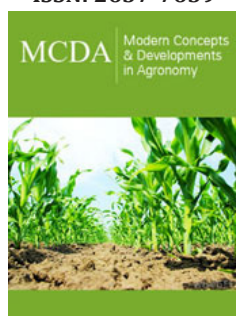


A Comprehensive Review on Medicinal Importance of *Nigella Sativa*

Ali Zeeshan*

Department of Biological Sciences, Pakistan

ISSN: 2637-7659



*Corresponding author: Ali Zeeshan,
Department of Biological Sciences,
University of Veterinary and Animal
Sciences Lahore Pakistan

Submission: 📅 November 18, 2024

Published: 📅 March 19, 2025

Volume 15 - Issue 1

How to cite this article: Ali Zeeshan*. A Comprehensive Review on Medicinal Importance of *Nigella Sativa*. Mod Concep Dev Agrono. 15(1). MCDA. 000854. 2025. DOI: [10.31031/MCDA.2025.15.000854](https://doi.org/10.31031/MCDA.2025.15.000854)

Copyright@ Ali Zeeshan. This article is distributed under the terms of the Creative Commons Attribution 4.0 International License, which permits unrestricted use and redistribution provided that the original author and source are credited.

Abstract

Background: Black seed, scientifically known as *Nigella sativa* and belonging to the family Ranunculaceae, has gained a reputation as a “miracle cure” due to its potential to alleviate various ailments and support the body’s self-healing processes.

Objectives: This review aims to discuss the medicinal importance *Nigella sativa*.

Results: It plays an important role in anti-cancer and anti-tumor activities, helps to prevent pancreatic and hepatic cancer and cervical cancer due to its TQ property. *Nigella sativa* also has antioxidant property due to which it plays an important role allergic and immunological reactions. *Nigella sativa* also acts for immuno-pathogenesis of asthma. It also has anti-fungal, anti-microbial and anti-bacterial activity due to various elements like Thymoquinone (TQ), present in different quantities in it. *N. sativa* is also used in many folk remedies. It also helps to maintain blood pressure, helps to balance lipid profile and also have role in hypoglycemic mechanisms. Identifying knowledge gaps, our current effort will direct future research to advance potential applications of *Nigella sativa* in health and diseases.

Keywords: *Nigella sativa*; Anti-fungal; Anti-microbial; Hypoglycemic

Introduction

Black seed (*Nigella sativa*) is also referred to as a plant that blooms every year in the Ranunculaceae family. Southeast Asia, the coast of the North Sea area, and western and southern Europe are home to the bulk of black seeds. The black seed is also known as “salvation black kernel” in the word of God, Melanthion by Aristotle and Discroides, and Gith by Paul the Elder [1] (Figure 1). Pakistan generates 40.29million metric tons of refined seed, though the world consumption is 607.3million metric tons [2]. The extract of *N. sativa* has been indicated to be highly beneficial in the treatment of a range of health conditions, depending on the Unani-Tibb healing system. *N. sativa* has been historically used in many civilizations throughout the entire globe throughout the beginning of time, and it is known as a “miracle cure” because of its capacity to cure a variety of maladies and regulate the process of self-healing in the human body [3]. In Indian medicine, the seeds serve as a sour, a parasitic agent sharp, pigmentation, stimulant in nature, sporadic high temperature, diuretic medication, paralytic, emmenagogue, stakes, dermatological issues, and indigestion treatment [4,5]. They have suppressive-cancer, xenophobic-diabetic, suppressive-bacterial, known to inhibit-parasitic, suppressive-fungal, and cytotoxic-parasitic properties, as well as therapeutic value. Black seeds are used immediately as a therapeutic compound in traditional medicines or as tea with herbs. Black seed extracts have antioxidant and anti-inflammatory qualities. Patients have used it to treat sneeze dissolving stones in the kidneys, halt the carcinogenic process, relieve stomach discomfort, diarrhea, gas, and polio, and it has choleric and uricosuric qualities [4,6]. *N. sativa* is utilized in both conventional and Unani medicinal products in Pakistan. According to previous research, *N. sativa* is a plant that has great potential for sickness repair as well as wellness augmentation; yet additional study will be required to transition botanical therapeutic civilization into fresh medicine systems. Nigellon is a thymoquinone-derived

carbonyl polymer. The oil and active components of *N. sativa* seeds have antiviral, antiseptic in nature blood sugar reducing, cancer-preventing, suppressive-oxidation, neuromuscular relaxing, and inflammatory properties [7-9]. Numerous biological compounds have been historically determined in *Nigella sativa* species [10]. *N. sativa* is an annual herbaceous plant in the Ranunculaceae family that is widely farmed in many countries of southern Europe as well as a few locations of Asia, including Saudi Arabia, Pakistan, Syria, India, and Turkey [11]. Its blooms are generally white, pink, yellow, light blue, or lavender in color, with 6-10 petals. The fruit of the plant is a bulky and balloon-like capsule containing numerous black seeds with a bitter and pungent flavor. *N. sativa* grows throughout November and April each year, and its sprouting phase lasts two

weeks following seed sowing. Nevertheless, the berries are typically harvested from vines between January and April [12]. *N. sativa* seeds have oil, and its medicinal properties were previously used to cool and flavor a variety of meals [13]. *N. sativa* seeds contain 28-36% fixed oil, which contains a variety of unsaturated fats, such as linolenic, arachidonic, linoleic, and eicosadienoic acids. Myristic, stearic, and palmitic acids are examples of saturated fatty acids [14]. This crude oil has a protective impact, primarily on cells in the brain [15] in the hepatocytes [16]. *N. sativa* crude oil has just a trace of oil that is volatile and displays functional properties due to thymoquinone, as well as other biological activities. In addition to its modest toxicity, this petroleum product is frequently utilized in nutritional supplements [17] (Figure 2).

