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Review Article

A Comprehensive Review on the Morphological, Phytochemical and Pharmacological Properties of *Nigella sativa* Linn

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Abstract

Objective(s): The present review aims to comprehensively summarize the traditional, phytochemical, pharmacological, and therapeutic aspects of *Nigella sativa* Linn. from both modern and Unani perspectives.

Data Sources: Relevant literature was collected from classical Unani texts, scientific databases, published review articles, pharmacological studies, and clinical research papers related to *Nigella sativa*.

Study Selection: Published literature describing the historical background, morphology, phytochemistry, pharmacological activities, therapeutic uses, dosage, formulations, and correctives of *Nigella sativa* was included in this review.

Summary of Contents: *Nigella sativa* Linn., commonly known as Black seed, Black cumin, or Kalonji, is widely recognized for its remarkable therapeutic properties and has been extensively used in traditional medicine systems and the food industry. In *Tibb-e-Nabwi* (Prophetic Medicine), it is regarded as one of the most valued healing remedies. The plant contains several important phytoconstituents including fixed oils, essential oils, proteins, alkaloids, and saponins. Thymoquinone, the major active constituent, is responsible for many of its pharmacological activities. According to Unani literature, Kalonji possesses actions such as carminative, anti-inflammatory, analgesic, diuretic, emmenagogue, galactagogue, and expectorant effects. Various experimental and clinical studies have reported its antidiabetic, anticancer, antimicrobial, antioxidant, immunomodulatory, bronchodilator, hepatoprotective, nephroprotective, gastroprotective, and anti-inflammatory activities. Despite extensive information, consolidated data combining both Unani and modern scientific perspectives remain limited.

Conclusion: *Nigella sativa* is a medicinally significant plant with broad therapeutic potential supported by traditional Unani concepts and contemporary scientific evidence. This review provides comprehensive information regarding its pharmacological importance and therapeutic applications, which may support future research and clinical use.

Keywords: *Nigella sativa* Linn., Healing Medicine, Kalonji, Thymoquinone, Prophetic Medicine, Anti-inflammatory, Unani Medicine.

Introduction

Indian plants have been used for treating diseases for several decades in various indigenous and traditional systems of medicine. Among the various potential medicinal plants, Kalonji, also known as *Nigella sativa* Linn., is a miraculous herb of the Ranunculaceae family with a strong historical and religious background.^{1,2} The seeds of kalonji are the source of the active ingredient, which has been utilised for thousands of years for medicinal purposes, as a spice, and as a food preservative. Historical uses of kalonji have been mentioned in various religious and ethnic books. In Islam, it is considered one of the greatest forms of

healing medicine, existing as a remedy for all diseases except death. It is also recommended for use consistently in *Tibb-e-Nabwi* (Prophetic Medicine).^{1,2,3} In the Unani system of Medicine, it is described as the melanthion (little black seed) by Hippocrates and Dioscorides. Galen and Ibn-Sina have also regarded kalonji as a valuable remedy for hepatic and digestive disorders. The famous book of medicine by Ibn-Sina, "The Canon of Medicine (980-1037), revealed the historical importance of kalonji as seeds that stimulate the body's energy and help recovery from fatigue and dispiritedness.^{2,3,4} There is so much therapeutic potential in this drug that it is also referred to as a

magical herb. The aim of the current review is to emphasise the morphological, phytochemical, and pharmacological characteristics, as well as the traditional uses and pharmacological investigations,

that have been carried out on the plant, so that the therapeutic potential of the said herb can be further explored for the betterment of humanity and the world (Figure 1).

