



A REVIEW ON ANTIBACTERIAL, ANTIFUNGAL AND ANTIOXIDANT ACTIVITY OF *NIGELLA SATIVA*

**Haridas D. Mahale^{*1}, Dr. Ravi S. Wanare², Dr Ravikiran B. Wakde³, Dr. Arun M. Mahale⁴ and
Dr. Swati P. Deshmukh⁵**

¹Student of Master of Pharmacy, Sudhakar Rao Naik Institute of Pharmacy, Pusad.

^{2,3,4}Professor Department of Pharmaceutics, Sudhakar Rao Naik Institute of Pharmacy, Pusad Professor Department of Pharmacology, Shradhha Institute of Pharmacy, Washim.

***Corresponding Author: Haridas D. Mahale**

Student of Master of Pharmacy, Sudhakar Rao Naik Institute of Pharmacy, Pusad.

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ABSTRACT

Nigella sativa (family Ranunculaceae) is a widely used medicinal plant throughout the world. It is very popular in various traditional systems of medicine like Unani and Tibb, ayurveda, and Siddha. Seeds and oil have a long history of folklore usage in various systems of medicine and food. The seeds of *n. Sativa* has been widely used in the treatment of different diseases and ailments. In Islamic literature, it is considered as one of the most significant forms of healing medicine. It has been recommended for use regularly in Tibb-e-nabi (prophetic medicine). It has been widely used as an antihypertensive, liver tonic, diuretic, digestive, anti-diarrheal, appetite stimulant, analgesic, anti-bacterial, and in skin disorders. Extensive studies on *n. Sativa* has been carried out by various researchers and a wide spectrum of its pharmacological actions have been explored which may include antidiabetic, anticancer, immunomodulator, analgesic, antimicrobial, anti-inflammatory, spasmolytic, bronchodilator, hepato-protective, renal protective, gastro-protective, antioxidant properties, etc. Due to its miraculous power of healing, *n. Sativa* has got a place among the top-ranked evidence-based herbal medicines. This also revealed that most of the therapeutic properties of this plant are due to the presence of thymoquinone which is a major bioactive component of the essential oil. The present review is an effort to provide a detailed survey of the literature on scientific research on pharmacognostic characteristics, chemical composition, and pharmacological activities of the seeds of this plant.

KEYWORDS: *Nigella sativa*, antibacterial antifungal, antioxidant.

INTRODUCTION

Nigella sativa, which belongs to the family Ranunculaceae, is one of the herbal medicines that has been extensively investigated and gained worldwide recognition. *Ns* is a native dicotyledonous plant to southern Europe, north Africa, and as a minor, and is widely cultivated in Pakistan and India, thus, becoming a household traditional medicinal plant in the region. Over the years, immigration helped plant cultivation to spread extensively throughout Eastern Europe and North America. It is also known as the black seed because when the seeds are exposed to air, they turned black. Among the Muslim community, this plant is referred to as habbatus sauda, Alabama alsawda, and alkamoun alaswad about the color of its seeds. In some other parts of the world, it is also known as shun, khodhira, black cumin, or black caraway.^[7] *Nigella sativa* is a herbaceous plant found in the middle east, Europe, and Western and Middle Asia.^[2] Also known as black cumin, nigella, or by its scientific name *nigella sativa*, kalonji belongs to

the buttercup family of flowering plants. It grows up to 12 inches (30 cm) tall and produces a fruit with seeds that are used as a flavorful spice in many cuisines. Black seed (*Nigella sativa*) is a flowering plant native to Asia and the Mediterranean. Its seed has been used to make medicine for thousands of years. Black seed might have effects on the body that help boost the immune system, fight cancer, prevent pregnancy, reduce swelling, and lessen allergic reactions by acting as an antihistamine. People commonly use black seed for asthma, hay fever, diabetes, high blood pressure, eczema, weight loss, menstrual cramps, and many other conditions, but there is no good scientific evidence to support many of these uses. There is also no good evidence to support using black seed for covid-19.

