

# A REVIEW ON THERAPEUTIC POTENTIAL & PHARMACOLOGY OF NIGELLA SATIVA

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**Abstract:** *Nigella sativa* (black cumin or black cumin), a member of the buttercup family, is an annual herb with many pharmacological properties. It is very popular in various traditional medicine systems such as Unani and Tibb, Ayurveda and Siddha. *N. sativa* seeds have been used extensively in the treatment of various diseases and ailments. Extensive studies on *N. Sativa* have been carried out by various researchers and a wide range of their pharmacological effects have been studied, including antidiabetic, anticancer, immunomodulatory, analgesic, antimicrobial, anti-inflammatory, spasmolytic, bronchodilator, hepatoprotective, renal protective, gastro- properties: protective, antioxidant, etc.

It Commonly used as an antihypertensive, liver tonic, diuretic, digestive, antidiarrheal, appetite stimulant, analgesic, antibacterial and for skin conditions has been demonstrated for its ability to reduce oxidative stress and inflammation and to promote immunity, cell survival and energy metabolism which is the foundation for various health benefits. Thymoquinone, the main bioactive component of the essential oil. The present review is an attempt to provide a detailed review of the scientific research literature on the pharmacological properties, chemical composition and pharmacological activities of the seeds of this plant. Black seed (*Nigella sativa* L.), a prized nutraceutical herb with a wide range of health benefits, has attracted increasing interest from health-conscious individuals, the scientific community and pharmaceutical industries.

**Keywords:** black seed, thymoquinone, *Nigella sativa*, Miracle herb, Ranunculaceae, Anti-diabetic, Antioxidant

## Introduction

Medicinal plants have been used in various indigenous medical systems as well as in folk medicine to cure diseases for many centuries. In addition, medicinal plants are also used to make herbal medicines because they are considered safe compared to modern medicines. allopathic medicines. Many researchers focus on medicinal plants as few plant species have been thoroughly studied for their medicinal properties, potentials, mechanisms of action, safety assessments, and toxicological studies (1).

A hot medicinal herb is *Nigella sativa* L. (Ranunculaceae), also called black cumin or black cumin, famous for its culinary uses and historically valuable in traditional medicine. Black cumin is native to a vast region of the eastern Mediterranean, North Africa and the Indian subcontinent. and Southwest Asia and is grown in many countries including Egypt, Iran, Greece, Syria, Albania, Turkey, Saudi Arabia, India and Pakistan. As a panacea, Black Seed in essential oil, paste, powder and extract form is indicated in Traditional Medicine for many diseases/conditions such as asthma, bronchitis, rheumatism, headache, back pain, anorexia, amenorrhea, paralysis, inflammation, mental weakness, eczema and high blood pressure, to name a few (2).

The black seeds and their oil have a long history of folkloric use in Indian and Arabic civilizations as food and medicine, and were commonly used to treat a variety of Health conditions related to the respiratory system, digestive tract, kidney and liver function, cardiovascular system and immune system support and general well-being (3). Most of the therapeutic properties of this plant are due to the presence of thymoquinone (TQ), which is an important active chemical component of the essential oil. Black seed is also used in food as a flavoring additive in bread and pickles as it has very low toxicity (4).

**Pharmacognostical characteristics:**

Fig.1

**Kingdom:** plantae  
**Division:** Magnoliophyta  
**Class:** Magnoliopsida  
**Order:** Ranales  
**Family:** Ranunculaceae  
**Genus:** Nigella  
**Species:** N. sativa

**Morphology of the plant:**

**Sativa** is an annual flowering plant that grows 20-90 cm tall with finely divided leaves, the leaf segments being narrowly linear or thread-like.

**Roots:** It has well developed yellow-brown tap root, producing many secondary & tertiary roots.

**Stem:** The stem up to 70 cm, is profusely branched, subterete, ribbed, often becoming hollow with edge, tuberculous & light to dark green.