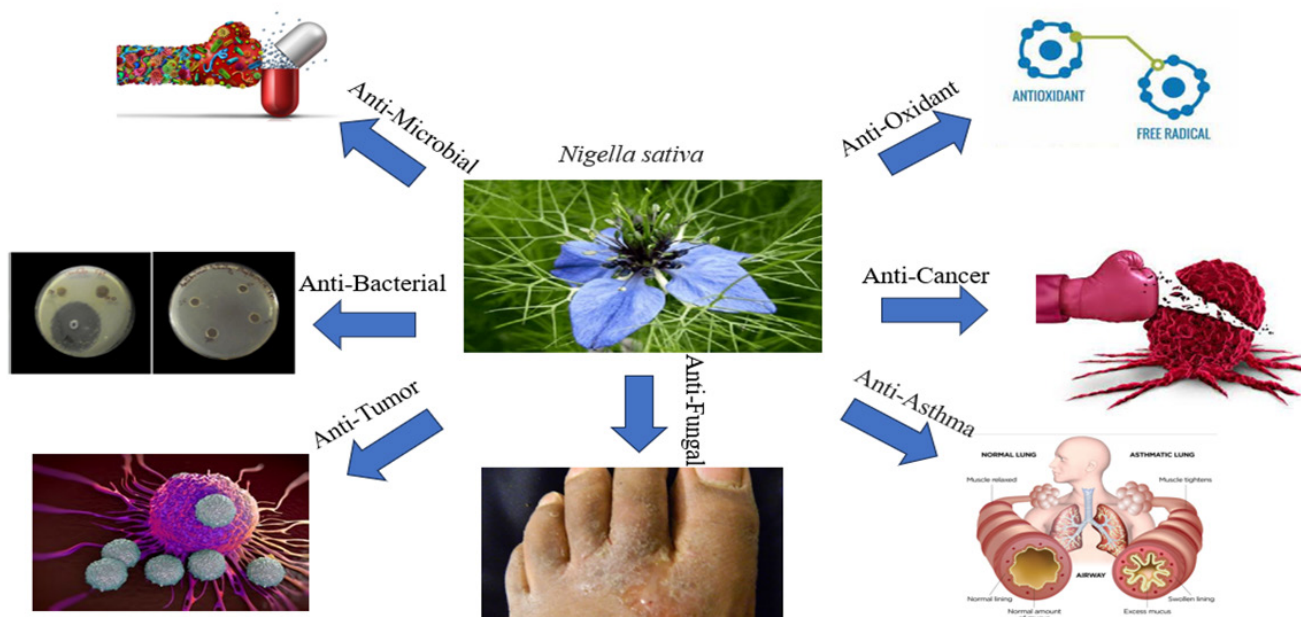


Figure 1: Graphical abstract.

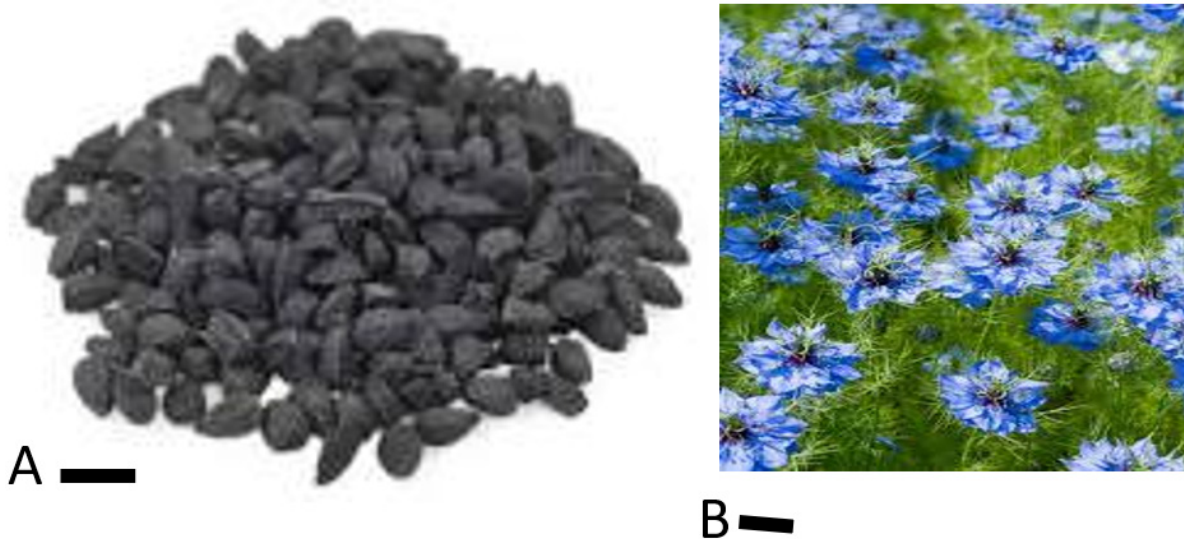


Figure 2: A) *Nigella sativa* seeds B) *Nigella sativa* plant.

