



## NIGELLA SATIVA L.: AN OVERVIEW

### NIGELLA SATIVA L.: GENEL BAKIŞ

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### ABSTRACT

**Objective:** *Nigella sativa* L. (Ranunculaceae) is an annual herbaceous plant indigenous to the Mediterranean region and Western Asia globally. It is cultivated in Türkiye, especially in Isparta, Burdur and Afyonkarahisar. While its seeds are known for their characteristic black color in many languages, in Türkiye, it is recognized as "çörek otu". Traditionally, its seeds have been utilized for addressing rheumatism, bronchitis, colds, asthma and inflammatory conditions, as well as to enhance milk production in lactating mothers, aid digestion, and combat parasitic infections. Meanwhile, its oil is applied to address skin issues like boils and eczema. Additionally, because of its pungent bitter flavor and fragrance, it serves as a seasoning in Middle Eastern and Indian cuisines. The purpose of this review is to undertake a thorough analysis of the literature concerning the scientific classification and morphology, traditional uses pharmacological effects and phytochemistry of the plant.

**Result and Discussion:** *Nigella* seeds contain abundant carbohydrates, proteins, fat, essential amino acids, diverse minerals and vitamins. The seeds contain 30-40% fixed oil, with 50-60% of the fixed oil consisting of unsaturated fatty acids such as oleic acid and linoleic acid. The seeds furthermore contain 0.4-0.45% essential oil. The primary constituents of the essential oil include thymoquinone, carvacrol, p-cymene, thymol, t-anethole,  $\alpha$ -terpinene and pinene. Additionally, the seeds comprise alkaloids like nigellimine, nigellicine, nigellamine, and nigellidine; saponins such as hederin and hederagenin; and compounds carrying various coumarin structures. The aerial parts are rich in flavonoid compounds such as nigelflavonoside B, nigelloside, quercetin, kaempferol, and rutin. The antioxidant, anti-inflammatory, antihistaminic, anti-aging, antihypertensive, anticoagulant, antimicrobial, antihelminthic, antineoplastic, hepatoprotective, nephroprotective, neuroprotective, and wound healing activities of *Nigella sativa* have been identified through in vitro, in vivo, and clinical research. In conclusion, *Nigella sativa* L. (black cumin) is a valuable medicinal plant with versatile health benefits. Further exploration of its therapeutic applications holds great promise for the development of new pharmaceuticals and nutraceuticals to combat various ailments and improve human health.

**Keywords:** Black cumin, *Nigella sativa*, pharmacological activity, phytochemistry, Ranunculaceae

### ÖZ

**Amaç:** *Nigella sativa* L. (Ranunculaceae), dünyada Akdeniz Bölgesi ve Batı Asya'ya özgü tek yıllık otsu bir bitkidir. Türkiye'de özellikle Isparta, Burdur ve Afyonkarahisar'da yetiştirilmektedir. Pek çok dilde tohumları karakteristik siyah rengiyle tanınırken, Türkiye'de "çörek otu" olarak bilinmektedir. Geleneksel olarak tohumları astım, bronşit, soğuk algınlığı, romatizma ve iltihaplı

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*hastalıkların tedavisinde, emziren annelerde süt üretimini artırmada, sindirimi kolaylaştırmada ve parazit enfeksiyonlarıyla mücadelede kullanılırken, yağı ise egzama, çıban gibi cilt problemlerinde kullanılmaktadır. Ayrıca keskin acı tadı ve aroması nedeniyle Hint ve Orta Doğu mutfaklarında baharat olarak tercih edilmektedir. Bu derlemenin amacı, bitkinin bilimsel sınıflandırılması ve morfolojisi, geleneksel kullanımı, farmakolojik etkileri ve fitokimyası ile ilgili literatürün kapsamlı bir analizini yapmaktır.*