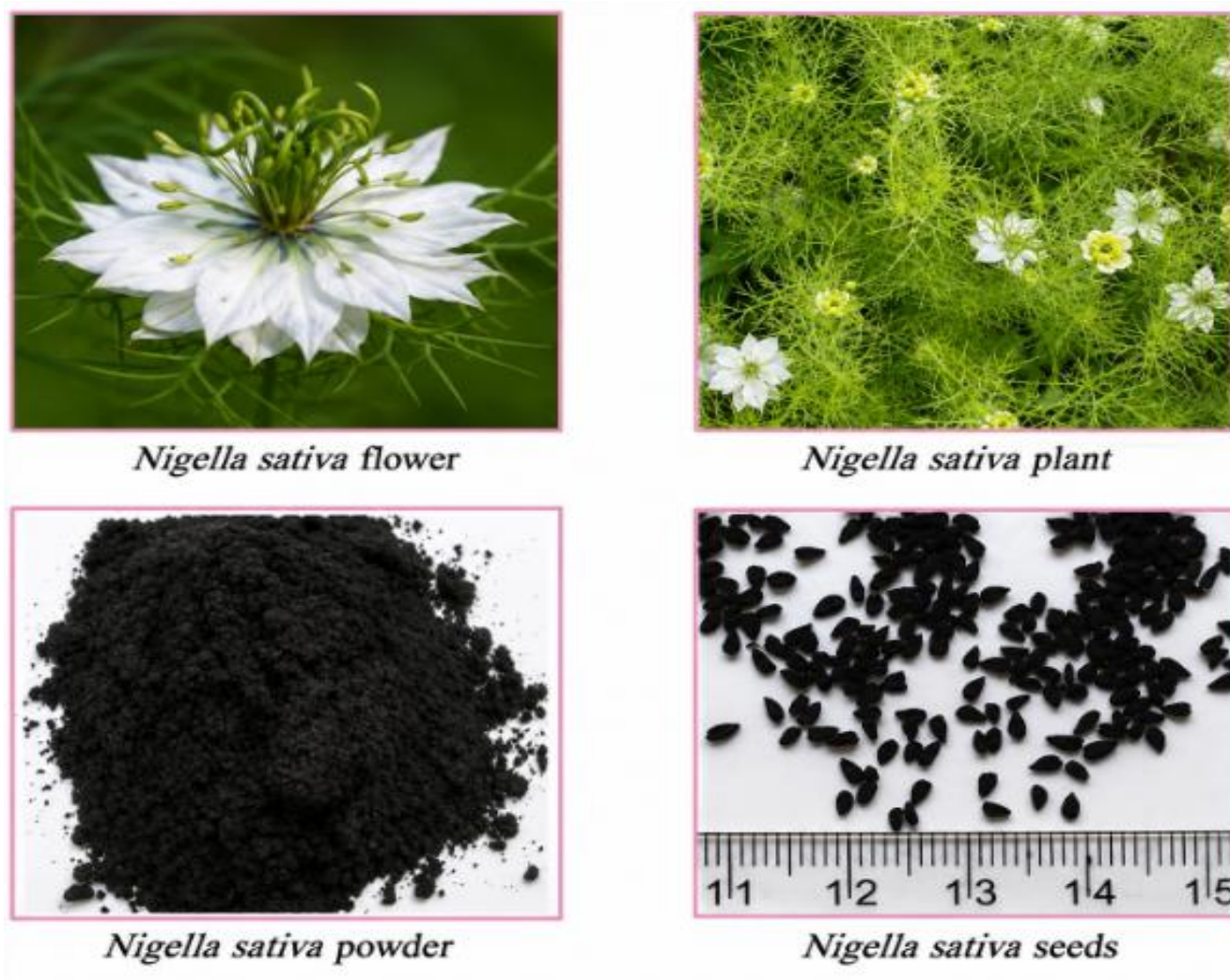


Figure 1: *Nigella sativa* Linn.

Methodology

This systematic review was conducted to explore the morphology, phytochemical composition, and pharmacological properties of *Nigella sativa* Linn. A comprehensive literature search was conducted across PubMed, Scopus, ScienceDirect, Web of Science, and Google Scholar, as well as traditional Unani textbooks and ethnobotanical literature, encompassing studies published up to October 2025. Keywords such as "*Nigella sativa*," "black seed," "black cumin," "Kalonji," "thymoquinone," and "Unani medicine" were used. Articles focusing on the morphology, phytochemistry, pharmacology, and therapeutic uses of *Nigella sativa* published in English or Urdu were included, while non-scientific or duplicate studies were excluded. Relevant data were extracted and synthesised to integrate traditional Unani knowledge with modern pharmacological findings, highlighting key bioactive constituents and therapeutic applications.

