

## Review Article

## Nigella Sativa and Its Role in the Immune System – A Review

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**Abstract:** Nigella sativa (black cumin), a small shrub native to Western Asia, Middle East and Eastern Europe, has been used for centuries for cooking as well as home remedies for various ailments. Its miraculous beneficial properties has made it to be of key interest in the modern medicine. Its use has been extensively studied for medicinal purposes owing to the fact that it has little to no side effects. With a wide range of uses in multiple fields, its role in strengthening the body's immunity has emerged to be of significant value. Owing to its antioxidant, anti-inflammatory and antimicrobial properties, nigella sativa and its most active component thymoquinone has been studied in countless researches to be proven as a potent antioxidant, anti-inflammatory and antimicrobial agent.

**Keywords:** immunity, antioxidant, anti-inflammatory, antimicrobial, black cumin, thymoquinone.

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## INTRODUCTION

The use of therapeutic herbs for the treatment of various ailments can be dated back to the early times. Their use in home remedies is well practiced. (Beheshti, Khazaei, & Hosseini, 2016) In the pharmacology world, they are being extensively studied for their benefits due to their added bonus of having fewer side effects. (Aisa, Xin, & Tang, 2019)

*Nigella Sativa* (NS) is an example of such a medicinal herb. Belonging to the family of *Ranunculaceae*, it mainly grows in the Western Asia, Middle East and Eastern Europe. (Shabana, El-Menyar, Asim, Al-Azzeh, & Al Thani, 2013) It is known by various names including black caraway, black cumin, black seed or black sesame in English; Habatul-barakah (seed of blessing) in Arabic; jintanhitam in Indonesian; kalonji in Urdu; Kaljeera in Hindi and çörek out in Turkish language. (Mollazadeh, Afshari, & Hosseinzadeh, 2017)(Datta *et al.*, 2012) It is a small shrub that grows upto 20-90 cm in length with five to ten petals. The petals are mostly light purple, blue, pink, yellow or white color. (Beheshti *et al.*, 2016) The fruits contains tiny black seeds which are the main source of various nutrients contributing to the plants therapeutic power. (Eid, Elmarzugi, Abu Ayyash, Sawafta, & Daana, 2017) It has great significance in the Islamic religion (Beheshti *et al.*, 2016) Islamic Prophet Muhammad (P.B.U.H.) stated the black seed to have

powers to heal any ailment except death. (Amin & Hosseinzadeh, 2016)

NS has been used in folk medicine for a wide range of ailments. With regard to its impressive healing ability, extensive researches are carried out to study its role in various pharmacological aspects. Based on its notable effects, it has been identified as the top evidence based therapeutic herb. (Ahmad *et al.*, 2013)

## USES

Black cumin is widely used in the Middle Eastern cuisine owing to its characteristic aroma and bitter taste as a spice in various dishes including curry, lentils and vegetables and flavor additive in pickles and bread. Its use has also been accounted in the ancient Egyptian times as a preservative during mummification. (Srinivasan, 2018)

NS has uses in pharmacological medicine and home remedies as well as cooking. (Kooti, Hasanzadeh-Noohi, Sharafi-Ahvazi, Asadi-Samani, & Ashtary-Larky, 2016) Quite famous in Middle East due to its religious importance, the use of black cumin goes back for more than 2000 years. The seeds have been used to treat many conditions including eczema, flu, fever, cough, asthma, anorexia, amenorrhea hemorrhage hypertension, diabetes rheumatism, dyspepsia, conjunctivitis, jaundice, skin diseases, (Forouzanfar,

