

# *Nigella Sativa* (Kalonji), Its Essential Oils and Their Therapeutic Potential

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## ABSTRACT

*Nigella sativa* originated from the Mediterranean region. It belongs to the family Ranunculaceae (butter-cup family). Used as spice and also generally used therapeutic plant all over the world. Customarily it is used to treat allergic disorders. Important medication in the Indian conventional methods of medication like Ayurveda (herbs) and Unani (roots of plants). Seeds are used as flavoring agent and preservatives. Black cumin seeds were extensively utilized for the cure of various ailments and conditions. In Islamic Literature, it is recognized as one of the ultimate forms of therapeutic medication. It has been widely used as aromatic, respiratory stimulant, diuretic, hypoglycemic, anti-tumor and an analgesic. *N. sativa* oil also have therapeutic properties and many active compounds. It is usually extracted by hydro-distillation method. Thymoquinone isolated from the black cumin is the principle main dynamic constituent of its volatile oil that involves in numerous biochemical and physical properties of this plant. The current review paper tries to describe the essential oils of *N. sativa*, their chemical composition as well as therapeutic activities.

## Introduction

There is a Hadith of Hazrat Muhammad (PBUH) that, 'black seed is treatment of every disease but death' (Bellir, Bellir, & Rouabah, 2014).

There is a Hadith of Hazrat Muhammad (PBUH) that, 'black seed is treatment of every disease but death' [1]. Kalonji word is used to address the *N. sativa* in south Asia and in Arab it is referred as "Habat-ul Sauda". English journals uses the name Black cumin for *N. sativa* [2]. *Nigella sativa* belongs to the family Ranunculaceae, cultivates as a small herb and is produced all throughout the India and other tropical areas of the world [3]. *Nigella sativa* originate from the Mediterranean region [4] and it is local to North Africa, southern Europe, south and southwest Asia [5]. *N. sativa* is one of the most olden known tamed plants and its seeds were supposedly found in Tutankhamon's burial chamber [6]. The genuine significance of *Nigella sativa* arises from the heavenly saying of the Prophet Mohammed (PBUH). It is a similar black cumin seed described by Prophet Mohammed as a panacea (all inclusive healer).

Chroniced utilization of black seeds has been referenced in different holy and cultural books. Kalonji is recognized as the therapeutic black cumin in the sacred book of scriptures (bible) and additionally portrayed as the melanthion (little black seeds) of Hippocrates and Dioscorides. In Greco Middle Easterner/Unani Tibb arrangement of medication that is started by Hippocrates, his contemporary Ibn-sina and Galen has viewed Kalonji as an important cure in liver and stomach related turmoil. The renowned book of medication by Ibn-sina "The cannon of medication (980-1037) uncovered verifiable significance of *Nigella sativa* such as seeds "That enhances energy of the body and help recuperation from tiredness [7].

## Therapeutic Importance of *N sativa*

The oil and seeds of black cumin have been broadly utilized for quite a long time in the cure of different illnesses all through the world. Also, it is a significant medication in the Indian conventional arrangement of medication such as Ayurveda and Unani [8]. It has been conventionally utilized since antiquated occasions as a

significant therapeutic plant and seasoning [5]. It is dynamic as a fragrant, respiratory energizer, diuretic, hypoglycemic, hostile to tumor and a pain relieving [3]. Generally, in present studies it is documented that seeds of *Nigella sativa* are recognized by old Egyptian and Greek doctors to treat cerebral pain, adenoidal clog, pain in teeth and worms that are present in intestine, are used as a substance that promotes diuresis to advance monthly cycle of periods and creation of milk [9]. In the customary arrangement of medication, it is suggested in a wide scope of infirmities including asthma, constant migraine, headache, chest clog, dysmenorrhea, heftiness, loss of motion, hemiplegia, back ache, stiffness, hypertension and gastrointestinal issues, for example, dyspepsia, gassiness and diarrhea.