Vernacular names^{5,6,7,8}

Arabic: Shoneez, Habbah sauda, Habbet el baraka, Kamun-Aswad, Habbe- aswad, Kamoon-e-Hindi

Persian: Siyah Dana, Shoniz, Siyah Daru, Shoniz, Shonoz, Siyah Biranj

Urdu: Kalonji

Hindi: Kalaunji, Mangaraila, Kalonji

Sanskrit: Sthulajiraka, Upakuncharika, Susavi, Krishna-jiraka, Upakunchika. Bshpika, Kalajaji, karavi, Kunchi, Kunchika, Kunjika Musavi,

Tamil: Karunjarakam, karungiragam

Bengali: Kalajira, Mungrela, Mota Kalajira

Unani: Kalonji, Shoniz

English: Black cumin, small fennel, Nutmeg flower

Gujrati: Kalonji, Jirum, Kalaunji

Kannada:	Karijirige
Marathi:	Kalaunji-Jire, Kalerjire
Malayalam:	Karinchirakam
Punjabi:	Kalvanmji
Telugu:	Peeajila Karra, Nallajilakara

Taxonomic hierarchy^{2,9}

Kingdom	Plantae
Clade	Angiosperm
Class	Eudicots
Order	Ranunculaceae
Family	Ranunculaceae
Genus	<i>Nigella</i>
Species	<i>sativa</i>

Origin, habitat and distribution

N. sativa is an annual flowering plant. It most probably belongs to the Mediterranean region. The seeds of this plant were first discovered in Tutankhamun's tomb in Egypt during the 18th dynasty (1549/1550–1292 BCE), indicating that the origin of this plant is likely Egypt and its adjoining regions. However, *Nigella sativa* is distributed worldwide and cultivated in many countries and regions, including the Middle Eastern Mediterranean region, Central and Southern Europe, the former Soviet Union (Central Asia, Eastern Europe, Russia, and Transcaucasia), Northern Africa, Sudan, Ethiopia, Kenya, Somalia, India, Pakistan, Bangladesh, Sri Lanka, Nepal, Iran, Syria, Turkey, and Saudi Arabia. This plant is grown in many northern Indian states for commercial purposes, and India is the world's largest producer and exporter of *Nigella sativa*. In India, it is found in Uttar Pradesh, Punjab, Himachal Pradesh, Bihar, Bengal, Assam, and Maharashtra.^{2,7,8,9}

It is cultivated in the northern plains, central, and peninsular regions of India, with a temperature range of 20-25°C during the period of sowing and seed formation. Therefore, warm and sunny climates are required for its cultivation. It grows well in the cool-dry regions of other parts of the world. *Nigella sativa* is frost-sensitive at all growth stages; therefore, its cultivation in Europe and tropical highlands is rarely possible. The sowing period of *Nigella sativa* depends on its location; therefore, in the Northern Hemisphere, it is sown during spring or early summer, but in regions with a monsoon climate, it is sown during the early rainy period. Flowering and seed setting occur in cool and humid weather. It cannot grow in shade. *Nigella sativa* can be grown on well-drained, light (sandy), medium (loamy) and heavy soils. Soils with slightly acidic, neutral, and slightly basic (alkaline) pH values are ideal for its growth, and sandy/loamy soils rich in microbial activity are the most suitable soils for cultivation. A soil pH of 7.0 to 7.5 is the most favourable for its cultivation.^{7,9,10}