**Flowers:** The flowers are pale green when young, light blue when mature, solitary & terminal, initially pale green, becoming pale blue or white; the pedicel is 4-8 cm, inserted on 2mm diameter yellow or brownish, depressed receptacle. There are 5 ovate sepals up to 17 x 22 mm, tapering at the base into a claw 2-3 mm. There are normally 8 petals, each with a short glabrous claw; the stamens in 8 groups of 3-7, are initially upright become horizontal with edge. The ovary is compound, 4-9 mm with a free stigma 5-mm.

**Seeds:** The black triangular or pyramidal seeds are borne in a capsule with five or six segments, each of which terminates in an elongated projection. The fruit is a large, inflated capsule composed of 3-7 connected follicles, each containing numerous seeds (1).

**Leaves:** The leaves are alternate & exstipulate, the petal 1-6 cm, present only on basal leaves. The blade is 7 x 5 cm, pinnately dissected into thin sublinear lobes usually describes as feathery & normally green but may become red/ brown with edge.



Fig.2

#### Chemical composition of black cumin:

Many active substances have been isolated, identified and described in different varieties of black cumin. The main active ingredients are thymoquinone (30%-48%), thymohydroquinone, dithymoquinone, p-cymene (7%-15%), carvacrol (6%-12%), 4-terpineol (2%-7%), t- Anethole (1%-4%), sesquiterpenes longifolene (1%-8%),  $\alpha$ -pinene and thymol, etc. Black seeds also contain some other compounds in small amounts. The seeds contain two different types of alkaloids; I. Isoquinoline alkaloids e. Nigellitimine and nigellitimine N-oxide and pyrazole alkaloids or indazole ring alkaloids, including nigelidine and nigelicine. In addition, N. sativa seeds also contain alpha-hederin, a water-soluble pentacyclic triterpene, and saponin, a potential anti-cancer agent (6). The seeds are said to contain a fatty oil rich in unsaturated fatty acids, principally linoleic acid (50-60%), oleic acid (20%), eicodadienoic acid (3%) and dihomolinoleic acid (10%). Acids (palmitic acid, stearic acid) can be about 30% or less. A-Sitosterol is an important sterol, accounting for 44% and 54% of total sterols in Tunisian and Iranian varieties of black seed oil, respectively, followed by stigmasterol (6.57–20.92% of total sterols).

Compositions by N.Sativa are vitamins, carbohydrates, minerals, fats and proteins that contain eight or nine essential amino acids. N. sativa whole seeds were fractionated by sodium dodecyl sulfate-polyacrylamide gel electrophoresis (SDS-PAGE) and showed bands with a molecular mass of 94-100 kDa. Black cumin seeds also have saponin and alpha-hederin, and trace amounts of carvone, limonene, and citronellol, as well as relatively good amounts of different vitamins and minerals such as Fe, Ca, K, Zn, P, Cu (7).

#### Traditional uses of folk remedies:

Nigella sativa is commonly used as a spice and flavoring in a variety of food preparations such as bread, yogurt, pickles, sauces and salads. Black cumin or black cumin (English), Habbatul Barakah (Arabic), Tikur Azmud (Amharic) has long been used as a traditional remedy in Arabic countries, Far East Asia, Europe and Africa. Nigella sativa was also described as a miracle plant and considered “the herb of heaven” by early herbalists. The Prophet Muhammad (peace be upon him) of described the healing powers of black cumin as “Expect to use this black cumin as it is a cure for all diseases except death.” Avicenna, a well-known 10<sup>th</sup>-century physician, famous for his book The Canon of Medicine, recommended the use of Nigella seeds to improve the body’s energy and also aid in recovery from fatigue and stress support. Nigella sativa is also mentioned in the Bible for its healing properties and also referred to as melanthion by Hippocrates and Dioscurides (8).