It has additionally been utilized as an energizer, diuretic, emmenagogue, lactagogue, anthelmintic and carminative. Phytochemicals of seeds were analyzed and uncovered the occurrence of unstable oil (1.5%), fixed oil (37.5%) nigellin, melanthin and Arabic acid, carvene, carvone and cymene, thymohydroquinone and thymoquinone. Thymoquinone is major active compound confined from the volatile oil of black cumin [10]. The existence of various alkaloids (nigellidine, nigellimine and nigellicine) has likewise be present in the seeds of *Nigella sativa* [2]. It has been utilized in societies around there since ancient time. The well-known spice has ebony seeds darker than black, with blue or purple undertones renowned for terpenoids substances that are present in them, especially thymoquinone and fatty acids. Experimental preliminaries have approved this current spice's expected use for handling allergic conditions.

There is additionally medical preliminary help for the utilization of kalonji seeds in individuals moving out from, and with-drawing from, narcotics, and individuals who need to improve lipid profiles as well as decline seizure recurrence [11]. Thymoquinone is the significant dynamic constituent of *N. sativa* and establishes about 30% of its essential oil or ether extract. Because of the presence of thymoquinone *N. sativa* have a large number of the biochemical, physiologic, and molecular impacts. There are just couple of reports in writing on the harmfulness of thymoquinone and in view of the wide spread utilization of *N. sativa*, it is important to check the harmfulness of its components in the research facility creatures [12]. Black seeds a zest that can be utilized as a therapeutic plant and a food additive. The seeds and the oil of *N. sativa* indicated a likely treatment in customary prescriptions. Black cumin has flavonoid mixes.

This plant has one cluster with *N. damascene*. That to be known has a high estrogenic impact. It also displayed antifertility, anti-oxytotic action, act as emmenagogues and also possess numerous different properties [13]. In various mixes, the seeds of black cumin were utilized in fatness and for the prophylaxes of difficult breathing. They have ability to counter liver disorder and are directed inside in discontinuous fever. Steady inward breath of fry

up seeds reduces cold and inflammation of the mucous membrane. They likewise been utilized in mercury harming, injuries and leprosy [14]. Black cumin is one of home grown medication with a few pharmacological properties, for example, antiparasitic, antitumor, anticancer, hepato-protective, gastro protective, antifungal, antibacterial, and immuno-energizer. A few logical reports have additionally upheld the *N. sativa* activities as an anti-diabetic compound by advancing typical digestion of glucose in rodent that have diabetes and recuperating the harm of pancreatic  $\beta$  cell, just as upgrading the insulin emission.

The other pharmacological actions shared by the home grown are connected with the estrogenic impact and its capacity in diminishing the clinical indications of the osteoporosis in ovariectomized rodents. The black cumin can control cell development and separation of monocyte and monocyte-determined macrophages, just as regulating amino acid discharge in refined neurons *in vitro* [15].

#### Taxonomy of *N. sativa*:

Kingdom: Plantae.

Subkingdom: Tracheobionata (vascular plant).

Supervision: Spermatophyte.

Order: Ranunculales.

Family: Ranunculaceae (Butter cup family).

Genera: *Nigella*.

Species: *sativa* [16].

#### Physical Characteristics of *N. sativa*:

**a) Morphology:** Kalonji is an annually blossoming plant which develops to 20-90cm tall, along with excellently partitioned leaves, the section of leaves hardly linear to thread-like structure. The blooms are delicate, and typically yellow, pink, light blue or pale purple in color, with 5-10 petals. The fruitlet is a huge and swelled case made out of 3-7 joined follicles, each one comprising numerous seeds [17].