Botanical description

It is an annual, small-flowering plant, 20-30 cm tall, originating in the Middle East, South Asia, and Southwest Asia. The plant has tapering, finely divided, linear, green leaves, 2-3 pinnatisect, 2.5-5 cm long, cut into linear or linear-lanceolate segments. It also features delicate, white, yellow, pink, pale blue, or purplish flowers with 5 to 10 petals. The flowers are terminal, greyish-blue in colour, on solitary, long peduncles (2-2.5 cm). The sepals are ovate, acute, and clawed, and the petals are nectarial, 8 in number, genticulate with a saccate gland in the knee, one on the face, and one on the apex of each lobe. Carpals are 5-7 in number, inflated, warty at the sides, united to the top, and beak as long as the ovary. The fruit has a large and inflated capsule composed of three to seven united follicles, each containing numerous seeds. Seeds are trigonous, rugulose-tubercular, and black seeds are three-cornered with two sides flat and one convex, black or brown externally, oleaginous within, of a strong, agreeable odour, like that of nutmeg, and a spicy, pungent taste.^{3,7,9,11,12}

Macroscopic:

Seeds flattened, oblong, angular, rugulose tubercular, small, funnel-shaped, 0.2 cm long and 0.1 cm wide, black in colour, odour slightly aromatic, taste bitter.^{5,6,9,11}

Microscopic:

The transverse section of the seed shows a single layer of epidermis consisting of elliptical, thick-walled cells externally covered with a papillose cuticle filled with reddish brown content, epidermis followed by 2-3 layers of thick-walled, tangentially elongated, parenchymatous cells, followed by a pigmented layer with reddish brown pigment, below pigmented layer, parenchyma composed of thick-walled rectangular, radially elongated cells, present in a layer, and endosperm consisting of moderately thick-walled rectangular to polygonal cells, a few filled with oil globules, and an embryo embedded in the endosperm.^{5,6}

Mahiyat (Unani description)

Kalonji is an herb, and its branches are large, thin and resemble those of the fennel plant. Its leaves look more like the leaves of the *sa'atar* (*Zataria multiflora*) plant, but are thinner. The upper part of the leaves resembles the upper part of the leaves of *Khashkhash* (*Papaver somniferum*). The flowers are usually yellow and white, but some flowers have blue hues. Its seeds are enclosed within capsules that resemble onion seeds. The seeds are black in colour, almost triangular in shape, and contain white oily kernels. Seeds have strong aromatic odours and are bitter (**Figure 1**).^{13, 14}

Juze mustamela (part used)

Dried fruit and seeds^{8,9,13,14}

Mizaj (temperament)

Hot 2° and Dry 2°^{7,15,16,17}

Hot 3° and Dry 3° 4,13,18,19

Miqdar-e-khuraq (Therapeutic Dose)

1-2 g 5,14,17

3 g 6,18

Mazarrat (Adverse Effects)

It causes Diphtheria (*Khunaaq*) 7,18,19,20

It causes Giddiness (*Dauran-e-Sar*) 18,19,21

It is harmful to the lungs 18 and kidneys 20

Musleh (Correctives)

Kateera (*Astragalus gummifer*) 18,19,21, *Sirka* 17,21, *Samagh-e-arabi* (*Acacia arabica*), *Sard ashiya* 17,20, *Tabasheer* (*Bambusa arundinaceae*), *Kasni* (*Chicorium*

intybus)¹⁸, *Tukhm-Kheyar* (*Lactuca sativa*), *Khurfa* (*Portulaca oleraceae*)¹⁸.

Badal (Substitute)

Anisoon (*Pimpinella anisum*) 17,18,21, *Gond Zaitoon* (*Olea europea*), *Tukhme Rashad* (*Lepidium sativum*), *Ajwayen khurasani* (*Hyoscyamus niger*) 18, *Soye ke Beej* (*Anethum graveolens*) 21.

Important formulations

Majoon-e-Kalkalanaj, *Majoon-e-Fanjnosh*, *Majoon-e-Kundur*, *Majoon-e-Fotnaji* 5,6,22

Af'al (Pharmacological Actions) (Table 1)

Table 1: Pharmacological actions of drug *Nigella sativa* Linn.