The seeds have been used as a pungent, aromatic, thermogenic, diuretic, expectorant, laxative, stimulant, diaphoretic, sedative and digestive aperitif. Black cumin seeds have a history of use in traditional Arabic herbal medicine to treat many ailments including skin diseases, jaundice, gastrointestinal -Problems anorexia, conjunctivitis, dyspepsia, rheumatism, diabetes, hypertension, autohemorrhage, paralysis, amenorrhea, anorexia, asthma, cough, bronchitis, headache, fever, flu and eczema (9)

#### Pharmacological properties:

In recent years, a large number of studies have been conducted highlighting recognized medicinal properties in various pharmacological effects of N.sativa seeds, such as , immunomodulatory and antitumor properties, hepatoprotective effect, also gastric ulcer healing, suppression of tumor growth, improvement of male infertility, cardiovascular diseases, improvement of memory, stimulation of milk production, protective effect on lipid peroxidation, antibacterial activity, antidermatophyte, antiviral activity against cytomegalovirus, have been reported for this medicinal plant(7).



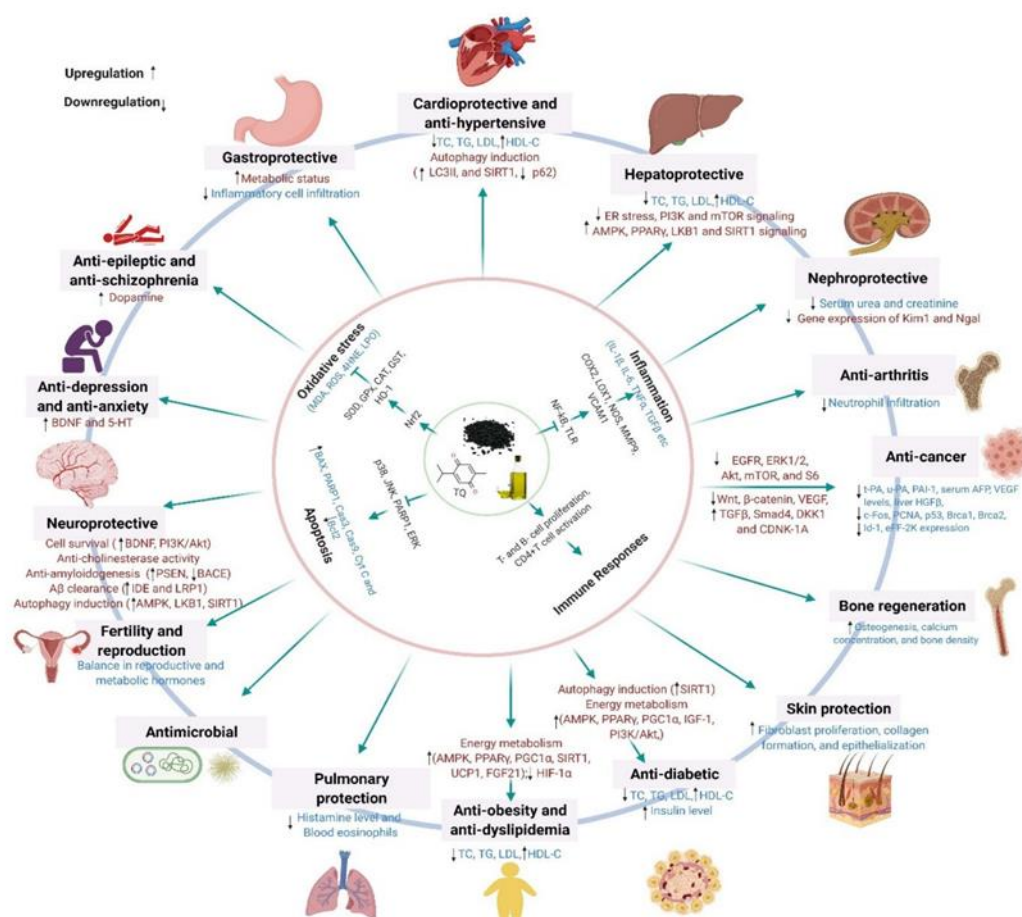


Fig.3

### Antioxidant activity

Oxidative pressure and an intensification within the ranges of loose radicals are among the foremost valuable markers related to numerous innovative pathological conditions, inclusive of neurological disorder, cancer, aging, and endocrine illness (10). The concomitant utilization of *Allium sativum* and *N. sativa* seed in thirty postmenopausal girls after months of intake found out a significant discount in plasma malondialdehyde (MDA) ranges with elevated pastime in erythrocyte glutathione peroxidase (GSH-Px) and superoxide dismutase (11). The antioxidant and antiarthritic pastime of TQ in Wistar Rat via way of means of collagen caused arthritis turned into evaluated. TQ turned into Administered at a dose of five mg/kg frame weight as soon as each day for 21 d.