**b) Structures of the Powder and Seeds:** Visibly, seeds are little dicotyledonous, having three angles or corners and regular tubes like structure, pointed, 2-3.5mm×1-2 mm, dark remotely and white inside, scent marginally fragrant and flavor unpleasant. Thoroughly, cross over segment of seeds appears epidermis that contains a single layer comprising of curved, thick-walled cells, covered the slightest bit by a papillose cuticle layer and loaded-up with dull earthy colored material. Epidermis tailed by 2-4 layers of dense walled loosely prolonged cells that are parenchymatous in nature, followed by a rosy earthy colored layer made-up of impenetrable walls, quadrilateral stretched cells. Inside to the shade layer, is available a layer made-up of dense walled four-

sided stretched or almost columnar, prolonged cells. Endosperm comprises of cells that have fragile walls and are rectangular or polygonal generally oil globs are filled in them. The microscopic study of powder of seeds shows earthy dark, parenchymatous cells and bubbles of oil [16].

**c) Chemical Structure of *N. sativa*:** *N. sativa* substance structure is assorted and comprises of scope of various parts including starches, proteins, fats, oils, strands, nutrients, minerals (Fe, Cu, Zn and P and so on), alkaloids, saponins and numerous other naturally dynamic mixes [18]. Significant alkaloids distinguished in *Nigella sativa* are: pyrozol alkaloid (for example nigellicine and nigellidine) and isoquinoline alkaloids (for example nigellicimine and nigellicimine-N-oxide) [19]. Level of naturally dynamic mixes that are discovered in black cummin that incorporates: thymoquinone, thymohydroquinone, dithymoquinone (DIM), 4-terpineol, carvone, carvacrol, t-anethol, thymol,  $\alpha$ -pinene,  $\alpha$ -hederin, limonene and numerous different mixes that are discovered in various amount [20]. The vast majority of the therapeutic activities of *Nigella sativa* are due to the presence of its quinine components [19]. The seed is likewise wealthy in unsaturated fats including linolenic acid, oleic acid, eicodadienoic acid, linoleic acid, palmitoleic acid, arachidic acid, palmitic acid, myristic acid and stearic acid [21].

**d) Essential Oils:**

The oils are perplexing common combinations of unstable secondary metabolites, extracted from plants by expression (citrus shell oil) and by refining through hydro-steam distilling method. The primary components of volatile oils mono and ses-qui-terpenes including sugars, ethers, alcohols, ketones and aldehydes are liable for the aromatic and medicinal properties of sweet-smelling and therapeutic plants. Because of these characteristics, ever since old time's flavors and spices have been added to food, as seasoning specialists as well as additives. For quite a long time volatile oil were extracted from various parts of plants and also utilized for comparative motives. They are exploited for counter a wide scope of living beings, for example, microscopic organisms such as parasites (fungi), bacteria, infectious viruses, protozoa, bugs and plants [22].

Oils have been appeared to have activities against bacteria, fungi, virus, insects and act as cancer prevention agent. A few oils have been utilized in malignancy treatment. Some different oils have been utilized in food protection, fragrance based treatment and scent manufacturing. Volatile oils are a rich basis of composites that are dynamic in nature. There has been an expanded interest in studying about the properties of extracted material against microorganisms from fragrant plants especially essential oils. Thus, it is sensible to anticipate a collection of plant mixes in these oils with particular as well as broad antimicrobial properties and anti-biotic activities [23]. Around 3000 volatile oils are found, and 10% of them have business significance in the production of different foods, beautifying agents and medicines. Therefore, they are commonly accepted as harmless by the US Food and Drug Administration

(FDA). Their organization possibly will change extensively between sweet-smelling plant species and their collections, and in similar variety from various geographic territories [24].

Particular volatile oils of plants, commonly utilized as essences and scents in the food and perfumes manufacturing [25] have long been supposed to resist pests. Current examinations in a few nations affirm that some plant volatile oils not only repulse pests, however, have connection and fumigant anti-insecticidal activities against explicit vermin, and antifungal activities against some significant plant microbes [26]. The ongoing years have likewise seen a re-establishment of materials that have traditional characteristics in medications and in food and beautifying agents' maintenance. Notwithstanding the improvement of anti-toxins, bacterial and parasitic contaminations are as yet a significant problem in medication, and the presence of various strains that are resistant to drugs represents another concern. Medicines made up of herbs have been widely utilized in this area for a long time. In recent times, there has been a developing interest in common items because of their accessibility, less harmful impacts or less poisonousness as well as great biodegradable property when contrasted with the accessible anti-infection agents and additives [27].