Pharmacological Action (Afa'al)	Unani References	Ethnobotanical References
<i>Muhallil-e-awram</i> (Anti-inflammatory)	5,13,14,21	1,2,9,11,33,42,43
<i>Musakkin</i> (Analgesic)	13,14	1,2,9,11
<i>Munaffis-e-balgham</i> (Expectorant)	13,14	7,2,9
<i>Mudir-e-Haiz</i> (Emmenagogue)	14	7,2,9
<i>Qatil-e-Kirm-shikam</i> (Antihelmintic)	13,14	1,2,9,11
<i>Kaseer-e-Riyah</i> (Anti-flatulence)	13,14	2,9,11
<i>Da'afae Humma</i> (Anti-pyretic)	13	7,11
Hair growth	13	24
<i>Mudir-e-Labn</i> (Galactagogue)	13,23	7,12
<i>Jali</i> (Detergent)	14,23	25
<i>Mudir-e-Baul</i> (Diuretic)	13,14	7,11
<i>Muqawwi-e-Meda</i> (Stomachic)	14	1,11
<i>Mulaiyin</i> (Laxative)	14	11
<i>Qatil-e-Jaraseem</i> (Anti-microbial)	23	1,36,26,39
<i>Musakhin</i> (Rubefacient)	14,23	25
Antioxidant activity	-	1,11
Anticancer activity	-	1,11,54
Immunomodulatory activity	-	1,11,46
Cardioprotective activity	-	1,11
Antidiabetic activity	-	1,11,49
Nephroprotective activity	14	1
Neuroprotective activity	14	1

Mawaq-e-istamal (Therapeutic Uses) (Table 2)**Table 2: Therapeutic uses of drug *Nigella sativa* Linn.**

MAWAQ-E-ISTEMAL (THERAPEUTIC USES)	UNANI REFERENCES	ETHNOBOTANICAL REFERENCES
<i>Waj'a-ul-mufasil</i> (Arthritis)	14,21	1,11,42
<i>Zeequn nafas</i> (Asthma)	13,17,21,33	1,27,28
<i>Nafakhe Shikam</i> (Flatulence)	17,19,21	7,11
<i>Ehtebase Haiz</i> (Amenorrhoea)	17,19,21	7,11
<i>Qillate Laban</i> (Agalactorrhoea)	13,17,19,20	7,12,25
<i>Zaufe Meda</i> (Weakness of Stomach)	5,17,20	1,11,51
<i>Nazla-wa-Zukam</i> (Cold & Coryza)	13,17,19,20	1,43,42
<i>Qabz Daimi</i> (Chronic constipation)	17	11
<i>Istisqa</i> (Ascites)	13,14	11
<i>Yarqan</i> (Jaundice)	13,14,23	11
<i>Ehtebas-e-Baul</i> (Retention of Urine)	19,29	11
<i>Dard-e-kamar</i> (Backache)	14,23	11,42
<i>Sudaa</i> (Headache)	14,23	11,42
<i>Bars</i> (Vitiligo), <i>Da'ad</i> (Tinea)	14,23	26,30
<i>Kirm-e-Shikam</i> (Helminthiasis)	13,14,21,23	1,11,36
<i>Sa'afa</i> (Baldness)	13,14,23	24,31
<i>Basoor labn</i> (Acne)	13	32

Phyto-chemical studies

Numerous phytochemical studies have been conducted to isolate and identify the chemical composition of *Nigella sativa* Linn. plants. The majority of the metabolites were obtained from seeds, followed by roots and shoots. Thymoquinone is the main active constituent of *N. sativa* (Table 3). The seeds of *Nigella sativa* Linn. contain: protein, 26.7%; fat, 28.5%; carbohydrates, 24.9%; crude fibre, 8.4%; and Total ash, 4.8%. The seeds also contain a good quantity of various vitamins and minerals, including Cu, P, Zn, and Fe. Carotene is also present in the seeds and is converted by

the liver to vitamin A. Phytoconstituents are found in different categories:

Volatile oil (0.5-1%)

Fixed oil (35.6 – 41.6%)

Alkaloids (1–12)

Fatty acids (13–25)

Polyphenols (26–54)

Phytosterols (55–60)

Terpenes and terpenoids (61–151) and others (152–171) ^{1,5,6,8,9,11,33,34,35}.