The consequences of remedy within the rats have been assessed via way of means of Biochemical (articular elastase, myeloperoxidase (MPO), LPO, Glutathione (GSH), catalase (CAT), SOD and NO), inflammatory Mediators [IL-1 $\beta$ , IL-6, TNF- $\alpha$ , IL-10, IFN- $\gamma$  and PGE (2)] And histological research in joints. The Antioxidant, anti-inflammatory, anticancer and antibacterial Activities of the shoots, roots and seeds methanol extracts From *N. sativa* have been studied. The 3 organs exhibited sturdy Antioxidant pastime the use of the oxygen radical absorbance Capacity technique and a cell-primarily based totally assay. TQ has been Shown to suppress the Fe-NTA-caused oxidative pressure, Hyperproliferative reaction and renal carcinogenesis in the mechanism of the antimicrobial impact of *N. sativa* seeds has now no longer been reported, its Wistar rats (1).

### Antibacterial activity:

antimicrobial belongings may be attributed to the lively ingredients specifically TQ and melanin. Their wide spectrum of pastime can be the motive of that the important thing techniques of the organisms are affected (7). Tymoquinone acquired from Seeds of *N. sativa* discovered broader spectrum sports Against more than one traces of gram-advantageous and gram-bad Bacteria, which include *Bacillus*, *Listeria*, *Enterococcus*, *Micrococcus*, *Staphylococcus*, *Pseudomonas*, *Escherichia*, *Salmonella*, *Serovar*, and *Vibrio parahaemolyticus* further to inhibit-Ing bacterial biofilm formation.

The methyl alcoholic Extract of the seed additionally displayed a bigger inhibition area on Gram-advantageous (*S. pyogenes*) compared to gram-bad Bacteria (*P. aeruginosa*, *K. pneumoniae*, and *P. vulgaris*). For different isolates of methicillin-resistant *S. aureus*, diverse Concentrations of (100%, 80%, 50%, 40%, 30%, and 20%) *N. Sativa* oils displayed an expressively better area of inhibitions Against all of the examined bacterial traces. Tymoquinone Also discovered a significant bactericidal pastime towards gram-Positive cocci with MICs starting from eight to 32 g/mL and proved the minimal biofilm inhibition awareness at 22 And 60 g/mL for *S. aureus* and *S. epidermidis*, respectively. Moreover, black seed (2 g/day) owed clinically precious Anti-*H. pylori* effect corresponding to triple therapy and This can offer a scientific foundation for the exploration of Potential makes use of of this valued seed for the remedy of *H. Pylori*-brought about gastric ulcers (8).

**Antidiabetic activity:**

Diabetes mellitus is a chronic metabolic disorder characterized by prolonged hyperglycemia with abnormalities in the metabolism of carbohydrates, fats and proteins in the body, mainly due to impaired secretion and/or action of insulin. The pathobiology of diabetes is closely related to dysregulated inflammation, increased oxidative stress through altered redox homeostasis, and imbalanced blood lipid profiles.

Complications associated with diabetes include neuropathy, nephropathy and retinopathy. As a component of traditional medicines, black cumin and essential oil (NSO) have great potential as antidiabetics. Black seed extracts have been shown to improve disease outcomes in alloxan- or streptozotocin-induced diabetic rats or mice through the mechanism involving the attenuation of oxidative stress by increasing the activity of antioxidant enzymes, regulating blood lipid profiles, enhancing endothelial dysfunction, and enhancing tissue regeneration and wound healing. It has been shown to alleviate STZ-induced diabetic neuropathy in rats by inhibiting inflammatory signals, restoring the antioxidant system and increasing nerve growth factor in the brain (12).