Anti-Cancer and Anti-Tumour Activities

The molecular compound Thymoquinone (TQ) can be identified in black seed vital oil and has been believed to be vital for many of the seed's therapeutic effects [18]. TQ is recognized for its capacity to inhibit the degradation of lipids and neutralize free radicals. Similarly, combination of TQ with ifosfamide raises the indication of treatment effectiveness and protects non-malignant tissues from the harm induced by chemotherapy [19]. Investigators encountered the therapeutic effects of TQ in safeguarding the wellness of humans and combating malignancy using biological sequence alteration. As a result, compounds which prompt carcinoma cells to die may lead to successful therapies for cancer in the future [20]. TQ has been proven to be efficacious across a wide range of multidrug-resistant human cancer cells and to aid in the suppression and stimulation of necrosis in cancer cells. The research investigation showed that TQ could potentially be administered as a nutritional product to enhance the potency of other anti-cancer drugs. A clinical trial integrating TQ with anti-cancer drugs might reduce side effects and increase therapeutic efficacy [19]. *N. sativa* has an array of other active compounds that help to prevent neoplasia in addition to thymoquinone. Alkaloids, also peptides, essential as well as vital fats, and tannin are a few categories. Previous study determined the precise mechanism whereby *N. sativa* volatile crude oil blocks development of cancer [21]. One plausible explanation of TQ's chemo preventive effects, anti-inflammatory and antioxidant qualities as well as its elimination technologies improvement [19].

Pancreatic cancer

TQ from *N. sativa* oil extract promoted apoptosis and reduced the proliferation of PDA (Pancreatic Ductal Adenocarcinoma) cells, as demonstrated [22]. It was previously shown to have cancer prevention activities among human hepatic cancer, endometrial a cancerous tumor, Edwards's peritoneal tumors, and the work of Dalton diarrhea, leukemia or with typical lymphocytes illustrating barely any mortality [18].

Hepatic cancer

It is discovered that swallowing TQ greatly improved the purpose of Quinone aminotransferase and cysteine transferase, presenting a possible preventive approach for the development of tumors and severity in liver carcinoma [23].

Cervical cancer

Based on infections with HPV are the underlying an etiology of all carcinogenic malignancies, with varieties of HPV 16 and 18 contributing to around 70% of all genital cinomas. TQ drastically decreases the lifespan of Siha cells, C33A, and several HPV-positive lineages of cells [24].

Antioxidant Activity

Numerous studies have linked the antioxidant value of *N. sativa* to its fascist-allergic and immunomodulatory actions. Multiple studies inquiries have revealed that unstable oxygen radicals have a role in immunological and antimicrobial properties [25].

Nutritional deterioration is caused by the formation of Reactive Oxygen Species (ROS), who additionally alter the structure and activity of biomolecules such as DNA, dietary fiber, peptides, and fatty substances [26]. In contradiction to preventative defensive mechanisms which include the enzyme catalase gsh-s-transferase (GST), the enzyme super oxide dismutase, glucose peroxidase, and superoxide dismutase (GPx), oxidative damage results in the synthesis of a large number of reactive oxygen species. Antivirus protecting the functioning of cells from the harmful impacts of volatile oxygen as well as nitrogen oxides. Antibodies perform an integral part as ROS investigators. It can be synthesized alternatively locally or intentionally by cells. The antioxidant abilities of *N. sativa* essence are owed to the presence of chemical compounds that include carvacrol in sulfuric acid, and several [27]. Further, TQ and black seed enhanced diets enhance simultaneously physiological (SOD, CAT, GPX, and GST) and free of enzymes (GSH and ascorbic acid) antioxidant capacities. Medication with *N. sativa* elevated haemoglobin concentrations in red blood cells besides possessing an adequate anti-oxidative armour towards reactive nitrogen species and oxygen and hampering neutrophil proliferation in the brain and spinal cord [28]. Superoxide, peroxide from hydrogen, and numerous other exceptionally reactive molecules made up of nitrogen are inhibited by *N. sativa* [29]. The breakdown of parts of the matrix by physiological reactive oxygen species via activation of latent collagen enzymes has been scientifically associated to articular Radicals and rheumatism [30]. Malondialdehyde and the Thiobarbituric Acid Responding Material (TBARS) are oxidative lipid crayons. Multipurpose oxidation of fatty acids develops throughout an assortment of cascade processes that ultimately result in barrier rupture. The robust antioxidant qualities of *N. sativa* mitigated ROS emergence, which in turn diminished the breakdown of lipids [31,32]. Moreover, *N. sativa* suppressed MDA levels in the mouse brain's activity, lymph nodes, liver, and serum in the blood [33,34,28].

Immunopathogenesiso Asthma and Dietary Intervention

Difficulty in breathing, an ongoing aggressive ailment of the bronchial arrangement, are triggered by an accumulation of periodically adjusting inflammatory mediators, cells that are inflammatory (mast tissue cells, plasma cell lymphocytes, etc.), and overproduction of mucus formation. According to worldwide asthmatic estimations, over 300 million people worldwide are affected, with more than 100 million at risk by the conclusion of 2025 [35]. Asthma affects people of every generation. Glucocorticosteroids are often prescribed for treating respiratory conditions, disregarding being aware that they have unidentified negative consequences such as deficient bone metabolism, slower expansion, and pituitary protection [36]. In addition, some with allergies reacted harshly or significantly to medication with steroids [37]. As an outcome, initiatives are underway towards creating specific, secure and suppressive-asthmatic pharmaceuticals that utilize naturally occurring substances. In accordance with study, certain naturally appearing seed varieties, especially the famous