Common names English

Fennel flower, nutmeg flower, roman coriander, blackseed or black caraway, black sesame; India: Assamese - kala jeera or kala jeera, Bengali - kalo jeera,

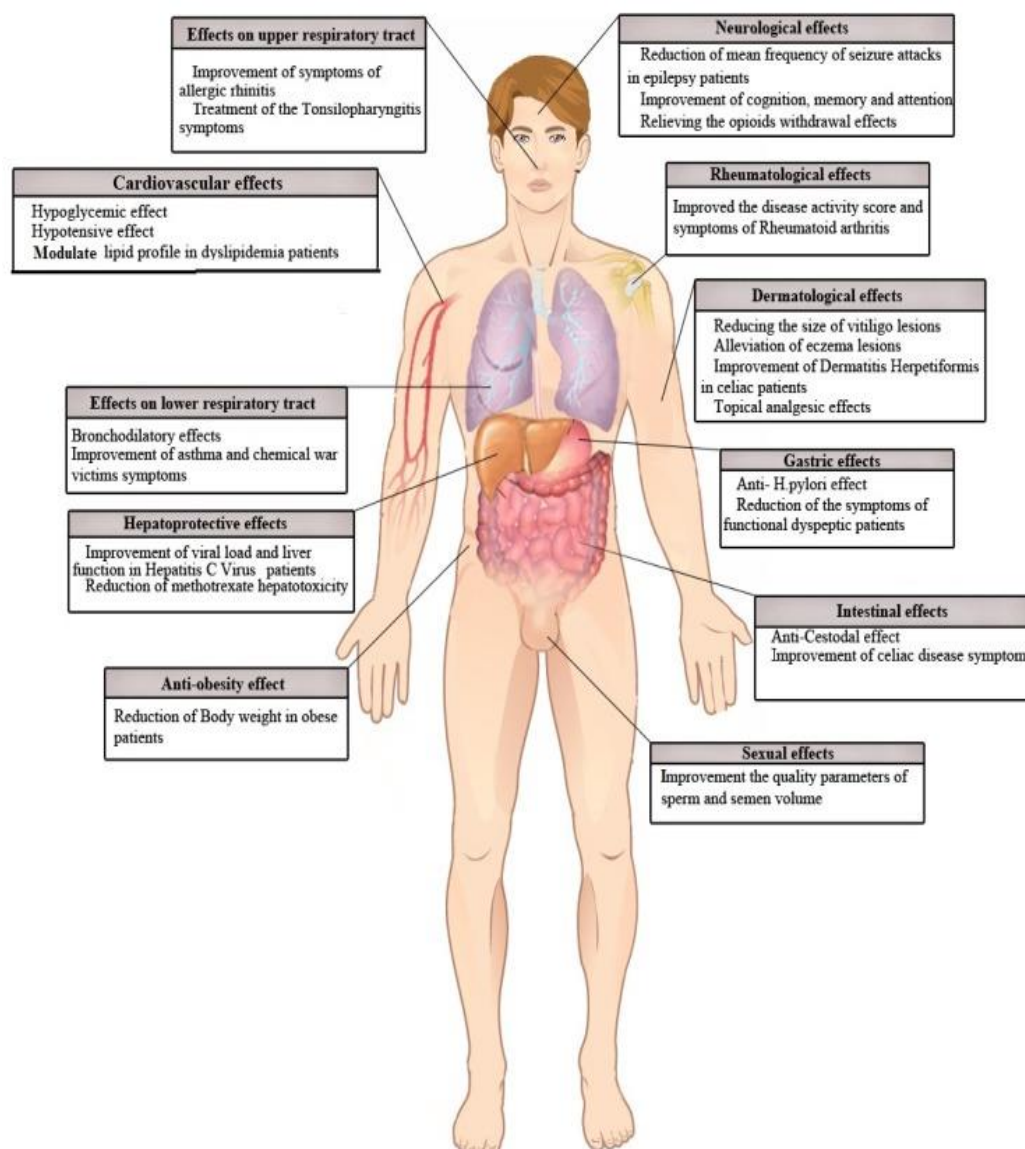
kannada – Krishna jeering, Tamil - Karim jeerakam, Hindi/urdu - kalonji/mangrail; Russian: chernushka; Hebrew: ketzakh; turkish: çörek out; Arabic: Shabbat al-barakah; Persian: siyâh dâne; Indonesian: jintan hitam; Bosnian: þurekot6; french: nigella de crête, toute épice; Germany: schwarzkümmel; Portuguese: cominho-negro; spanish: ajenuz, arañuel; swedish: svartkummin.^[1]