**Antiviral activity:**

Apoptosis is caused by viral infections that lead to depletion of lymphocytes in the host cell, and antioxidants can inhibit virus-induced apoptosis in addition to inhibiting viral replication in target cells, allowing antiviral effects and antioxidants to combine. To study the antiviral effect of NSO, murine cytomegalovirus (MCMV) was used as a model. Intraperitoneal administration of NSO to mice completely inhibited virus titers in spleen and liver by day 3 of infection.

In one study, the patient had hepatitis C virus (HCV) unsuitable for IFN- $\alpha$  therapy who received the NSO capsule (450 mg) for three consecutive months, three times a day, and the results showed that the viral load decreased significantly and the oxidative stress decreased due to the increased total antioxidant activity, total protein and albumin, red blood cell count and the Platelet count was improved in HCV patients. The increased red blood cell count can be attributed to a low Laugh The level of lipid peroxide in the membrane leads to a reduction in the frequency of hemolysis. It lowers blood glucose levels, suggesting that it may have a modulating effect on HCV-induced glucose intolerance, improvement in lower extremity edema has also been observed (7).

**Antischistosomiasis activity:**

Two weeks treatment with N. sativa oil (NSO) in mice that infected with *Schistosoma mansoni* results in diminish the quantity of Sch. Mansoni worms within the liver and conjointly reduced the entire number of ova deposited in each the liver and therefore the intestine. Moreover, it increased the number of dead ova in the enteric wall and clearly diminished the neoplasm diameters. The infected mice with Sch. Mansoni made a marked rising in the bodily fluid activity of L-alanine aminopherase (ALT), gamma-glutamyl transferase (GGT), with a coffee increase in base-forming enzyme (AP) level, whereas reduced albumin level.

The protection is also because of the flexibility of NSO and TQ to scale back the genetics injury caused by infection infection. The results of in vitro tests of N. sativa seeds against Sch. Mansoni, miracidia, cercariae, and adult worms show its sturdy results against all stages of the parasite and a repressive effect on giving birth of female person worms. Besides, N. sativa seeds evoked an aerophilous stress against adult worms that shown with diminish within the activities of glutathione reductase, inhibitor enzymes, glutathione peroxidase, enzyme and enzymes of aldohexose metabolism, glucose-6-phosphate dehydrogenase and hexokinase. Perturbing of those enzymes of adult worms' victimization N. sativa seeds may flip render the parasite susceptible to injury by the host and should play a task within the anti-schistosomal potency (13).

**Antihypertensive activity:**

Numerous antihypertensive drugs have been used clinically to control hypertension and alleviate comorbidities. However, the effectiveness of these agents is only given in 40-60% of hypertensive patients and usually consists of a combination of two or more antihypertensive agents. Classes are required to achieve desired results. This ultimately increases the likelihood of side effects and also increases the cost of therapy. A number of herbal products such as B. N. Seeds.

Sativa has been used and claimed to have beneficial effects against high blood pressure (BP). In addition, it was used to determine the blood pressure lowering potential and possible mechanisms of N. sativa in the rat model and it was found that the groups receiving seed oil and nicardipine showed significant reductions in blood pressure. The antihypertensive effect was associated with a reduction in cardiac lipid peroxidation product and angiotensin converting enzyme inhibitory activity in both groups but plasma nitric oxide levels were significantly increased when N. sativa oil was administered Than the groups receiving placebo and nicardipine. Black seed and its active ingredient thymoquinone have been shown to reduce oxidative stress by blocking calcium channels and increase urinary excretion activity, which may be associated with lowering blood pressure. Based on most of these reports, various N. sativa preparations have shown sustained reductions in blood pressure in animal models and therefore clinical trials can be explored as a promising basis for natural Antihypertensives (8).

**Cardiovascular activity:**

The acute effect (after 4 and 18 h) of diesel particulate matter (DEP) on cardiopulmonary parameters in mice and the protective effect of TQ were investigated. Mice were administered intratracheal saline (control) or DEP (30  $\mu$ g per mouse). There was pneumonia and loss of lung function 18 hours (but not 4 hours) after DEP administration. At both 4 and 18 h, DEP caused systemic inflammation characterized by leukocytosis, elevated IL-6 levels, and decreased blood pressure. The activity of SOD Was reduced by only 18 h.