N. sativa, have a substantial impact on decreasing the seriousness of bronchitis [38,39]. Asthma is triggered by an assortment of cell connections, inflammatory disorders, completely impervious-boosting drugs, and other factors. Cells in the mast dendritic cells, with the goal of T helper cells (especially Th1, Th2, and Th9 cells), B cells, lymphocytes, lymphoid stem cells eosinophils, and neutrophils basophils, phagocytes, and epithelial cells constituted the key immune cells that were associated with lung disease-related irritation [38,39]. They also have an importance in the fundamental reasons of respiratory and lung damage in the emergence of asthma. Actually, the cells contribute considerably to the onset of severe asthmatic bronchitis by releasing cytokines [40,41]. The study's findings supported the notion that cytokine multiplication is the main mediator of the activity during inflammation. The primary cytokines generating influenza have been determined as pro-inflammatory mediators manufactured by the cells, such as IL-4, IL-5, and IL-13, as well as IFN- and IL-6 (cytokines emitted by Th1 cells) [42,43]. Unexpectedly, each person's blood has a high level of fall dramatically, that contributed to the documented recovery. It's important to remember because [44] additionally described a double-blind study standardized investigation which includes individuals with asthma, which revealed a transient pulmonary effect after receiving just a single dosage of *N. sativa* (50mg/kg) [44].

Effect of black seed (*N. sativa*) on immunomodulation

Nigella sativa is a plant that has played an important part in immune response strengthening and ailments therapies, especially irritation of the skin, autoimmune diseases, allergic rhinitis, thyroiditis caused by Hashimoto's, and others. Drug sensitivity and leftover immunomodulatory agents such as lenalidomide, antibiotics, pomalidomide, thalidomide have become prevalent when administered combat infectious agents. On the contrary, herbal medicine may be favorable than conventional medicinal products. *N. sativa* kernels and their purified biologically active elements are frequently utilized to treat and prevent a wide range of illnesses related to the immune system. *N. sativa* exhibits the ability to boost cellular immunity via T lymphocytes, which are associated with immune response [45]. In a Streptozotocin-induced diabetes with a type 1 diagnosis rat framework, the oil extracted from *N. sativa* minimized the concentration of militant-islet cell immune system antibodies as well as the main antibody molecules produced in the autoimmune conditions procedure, resulting in a substantial decrease in the amount of immunological barriers indications Pan B-lymphocytes (CD19), Pan innate cells (CD 1 lb), and Pan T-lymphocytes (CD90). According to Hmza AJ et al. [46] *N. sativa* oil stimulates elderly immunologic sensitivity and T responder cell generation [47]. In a mouse model, *N. sativa* significantly raised the total (leukocyte) frequency and the amount of hemoglobin generated by doxorubicin while also increasing T-lymphocyte cell development. A study realised that the extract of *N. sativa* decreases the number of militant-islet cell immunoglobulins which are also the main antigens produced in the autoimmune illnesses manipulate, and leads to an impressive

decrease of immune-mediated indications Pan B-lymphocytes (CD19), Pan innate cells (CD 1 lb), and Pan T-lymphocytes (CD90) in a Streptozotocin-induced diabetic rat framework [46]. It is observed that *N. sativa* oil enhances ageing immunologic protection and T lymphocyte cell generation [47]. In an animal study, *N. sativa* significantly boosted the total (leukocyte) frequency and haemoglobin concentrations caused by cisplatin, while likewise boosting T-lymphocyte cell development [48,49]. This is comparable to a research investigation that discovered *N. sativa* promotes total erythrocyte and anemia content in an irinotecan-induced mice model. Therefore, the mentioned seed boosted T-lymphocyte cells (cluster of differentiation 3), helper T-lymphocyte cells (cluster of differentiation 4), and repressor to harmful T lymphocyte cells (cluster of differentiation 8) [50]. It is concluded that individuals that acquired hypersensitivity reaction-specific immunotherapy, which is in conjunction with *N. sativa* (2g/day) utilization along with vaccinations made more improvements (polymorph-nuclear erythrocyte acts (PMNs) and group of proliferation 8 (CD8 counts) than individuals to which obtained solely the immune system for the duration of two months. He concluded that treatment with *N. sativa* gave rise to greater efficacy chemotherapy [51].

Antimicrobial Activity

Antibiotics serve as the backbone for medical practice throughout the latter half of the 20th century, sparing numerous individuals from major bacterial infections. Nevertheless, during the late twentieth and early twenty-first century, antimicrobial resistance in harmful microbes slowly started to emerge internationally [52,53]. The growing fear of pathogenic infections and antibiotic-resistant microbes needs a worldwide search for imaginative therapies that may be centered on natural commodities including vegetation whose are selected depending on well-known ethnomedicinal usage. Black cummin is one of the most inspiring therapeutic plants, with antiviral, antibacterial, antifungal, and antiparasitic qualities [54,55].