Origin of the name:- originally black cumin was the common name for *Bunium persicum* and was later named *Carum bulbocastanum*, which is now near extinction slowly *carum carvi* graduated to the name, and due to the inability of the species to all over India, later

n. Sativa was adopted by Portuguese or Turkish merchants.

Varieties following varieties of cultivated kala-zira reported with seed yield (g/plant) from zira and saffron research station, Sangla, district Kinnaur (Himachal pradesh), India: racing, Pangi, stang, Barang, Sanji, rispa, Janam, kilba, ribbon, single, Selangor, change, Lobsang, mailer, rogi, Kothi, pillow, Morang, Gurbani, harbor and surname. A variety of grass an different agro techniques is also reported. Cheikh-Touhou et al. Also reported varieties namely, Tunisian and Iranian.

Effect of *Nigella sativa* on Different Parts of the Body



Morphology of the plant

N. Sativa is an annual flowering plant that grows at 20-90 cm tall, with finely divided leaves; the flowers are white, yellow, pink, pale blue, or pale purple in color, with 5-10 petals the fruit is large and inflated capsule

consists of 3-7 united follicles, each containing several seeds. Seeds are small dicotyledonous, trigonous, angular, tubercular, black externally and white inside, odor slightly aromatic, and taste bitter.

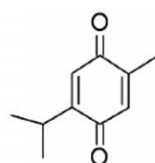


Chemical composition of *nigella sativa*

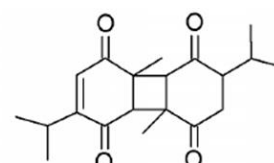
Extensive studies were done to identify the composition of the black cumin seed, the ingredients of *N. Sativa* seed includes fixed oil, proteins, alkaloid, saponin, and essential oil.

The fixed oil (32-40 %) contains unsaturated fatty acids which include: arachidonic, eicosadienoic, linoleic, linolenic, oleic, palmitoleic, palmitic, stearic, and myristic acid as well as beta-sitosterol, cycloeucalenol, cycloartenol, sterol esters, and sterol glucosides.

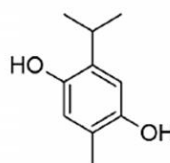
The volatile oil (0.4-0.45 %) contains saturated fatty acids which include: nigellone which is the only component of the carbonyl fraction of the oil, thymoquinone (TQ), thymohydroquinone (the), thymoquinone, thymol, carvacrol, α and β -pinene, d-limonene, d-citronellol, p-cymene volatile oil of the seed also contains: p-cymene, carvacrol, t-anethole, 4-terpineol, and longline. black cumin seed have two different forms of alkaloids: isoquinoline alkaloid that includes: nigellicimine, nigellicimine n-oxide, and pyrazole alkaloid that includes: nigellone and nigellicine. the nutritional compositions of *N. Sativa* are vitamins, carbohydrates, mineral elements, fats, and proteins that include eight or nine essential amino acids. by sodium dodecyl sulfate-polyacrylamide gel electrophoresis (SDS-page) the fractionation of whole *N. Sativa* seeds were done which shows the bands ranged from 94 to 100 kDa molecular mass. black cumin seeds also have saponin and alpha heroine and in trace amount has carvone, limonene, and citronellol, as well as provide relatively good amounts of different vitamins and minerals such as Fe, Ca, K, Zn, P, Cu. most of the pharmacological effects are due to quinine constituent, of which it is mainly abundant. Tq possesses anticonvulsant activity, antioxidant, anti-inflammatory, anti-cancer antibacterial, and antifungal activity.^[8]