A few creators have researched the essential oil of *Nigella* seeds and extracted and distinguished dynamic components that have valuable medical impacts. Egyptians accept that *nigella* seeds enhance and improve the immune system of individual. The oil has been created by squeezing the crude or cooked seeds [23]. *Nigella sativa* seed oil comprises of oleoresins and volatile oil constituents, including thymoquinone, thymohydroquinone, dithymoquinone,  $\alpha$ -thujene, carvacrol, longifolene, p-cymene, 4-terpineol, t-anethol, pinene and thymol. p-cymene (7–25.8%) and Thymoquinone (30–52.6%) were accounted for as its key constituents [28]. Anti-microbial properties of essential oil is credited predominantly to its phenolic components of the volatile oil section. Subsequently, thymoquinone followed by its connected compounds, for example, thymol, dithymoquinone, and thymohydroquinone alongside carvacrol indicates significant function against microorganisms [29]. Different components, linoleic acid, oleic acid and oleoresins may likewise appears slight effects against microbes [28].

Undoubtedly, entire volatile oil existed accounted for greater activity against bacterial infections than the mixtures of its noticeable components, recommending that the negligible parts enhance the action of *N. sativa* essential oil against microorganisms [30]. *Nigella sativa* oil is more powerful as compared to thymoquinone. It is a better source of biologically active mixes, for example,  $\alpha$ -pinene, p-cymene and limonene, those are considered as incredible bactericides. It indicated a significant property against microbes, in spite of the fact that the extremely low quantity of thymoquinone. It stays a better usual basis for the creation of new anti-microbial medications, in this manner supporting the

more extensive utilization of *Nigella sativa* as regular medication for the infections that are caused by micro-organisms [31]. *N. sativa* volatile oils are more functional against gram +ve bacteria, as compared to the gram -ve bacteria. A firmly related component thymohydroquinone, separated from *Nigella sativa* essential oil, was discovered to be a profoundly dynamic constituent, resisting gram positive bacteria, for example, *Staphylococcus epidermidis*, *Bacillus cereus* and *Staphylococcus aureus*, have been generally assigned as the most vulnerable species to *Nigella sativa* oil [32].

Various compounds got from plants regularly show significant action against bacteria that are Gram positive do not show any activity against Gram negative bacteria. Gram -ve microorganisms have a powerful porousness hindrance, included the external layer, which limits the infiltration of molecules which have both hydrophilic and hydrophobic parts and have resistant multidrug taps that expel toxic substances over the border line. It is probable that the apparent insufficiency of plant compounds that are attacking on microorganisms generally because of the permeable blockade [33]. *N. sativa* volatile oil have more grounded anti-bacterial activities contrast with Tetracyclin, Cefuroxime, and about a similar quality contrast with Ciprofloxacin and equal activity against fungi contrast with Clomatrizol [34]. Black cummin volatile oils containing higher amounts of (30ug) carvacrol and thymol are more sensitive bacterial species as compared to those that contains low amount (10ug) perhaps for the reason that they are accountable for the action against bacteria. Methanol concentration that is extracted from *N. sativa* showed higher activity against bacteria and fungi as compared to the ether extracts [34].