Antibacterial Activities

In besides hindering lactic acid biofilm formation, thalidomide obtained from *N. sativa* seeds revealed wider spectrum endeavors contrary to a variety of bacterial genera, which includes *Pseudomonas*, *Escherichia Bacillus*, *Enterococcus*, *Staphylococcus*, *Pseudomonas*, *Listeria*, *Serovar*, and *Vibrio parahaemolyticus* and *Micrococcus* [56]. The dimethyl alcohol obtained from the inside of the seed significantly reduced larger gram-positive microorganisms (*S. pyogenes*) versus gram-negative bacteria (*P. aeruginosa*, bacteria such as *K. pneumoniae*, and *P. vulgaris*) [57]. Different quantities for *N. sativa* hydrocarbons (100%, 80%, 50%, 40%, 30%, and 20%) prevented each of the microbial isolates investigated towards products which are produced-resistant *S. aureus* isolates [58]. Thymoquinone displayed significant bactericidal properties towards gram-negative bacteria, exhibiting MICs spanning 8 to 32g/mL, and creating the cheapest inhibitors of biofilm concentrations both *S. aureus* and *S. epidermidis*, at 22 and 60g/mL, accordingly [59]. Additionally, black seed (2g/day) demonstrated a known

effectiveness to inhibit *H. pylori* effect equivalent to triple medical care. This establishes an excellent basis for additional investigation into the potential uses of this unique seed for the treatment of *H. pylori* latent infection-induced ulcers in the stool [60].

Antifungal Activity

It was recently proven that the vital oil of *N. sativa* with various origins has considerable protective properties towards pathogenic bacteria, dermatological fungi and non dermatophytic filamentous fungal organisms, along with mycotoxins-producing microorganisms. The *N. sativa* treatments addressed the cell's inner wall, the membrane of the plasma cell, and membranous organelles that are present especially in the nucleus and mitochondria, considering the physical appearance of these toxigenic fungi [61]. Besides, black cumin and TQ extracts show substantial fungicidal action contrary to dermatophyte isolates which include *Trichophyton mentagrophytes* and *Microsporum gypseum*, being superior to fluconazole but not as effective as ketoconazole [62].

When contrasted with Amphotericin-B, Thymoquinone hindered the proliferation of *Fusarium olani* and *Aspergillus niger* or was beneficial regarding the colonies of *Candida albicans*, yeast *tropicalis*, and *Candida krusei* [63,64] researched the constituents of *Nigella sativa* such as thymo, TQ, and thymo hydro-quinone and discovered that the ingredient of black cumin exhibited antifungal activity against yeast, dermatophytes, and molds. *N. sativa* has antimicrobial properties and can help preserve food from spoiling (Table 1) [65-71].

Table 1: Some traditional uses of *Nigella sativa* seeds.

Traditional Use	Country	References
Curative effects in bacterial-caused diseases, sexual tonic, to manage lactation and to decrease mental disturbances	Pakistan	[65,66]
To ease bowel and indigestion problems and to manage diabetes	India	[67,68]
To treat lung, brain and skin	Palestine	[69]
To manage pain during menstruation and diabetes	Bangladesh	[70]
Hypoglycemic and hypotensive agent	Algeria	[71]

Future Perspectives

The mechanisms by which *N. sativa* seeds and their contents exert their therapeutic benefits must be studied in more detail. Future research on the molecular structure of TQ, alpha-hederin, and other components of *N. sativa* seeds may result in the development of more potent and secure medications for the treatment of a wide range of ailments. For a successful treatment of numerous infectious illnesses and to circumvent the resistance issue, *N. sativa* seeds, its oil, and components such as TQ, alpha-hederin, or others might be utilised in appropriate combinations with currently available chemotherapeutic drugs. Additionally, additional studies should concentrate on and investigate the precise cellular and molecular targets of numerous *N. sativa* components, including TQ. This review article is dedicated to all researchers

interested in concentrating their research on this wonder plant. It is our hope that this review article will assist researchers in their investigation and further preclinical and clinical studies on the use of *N. sativa* for the treatment of a variety of diseases.

Conclusion

Nigella sativa is a versatile plant with a wide range of potential health benefits. Its seeds are rich in Thymoquinone (TQ), a molecular compound with potent antioxidant and anti-inflammatory properties. Research has shown that TQ has the potential to prevent tumor development and reduce the proliferation of cancer cells. Additionally, *N. sativa* has been found to strengthen immune response, combat pathogenic bacteria and fungi, and lower blood pressure and cholesterol levels. Its potential therapeutic uses include the treatment of skin inflammation, autoimmune diseases, and Hashimoto's thyroiditis. *N. sativa* is also commonly used as a seasoning in various food preparations. However, further research is needed to fully understand the plant's medicinal properties and potential side effects. *Nigella sativa*, also known as black seed, is an annual herbaceous plant that is widely cultivated in many countries of southern Europe and Asia. Its fruit contains numerous black seeds that are rich in thymoquinone (TQ), a molecular compound that has been linked to many of the seed's therapeutic effects. *N. sativa* has been shown to be highly beneficial in the treatment of a range of health conditions and has been referred to as a "miracle cure." The plant possesses immunological and antimicrobial properties and has been proven to inhibit the growth of pathogenic bacteria, dermatological fungi, and non-dermatophytic filamentous fungal organisms. *N. sativa* is also used as a flavouring ingredient and seasoning in various food preparations. It has been shown to lower blood pressure, reduce cholesterol levels, and improve glucose balance, making it an effective therapeutic agent for diabetes management. Furthermore, studies have indicated that *N. sativa* extract could potentially be a preventive approach for the development of tumors and severity in liver carcinoma. *In vitro* studies have also demonstrated that *N. sativa* extract could decrease the electrogenic gastrointestinal absorption of glucose. Overall, *N. sativa* is a promising therapeutic plant with a wide range of potential health benefits.