Table 3: Phytoconstituents of drug *Nigella sativa* Linn.⁹

ALKALOIDS	FATTY ACID	POLYPHENOL	TERPENES AND TERPENOID	PHYTOESTEROL	OTHERS
Nigellidine	Methylnonadeca-15, 17-dienoate	Vanillic acid	Thymoquinone, Camphene, Linalool, Camphor, β -pinene oxide, Cis, pinocarveol	Cholesterol	Eugenol
Nigellicine	Pentyl hexadec-12-enoate	Salicylic acid		Campesterol	Methyl-eugenol
Nigellicimine	Pentyl pentadec-11-enoate	p-dihydroxybenzoic acid	α -terpineol, Nerol- α -pinene, Fenchone, Dihydrocarvone	Stigmesterol	(E)-cinnamaldehyde
Nigellicimene-N-oxide		p-coumaric acid	Carvone, Trans- β -terpineol, Terpinen-4-ol, Umbellulone	β -sitosterol	3-methylnonane
Nigellamine	Myristic acid	Chlorogenic acid	Carvacrol, p-cymene-8-ol	δ -7-stigmasterol	n-nonane
Nigellidine-4-O-sulfite	Palmitic acid	Syringic acid		δ -7-avenasterol	Dodecanal
Nigellamine A1	Lauric acid	Ferulic acid	α -ionone, α -longipinene, Longifolene,		n-decane
Nigellamine A2	Stearic acid	Trans-2-hydroxycinnamic acid	(Z)-caryophyllene, Cyclosativene, α -copaene, Aromadendrene, α -longicyclone, 2,4(10)-thujadiene, Dihydrofarnesyl acetate		1-methyl-3-propyl benzene
Nigellamine A3	Oleic acid	Caffeic acid	Pimaradiene, Myrcene, Limonene		benzaldehyde
Nigellamine A4	Lenoleic acid	Trans-cinnamic acid	p-cymene, 1,5,8-p-menthatriene		1-ethyl-2,3-dimethyl benzene
Nigellamine A5	Lenolenic acid	4-hydroxybenzoic acid	Γ -terpinene, terpinolene		n-tetradecane
Nigellamine B1	Eicosadienoic acid	5-hydroxybenzoic acid	Thymohydroquinone dimethylether		n-hexadecane
Nigellamine B2	n-decanoic acid	3-hydroxybenzoic acid	Thymohydroquinone methyl ether		Citronellyl n-butyrate
Nigellamine C	Butyric acid	Protocatechuic acid	Trans-sabinene hydrate acetate, Ocimenone, β -farnesene, Citronellyl acetate, α -phellandrene, Tricyclone, α -terpinene, p-cymene, Trans- α -bergamotene, 1,8-cineole, Cis-sabinene hydrate, Trans-sabinene hydrate, Borneol, Pinocarvone, Trans-dihydrocarvone, Iso-dihydrocarveol, Myrtenol, trans-carveol, cis-carveol, Bornyl acetate, Thymol, anisaldehyde, Methyl geranate, trans-anethol, β -bisabolol, β -bisabolene, p-cymen-7-ol, neryl acetate, Z,E-farnesyl acetate, Sabinene, Estragol, β -Elemene		methyl linoleate
	hexadecyl ester	Quercetin	Cis-thujopsene, β -caryophyllene, δ -cadinene, Myristicin, Cis-carvyl acetate, 6-methyl- α -(E)-ionone, farnesyl acetate, Davanone, geranyl acetone, Iso-longifolene, geranial, γ -Elemene, α -curcumene, Cis-piperitol		α -hederin
		Sinapinic acid	trans-piperitol, α -longifolene		dodecanal
		Rosmarinic acid	α -zingiberene, γ -himachalene		2-undecanone
		Catechin hydrated	α -himachalene, α -humulene		(Z)-isoeugenol acetate
		Apigenin			Tetradecanal
		Epicatechin			Iso-longifolol
		Myricetin			coumarin
		Flavone			
		Gallic acid			
		Amentoflavone			
		Naringenin			
		Chrysin, Galangin			
		Kaempferol			