**Sonuç ve Tartışma:** Çörek otu tohumları karbonhidratlar, yağlar, proteinler, esansiyel amino asitler, çeşitli vitaminler ve mineraller açısından zengindir. Tohumlar %30-40 oranında sabit yağ içerir ve sabit yağın %50-60'ı linoleik asit ve oleik asit gibi doymamış yağ asitlerinden oluşur. Tohumlar ayrıca %0.4-0.45 oranında esansiyel yağ içerir. Esansiyel yağın ana bileşenleri timokinon, p-simen, karvakrol,  $\alpha$ -terpinen, timol, pinen ve t-anetoldür. Ayrıca tohumlar nigellisin, nigellidin, nigellimin ve nigellamin gibi alkaloidler; hederin ve hederagenin gibi saponinler ve çeşitli kumarin yapıları taşıyan bileşikler içerir. Toprak üstü kısımları nigelflavonozit B, nigellozit, kersetin, kemferol ve rutin gibi flavonoid bileşikler açısından zengindir. *Nigella sativa*'nın antioksidan, anti-inflamatuar, antihistaminik, anti-aging, antihipertansif, antikoagülan, antimikrobiyal, antihelmintik, antineoplastik, hepatoprotektif, nefroprotektif, nöroprotektif ve yara iyileştirici aktiviteleri *in vivo*, *in vitro* ve klinik çalışmalarla belirlenmiştir. Sonuç olarak çörek otu sağlık açısından çok yönlü faydaları olan değerli bir şifalı bitkidir. Terapötik uygulamalarının daha fazla araştırılması, çeşitli rahatsızlıklarla mücadele etmek ve insan sağlığını iyileştirmek için yeni farmasötiklerin ve nutrasötiklerin geliştirilmesi için büyük umut vadetmektedir.

**Anahtar Kelimeler:** Çörek otu, farmakolojik aktivite, fitokimya, *Nigella sativa*, Ranunculaceae

## INTRODUCTION

*Nigella sativa* L. (Syn: *Nigella cretica* Miller) is an annual herbaceous plant belonging to the Ranunculaceae family. This plant boasts a lengthy history and has been extensively utilized across numerous countries. The first evidence of its historical use dates back to the seeds discovered within the burial site of the Egyptian pharaoh Tutankhamun in the Valley of the Kings, dating between 1333 and 1323 BC. It is known that the Egyptian queen Cleopatra also used the seed oil for skincare. In ancient texts and historical records, it is referred to as the "miracle plant," "universal remedy," "sacred plant," and "plant from heaven" by ancient healers [1-4].

Black cumin has also been prescribed and used by Hippocrates and Dioscorides for digestive complaints and colds [2,3]. The statement attributed to the Prophet Muhammad (PBUH), "Utilize this black seed, for it is a cure for all ailments except death." and the Arabic term "Habbah Al-Baraka," meaning endless wealth, reflect the importance of this plant [1,2]. Its local names in many languages usually emphasize the characteristic black color of its seeds. In French, it is called "Cumin Noir," in German "Echter Schwarzkümmel," and in Hindi "kalonji." In Turkish, it is traditionally referred to as "çörek otu," mainly because it is commonly used in baking [1,2].

The native habitat of *Nigella sativa* is the Western Asia and Mediterranean region, with its cultivation expanding from Asia to America and Africa. North Africa, India, and Türkiye are considered its secondary homeland. Currently, it is cultivated in many countries, spanning Asia, the Middle East and Europe, including Saudi Arabia, Syria and Türkiye (Figure 1) [5-13].



**Figure 1.** Geographical distribution of *Nigella sativa* [14]

There are 14 species of the genus *Nigella* growing in Türkiye, including 5 endemic taxa. However, the cultivated and commercially important species are *Nigella sativa* and *Nigella damascana* L. [4,15,16].

### Scientific Classification and Morphology

Division	: Spermatophyta
Subdivision	: Angiospermae
Class	: Dicotyledones
Subclass	: Dialypetalae
Order	: Ranales
Family	: Ranunculaceae
Genus	: <i>Nigella</i> L.
Species	: <i>Nigella sativa</i> L. [1,4].

*Nigella sativa* is 15-30 cm tall, branched, pubescent, or shortly viscid-hirsute or absent. It has finely dissected leaves, each segment oblong-lanceolate and rather short. Flowers non involucrate. Sepals ovate, whitish and shortly clawed. Petals bluish, bluntly acuminate, ovate and shortly stalked (Figure 2). Fruits swollen, hard capsule formed by the fusion of 5 follicles up to the apex. Involucre is filiformly divided. Styles are long and erect, persisting at the apex of the follicles. Seeds are numerous, black-colored, angular, and three-sided. *Nigellae semen* is rich in essential oil. Flowering occurs between the 5<sup>th</sup> and 7<sup>th</sup> months. It is locally cultivated in fields [4,9,17].