References

- Huchchannanavar S, Yogesh LN, Prashant SM (2019) The black seed *Nigella sativa*: A wonder seed. *Int J Chem Stud* 7(3): 1320-1324.
- Sands RD, Suttles SA (2022) World agricultural baseline scenarios through 2050. *Appl Econ Perspect Policy*.
- Goreja WG (2003) Black seed. *Nature's Miracle Remedy*; Karger Publishers, Basel, Switzerland.
- Ahmad, Tripathi J, Manik S, Umar L, Rabia J (2013) Preliminary phytochemical studies of the miracle herb of the century, *Nigella sativa* L. (black seed). *Indo American J Pharma Res* 3(4): 3000-3007.
- Warrier PK, Nambiar VPK, Ramankutty C (2004) *Indian medicinal plants: A Compendium of 500 Species*; Orient Blackswan: Hyderabad, India, p. 4.
- Al-Khalaf MI, Ramadan KS (2013) Antimicrobial and anticancer activity of *Nigella sativa* oil-a review. *Aus J Basic Appl Sci* 7(7): 505-514.

7. Salem M (2005) Immunomodulatory and therapeutic properties of the *Nigella sativa* L. seed. *J Int Immunopharmacol* 5(13-14): 1749-1770.
8. Ojueromi OO, Obboh G, Ademosun AO (2022) Effect of black seeds (*Nigella sativa*) on inflammatory and immunomodulatory markers in Plasmodium berghei-infected mice. *J Food Biochem* 46(11): e14300.
9. Janfaza S, Janfaza E (2001) The study of pharmacologic and medicinal valuation of thymoquinone of oil of *Nigella sativa* in the treatment of diseases. *Ann Biol Res* 3(4):1953-1957.
10. Ahmad I, Tripathi J, Sharma M (2014) *Nigella sativa*-A medicinal herb with immense therapeutic potential (A Systematic Review). *Int J Biol Pharm Res* 5: 755-762.
11. Rajsekhar S, Kuldeep B (2011) Pharmacognosy and pharmacology of *Nigella sativa*-A review. *Int Res J Pharm* 2(11): 36-39.
12. Paarakh PM (2010) *Nigella sativa* Linn. A comprehensive review. *Indian J Nat Prod Resour* 1(4): 409-429.
13. Burdock GA (2022) Assessment of black cumin (*Nigella sativa*) as a food ingredient and putative therapeutic agent. *Regul Toxicol Pharmacol* 128:105088.
14. Hajhashemi V, Ghannadi A, Jafarabadi H (2004) Black cumin seed essential oil, as a potent analgesic and anti-inflammatory drug. *Phytother Res* 18(3): 195-199.
15. Hobbenaghi R, Javanbakht J, Sadeghzadeh SH, Kheradmand D, Abdi F, et al. (2014) Neuroprotective effects of *Nigella sativa* extract on cell death in hippocampal neurons following experimental global cerebral ischemia-reperfusion injury in rats. *J Neuro Sci* 337(1-2): 74-79.
16. Develi S, Evran B, Kalaz E, Koçak-Toker N, Erata G (2014) Protective effect of *Nigella sativa* oil against binge ethanol-induced oxidative stress and liver injury in rats. *Chin J Nat Med* 12(7): 495-499.
17. Sultan M, Butt M, Karim R, Ahmad A, Suleria H, et al. (2014) Toxicological and safety evaluation of *Nigella sativa* lipid and volatile fractions in streptozotocin induced diabetes mellitus. *Asian Pac J Trop Dis* 4(Suppl 2): S693-S697.
18. Muhtasib GH, Diab AM, Boltze C, Hmaira JA, Hartig R, et al. (2004) Thymoquin-one extracted from black seed triggers apoptotic cell death in human colorectal cancer cells *via* a p53- dependent mechanism. *International Journal of Oncology* 25(4): 857-866.
19. Edris AE (2009) Anti-cancer properties of *Nigella spp.* essential oils and their major constituents, thymoquinone and β -elemene. *Curr Clin Pharm* 4(1): 43-46.
20. Kus G, Ozkurt M, Kabadere S, Erkasap NG, Goger G, et al. (2022) Antiproliferative & antiapoptotic effect of thymoquinone on cancer cells *in vitro*. *Bratisl Lek Listy* 119(5): 312-316.
21. Rahmani AH, Aly SM (2015) *Nigella sativa* and its active constituent's thymoquinone show pivotal role in the diseases prevention and treatment. *Asian J Pharm Clin Res* 8(1): 48-53.
22. Chehl N, Chipitsyna G, Gong Q, Yeo CJ, Arafat HA (2009) Anti-inflammatory effects of the *Nigella sativa* seed extract, thymoquinone, in pancreatic cancer cells. *Hpb* 11(5):373-381.
23. Nagi MN, Almakki HA (2009) Thymoquinone supplementation induces quinone reductase and glutathione transferase in mice liver: possible role in protection against chemical carcinogenesis and toxicity. *Phytotherapy Research: An International Journal Devoted to Pharmacological and Toxicological Evaluation of Natural Product Derivatives* 23(9):1295-1298.