Pharmacological studies

Antimicrobial activity

The antimicrobial activity of *Nigella sativa* Linn. seeds was determined by Shafodino *et al.* using different extracts with different solvents (petroleum spirit, ethyl acetate, methanol, water, and hexane). For the antimicrobial activity of undiluted extracts of *Nigella sativa* Linn. seeds, as determined using the disc diffusion assay on nutrient agar plates, the inhibitory effect of the hexane oil extract against the bacteria followed the order: *B. subtilis* > *S. aureus* > *E. coli* > *P. aeruginosa*. A similar trend was observed in the zones of inhibition for the oil extracted using absolute ethanol, but *P. aeruginosa* was the most susceptible to *E. coli*. The undiluted methanol extract was more effective against both Gram-negative and Gram-positive bacteria to nearly the same extent, and its inhibitory effects on the bacteria followed the order *P. aeruginosa* > *E. coli* > *B. subtilis* > *S. aureus*, unlike the other extracts. This can be attributed to the better extraction of phytochemicals, as demonstrated by both qualitative and quantitative analysis, particularly in the case of methanol, and to the differences in the chemical composition of solvent extracts. The aqueous extract exhibited antibacterial activity only against *B. subtilis*.³³

Chaieb *et al.* investigated the antibacterial activity of thymoquinone (an active component of *Nigella sativa* Linn. seeds) and its biofilm inhibition potency against 11 human pathogenic bacteria. Thymoquinone exhibited significant bactericidal activity against various bacteria, including *Staphylococcus aureus* and *Staphylococcus epidermidis*. The inhibition of biofilm development (%) was 85% for *Enterococcus faecalis*, 22% for *Staphylococcus aureus*, and 60% for *Staphylococcus epidermidis*.³⁶

In an experimental study conducted by Khan *et al.*, an aqueous extract of *Nigella sativa* Linn. seeds exhibited inhibitory effects against candidiasis in mice. A 5-fold (41300 ± 55) decrease in *Candida* in the kidneys, 8-fold (690 ± 83) in the liver, and 11-fold (901 ± 99) in the spleen were observed in the groups of animals post-treated with the plant extract. Upon histopathological examination, it was observed that the tissue architecture was preserved, and there was less infiltration of inflammatory cells in the post-treated group compared to the control group. There was no difference in tissue architecture between the specimens from animals in group 1 (control) and group 3 (pre-treated) at.³⁷

The antidermatophyte activity was evaluated by Aljabre *et al.*, with the ether extract of *Nigella sativa* Linn. and thymoquinone against eight species of dermatophytes, four species of *Trichophyton rubrum*, and one each of *Trichophyton interdigitale*, *Trichophyton mentagrophytes*, *Microsporum canis*, and *Epidermophyton floccosum*, using the agar well diffusion method. The MICs of the ether extract of *N. sativa* and thymoquinone were 10-40 and 0.125-0.250 mg/mL, respectively. Hence, the results showed anti-dermatophyte activity of

the ether extract of *N. sativa* seeds and its active principle, thymoquinone.³⁸

Another study by Hannan *et al.* showed that all tested strains of methicillin-resistant *Staphylococcus aureus* (MRSA) were sensitive to the ethanolic extract of *Nigella sativa* Linn. at a concentration of 4 mg/disc, with an MIC range of 0.2-0.5 mg/ml. Therefore, it may be concluded from this study that *Nigella sativa* Linn. seed extract has antimicrobial activity against MRSA.³⁹

Anti-inflammatory activity

A study conducted by Dwita *et al.* evaluated the anti-inflammatory activity of *Nigella sativa* Linn. oil in a simple balm stick through topical application on Wistar rats (*Rattus norvegicus* L.). Fifty rats were used in this study. The activity was evaluated using two methods: carrageenan-induced paw oedema and granuloma pouch in rats. The results indicated that balm sticks containing 10% *Nigella sativa* Linn. can overcome both acute and subacute inflammation by showing high oedema inhibition (60.64%), low leukocyte count (43.55% lower than control), and a significant TNF- α concentration (50% lower than control) in the inflamed area of rats. Therefore, it can be concluded that *Nigella sativa* Linn. possesses anti-inflammatory properties.⁴⁰