DEP reduced platelet counts and aggravated thrombosis in the piatric arterioles in vivo. In vitro, the addition of DEP (0.1–1  $\mu$ g/mL) to untreated blood-induced platelet aggregation. Pretreatment of mice with TQ prevented DEP-induced decreases in systolic blood

pressure and leukocytosis, increased IL-6 concentration, and decreased plasma SOD activity. TQ also prevented platelet count decreases and prothrombotic events, but not platelet aggregation in vitro (14).

#### **Pulmonary protective activity and antiasthmatic effects:**

Wienkotter et al. reported the effect of Nigellone and TQ on the trachea (antispasmodic effect) and their influence on respiratory clearance. The ciliary action in the tracheal area was studied using a microdialysis technique. Nigellone and high concentrations of TQ had a concentration-dependent inhibitory effect on the trachea when contracted by the depolarizing effect of Ba<sup>2+</sup>.

Tracheal contractions induced by leukotriene-d (4) LT<sub>4</sub> were inhibited by Nigellone and by TQ. It was concluded that Nigellone has an antispasmodic effect and an increase in mucociliary clearance, but TQ has no such effects. Therefore, it is suggested that Nigellone, but not TQ, may be useful in treating various respiratory diseases. The possible beneficial effects of *N. sativa* L. seeds. Experimental lung damage was investigated in male Wistar rats after lung aspiration of various materials. Results showed that *N. sativa* treatment inhibited pulmonary inflammatory responses and significantly ( $P < 0.05$ ) reduced peribronchial inflammatory cell infiltration, alveolar septal infiltration and alveolar edema, alveolar exudate, alveolar macrophages, interstitial fibrosis, granuloma formation and necrosis in various models ( $P < 0.05$ ). of lung aspiration.

The data showed a significant reduction in inducible nitric oxide synthase activity and an increase in surfactant protein D in lung tissue from different lung aspiration models after *N. sativa* therapy. It was concluded that *N. sativa* treatment could be beneficial to patients and have potential clinical benefit. The beneficial effects of NSO were evaluated in rats with hyperoxia-induced lung injury, since oxygen-induced lung injury is believed to lead to the development of bronchopulmonary Dysplasia in preterm infants. NSO significantly reduced the severity of lung damage due to hyperoxia (1)

#### **Antiparasitic activity:**

The effects of *N. sativa* seeds on children naturally infected with tapeworm were studied. A single oral administration of 40 mg/kg ethanolic extract of *N. sativa* without side effects at the doses tested reduced the percentage of fecal eggs (69). 25 g/kg of methanolic extract of *N. Sativa* seeds (MENS) resulted in suppression of *Plasmodium yoelii* infection (94%,  $P < 0.05$ ), while chloroquine, the drug of choice, resulted in 86%. Therefore, MENS is more effective than chloroquine in treating *Plas. Yoelii* infection.

The antimalarial effect is due to the fact that MENS has an antioxidant effect in mice infected with *Plasmodium*, thereby improving the oxidative status in red blood cells and hepatocytes of infected mice (70). At 400 mg/kg aqueous suspensions and oily emulsions of *N. sativa* seeds for the treatment of coccidiosis in rabbits. Anticoccid effects were seen with both treatments, but the most rapid antiparasitic effect was seen with the *N. sativa* oil emulsion.

Both treatments increased weight gain and decreased fecal oocyst shedding, and liver tissue histopathology improved remarkably. Improvements included a significant reduction in inflammatory cell infiltration into the portal area, the various stages of parasites in the bile ducts were also reduced. And the bleeding between the liver lobes disappeared, the hepatocytes returned to their natural radial arrangement, and all severe symptoms disappeared. Deadly influence on parasites (7).