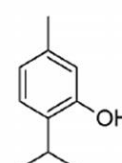
Thymoquinone



Dithymoquinone



Thymohydroquinone



Thymol

Traditional uses of *nigella sativa*

N. Sativa has been traditionally used for the treatment of a variety of disorders, diseases, and conditions in the respiratory system, digestive tract, kidney and liver function, cardiovascular system, and immune system support, as well as for general well-being. Avicenna refers to black seeds in the "canon of medicine", as seeds stimulate the body's energy and help recovery from fatigue and dispiritedness. Black seeds and their oil have a long history of folklore usage in Indian and Arabian civilizations as food and medicine. the seeds have been traditionally used in Southeast Asian and Middle east countries for the treatment of several diseases and ailments including asthma, bronchitis, rheumatism, and related inflammatory diseases. Its many uses have earned *Nigella* the Arabic approbation 'habbatul barakah', meaning the seed of blessing. A tincture prepared from the seeds is useful in indigestion, loss of appetite, diarrhea, dropsy, amenorrhoea, and dysmenorrhoea, and in the treatment of worms and skin eruptions. Externally the oil is used as an antiseptic and local anesthetic. Roasted black seeds are given internally to stop the vomiting.^[2]

Medicinal uses of *nigella sativa*

Nigella sativa has been used for medicinal purposes for centuries, both as a herb and pressed into oil, in Asia, the middle east, and Africa. It has been traditionally used for

a variety of conditions and treatments related to respiratory health, stomach and intestinal health, kidney and liver function, circulatory and immune system support, and for general well-being. In Islam, it is regarded as one of the greatest forms of healing medicine available. The Islamic prophet Muhammad once stated that the black seed can heal every disease except death. Avicenna, most famous for his volumes called the canon of Medicine, refers to *nigella* as the seed that stimulates the body's energy and helps recovery from fatigue and dispiritedness. It is also included in the list of natural drugs of 'tibb-e-nabavi', or "medicine of the prophet (Muhammad)", according to the tradition "hold onto the use of the black seeds for healing all diseases. In the unani tibb system of medicine, *n. Sativa* is regarded as a valuable remedy for several diseases. The seeds have been traditionally used in the middle east and southeast asian countries to treat ailments including asthma, bronchitis, rheumatism, and related inflammatory diseases, to increase milk production in nursing mothers, to promote digestion, and to fight parasitic infections. Its oil has been used to treat skin conditions such as eczema and boils and to treat cold symptoms. Its many uses have earned *nigella* the Arabic approbation 'habbatul barakah', meaning the seed of blessing karayal seeds and their oil have a long history of folklore usage in Arabian and Indian civilizations and are used in food as well as medicine. The seeds are used for flavoring, to improve digestion, and produce warmth, especially in cold climates. They are sometimes scattered in the folds of woolen fabrics to preserve them from insect damage. In India, the seeds are used as a carminative and stimulant to ease bowel and indigestion problems and are given to treat intestinal worms and nerve defects to reduce flatulence and induce sweating. Dried pods are sniffed to restore a lost sense of smell. It is also used to repel some insects, much like mothballs.^[9]

Anti-cancer effects of *n. Sativa*

Many of the anti-cancer activities of *n. Sativa* has been attributed to its major active constituent, thymoquinone (TQ). Tq has been shown to exert anti-proliferative, pro-apoptotic, anti-oxidant, anti-oxidant, anti-mutagenic, anti-angiogenic, and anti-metastatic effects against cancer cells. Tq seems to mediate its anti-cancer effects by targeting several cellular pathways involving p53, nf-kb, ppar γ , stat3, maps, and pi3k/akt transducing. Besides tq, other phytoconstituents of *n. Sativa* has also been shown to contribute to the anti-cancer potential of *n. Sativa* extracts. A-herein is a pentacyclic triterpene saponin found in *n. Sativa* seeds exert effective anti-cancer effects, both in vitro and in vivo. Moreover, thymol, thymohydroquinone, thymoquinone, nigellone-n-oxide, nigericin, nigellone, and carvacrol are phytoconstituents of *n. Sativa* that have been demonstrated to play anti-cancer and cytotoxic functions. Yet, the exact molecular mechanisms underlying the anti-cancer effects of these phytoconstituents are not fully known, and future studies are needed to elucidate