**Figure 2.** *Nigella sativa* L. [14]

*Nigella sativa* thrives in sunny, temperate, and warm climates, producing good seeds in well-drained soils that are slightly clayey and sandy-loamy, rich in nutrients. It does not require excessive watering due to its low moisture needs. Planting time is in the fall in regions with mild winters (usually the first half of November) and in the spring in regions with harsher climates (mostly March, no later than mid-April). After sowing, seeds germinate within about a week and emerge within two weeks. The period when the plant starts to yellow and the capsules turn black indicates the harvesting time. Harvesting should be done at the end of July and in August, preferably in the early morning hours. The harvested seeds are dried in the shade and in a dry environment with good air circulation [4,15].

### Traditional Use

*Nigella sativa* has a longstanding history of use across various countries and cultures as both a spice and a remedy for diverse ailments. Ibn Sina, in his most famous work "The Canon of Medicine - El-Kanun fit-Tib" describes black cumin as a seed that revitalizes the body and alleviates fatigue and boredom [2]. It has been frequently described and recommended in Prophetic Medicine, Unani Medicine, African, and Eastern Medicine, as well as in Arab, Chinese, and Ayurvedic Medicine. Both

the seeds and the oil have been utilized for medicinal purposes in Asia, Africa and the Middle East for centuries [7,11,18].

In the Southeast Asian and Middle East nations, the seeds have conventionally been employed to alleviate rheumatism, bronchitis, colds, asthma and inflammatory conditions, as well as to enhance milk production in lactating mothers, aid digestion, and combat parasitic infections. Meanwhile, its oil is applied to address skin issues like boils and eczema. Additionally, it has been used as an antiseptic and local anesthetic for scorpion, spider, snake, dog and cat bites. In India, the seeds are employed as anthelmintic, diaphoretic and carminative agents. Dried capsules are inhaled to regain lost sense of smell and are also utilized to deter certain insects and moths [1,7,11,19,20].

It is known that ancient Egyptian and Greek doctors prescribed seeds for various ailments such as headaches, toothaches, intestinal worms and nasal congestion. They were also used as regulators of menstruation, lactagogues, and diuretics. External applications of the seeds, mixed with a small amount of binding flour or soaked in water, have been mentioned for conditions such as abscesses, nasal ulcers, orchitis, rheumatism, and swelling of the hands and feet [10,21]. Additionally, because of its pungent bitter flavor and fragrance, it serves as a seasoning in Middle Eastern and Indian cuisines, especially in bread, yogurt, pickles, sauces, and salads. It is also known to have been used in ancient Egypt for mummification as a preservative [12,20,21].

In Türkiye, in the Central Anatolia region, decoctions of black cumin seed are used due to their abortifacient effects. After boiling the seeds and allowing them to cool, they are wrapped around the chest to treat the common cold. In Akşehir (Konya) and its surroundings, adults consume powdered black cumin seed for abdominal pain, while in children, 2-3 drops of the essential oil are used. In Ermenek (Karaman) and its surroundings, black cumin oil is dropped into the ear to treat earaches. In Muğla, seeds of black cumin are crushed or boiled and used as a syrup in the treatment of kidney stones [9,22,23,24].

### Phytochemical Content

Black cumin seeds are quite rich in content; they contain carbohydrates, proteins, fat, essential amino acids, diverse minerals, vitamins and essential oil. As monosaccharides, they contain glucose, rhamnose, xylose, and arabinose. They contain vitamins B<sub>1</sub>, B<sub>2</sub>, B<sub>3</sub>, B<sub>6</sub>, B<sub>9</sub>, C, A and minerals such as Mg, Fe, P, Cu, Ca, Zn, Se, Na, and Mn. About 30-40% of the fixed oil found in the seeds consists of 50-60% unsaturated fatty acids. These contents varies according to the climate, environmental conditions, and harvesting characteristics of the region where the plant grows [15,25,26,27,28,29].