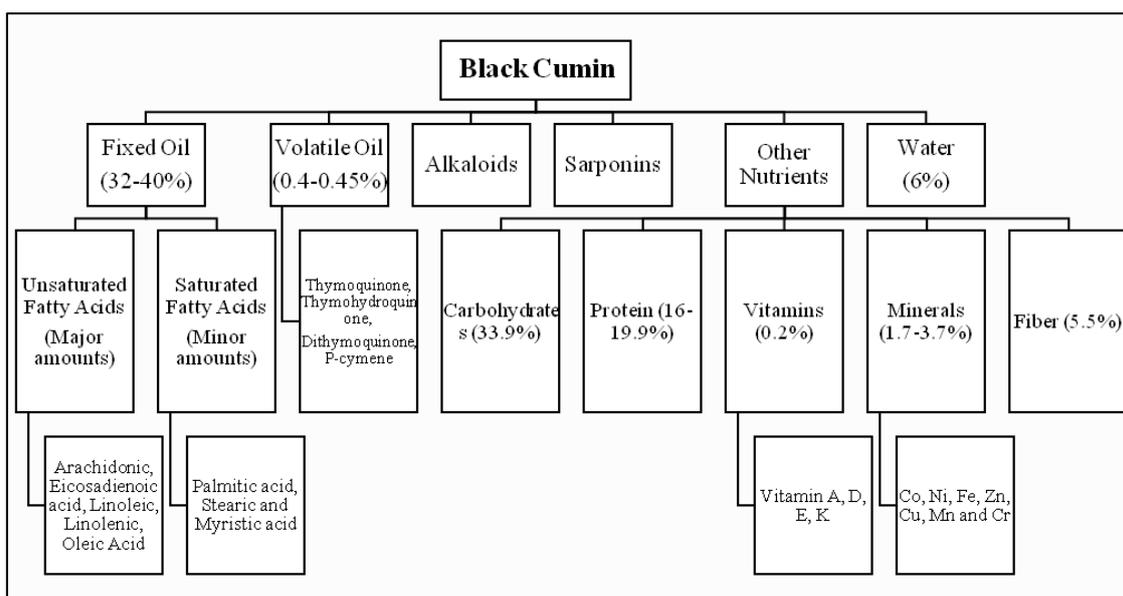
Bazzaz, & Hosseinzadeh, 2014)diarrhea, nasal ulcers, swollen joints, flatulence, dyspepsia, back pain, paralysis, obesity, congestion dizziness and migraine. (Datta *et al.*, 2012)

In the pharmacological world, its use has been widely studied with black cumin being recognized as having therapeutic effect on endocrine, immune, respiratory and cardiovascular system. (Gharby *et al.*, 2015)It has been acknowledged as having antitumor, antifungal, antibacterial, antimalarial, insecticidal, diuretic and antiseptic effect.(Hadi, Mohammed, & Hameed, 2016) Most of the medicinal effect has been ascribed to bedue to the presence of thymoquinone, a

major constituent of the black cumin. (Gharby *et al.*, 2015)

### Composition

The seed of *Nigella Sativa* contains both fixed as well as volatile oil. Other than this it also contains saponins, alkaloids and proteins and other nutrients. (Piras *et al.*, 2013) Studies show the seed to consist of thirty two volatile terpenes and 8 fatty acids. Thymoquinone has been isolated as the prime active component of black cumin. (Khan & Afzal, 2016)Some of the major constituents of black cumin are shown in table below.



**Figure – 1**(Amin & Hosseinzadeh, 2016; Ijaz *et al.*, 2017; Srinivasan, 2018; Tembhurne, Feroz, More, & Sakarkar, 2014; Vatansev *et al.*, 2013)

### Role in Immunity

For the protection of the human body against foreign attacks, there are a set of specific cells and organs collectively known as the immune system. To maintain the body’s homeostasis, it is essential that the immune system is functioning properly. (Sultan, Buttxs, Qayyum, & Suleria, 2014) The components of NS play a vital role in this.(Gheita & Kenawy, 2012)

NS has been reported to support the immune system in variety of ways. Studies show its potent activity as an antifungal, antibacterial, respiratory stimulation, antidiabetic, antihypertensive, analgesic, anti-inflammatory and antitumor. (Abdel-Moneim, Morsy, Mahmoud, Abo-Seif, & Zanaty, 2013) Studies show that thymoquinone obtained from NS can be used for its therapeutic effect through the regulation of immune system in combating a range of non-infectious and infectious disorders such as cancer, autoimmune disorders or allergies. (Majdalawieh & Fayyad, 2015)

Thymoquinone, a major component of NS, plays a role as in strengthening the body’s immune

response, is a potent antioxidant, controls the Akt pathway and prompts apoptosis. Moreover, studies also prove it to be effective in healing allergic conditions including allergic rhinitis, eczema and asthma. (Tavakkoli, Mahdian, Razavi, & Hosseinzadeh, 2017)