the detailed mechanisms of action that mediate the anti-cancer effects of *n. Sativa* phytoconstituents.^[10]

Effects of *n sativa* on the reproductive system

ns is one of the components of traditional Iranian remedies for the treatment of infertility. *Nso* had favorable effects on abnormal semen parameters in male fertility in normal and hyperlipidemic rats. *Nso* improved abnormal semen quality in infertile men without any adverse effects. The patients (n=34) in the no group received 2.5 ml so, and the placebo group received 2.5 ml of liquid paraffin two times a day orally for two months. Sperm count, motility and morphology, and semen volume, ph, and round cells were improved significantly in the no treated group compared with the placebo group after this period¹⁸⁶.^[11]

anti-inflammatory effects

Anti-inflammatory activities are critical pharmacological properties of black cumin and qt. Here, in addition to the antioxidant properties, recent developments on the anti-inflammatory potentials of black cumin seeds, covering the last five years, are focused on. In low-grade inflammation in human pre-adipocytes, freshly extracted so reduced the interleukin-6 (il-6) level, while stored so reduced the il-1 β level. Following no treatment (400 mg/kg) in rats with carrageenan-induced paw edema, there was a significant improvement in the pro-inflammatory cytokines il-6, il-12, and tumor necrosis factor (TNF)- α in paw exudates and sera. Moreover, topical application of balm stick containing 10% so in rats with paw edema substantially mitigated acute and sub-acute inflammation with a marked edema inhibition (60.64%), and a reduced leucocytes count (43.55% lower than control), and TNF- α level (50% lower than control) on the inflammation area.

As a major bioactive, qt is the key compound responsible for the anti-inflammatory property of black cumin. Hossen et al. Reported that tq inhibited pro-inflammatory factors, including nitric oxide (no), nitric oxide synthase (nos), TNF- α , il-6, il-1 β , and cyclooxygenase (cox) 2 in lps-stimulated murine macrophage-like raw264.7 cells, involving a mechanism that includes the inhibition of irak-linked ap-1/ nf-kb pathways. Tq also promoted the autophosphorylation of tank-binding kinase 1 (tbk1), reduced the mRNA expression of interferons (if- α and in- β), and downregulated the if-3 signaling pathways in lps-stimulated murine macrophage-like raw264.7 cells. Current evidence of the anti-inflammatory potentials of black cumin and qt are promising, however, most of the studies so far have been conducted in animal models. Future studies should focus on determining the anti-inflammatory potential in ameliorating human disease conditions.^[12]

Nigella in the urinary system

n. Sativa along with ascorbic acid (vitamin C) produced a nephroprotective effect by lowering serum creatinine (ck), blood urea nitrogen (bun), and antioxidant activity

in rabbits. Otherwise, it showed an effect on renal expression of organic ion transporters and multidrug resistance-associated proteins in rats. Increased protein levels of the efflux transporters mrp2 and mrp4 and decreased expression of oat1, oat3, oct1, and oct2 were observed in rats. Along with decreasing tubular necrosis score, *n. Sativa* is a good reducer of ck, urea, mda, no, ros, osi, and to levels and augments of tac, sod, and gpx in kidney tissue and blood. Tq is evident to have a complete reversal of the gentamicin (gm)-induced alteration of serum CK, bun, thiobarbituric acid substances (bars), total nitrite/nitrate content, gsh, gpx, cat, and atp values in rats. The black seed ethanol extract at 250-100mg/kg (p.o.) Female Wistar albino rats showed significant nephroprotective activity on paracetamol-induced nephrotoxicity. Otherwise, cd-induced nephroprotective is also evident in rats by Erboglu et al.