The main components of the fixed oil extracted from black cumin seeds include linoleic acid,  $\beta$ -sitosterol and oleic acid. The fractions of the fixed oil are given in Table 1. Additionally, black cumin seed contains 0.4-0.45% essential oil. The primary constituents of the essential oil include thymoquinone, dihydrothymoquinone, carvacrol, p-cymene,  $\alpha$ -thujene, thymol, trans-anethole,  $\alpha$ -terpinene,  $\alpha$ -pinene and  $\beta$ -pinene. The concentration of essential oil fractions is given in Table 2 [7,28,30].

**Table 1.** The chemical makeup of the fixed oil extracted from black cumin seeds [27]

Composition of fixed oil	Range % (w/w)
Arachidic acid	2-3
Eicosadienoic acid	2-2.5
Linoleic acid	44.7-56
Linolenic acid	0.6-1.8
Myristic acid	0.16
Oleic acid	20.7-24.6
Palmitic acid	12-14.3
Palmitoleic acid	3
Stearic acid	2.7-3
Sterols	0.5

**Table 2.** The chemical make up of the essential oil obtained from black cumin seeds [30]

Composition of essential oil	Concentration (%)
$\alpha$ -Pinene	1.48
$\alpha$ -Thujene	2.4
$\beta$ -Pinene	1.72
Carvacrol	10.8
Dihydrothymoquinone	3.84
Minor components	23.81
p-Cymene	32.02
t- Anethole	2.10
Thymol	2.32
Thymoquinone	23.25

Black cumin seeds contain alkaloids such as nigellicine, nigellidine containing an imidazole ring, nigellimine carrying an isoquinoline ring, and nigellimine N-oxide and nigellamine carrying a tropane ring in addition to fixed and essential oil. Additionally, various flavonoid compounds such as kaempferol-3-O-rutinoside, kaempferol-3,7-diglucoside, nigelloside, rutin and nigellflavonoside B have been detected. Furthermore, it has been observed that hederin (melanthin), hederagenin (melanthenin) saponins along with 6-methoxy coumarin, 7-hydroxy coumarin, and 7-oxo coumarin are present [7,12,28,31-33].

### Pharmacological Potential of *Nigella sativa* and Its Effect on Biological Activities

#### Antioxidant Effect

Studies have shown that *Nigella sativa* seeds and the essential and fixed oils obtained from the seeds exhibit antioxidant activity through linoleic acid-based and  $\beta$ -carotene antioxidant activity tests, ABTS Radical Cation Scavenging Activity Assay, Cupric Ion Reducing Antioxidant Capacity (CUPRAC) Assay and DPPH Radical Scavenging Capacity Assay, as well as *in vivo* animal experiments. This effect has been associated with the total phenolic content. It is believed that the compounds  $\alpha$ -thujene, p-cymene, and thymoquinone found in the essential oil are the main responsible components for this effect. Comparative studies have found that the essential oil has higher antioxidant activity compared to the fixed oil. Additionally, it has been observed that oil obtained by supercritical fluid extraction contains elevated levels of unsaturated fatty acids, tocopherols, phytosterols, and polyphenol content compared to oils derived from solvent extraction and cold pressing methods, and thus, is associated with a higher antioxidant effect [30,32,34-41].

#### Analgesic, Anti-inflammatory, and Wound Healing Effect

Various *in vivo* tests conducted on rats and rabbits have shown that black cumin hydrosol, essential and fixed oils can promote wound healing and have analgesic effects. Biopsy and histological examinations have revealed accelerated wound healing processes, while a decrease in licking and writhing counts in animals has indicated analgesic effects. Additionally, the applied treatment has been found to reduce acute inflammatory reactions [38,42,43].

In clinical trials involving patients with osteoarthritis, significant reductions in serum levels of the inflammatory and oxidative stress marker CRP (C-reactive protein) have been observed after oral administration of black cumin oil. Topical application of black cumin oil has also been thought to provide significant improvements in general, physical, and mental health sub-scales. Throughout the treatment, patients were evaluated based on VAS (Visual Analog Skala) and WOMAC (Western Ontario and McMaster Universities Osteoarthritis Index) scores, revealing a decrease in the dosage of analgesic drugs used by patients and the analgesic effect of black cumin oil [44-46].