### Antioxidant

For energy production, oxygen is a vital compound required by all organisms. During the process of oxygen metabolism, minute amounts of free radicals or reactive oxygen species (ROS) are released, which when accumulated, damage body cells. Antioxidants are compounds that prevent this damage by inhibiting or delaying the action of free radicals. They can be either made by the body or obtained through diet. Evidence shows NS to have potent antioxidants present in its seed extract. (A. Mohammed & Al-Suwaiegh, 2016) Its antioxidant effect has been suggested to be by the scavenging of free radicals as well as increasing the antioxidant production of the body by raising the transcription gene responsible. (Goyal *et al.*, 2017)Further studies indicate the existence of thymoquinone in NS to be responsible for

its antioxidant activities. (Kapil, Suresh, & Chandna, 2015) Its effectiveness as a potent antioxidant maybe due to its quinine structure enabling it to cross morphological barriers thereby obtaining access within the cellular structure and carrying out its scavenging action on the free radicals. (Alenzi *et al.*, 2013)

### Antiinflammatory

Numerous study indicate the anti-inflammatory action of black cumin through inhibition of cyclo-oxygenase and 5-lipoxygenase pathway involved in arachidonate metabolism with regard to lipid peroxidation. It also induces the inhibition of eicosanoids and cytokines that play key role in inflammatory response. Furthermore, its immunity strengthening effects are also attributed to its natural killer (Nk) and T-cell mediated response. (Ijaz *et al.*, 2017) In addition to this it has also been seen to inhibit inflammation mediators, prostaglandins, leukotrienes and B-cell mediated immune response. (Gholamnezhad, Keyhanmanesh, & Boskabady, 2015)

### Antimicrobial

Evidence shows that NS possesses anti-parasitic, antiviral and antimicrobial activity. Their antibacterial action was seen against multiple species of Gram positive and Gram negative bacteria. (A. Mohammed & Al-Suwaiegh, 2016) Studies show that NS can stimulate antiviral activities attributed to increased T-cell response. (Alenzi *et al.*, 2013) Investigation show that NS extracts employ inhibition actions against variety of infections due to bacteria. Moreover, it was seen that even in the lack of any disease, NS proved as an immune modulator by strengthening the activity of NK-cell as well as improving the function of T-cell. (Ishtiaq, Ashraf, Hayat, & Asrar, 2013).

## REVIEW LITERATURE

A study was conducted to study the antimicrobial actions of NS seeds. The extract obtained from the seeds was analyzed using agar well diffusion method against different microorganisms. Results showed that the presence of thymoquinone, thymohydroquinone, longiforene and p-cymene exhibited potent antimicrobial action against the bacteria including *P. aeruginosa*, *E.coli*, *S. epidermis*, *S. aureus*, *B. subtilis* and *B. cereus*. (Singh *et al.*, 2014)

Chaudhary *et al.* conducted a study to analyze the antibacterial and antioxidant effect of NS against Gram negative and Gram positive by suspension extracts. The results showed increased antioxidant and enzyme activity with regard to increased thymoquinone and thymol content. With the presence of phytochemical constituents, strong antibacterial activity was also seen against the bacteria present. (Chaudhry, Fatima, & Ahmad, 2015)

A study was carried out to investigate the antifungal action of NS extracts especially its active component, thymoquinone against *Microsporungypseum*, *Microsporum canis* and *Trichophyton mentagrophytes*. Disk diffusion methods was used to study the antifungal action. Results showed that the extract, especially thymoquinone, exhibited strong antifungal activity against the given strains. (Mahmoudvand, Sepahvand, Jahanbakhsh, Ezatpour, & Mousavi, 2014)

A study conducted by Goga *et al.*, studied the antioxidant effect of NS seed extracts using the ultrasound and Soxhlet extraction methods. ABTS test and DPPH method was used to analyze the radical scavenging activity. Results showed potent antioxidant effect with thymoquinone and ethanolic extract being the most prominent. (Goga, Hasic, Becirovic, & Cavar, 2012)

Research was done to analyze the antioxidant, antimicrobial and anti-inflammatory activity of NS extract. Results showed thymoquinone to be the strongest antioxidant and anti-inflammatory agent. It proved to be most active in decreasing oxidation. The extract proved to be very effective against bacteria especially *E.coli* and *Candida albicans*. (Kazemi, 2014)

