shown significant protection against maximal electroshock (MES) and PTZ-induced convulsions in mice. The antiepileptic effects of the volatile oils are likely due to p-cymene and TQ, the primary active compounds. Additionally, *N. sativa* seed extracts and their active components have been observed to cause varying degrees of minimal neurological deficit (MND) in the chimney test. The MND caused by the volatile oils is probably due to their content of TQ, p-cymene, and α-pinene, which constitute 63%, 23%, and less than 14% of the active compounds, respectively. It is likely that the enhancement of the GABAergic response is mediated by GABA receptors, while TQ increases the efficacy of valproate in both MES and PTZ animal models [34]. Noor and colleagues further demonstrated the anticonvulsant effects of curcumin and *N. sativa* oil in a pilocarpine-induced epilepsy model, highlighting their potential in mitigating this condition in comparison to valproate [35].

Antioxytocic Activity: Preliminary studies have suggested that black cumin may have antioxytocic properties. *N. sativa* seeds were found to inhibit uterine smooth muscle contractions induced by oxytocin, indicating the potential of NSO as an anti-oxytocic agent [36].

Antiviral Activity: *Nigella sativa* seeds contain active constituents, Thymoquinone (TQ) stands out for its broad antimicrobial properties, effective against Gram-negative and Gram-positive bacteria, viruses, parasites, schistosomes, and fungi. The effectiveness of *N. sativa* seeds and TQ varies depending on the target microorganism. This review focuses on the antiviral activities of *N. sativa*, highlighting its potential against viruses such as murine cytomegalovirus, avian influenza (H9N2), *Schistosoma mansoni*, PPR virus, Broad bean mosaic virus, HIV, Hepatitis C virus, Zucchini yellow mosaic virus, and Papaya ring spot virus [37].

Contraceptive Activity: The hexane extract of the seeds effectively prevented pregnancy in Sprague-Dawley rats when administered orally at a daily dose of 2 g/kg during days 1-10 post-coitum. This active extract showed mild uterotrophic activity, similar to ethinylestradiol, but lacked any estrogenic effects in the immature rat bioassay [38]. Agarwal et al. [39] also noted that the ethanolic seed extract exhibited antifertility effects in male rats, likely due to its inherent estrogenic activity.

Pulmonary Activity: Nigellone has been found to effectively inhibit histamine release from mast cells, suggesting its potential use in treating asthma [40]. Padmalatha *et al.* [41] studied the antianaphylactic effects of a polyherbal formulation containing *Nigella sativa* (NS) on mesenteric mast cells, attributing its activity to membrane stabilization, suppression of antibody production, and inhibition of antigen-induced histamine release. Gilani *et al.* [42] proposed that the bronchodilatory effect of NS seeds might be mediated through calcium channel blockade.

Keyhanmanesh *et al.* [43] investigated the prophylactic effects of thymoquinone (TQ) on tracheal responsiveness and white blood cell (WBC) count in the lung lavage of sensitized guinea pigs, with results indicating a preventive effect on tracheal responsiveness and inflammatory cells in the lung lavage. Suddek [44] suggested that TQ-induced relaxation of the precontracted pulmonary artery likely occurs through the activation of ATP-sensitive potassium channels and possibly by non-competitive blockade of serotonin, alpha-1, and endothelin receptors.

Immunomodullary Activity: A group of medicinal plants, including black seed, were evaluated for their immunomodulatory effects in BALB/c mice. Treatment with five doses of methanolic extract of black seed via intraperitoneal injection significantly increased the total white blood cell count to 1.2×10^4 cells/mm³. Additionally, bone marrow cellularity showed a significant increase ($P<0.01$) following administration of the black seed extract. The spleen weight of the black seed-treated groups also increased significantly ($P<0.01$). In two groups of mice immunosuppressed with cyclophosphamide, those pretreated with the black seed extract exhibited a significant ($P<0.01$) restoration of resistance against lethal infection by the predominantly granulocyte-dependent *Candida albicans*. These findings confirm the immunomodulatory activity of black seed, suggesting potential therapeutic applications in the prophylactic treatment of opportunistic infections and as supportive care in oncogenic cases [45].

Antibacterial Activity: Numerous studies have reported the antibacterial activity of *Nigella sativa*. Thymoquinone, the primary chemical constituent isolated from this plant, has been found to exhibit antibacterial effects against various bacteria, particularly Gram-positive cocci, including *Staphylococcus aureus* and *Staphylococcus* [46, 47].