### Chemical Composition of Essential Oil of *Nigella Sativa*

The steam distillation of the concentrate from the seeds of *Nigella sativa* presented a yellowish essential oil. 32 complexes, comprising (86.7%) of the essential oil, were distinguished. The oil comprised of 9 monoterpenoid hydrocarbons (26.9%), 6 phenyl

propanoid compounds (46.1%), 8 non-terpenoid hydrocarbons (4.0%), 4 monoterpenoid ketones (6.0%), 2 sesqui-terpenoid hydrocarbons (1.0%), 3 monoterpenoid alcohols (2.7%). In this way, oil of black cummin is described by a larger quantity of propanoids of phenyl. These oils of *Nigella sativa* introduced elevated concentrations of p-cymene (14.8%) and trans-anethole (38.3%). Other significant components were carvone (4.0%) and limonene (4.3%) [21]. The monoterpene thymoquinone that are enriched with oxygen and the essential unsaturated fat 18:2 n – 6 were the significant components volatile oils. Essential oils showed fascinating properties against tuberculosis and fungal infections. Egyptian *N. sativa* essential and fixed oils demonstrated the best activity against microorganisms [35].

### Methods Used for the Extraction of Essential oils:

- 1) Hydro-distillation
- 2) Cold Pressing
- 3) Solvent Extraction
- 4) Supercritical Fluid Extraction
- 5) Ultrasound-Assisted Extraction (UAE)
- 6) Microwave-Assisted Extraction (MAE) [36].

### Hydro-Distillation (HD) /Steam Distillation Method

Steam distillation method is additionally one of the generally utilized approaches for the abstraction of volatile oils [37] generally hydro-distillation was accomplished with a Clevenger device to contrast with Microwave-Assisted Extraction technique. 100 g ground seeds were placed into a sample jar and blended in with 300 mL deionized water. Distillation is occurred in 3–4 h until not any more essential oil was extracted. The collection and storage of volatile oil was done at 0 °C till use. This procedure was completed in three-fold [37-58].

**Table 1:** Therapeutic Properties of Essential oil of *N. sativa*.

No	Properties	Activity	References
1	Anti-malarial Effects	<ul style="list-style-type: none"> <li>· <i>N. sativa</i> oil can possibly be utilized as both supplements and as adjuvant.</li> <li>· It has great importance when combine with chloroquine because the rate of loss and failure becomes less that's why it is safer for utilization.               <ul style="list-style-type: none"> <li>· This will lessen the side effects of CQ</li> </ul> </li> <li>· Total charge of treatment of malaria through chloroquine being the least expensive and mostly accessible.</li> </ul>	Emeka, Badger-Emeka, Eneh, & Khan [46]
2	Anti-bacterial Activity	<ul style="list-style-type: none"> <li>· <i>Nigella sativa</i> oil have shown great properties against bacterial specie that are producing wound infections.</li> <li>· The oil provided great preventing impacts on <i>Staphylococcus Aureus</i> and <i>Streptococcus</i> species.</li> <li>· Thymohydroquinone was separated from the essential oil known to possess higher actions against gram +ive bacteria.</li> </ul>	Khuder, El-Fatary [42,50]