An investigation was carried out to examine the antibacterial and antioxidant action of NS's component - thymoquinone. By the well diffusion method, the antibacterial action was studied against *Salmonella typhi*, *Staphylococcus* and *E. coli* strains. Results showed potent antioxidant effect as well as antimicrobial action proving thymoquinone to be therapeutic. (Nallamuthu, Parthasarathi, & Khanum, 2013)

Bordoni *et al.* conducted a study with the aim to investigate the antioxidant activity of NS extract containing thymoquinone. It was seen that NS oil containing high levels of thymoquinone exhibited strong antioxidant activity. (Bordoni *et al.*, 2019)

A study was carried out to examine the antioxidant property of black cumin and garlic extract on postmenopausal women. The consumed the required amount of black cumin and garlic extract for eight weeks. Increased superoxide dismutase erythrocyte glutathione peroxidase activity with decreased levels of glutathione peroxidase was seen. (Mostafa, Moustafa, Mirghani, AlKusayer, & Moustafa, 2013)

The purpose of an investigation was to study the antioxidant and anti-inflammatory effect of NS's thymoquinone on human lung cancer cell. For three days, the cells were exposed to different thymoquinone concentrations. It was seen that thymoquinone enhanced apoptotic cell death in the tumor cell. It was also seen that p53 expression that is another apoptotic

modulator in the cancer cell was upregulated by thymoquinone. By the activation of caspase-9 and -3, thymoquinone also caspase dependent apoptosis. It was concluded that thymoquinone possesses therapeutic properties in combating lung cancer. (Samarghandian, Azimi-Nezhad, & Farkhondeh, 2019)

A study was carried out by Ramadan *et al.* to analyze the antimicrobial activity of black cumin extract. The results showed black cumin extract exhibited potent antimicrobial effect against all microorganisms except *A.flavus* and *A.niger*. (Ramadan, Asker, & Tadros, 2012)

Research was done to analyze the antibacterial effect of black seed oil against wide range of bacteria. Results showed that black seed oil inhibited the growth of all bacteria particularly *Bacillus subtilis*. It was also seen the main agent responsible for the black seed oil's antimicrobial actions were due to the presence of thymoquinone. Strong antibacterial effect of black seed oil was concluded even to be effective against MRSA. (S. J. Mohammed *et al.*, 2019)

A study was conducted to examine thymoquinone and its antioxidant activity and its effectiveness in reducing free radicals. Free radical scavenging methods were used. Results showed thymoquinone to be a strong antioxidant. It inhibited the peroxidation of beta-carotene. It was seen to be a potent lipid peroxidation, hydroxyl scavenger and hydrogen peroxide inhibitor. (Khither, Sobhi, Khenchouche, Mosbah, & Benboubetra, 2018)

In 2015, a study was carried out by Hussein to investigate NS extract as an antibacterial (*E. coli* and *Staph. Aureus*) and antifungal (*A.niger*). To study the inhibition of bacterial growth, inhibition zone plate method was used while fungal activity was studied through radial growth and mycelia weight were used. Strong antimicrobial action was seen against both bacteria particularly *E.coli*. Moreover, a decrease in fungus was identified with increase in NS extract concentrations. (Hussein, 2015)

A study was carried out by Georgescu *et al.* with the purpose to examine the antimicrobial effect of NS seed extract on traditional cheese in the absence of any additives. 3 sets were made with varying concentration of the extract, one being a control set. Results showed the inhibition of bacterial growth in the presence of the extract without any alteration in the physiochemical structure of the product. It was concluded that NS seed extract can successfully be used as an antibiotic in supplements. (Georgescu *et al.*, 2018)

In a study aimed at analyzing the antimicrobial action of NS, its extract was obtained and its effect against *Bacillus subtilis*, *Staphylococcus aureus* and *E.coli* was studied. Agar well diffusion method and agar

disk method was applied. Results showed inhibition in the growth of all three bacteria owing to the presence of strong phytochemical agents in NS. It was concluded that the extract of NS can be widely used in preservative and preservative medicine composition. (Foroughi *et al.*, 2016)

## CONCLUSION

Evidence obtained from countless researches prove nigella sativa to be a very effective component in strengthening the body's immune system. Its active components, especially thymoquinone, play a vital role as an antioxidant, anti-inflammatory and antimicrobial activities. Further research is recommended to further identify, examine and study the phytochemical properties of nigella sativa and its seed in combating various illnesses in an effort for it become a vital part of the pharmacological world.