Antifungal Activity: Methanolic extracts of *Nigella sativa* have demonstrated the strongest antifungal activity, followed by chloroform extracts, particularly against various strains of *Candida albicans*. In contrast, aqueous extracts showed no antifungal activity. When *Candida albicans* was introduced intravenously, colonies of the organism formed in the liver, spleen, and kidneys. Treatment with *N. sativa* extract 24 hours after inoculation significantly inhibited the growth of the organism in all studied organs. Khan et al. (2003) reported that the aqueous extract of *N. sativa* seeds exhibits an inhibitory effect against candidiasis in mice, with a 5-fold reduction of *Candida* in the kidneys, an 8-fold reduction in the liver, and an 11-fold reduction in the spleen in post-treated animals. These results were further confirmed by histopathological examination of the respective organs [48].

Additionally, the antidermatophyte activity of the ether extract of *N. sativa* and thymoquinone (TQ) was tested against eight species of dermatophytes, with the Ns-D1 and Ns-D2 defensins isolated from *N. sativa* seeds displaying strong and diverse antifungal activity against several phytopathogenic fungi [49].

Anticancer Activity: Several studies have explored the anticancer effects of *Nigella sativa*. The extract was tested on cancer cells derived from mice, revealing that thymoquinone, a key compound in *N. sativa*, possesses chemopreventive potential. Khalife *et al.* found that thymoquinone induces apoptosis in human colon cancer cells through a p53-independent pathway involving p21 and arrests the cell cycle in the S phase. Thymoquinone has shown anticancer activity against various cancer cell lines, including MCF-7/Topo breast carcinoma cells, and has been observed to downregulate NF-κB and MMP-9 in Panc-1 cells, as well as bcl-2 in gastric cancer cells. An *in-vivo* study on 63 adult male rats demonstrated that *Nigella sativa* effectively prevents formaldehyde-induced apoptosis and epithelial damage [50, 51].

Neuro-pharmacologycal Activities: The aqueous and methanol extracts of defatted *Nigella sativa* L. seeds have been shown to exhibit significant neuropharmacological activities, particularly in terms of central nervous system and analgesic effects. The methanol extract, in particular, demonstrates notable depressant action [52]. An anxiolytic drug typically functions by increasing serotonin (5-HT) levels and decreasing the levels of its metabolite, 5-hydroxyindoleacetic acid (5-HIAA), in the brain. Long-term administration of *Nigella sativa* has been found to elevate 5-HT levels, which in turn enhances learning and memory in rats. Moreover, repeated administration of *N. sativa* reduces 5-HT turnover, leading to anxiolytic effects [53].

Anti-Schistosomiasis Activity: The study by Mahmoud *et al.* investigated the protective effects of *Nigella sativa* oil (NSO) against liver damage induced by *Schistosoma mansoni* (*S. mansoni*) infection in mice. When NSO was administered alone, it significantly reduced the number of *S. mansoni* worms in the liver and decreased the total number of ova deposited in both the liver and intestines. Notably, when NSO was combined with praziquantel (PZQ), there was a further reduction in the number of dead ova beyond that achieved with PZQ alone. *S. mansoni* infection in mice led to a significant increase in serum levels of ALT and GGT, with a slight increase in AP levels, and a reduction in serum albumin. Administration of NSO partially corrected these changes, improving ALT, GGT, AP activity, and albumin content in serum. These findings suggest that NSO may have a protective role against the alterations caused by *S. mansoni* infection [54].

In-vitro testing of *Nigella sativa* seeds demonstrated strong biocidal effects against all stages of the parasite, including miracidia, cercariae, and adult worms, and inhibited egg-laying in adult female worms. Additionally, *N. sativa* seeds induced oxidative stress in adult worms, as evidenced by decreased activities of antioxidant enzymes such as superoxide dismutase (SOD), glutathione peroxidase, glutathione reductase, and key enzymes in glucose metabolism like hexokinase and glucose-6-phosphate dehydrogenase. This disruption of enzyme activity in adult worms may render the parasite more susceptible to host defenses, contributing to the anti-schistosomal effects of *Nigella sativa* seeds [55].

Testicular-protective Activity: The protective effects of thymoquinone (TQ) against methotrexate-induced testicular toxicity were studied in male C57BL/6 mice (6 weeks old, 20±2 g). Treatment with TQ reduced total antioxidant capacity (TAC) and prevented the increase in myeloperoxidase activity. Light microscopy revealed that methotrexate caused interstitial space dilation, edema, severe disruption of the seminiferous epithelium, and reduced diameter of the seminiferous tubules. However, TQ administration significantly reversed these histological changes. It is suggested that TQ may help mitigate the harmful effects of methotrexate on testicular tissue in patients undergoing treatment with this drug [56].