#### **Nephroprotective activity**

There are approximately 13.3 million cases of acute kidney injury (AKI) worldwide with an estimated annual incidence of 11.3 million in the developing world annually. Patients with AKI are at increased risk of developing chronic kidney disease (CKD) and vice versa. Therapeutic management of renal disease involves pharmacological treatment of pathological events that contribute to disease progression

Black cumin seeds, NSO and TQ, comparable to some other natural products, have shown therapeutic promise against kidney diseases. A growing body of literature suggests protective effects of black seed, particularly NSO, against a variety of chemical/drug/heavy metal/pesticide induced nephrotoxicity. For example, black seed mitigated the harmful effects of commonly prescribed cancer chemotherapy drugs like methotrexate and cisplatin.

In addition, oral administration of NSO protected renal tissue from oxidative stress and inflammation induced by sodium nitrite and CCl<sub>4</sub>. In addition, black seed pretreatment has a protective effect against reperfusion-induced kidney damage by inhibiting apoptosis and cell proliferation. Cumin may also improve nephrolithiasis and kidney damage, as well as kidney damage from unilateral ureteral obstruction (UUO). In addition, the supplementary intake of black cumin or the preparation NSO CKD is beneficial Patients. Together, black seed and TQ can be expected to be useful against a variety of kidney complications (12).

#### **Anti-inflammatory and Analgesic activity:**

In animal models, the aqueous extract of *N. sativa* has been found to have anti-inflammatory and analgesic but no antipyretic effects, while the anti-inflammatory effects of the alcoholic extracts of *N. sativa* seeds and their callus appear in rat glial cells mixed with its TQ content examined. Mixed glial cells inflamed by lipopolysaccharide were subjected to anti-inflammatory studies in the presence of varying amounts of TQ and alcoholic extracts. The results confirmed that TQ

The level of leaf callus was 12 times higher than that measured in the seed extract. Studies in pooled inflamed rat glial cells showed a significant reduction in nitric oxide production in the presence of 0.2 to 1.6 mg/ml callus extract. And 1.25 to 20 µl/ml of the seed extracts.

Osteoporosis has been linked to oxidative stress and inflammation. Studies have been conducted on the anti-osteoporotic effects of *N. sativa* and TQ. *N. sativa* and TQ have been shown to inhibit inflammatory cytokines such as interleukin-1 and 6 and the transcription factor nuclear factor κB. Both NS and TQ have shown potential as anti-osteoporosis agents. The antioxidant, anti-inflammatory, anti-cancer and anti-bacterial activities of methanolic extracts from *N. sativa* sprouts, roots and seeds were examined. The hexane fraction of the seeds of the methanol extract showed significant anti-inflammatory activity and inhibited nitric oxide

release with an IC<sub>50</sub> of 6.20 µg/mL in RAW 264.7 macrophages stimulated with lipopolysaccharide. The antiallergic effects of the *N. sativa* components could be attributed to allergic rhinitis. Also *N. Sativa* should be considered for the treatment of allergic rhinitis when it is necessary to avoid the effects of other antiallergic drugs (1).

#### Antimicrobial activity:

Antimicrobials have been the mainstay of clinical medicine since the second half of the 20<sup>th</sup> century and have saved significant numbers of people from serious microbial infections. However, in the late 20<sup>th</sup> century and early 21<sup>st</sup> century, the arrival and generalization of antimicrobial resistance in pathogenic microorganisms was perceived around the world. The growing horror of microbial infections and antimicrobial resistant bacteria requires a global struggle to discover novel solutions that can be based on natural products such as plants, chosen on the basis of recognized ethnomedical uses. Among the inspirational medicinal plants, black cumin is the one that has potent antibacterial, antifungal, antiviral, and antiparasitic effects (15).

#### Conclusion:

The use of herbal medicines as complementary medicine is widespread and gaining popularity around the world. Many medicines are derived directly from plants; while the others are chemically modified natural products. The original research articles published to date have demonstrated the pharmacological potential of *N. sativa* seeds, their oil and extracts, and some of their active ingredients, notably TQ and alpha-hederin, with remarkable in vitro and in vivo pharmacological activities against a wide range of Confirmed diseases and have been shown to be relatively safe

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