#### Antihistaminic Effect and Effect on Asthma

*In vivo* studies conducted on mice and rats have shown that black cumin oil reduces the frequency of nasal itching observed in allergic rhinitis, significantly alleviates nasal symptoms, reduces the

gathering of inflammatory cells in the nasal lavage fluid, nasal mucosa, and prevents typical inflammatory changes and inflammation [47,48].

Clinical trials conducted on patients with asthma have found that black cumin oil regulates the TH 17/Treg balance. Additionally, improvements in Asthma Control Test scores, significant reductions in blood eosinophils, fractional exhaled nitric oxide (FeNO), immunoglobulin E, and interferon- $\gamma$  levels have been observed [49-51].

### **Anti-aging and Anti-alopecia Effect**

The anti-aging and anti-melanogenic properties of black cumin seed extract and oil have been demonstrated through various tests, suggesting its potential as a cosmetic agent. *In vitro* tests have shown that black cumin inhibits advanced glycation end product formation, elastase and collagenase activity and collagen cross-linking while reducing melanin content and cellular tyrosinase activity in B16-F10 cells. Additionally, it has been found to significantly suppress the mRNA expression levels of genes linked to melanogenesis and tyrosinase-related proteins 1 and 2. In a 42-day study conducted on mice, black cumin oil was observed to reduce lipid peroxidation, fat, Bax/Bcl-2 proteins levels, and regulate the expression of caspase-3 proteins in brain and liver tissues [52,53].

Research on both mice and humans has indicated that topical application of *Nigella sativa* essential oil and decoction effectively prevents hair loss in mice and significantly improves hair growth in 70% of individuals participating in the study. Videodermatoscopic analysis has also revealed patients experienced a notable increase in hair density and thickness [54-55].

### **Anti-infertility Effect**

Black cumin oil and flower honey have been found to significantly alleviate testicular and sperm abnormalities in male rats and mice with induced testicular damage, as observed through biochemical and histological examinations. They have corrected total testosterone (TT) and sex-hormone binding globulin (SHBG) levels, increased testis weight, and improved sperm quality. It has been discovered that black cumin oil is more efficacious than flower honey [56,57]. Female rats with polycystic ovary syndrome (PCOS) treated with hydroalcoholic extract derived from *Nigella sativa* seeds for 3 weeks have shown regulation of fertility-related hormones. Significant improvement in ovarian tissue, reduction in cysts, and normal luteinization have also been observed. These effects are attributed to the plant's phytosterol content and its hypoglycemic and antioxidant effects, which are believed to contribute to PCOS recovery [58].

### **Anticoagulant and Antihypertensive Effect**

The alcoholic extract of *Nigella sativa* seed has been found to prolong the prothrombin time (PT), thrombin time (TT) and activated partial thromboplastin time (aPTT) in clotting tests, while its oil has exhibited concentration-dependent clot lysis activity on clotted human blood and its aqueous extract has shown antiplatelet activity [59-61]. Its antihypertensive effect has been tested in both animals and humans. Intravenous injection of the aqueous extract of black cumin seeds in mice resulted in a decrease in mean arterial blood pressure and a reduction in heart rate, which is dependent on the dosage. In a clinical study involving hypertensive patients, significant reductions in diastolic and systolic blood pressure were recorded after an 8-week treatment period, along with a significant increase in glomerular filtration rate [62].

### **Antimicrobial and Anthelmintic Effect**

Different researches have indicated that black cumin seed extract, its essential oil, and flower honey exhibit antifungal and antimicrobial effects against various fungi, bacteria, and virus species. The essential oil has been effective against *Colletorichum gloeosporoides* and *Penicillium digitatum*, while the seed extract and flower honey have shown effectiveness against *Aspergillus flavus*, *A. parasiticus*, *Mucor rammanianus*, and *Candida albicans* species. It has been observed that the antimicrobial activity is higher against gram-positive strains than gram-negatives [36,63-66]. The anthelmintic properties of aqueous and methanol extracts derived from *Nigella sativa* seeds have been studied on different species

with the methanol extract being more active. It has been observed to cause a dose-related paralysis and reduce egg levels in fecal samples [67,68].