3	Anti-parasitic Effects	<ul style="list-style-type: none"> <li>· Nigella sativa oil serves to counter infection by tapeworms and also used in the treatment or control of nematode infestations.</li> <li>· It was demonstrated that oil have the ability to lessen the quantity of Schistosoma mansoni worms and ova that are produced in both the liver and in the intestinal tract.</li> <li>· It has ability to expel parasitic worms such as nodular worms, tapeworms, hookworms, earthworms and nodular worms.</li> <li>· Displayed great properties to attack the tapeworms and earthworms.</li> </ul>	Mahmoud, El-Abhar, & Saleh, Mehta & Anita [52,53]
4	Influence on blood	<ul style="list-style-type: none"> <li>· In an ongoing report it was seen that menthol dissolvable parts of Nigella sativa oil <ul style="list-style-type: none"> <li>· Counting thymol and carvacol</li> </ul> </li> <li>· Had extremely solid inhibitory impact on aggregated platelets that are induced by archidonic acid.</li> </ul>	Sayed [56]
5	Anti-Diabetic Activity	<ul style="list-style-type: none"> <li>· Black cumin oil was discovered to be successful by means of an extra treatment in patients suffer from insulin resistant disorder.</li> <li>· Oil of N.sativa shows important effects in individuals that are suffer from diabetes and dyslipidemia.</li> </ul>	Najmi, Haque, Naseeruddin, & Khan, [55]
6	Treatment of Acne	<ul style="list-style-type: none"> <li>· The Nigella sativa oil moisturizer has demonstrated its adequacy as an effective treatment for skin break out by acne vulgaris.</li> <li>· A new common plant extricate, which does not have any consequences. <ul style="list-style-type: none"> <li>· One of its constituents <math>\alpha</math>-pinene had in vitro impact against Propionibacterium acnes,</li> </ul> </li> <li>· That is one of the main considerations involve in the advancement of skin inflammation.</li> </ul>	El-Tahir & Bakeet, Al-Harchan, Hadi & Ashor, [44,39,47, ]
7	Anti-fungal Effects	<ul style="list-style-type: none"> <li>· The essential oil of Kalonji of various backgrounds has accounted for to have adequate inhibitory activity against disease causing strains of: <ul style="list-style-type: none"> <li>· yeasts,</li> <li>· dermatophytes and</li> </ul> </li> <li>· Non-dermatophytic filamentous parasites alongside aflatoxin-creating organisms.</li> </ul>	Yimer et al. [58]
8	Effects on immune system	<ul style="list-style-type: none"> <li>· By means of a characteristic cure, individuals take Kalonji oil as an advertiser of better wellbeing and for the treatment of normal cold and Asthma.</li> <li>· Daily up take of Nigella sativa oil through mouth by rodents before entire body gamma light brought about critical inversion of decrease of hemolysin antibodies titers.</li> </ul>	El-Kadi & Kandil, Boskabady, Keyhanmanesh, Khameneh, Doostdar, & Khakzad [40,43]
9	Anti-oxidant Effects	<ul style="list-style-type: none"> <li>· Nigella sativa oil has thymoquinone and its correlated mixes; thymol and dithymoquinone as significant dynamic components, which have cell anti-oxidant properties.</li> <li>· Scavenging oxygen free charged particles, produced during numerous degenerative sicknesses.</li> </ul>	Lutterodt et al. [51]
10	Effect on reproductive system	<ul style="list-style-type: none"> <li>· The uptake of 1ml/kg/day of black cumin oil enhances the release of sexual hormones that stimulated the increase protein production of liver enzymes, platelets numbers and in the blood it diminishing the level of cholesterol present in serum.</li> <li>· Nigella sativa oil possess anti-oxidative activities to neutralize the damage in the epididymal sperm characters brought about by hydrogen peroxide (<math>H_2O_2</math>) treatment.</li> </ul>	Juma, TawfeeK [49,57]
11	Effect on respiratory system	<ul style="list-style-type: none"> <li>· In Saudi Arab and neighboring nations Kalonji seeds and oils are commonly utilized for the cure of asthma.</li> <li>· Carbonyl polymer of thymoquinone (nigellone) ends up being an incredible preventive agent for both bronchial asthma and asthmatic bronchitis.</li> <li>· Essential oil can be utilized as probable respiratory energizer if thymoquinone is eliminated.</li> </ul>	MK, El Tahir, Ashour, & Al-Harbi [45,54]

## Conclusion

*Nigella sativa* is a herb that is used in traditional remedies of diseases. Since ancient time it is used for medicinal purpose and used as preservative and flavoring agent in food. The seeds of NS have a potential medicinal value and are relatively safe to consume. Its essential oil also contains many bioactive compounds and has beneficial clinical effects. However, it has some side effects, but the minor and/or negligible toxicological effects and wider therapeutic margin of *N. sativa* seeds, its oil and extracts and some of its active principles, particularly Thymoquinone, as evident by various scientific studies support its safe use for the long-term traditional food and medicinal purposes.

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