## Conflict Of Interest

There was no conflict of interest.

## Acknowledgements

None

## REFERENCES

1. Abdel-Moneim, A., Morsy, B. M., Mahmoud, A. M., Abo-Seif, M. A., & Zanaty, M. I. (2013). Beneficial therapeutic effects of *Nigella sativa* and/or *Zingiber officinale* in HCV patients in Egypt. *EXCLI journal*, 12, 943.
2. Ahmad, A., Husain, A., Mujeeb, M., Khan, S. A., Najmi, A. K., Siddique, N. A., . . . & Anwar, F. (2013). A review on therapeutic potential of *Nigella sativa*: A miracle herb. *Asian Pacific journal of tropical biomedicine*, 3(5), 337-352.
3. Aisa, H., Xin, X., & Tang, D. (2019). *Nigella sativa*: A medicinal and edible plant that ameliorates diabetes Bioactive Food as Dietary Interventions for Diabetes (pp. 629-640): Elsevier.
4. Alenzi, F., Alsakran Altamimi, M., Kujan, O., Tarakji, B., Tamimi, W., Bagader, O., . . . Al-Swailmi, F. (2013). Antioxidant properties of *Nigella sativa*. *J Mol Genet Med*, 7(3), 1-5.
5. Amin, B., & Hosseinzadeh, H. (2016). Black cumin (*Nigella sativa*) and its active constituent, thymoquinone: an overview on the analgesic and anti-inflammatory effects. *Planta medica*, 82(01/02), 8-16.
6. Beheshti, F., Khazaei, M., & Hosseini, M. (2016). Neuropharmacological effects of *Nigella sativa*. *Avicenna journal of phytomedicine*, 6(1), 104.
7. Bordoni, L., Fedeli, D., Nasuti, C., Maggi, F., Papa, F., Wabitsch, M., . . . & Gabbianelli, R. (2019). Antioxidant and anti-inflammatory properties of *Nigella sativa* oil in human pre-adipocytes. *Antioxidants*, 8(2), 51.
8. Chaudhry, H., Fatima, N., & Ahmad, I. Z. (2015). Evaluation of antioxidant and antibacterial