### **Antineoplastic Effect**

The aqueous extract of black cumin seeds, nanoemulsion prepared from its tincture, its fixed oil, and its essential oil, particularly the major component thymoquinone, has been tested on various cancer cell lines (for instance A2780, HepG2, HUVEC, MDA-MB-231 and MCF-7), suggesting the potential of *Nigella sativa* as an agent in cancer treatment. Studies have shown that black cumin triggers cell cycle cessation and enhances apoptosis, exhibiting molecular binding with apoptotic proteins like Bax, Bcl-2, p53, STAT3, and Caspase-3/9. It inhibits cell growth, modifies the morphology of cancer cells, and reduces cell multiplication and survival [69-73].

### **Gastrointestinal System Effect**

The effect of *Nigella sativa* oil and seed hydroalcoholic extract on gastric ulcers has been investigated in rats, showing a gastroprotective effect. After 7 days of treatment, black cumin reduced the gastric ulcer index, malondialdehyde, and protein content, while increasing total thiol, mucus content and total hexose. However, it had no impact on the secretion of gastric acid [74,75]. Following oral administration of the seed hydroalcoholic extract in rats, a dose-dependent decrease in gastrointestinal motility, defecation frequency, and water content in feces was observed, indicating an antidiarrheal effect. Moreover, intraperitoneal application of black cumin seed oil markedly decreased the extent of intestinal injury in rats with enterocolitis. Additionally, an increase in villus length, width, and percentage of goblet cells was observed in the duodenum, jejunum, and ileum of rats. Black cumin is suggested to have enhanced and protective effects on food absorption [76-78].

### **Hypoglycemic, Hypolipidemic, and Hepatoprotective Effect**

Alcoholic extracts of *Nigella sativa* seed and aerial parts have been studied through *in vitro*, *in vivo*, and clinical trials, investigating their hypoglycemic and hypolipidemic effects. *In vitro* tests for inhibiting  $\alpha$ -glucosidase and PTP1B (Protein Tyrosine Phosphatase 1B) have shown that the aerial parts exhibit antidiabetic effects. After 28 days of treatment in diabetic rats, significant decreases in glucose, urea, creatinine, uric acid, total protein, total cholesterol, and LDL (Low Density Lipoprotein) stages, along with an enhance in HDL (High Density Lipoprotein), were observed. Additionally, impaired AST (Aspartate Aminotransferase), ALP (Alkaline Phosphatase) and ALT (Alanine Aminotransferase) values returned to normal levels. In mice with liver damage, improvement was observed in serum oxidative stress indicators, liver function markers, biochemical parameters and histopathological assessments, with a reduction in ALT and AST levels, which were caused by concavalin A-induced injuries [32,79,80,81].

Clinical studies conducted with diabetic patients have observed a decrease in insulin, HbA1c, glucose, CRP, TG (Triglyceride), LDL, ALP, AST and ALT grades, along with a rise in HDL, following the administration of the plant extract. Moreover, when *Nigella sativa* was used in conjunction with exercise, the observed effects were further enhanced [82,83].

### **Nephroprotective and Neuroprotective Effects**

*In vivo* studies with rats and clinical trials with humans have shown that the fixed oil and ethanol extract of *Nigella sativa* seeds reduce serum creatinine, 24-hour total urinary protein, blood glucose and urea levels, while increasing 24-hour total urinary volume, glomerular filtration rate and hemoglobin levels. Additionally, histopathological examinations have demonstrated a significant protective effect against kidney toxicity [84-86].

The impact of black cumin seed extract and fixed oil on the central nervous system have been investigated in various experimental animal models with rats and mice. Black cumin has been found to exhibit anxiolytic and anticonvulsant effects, reduce locomotor activity and the frequency of various stages of epileptic seizures, decrease brain 5-Hydroxyindoleacetic Acid (5-HIAA) levels, increase open field activity, brain serotonin (5-HT) levels, and significantly increase brain and plasma tryptophan levels. Furthermore, the primary constituent of the essential oil, thymoquinone, has been shown to have

protective effects against cytotoxicity and neurotoxicity caused by amyloid beta specific to Alzheimer's disease, as well as against synaptic toxicity induced by alpha-synuclein accumulation in individuals diagnosed with Parkinson's disease and Lewy body dementia [87-91].