Antioxidant activity of *Nigella sativa*

Nigella sativa has a special chemical component that acts as an antioxidant. This component is thymoquinone (qt). An experiment was set up using rats to approve the antioxidant property of the tq. the rats were injected with collagen that induced arthritis, which caused an elevation in the inflammatory mediators' level administration of qt reduced the inflammatory mediators' level and that result indicated the antioxidant activity of thymoquinone *nigella sativa* as antibacterial a unique chemical composition of *nigella sativa* drove the researchers to explore the potential effect of this seed against bacteria. One of these experiments used the ethanol extraction of ns against methicillin-resistant staphylococcus aureus (MRSA) and the strains showed sensitivity to the ethanol extraction of ns. Further, black seed has shown a powerful effect against helicobacter pylori therefore, *nigella sativa* was classified as an antibacterial.^[7]

Antibacterial activity of *nigella sativa* antimicrobial properties of herbal plants and their extracts have been recognized since ancient times, while attempts to illustrate these qualities in the laboratory date back to the early 1900s. Now, the development of resistance via a pathogen to several of the usually used antibiotics provides a drive for additional attempts to find new antimicrobial agents to eradicate the infection and defeat the problems of resistance and side effects of the antimicrobial drugs that are currently used. the mechanism of the antimicrobial effect of *n. Sativa* seeds have not been reported, its antimicrobial property could be attributed to the active constituents, particularly qt and melanin .their broad spectrum of activity may be the reason why the key processes of the organisms are affected.^[6]

Antifungal activities of *nigella sativa*

From the reported studies it is clear that *nigella sativa* possesses antiviral activity against most pathogenic fungi. Thymoquinone was examined for antifungal activity against most fungal strains. A comparative study

reported that the antifungal activity of *nigella sativa* was more potent than the amphotericin b drug (an antifungal drug). One more study reported the antifungal activity of *n. Sativa*. The methanolic and ethanolic extract of the seeds of *n. Sativa* was examined on different pathogenic fungal strains. These strains were *Aspergillus*, *Candida*, *cryptococcus*, and *Issatchenkia* species. The decoction was prepared by the cold maceration technique and assessed by "the national committee of clinical laboratory science" (nucleus) method. It was found that the methanolic extract of the plant showed major inhibition of fungal growth against *candida parapsilosis* and *issatchenkia orientalis* and ethanolic extract showed significant inhibition against *issatchenkia orientalis* respectively. In another study, the essential oil and various extracts of *n. Sativa* was evaluated against trichophyton mentagrophytes, *Microsporum canis*, and *microsporum gypsum* as dermatophyte fungal strains. The antifungal activity of *n. Sativa* was studied by the disk diffusion method. The result showed a potent antifungal effect on *t. Mentagrophytes*, *m. Canis* and *m. Gypsum*. In another study, it was concluded that *c. Cyminum*, *z. Clinopodioides* and *n. Sativa* oils possess antifungal properties. The result showed inhibition in the growth of *a. Fumigatus* and *a. Flavus*. Some researchers reported various treatments for fungal infection by using natural products. *N. Sativa* was also reported for enhancing the antifungal effect. To evaluate the anti-fungal activity a microwell dilution assay was performed against three human pathogenic fungal strains that are *aspergillus flavus*, *aspergillus niger*, *candida albicans*, and four bacteria i.e. *Escherichia coli*, *staphylococcus sp.*, *pseudomonas syringae* and *bacillus subtilis*. It was found that the methanolic extract of *n. Sativa* shows maximum inhibitory potential against all the test fungi.^[8]

CONCLUSION

n. Sativa has been considered worldwide as an essential medicinal herb. all findings discussed above indicate that *n. Sativa* seeds have antimicrobial antifungal, and antioxidant effects against different pathogens, including bacteria, viruses, and fungi.

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