- potentials of *Nigella sativa* L. suspension cultures under elicitation. *BioMed research international*, 2015.
9. Datta, A. K., Saha, A., Bhattacharya, A., Mandal, A., Paul, R., & Sengupta, S. (2012). Black cumin (*Nigella sativa* L.)—a review. *Journal of plant development sciences*, 4(1), 1-43.
  10. Eid, A. M., Elmarzugi, N. A., Abu Ayyash, L. M., Sawafta, M. N., & Daana, H. I. (2017). A Review on the Cosmeceutical and External Applications of *Nigella sativa*. *Journal of tropical medicine*, 2017.
  11. Foroughi, A., Pournaghi, P., Tahvilian, R., Zangeneh, M. M., Zangeneh, A., & Moradi, R. (2016). Ethnomedicinal plants: Study on the chemical composition and antibacterial activity of the *Nigella sativa* (Black seed) oil's. *International Journal of Pharmaceutical and Clinical Research*, 8(11), 1528-1532.
  12. Forouzanfar, F., Bazzaz, B. S. F., & Hosseinzadeh, H. (2014). Black cumin (*Nigella sativa*) and its constituent (thymoquinone): a review on antimicrobial effects. *Iranian journal of basic medical sciences*, 17(12), 929.
  13. Georgescu, M., Tăpăloagă, P. R., Tăpăloagă, D., Furnaris, F., Ginghină, O., Negrei, C., . . . & Popescu, I. A. (2018). Evaluation of antimicrobial potential of *Nigella sativa* oil in a model food matrix. *Farmacia*, 66(6), 1028-1036.
  14. Gharby, S., Harhar, H., Guillaume, D., Roudani, A., Boulbaroud, S., Ibrahimi, M., . . . & Chafchaoui-Moussaoui, I. (2015). Chemical investigation of *Nigella sativa* L. seed oil produced in Morocco. *Journal of the Saudi Society of Agricultural Sciences*, 14(2), 172-177.
  15. Gheita, T. A., & Kenawy, S. A. (2012). Effectiveness of *Nigella sativa* oil in the management of rheumatoid arthritis patients: a placebo controlled study. *Phytotherapy research*, 26(8), 1246-1248.
  16. Gholamnezhad, Z., Keyhanmanesh, R., & Boskabady, M. H. (2015). Anti-inflammatory, antioxidant, and immunomodulatory aspects of *Nigella sativa* for its preventive and bronchodilatory effects on obstructive respiratory diseases: A review of basic and clinical evidence. *Journal of Functional Foods*, 17, 910-927.
  17. Goga, A., Hasic, S., Becirovic, S., & Cavar, S. (2012). Phenolic compounds and antioxidant Activity of extracts of *Nigella sativa* L. *Bull Chemists Technol Bosnia Herzegovina*, 39, 15-19.
  18. Goyal, S. N., Prajapati, C. P., Gore, P. R., Patil, C. R., Mahajan, U. B., Sharma, C., . . . & Ojha, S. K. (2017). Therapeutic potential and pharmaceutical development of thymoquinone: a multitargeted molecule of natural origin. *Frontiers in pharmacology*, 8, 656.
  19. Hadi, M. Y., Mohammed, G. J., & Hameed, I. H. (2016). Analysis of bioactive chemical compounds of *Nigella sativa* using gas chromatography-mass spectrometry. *Journal of Pharmacognosy and Phytotherapy*, 8(2), 8-24.
  20. Hussein, A. O. A. (2015). Biological Activities and some Physiochemical Characteristics of the Black Cumin (*Nigella sativa* L.) Seed Oil. University of Gezira.
  21. Ijaz, H., Tulain, U. R., Qureshi, J., Danish, Z., Musayab, S., Akhtar, M. F., . . . & Waheed, I. (2017). *Nigella sativa* (Prophetic Medicine): A Review. *Pakistan journal of pharmaceutical sciences*, 30(1).
  22. Ishtiaq, S., Ashraf, M., Hayat, M. Q., & Asrar, M. (2013). Phytochemical analysis of *Nigella sativa* and its antibacterial activity against clinical isolates identified by ribotyping. *International Journal of Agriculture and Biology*, 15(6).
  23. Kapil, H., Suresh, D., & Chandna, S. (2015). Thymoquinone: A natural remedy for treatment of various diseases: A review. *J Periodontol Med Clin Prac*, 2(1), 5-11.
  24. Kazemi, M. (2014). Phytochemical composition, antioxidant, anti-inflammatory and antimicrobial activity of *Nigella sativa* L. essential oil. *Journal of Essential Oil Bearing Plants*, 17(5), 1002-1011.
  25. Khan, M. A., & Afzal, M. (2016). Chemical composition of *Nigella sativa* Linn: part 2 recent advances. *Inflammopharmacology*, 24(2-3), 67-79.
  26. Khither, H., Sobhi, W., Khenchouche, A., Mosbah, A., & Benboubetra, M. (2018). In-vitro Antioxidant Effect of Thymoquinone. *Annual Research & Review in Biology*, 1-9.
  27. Kooti, W., Hasanzadeh-Noohi, Z., Sharafi-Ahvazi, N., Asadi-Samani, M., & Ashtary-Larky, D. (2016). Phytochemistry, pharmacology, and therapeutic uses of black seed (*Nigella sativa*). *Chinese journal of natural medicines*, 14(10), 732-745.
  28. Mahmoudvand, H., Sepahvand, A., Jahanbaksh, S., Ezatpour, B., & Mousavi, S. A. (2014). Evaluation of antifungal activities of the essential oil and various extracts of *Nigella sativa* and its main component, thymoquinone against pathogenic dermatophyte strains. *Journal de mycologie medicale*, 24(4), e155-e161.
  29. Majdalawieh, A. F., & Fayyad, M. W. (2015). Immunomodulatory and anti-inflammatory action of *Nigella sativa* and thymoquinone: A comprehensive review. *International immunopharmacology*, 28(1), 295-304.
  30. Mohammed, A., & Al-Suwaiegh, S. (2016). Effects of *Nigella sativa* on mammals' health and production. *Adv. Anim. Vet. Sci*, 4(12), 630-636.
  31. Mohammed, S. J., Amin, H. H., Aziz, S. B., Sha, A. M., Hassan, S., Aziz, A., . . . & Rahman, H. S. (2019). Structural Characterization, Antimicrobial Activity, and In Vitro Cytotoxicity Effect of Black Seed Oil. *Evidence-Based Complementary and Alternative Medicine*, 2019.
  32. Mollazadeh, H., Afshari, A. R., & Hosseinzadeh, H. (2017). Review on the potential therapeutic