### Allelopathic Effect

The chemical compositions of *Nigella sativa* at different growth stages and its allelopathic effects on *Lactuca sativa* L. have been studied, revealing that the quantity of secondary metabolites fluctuates depending on the plant's growth stages. Consequently, it has been determined to possess allelopathic effects. The aqueous extract obtained from the above-ground parts during the vegetative stage demonstrated the highest toxicity towards lettuce germination. Similarly, the aqueous extract derived from *Nigella sativa* during the flowering stage was found to be the most detrimental to lettuce growth. [92,93].

### Toxicity

Various studies have found *Nigella sativa* seeds and its components to be quite safe. LD<sub>50</sub> (Median Lethal Dose) values have been examined in studies conducted on mice and rats, along with possible biochemical, hematological, and histopathological changes. Histological examinations have shown no changes in heart, liver, kidney, and pancreatic tissues, stable liver enzymes, and high LD<sub>50</sub> values (794.3 mg/kg for oral intake in rats, 57.5 mg/kg for intraperitoneal administration). *Nigella* seeds have shown little to no toxic effects in practice, indicating a wide safety margin for therapeutic doses [3,12,21].

## RESULT AND DISCUSSION

*Nigella sativa* L., commonly called as "çörek otu" in Türkiye, is an annual herbaceous plant with a long-standing history of traditional medicinal uses. Originating from the Mediterranean regions and Western Asia, it is cultivated extensively in Türkiye, particularly in regions like Afyon, Burdur, and Isparta. The *Nigella sativa* seeds, renowned for their characteristic black color, have been employed traditionally to address a wide array of health issues, ranging from respiratory ailments like asthma and bronchitis to inflammatory conditions, digestive problems, and skin disorders. Moreover, these seeds serve as a flavoring in Middle Eastern and Indian cuisines, adding both flavor and nutritional value.

Chemical analysis reveals that *Nigella* seeds are packed with essential nutrients, including fats, carbohydrates, proteins, minerals and vitamins. Notably, they contain a significant amount of fixed oil, predominantly comprising unsaturated fatty acids like oleic acid and linoleic acid, along with essential oils abundant in compounds like thymoquinone, p-cymene, and carvacrol. Furthermore, *Nigella* seeds harbor alkaloids, saponins, and flavonoids, among other bioactive constituents, which contribute to their diverse pharmacological properties.

Extensive research, encompassing *in vitro*, *in vivo*, and clinical studies, has unveiled the remarkable therapeutic potential of *Nigella sativa*. Its extracts and derivatives exhibit antioxidant, anti-inflammatory, antimicrobial, antihypertensive, and hepatoprotective activities, among others. Additionally, *Nigella sativa* demonstrates promising prospects in the fields of wound healing, neuroprotection, and anticancer therapy.

In conclusion, the comprehensive examination of the literature regarding the phytochemistry, pharmacognosy and pharmacological effects of *Nigella sativa* underscores its significance as a valuable medicinal plant with multifaceted health benefits. Further exploration of its therapeutic applications holds great promise for the development of novel pharmaceuticals and nutraceuticals to combat various ailments and enhance human health.

## AUTHOR CONTRIBUTIONS

Concept: Ş.H.G., D.Ç.P.; Design: Ş.H.G., D.Ç.P.; Control: D.Ç.P.; Sources: Ş.H.G., D.Ç.P.; Materials: Ş.H.G., D.Ç.P.; Data Collection and/or Processing: Ş.H.G., D.Ç.P.; Analysis and/or Interpretation: Ş.H.G., D.Ç.P.; Literature Review: Ş.H.G.; Manuscript Writing: Ş.H.G., D.Ç.P.; Critical Review: Ş.H.G., D.Ç.P.; Other: -



## CONFLICT OF INTEREST

The authors declare that there is no real, potential, or perceived conflict of interest for this article.

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