24. Ichwan SJ, Al-Ani IM, Bilal HG, Suriyah WH, Taher M, et al. (2014) Apoptotic activities of thymoquinone, an active ingredient of black seed (*Nigella sativa*), in cervical cancer cell lines. *Chin J Physiol* 57(5): 249-55.
25. Islam MN, Hossain KS, Sarker PP, Ferdous J, Hannan MA, et al. (2021) Revisiting pharmacological potentials of *Nigella sativa* seed: a promising option for COVID-19 prevention and cure. *Phytother Res* 35(3): 1329-1344.
26. Yousefi M, Adineh H, Reverter M, Hamidi MK, Vatnikov YA, et al. (2021) Protective effects of black seed (*Nigella sativa*) diet supplementation in common carp (*Cyprinus carpio*) against immune depression, oxidative stress and metabolism dysfunction induced by glyphosate. *Fish Shellf Immunol* 109: 12-19.
27. Feng Y, Dunshea FR, Suleria HA (2020) Lc-esi-qtof/ms characterization of bioactive compounds from black spices and their potential antioxidant activities. *J Food Sci Technol* 57(12):4671-4687.
28. Majdalawieh AF, Fayyad MW (2015) Immunomodulatory and anti-inflammatory action of *Nigella sativa* and thymoquinone: a comprehensive review. *Intl Immunopharmacol* 28(1):295-304.
29. Gius D, Spitz DR (2006) Redox signaling in cancer biology. *Antioxid Redox Signal* 8(7-8): 1249-1252.
30. Luchian I, Goriuc A, Sandu D, Covasa M (2022) The role of matrix metalloproteinases (MMP-8, MMP-9, MMP-13) in periodontal and peri-implant pathological processes. *International Journal of Molecular Sciences* 23(3): 1806.
31. Burits M, Bucar F (2000) Antioxidant activity of *Nigella sativa* essential oil. *Phytother Res* 14(5): 323328.
32. Al-Majed AA, Al-Omar FA, Nagi MN (2006) Neuroprotective effects of thymoquinone against transient forebrain ischemia in the rat hippocampus. *Eur J Pharmacol* 543(1-3): 40-47.
33. Perera WPRT, Liyanage JA, Dissanayake KGC, Chandrasiri WAL, Gunathilaka H (2021) A review on pharmacological activities and antimicrobial properties of *Nigella sativa* and isolated Thymoquinone. *J Med Plants* 9(3):118-122.
34. Ardiana M, Pikir B, Santoso A, Hermawan H, Al-Farabi MJ (2020) Effect of *Nigella sativa* supplementation on oxidative stress and antioxidant parameters: a meta-analysis of randomized controlled trials. *Sci World J* 2020: 2390706.
35. Afzal S, Ramzan K, Ullah S, Jamal A, Basit S, et al. (2022) Association between 17q21 variants and asthma predisposition in pashtun population from Pakistan. *J Asthma* 60(1): 63-75.
36. Ora J, Calzetta L, Matera MG, Cazzola M, Rogliani P (2020) Advances with glucocorticoids in the treatment of asthma: state of the art. *Expert Opin Pharmacother* 21(18): 2305-2316.
37. Henderson I, Caiazzo E, McSharry C, Guzik TJ, Maffia P (2020) Why do some asthma patients respond poorly to glucocorticoid therapy? *Pharm Res* 160: 10189.
38. Koshak AE, Yousif NM, Fiebich BL, Koshak EA, Heinrich M (2018) Comparative immunomodulatory activity of *Nigella sativa* L. preparations on proinflammatory mediators: a focus on asthma. *Front Pharmacol* 9: 1075.
39. Ikhsan M, Hiedayati N, Maeyama K, Nurwidya F (2018) *Nigella sativa* as an anti-inflammatory agent in asthma. *BMC Res Notes* 11(1): 744.
40. Chang JH, Chuang HC, Hsiao G, Hou TY, Wang CC, et al. (2022) Acteoside exerts immunomodulatory effects on dendritic cells *via* aryl hydrocarbon receptor activation and ameliorates Th2-mediated allergic asthma by inducing Foxp3⁺ regulatory T cells. *Intl Immunopharmacol* 106: 10860.
41. Chen X, Bi M, Yang J, Cai J, Zhang H, et al. (2022) Cadmium exposure triggers oxidative stress, necroptosis, Th1/Th2 imbalance and promotes inflammation through the TNF- α /NF- κ B pathway in swine small intestine. *J Haz Mater* 421:126704.
42. Koshak A, Wei L, Koshak E, Wali S, Alamoudi O et al. (2017) *Nigella sativa* supplementation improves asthma control and biomarkers: a randomized, double blind, placebo-controlled trial. *Phytotherap Res* 31(3): 403-409.