- roles of nigella sativa in the treatment of patients with cancer: Involvement of apoptosis:-black cumin and cancer. *Journal of pharmacopuncture*, 20(3), 158.
33. Mostafa, R. M., Moustafa, Y. M., Mirghani, Z., AlKusayer, G. M., & Moustafa, K. M. (2013). Antioxidant effect of garlic (*Allium sativum*) and black seeds (*Nigella sativa*) in healthy postmenopausal women. *SAGE open medicine*, 1, 2050312113517501.
34. Nallamuthu, I., Parthasarathi, A., & Khanum, F. (2013). Thymoquinone-loaded PLGA nanoparticles: antioxidant and anti-microbial properties. *International Current Pharmaceutical Journal*, 2(12), 202-207.
35. Piras, A., Rosa, A., Marongiu, B., Porcedda, S., Falconieri, D., Dessi, M. A., . . . & Koca, U. (2013). Chemical composition and in vitro bioactivity of the volatile and fixed oils of *Nigella sativa* L. extracted by supercritical carbon dioxide. *Industrial Crops and Products*, 46, 317-323.
36. Ramadan, M. F., Asker, M. M. S., & Tadros, M. (2012). Antiradical and antimicrobial properties of cold-pressed black cumin and cumin oils. *European Food Research and Technology*, 234(5), 833-844.
37. Samarghandian, S., Azimi-Nezhad, M., & Farkhondeh, T. (2019). Thymoquinone-induced antitumor and apoptosis in human lung adenocarcinoma cells. *Journal of cellular physiology*, 234(7), 10421-10431.
38. Shabana, A., El-Menyar, A., Asim, M., Al-Azzeh, H., & Al Thani, H. (2013). Cardiovascular benefits of black cumin (*Nigella sativa*). *Cardiovascular toxicology*, 13(1), 9-21.
39. Singh, S., Das, S., Singh, G., Schuff, C., de Lampasona, M. P., & Catalan, C. A. (2014). Composition, in vitro antioxidant and antimicrobial activities of essential oil and oleoresins obtained from black cumin seeds (*Nigella sativa* L.). *BioMed research international*, 2014.
40. Srinivasan, K. (2018). Cumin (*Cuminum cyminum*) and black cumin (*Nigella sativa*) seeds: traditional uses, chemical constituents, and nutraceutical effects. *Food quality and safety*, 2(1), 1-16.
41. Sultan, M. T., Butt, M. S., Qayyum, M. M. N., & Suleria, H. A. R. (2014). Immunity: plants as effective mediators. *Critical reviews in food science and nutrition*, 54(10), 1298-1308.
42. Tavakkoli, A., Mahdian, V., Razavi, B. M., & Hosseinzadeh, H. (2017). Review on clinical trials of black seed (*Nigella sativa*) and its active constituent, thymoquinone. *Journal of pharmacopuncture*, 20(3), 179.
43. Tembhumne, S., Feroz, S., More, B., & Sakarkar, D. (2014). A review on therapeutic potential of *Nigella sativa* (kalonji) seeds. *J Med Plants Res*, 8(3), 167-177.
44. Vatansev, H., Ciftci, H., Ozkaya, A., Ozturk, B., Evliyaoglu, N., & Kiyici, A. (2013). Chemical composition of *Nigella sativa* L. seeds used as a medical aromatic plant from East Anatolia Region, Turkey. *Asian journal of chemistry*, 25(10), 5490-5492.