Gastro-Protective Activity: The gastro-protective potential of *Nigella sativa* (*N. sativa*) aqueous suspension was evaluated in rats with experimentally induced gastric ulcers and basal

gastric secretion to support its traditional use by herbal and Unani medicine practitioners. Acute gastric ulcers were induced using various harmful chemicals (80% ethanol, 0.2 mol/L NaOH, 25% NaCl, and indomethacin) in Wistar albino rats. Anti-secretory effects were also studied in a separate group of rats. The gastric wall mucus content and non-protein sulfhydryl concentration were measured, and the gastric tissue was examined histopathologically. The aqueous suspension of *N. sativa* seeds significantly prevented the formation of gastric ulcers caused by necrotizing agents. It also notably reduced ulcer severity and basal gastric acid secretion in pylorus-ligated Shay rats. Additionally, the suspension significantly restored the depleted gastric wall mucus content and non-protein sulfhydryl levels induced by ethanol. The anti-ulcer effect was further confirmed through histopathological analysis. The protective effects of *N. sativa* are likely mediated by prostaglandins and/or its antioxidant and anti-secretory properties [57].

Antihyperlipidemic and Antihypercholesteremic Activity: Hypercholesterolemia is marked by elevated levels of TG, TC, LDL, HDL, and very-low-density lipoprotein (VLDL). An increase in HDL levels and a decrease in LDL levels can significantly reduce the risk of cardiovascular disease. *Nigella sativa*, along with its active component thymoquinone, shows an antihypercholesterolemic effect by reducing the activity of HMG-CoA reductase, the rate-limiting enzyme in cholesterol synthesis, thereby providing protection against dyslipidemia. Additionally, *Nigella sativa* has been reported to exhibit antihyperlipidemic properties by activating the paraoxonase enzyme (PON1), which acts as an antioxidant. PON1 protects LDL from oxidation and neutralizes radicals like hydrogen peroxide, leading to increased arylesterase activity, the protein marker for PON1 [58].

Nephrolithiasis Activity: Several studies have investigated the effects of *N. sativa* and its active component thymoquinone on renal stones. Hadjzadeh *et al.* (2007) found that oral administration of an ethanolic extract of *N. sativa* for 30 days resulted in a 57% reduction in calcium oxalate (CaOx) deposits in the treatment group, although this effect was not statistically significant in the prevention group. The extract did not impact kidney weight due to the short duration of the treatment. Furthermore, urinary oxalate levels significantly decreased in the prevention group compared to the ethylene glycol group, with no notable difference between the treatment and control groups. Subsequent studies by Hadjzadeh *et al.* (2011) indicated that the preventive efficacy of N-butanol and its remnant fractions was superior to that of a 50% ethanolic extract. Additionally, Hadjzadeh *et al.* (2008) demonstrated that intraperitoneal injection of thymoquinone for 28 days had both preventive and disruptive effects on CaOx deposits. In another study, Khajavi Rad *et al.* (2008) reported that while the ethyl acetate phase remnant fraction exhibited significant preventive effects against renal calculi, the ethyl acetate fraction alone did not show any effect [59].

CONCLUSION: *Nigella sativa*, commonly known as black seed or black cumin, is a flowering plant native to South Asia and the Middle East, widely recognized for its extensive therapeutic properties. The plant is an annual herb that reaches a height of 20–30 cm, featuring finely divided linear leaves, pale blue or white flowers, and a large capsule fruit containing numerous small black seeds. Pharmacognostically, *Nigella sativa* is characterized by its rough-textured seeds, which have been a subject of modern scientific research due to their rich chemical composition, including thymoquinone, alkaloids, and essential oils. *Nigella sativa* belongs to the Ranunculaceae family and has a range of common names, including black caraway and kalonji.

Its medicinal uses are vast, encompassing anti-diabetic, antioxidant, anthelmintic, anticonvulsant, antioxytocic, antiviral, contraceptive, pulmonary, immunomodulatory, antibacterial, antifungal, anticancer, neuropharmacological, anti-schistosomiasis, testicular protective, gastro-protective, anti-hyperlipidemic, anti-hyper-cholesteremic, and nephrolithiasis activities. The seeds have shown significant potential in treating conditions like diabetes, oxidative stress, infections, convulsions, and cancer, among others, highlighting their broad-spectrum pharmacological efficacy. *Nigella sativa* continues to be a subject of intense study, with its wide range of bioactivities

making it a valuable plant in both traditional and modern medicine.

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CONFLICT OF INTEREST: Nil

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