43. Beasley R, Harper J, Bird G, Maijers I, Weatherall M, et al. (2019) Inhaled corticosteroid therapy in adult asthma. Time for a new therapeutic dose terminology. *Am J Respir Crit Care Med* 199(12): 1471-1477.
44. Boskabady MH, Mohsenpoor N, Takaloo L (2010) Antiasthmatic effect of *Nigella sativa* in airways of asthmatic patients. *Phytomed* 17(10): 707-713.
45. Salem M (2005) Immunomodulatory and therapeutic properties of the *Nigella sativa* L. seed. *J Int Immunopharmacol* 5(13-14): 1749-1770.
46. Hmza AJ, Osman MT, Adnan A, Omar E (2013) Immunomodulatory effect of *Nigella sativa* oil in the disease process of type 1 diabetic rats. *Res J Pharm Biol Chem Sci* 4(1): 980-988.
47. Paarakh PM (2010) *Nigella sativa* Linn. A comprehensive review. *Indian J Natl Prod* 1(4): 409-429.
48. Tutuncu S (2020) Black Seed (*Nigella sativa*) and immunomodulatory effect. *IJVAR* 3(1): 6-9.
49. Rahmani AH, Aly SM (2015) *Nigella sativa* and its active constituents thymoquinone shows pivotal role in the diseases prevention and treatment. *Asian J Pharm Clin Res* 8(1): 48-53.
50. Mills S, Bone K (2010) Principles and practice of phytotherapy. Modern herbal medicine, Churchill Livingstone, London, UK.
51. Alsamarai S, Adams JM, Murphy MK, Post MD, Hayden DL, et al. (2009) Criteria for polycystic ovarian morphology in polycystic ovary syndrome as a function of age. *J Clin Endocrinol Metabol* 94(12): 4961-4970.
52. Ventola LC (2015) The antibiotic resistance crisis: causes and threats. *Pharm and Therap* 40(4): 277-283.
53. Lee CR, Cho IH, Jeong BC, Lee SH (2013) Strategies to minimize antibiotic resistance. *Int J Environ Res Public Health* 10(9): 4274-4305.
54. Theuretzbacher U (2012) Accelerating resistance, inadequate antibacterial drug pipelines and international responses. *Int J Antimicrob Agents* 39(4): 295-299.
55. Andrade PHM, Schmidt Rondon E, Carollo CA, et al. (2015) Effect of powdered shells of the snail *Megalobulimus lopesi* on secondary-intention wound healing in an animal model. *Evid Based Complement Alternat Med* 2015: 120785.
56. Abdallah EM (2017) Black Seed (*Nigella sativa*) as antimicrobial drug: a mini-review. *Novel Approches in Drug Designing and Develop* 3(2): 1-5.
57. Hasan NA, Nawahwi MZ, Malek HA (2013) Antimicrobial activity of *Nigella sativa* seed extract. *Sains Malaysiana* 42(2): 143-147.
58. Maryam AJ, Fatimah AA, Ebtasam AK, Abdulrahman AS, Ineta BEL (2016) In-vitro studies on the effect of *Nigella sativa* Linn. Seed oil extract on Multidrug Resistant Gram positive and Gram-negative bacteria. *J Med Plants* 4(2): 195-199.
59. Chaieb K, Kouidhi B, Jrah H, Mahdouani K, Bakhrouf A (2011) Antibacterial activity of thymoquinone, an active principle of *Nigella sativa* and its potency to prevent bacterial biofilm formation. *BMC Comp Alt Med* 1(29).
60. Salem EM, Yar T, Bamosa AO, Quorain AA, Yasawy M, et al. (2010) Comparative study of *Nigella sativa* and triple therapy in eradication of *Helicobacter Pylori* in patients with non-ulcer dyspepsia. *Saudi J Gastroentero* 16(3): 207-214.
61. Shokri H (2016) A review on the inhibitory potential of *Nigella sativa* against pathogenic and toxigenic fungi. *Avicenna J Phytomed* 6(1): 21-33.
62. Mahmoudy and H, Sepahvand A, Jahanbakhsh S, Ezatpour B, Mousavi SAA (2014) Evaluation of antifungal activities of the essential oil and various extracts of *Nigella sativa* and its main component, thymoquinone against pathogenic dermatophyte strains. *J Med Mycol* 24(4): e155-e161.
63. Piras, Rosa AA, Marongiu B, Porcedda S, Falconieri D, et al. (2013) Chemical composition and *in vitro* bioactivity of the volatile and fixed oils of *Nigella sativa* L. extracted by supercritical carbon dioxide. *Ind Crops and Prod* 46: 317-323.
64. Taha M, Azeiz A, Saudi W (2010) Antifungal effect of thymol, thymoquinone and thymo hydro quinone against yeasts, dermatophytes and non-dermatophyte molds isolated from skin and nails fungal infections. *Egypt J Biochem Mol Bio* 28(2).
65. Khan N, Abbasi, AM, Dastagir G, Nazir A, Shah GM, et al. (2014) Ethnobotanical and antimicrobial study of some selected medicinal plants used in Khyber Pakhtunkhwa (KPK) as a potential source to cure infectious diseases. *BMC Complement Altern Med* 14: 122.
66. Aziz MA, Khan AH, Adnan M, Izatullah I (2017) Traditional uses of medicinal plants reported by the indigenous communities and local herbal practitioners of Bajaur Agency, Federally Administrated Tribal Areas, Pakistan. *J Ethnopharmacol* 198: 268-281.
67. Tajmiri S, Farhangi MA, Dehghan P (2016) *Nigella sativa* treatment and serum concentrations of thyroid hormones, transforming growth factor β (TGF- β) and interleukin 23 (IL-23) in patients with Hashimoto's Thyroiditis. *Eur J Integr Med* 8(4): 576-580.
68. Esakkimuthu S, Mutheeswaran S, Arvinth S, Paulraj MG, Pandikumar P, et al. (2016) Quantitative ethnomedicinal survey of medicinal plants given for cardiometabolic diseases by the non-institutionally trained siddha practitioners of Tiruvallur district, Tamil Nadu, India. *J Ethnopharmacol* 186: 329-342.
69. Jaradat NA, Al-Ramahi R, Zaid AN, Ayesh OI, Eid AM (2016) Ethnopharmacological survey of herbal remedies used for treatment of various types of cancer and their methods of preparations in the West Bank-Palestine. *BMC Complement Altern Med* 16: 93.
70. Hossan MS, Jindal H, Maisha S, Samudi Raju C, Devi Sekaran S, et al. (2018) Antibacterial effects of 18 medicinal plants used by the Khyang tribe in Bangladesh. *Pharm Biol* 56(1): 201-208.
71. Bouzabata A (2013) Traditional treatment of high blood pressure and diabetes in Souk Ahras district. *J Pharmacognosy Phyto-therapy* 5(1): 12-20.