Shady *et al.* examined the effect of *Nigella sativa* Linn. on the compact bone of streptozotocin-induced diabetic rats. Forty adult male rats were divided into four groups: control, *Nigella sativa* Linn. treated, diabetic, and diabetic with *Nigella sativa* Linn. Radiologically, diabetic rats treated with *Nigella sativa* Linn. showed remodelling of the bone with a slight decrease in cortical thickness. Histologically, the femoral sections of both control and *Nigella sativa* Linn. treated rats were similar, showing compact bone with smooth bone surfaces (periosteum and endosteum). Active osteoblasts with cubic nuclei appeared on the bone surface. Osteocytes are present in the lacunae between the Haversian canals. The collagen fibres were regularly arranged. Morphometrically, diabetic rats treated with *Nigella sativa* Linn. showed a highly significant improvement in osteoblast numbers compared to diabetic rats. Immunohistochemically, diabetic rats treated with *Nigella sativa* Linn. showed increased osteopontin protein expression compared to diabetic non-treated rats. Treatment of diabetic rats with *Nigella sativa* Linn. resulted in improved body weight, as well as enhanced biochemical, radiographical, histological, morphometric, and immunohistochemical outcomes. Therefore, it can be said that *Nigella sativa* Linn. exhibits anti-osteoporotic effects.⁴¹

An experimental study by Pise *et al.* evaluated the anti-inflammatory activity of *Nigella sativa* Linn. seed fixed oil in different models of inflammation in rats and compared it with that of the control and aspirin. In the model of acute inflammation, specifically carrageenin-induced paw oedema in rats, *Nigella sativa* Linn. demonstrated anti-inflammatory activity, which was statistically significant compared to the control ($P < 0.001$), but less pronounced than that of aspirin. In the

cotton pellet-induced granuloma method, *Nigella sativa* Linn. significantly decreased the formation of granulomatous tissue compared to the control ($P < 0.001$). *Nigella sativa* Linn. exhibited significant anti-inflammatory activity comparable to that of aspirin in a formaldehyde-induced arthritis model of chronic inflammation ($P > 0.05$). This suggests that *Nigella sativa* Linn. may act as an anti-inflammatory agent.⁴²

A clinical trial conducted by Nikakhlagh *et al.* investigated the anti-inflammatory effects of *Nigella sativa* Linn. and its effects on inflammatory factors in patients with allergic rhinitis symptoms. The present study included 66 patients with allergic rhinitis, including 22 males (33.3%) and 44 females (66.7%), with a mean age of 47.19 years. A total immunoglobulin E level of more than 100 was reported in 38 patients before treatment. Immunoglobulin E was detected in the nasal wash of 7 patients and was undetectable in 59 cases. Only 6.1% of the study population had nasal mucosal eosinophil. *Nigella sativa* Linn. has been shown to reduce the presence of nasal mucosal congestion, nasal itching, runny nose, sneezing attacks, turbinate hypertrophy, and mucosal pallor during the first 2 weeks. This indicated the anti-inflammatory role of *Nigella sativa* Linn.⁴³

Galactagogue action

Moty *et al.* found the effect of *Nigella sativa* Linn. seed supplementation on milk fat, milk protein, and milk energy in 20 lactating Ossimi ewes during the experimental period. They were randomly assigned to four groups: two groups, G1 and G2, that were single suckled, and the other two groups, G3 and G4, that were twins suckled. G1 and G2 were fed a basal diet and a basal diet supplemented with 100 mg of *Nigella Sativa* Linn. seeds daily for G2. Ewes in the third (G3) and fourth (G4) groups were fed on a basal twin diet (control-twins) and on a basal twin diet +100mg daily *Nigella sativa* Linn. seeds for G4. The results of this experiment showed that milk yield had insignificant differences in the first and second weeks of the experiment. However, from the third to the twelfth week, the difference among groups was highly significant ($P < 0.01$) in the G2 and G4 groups compared to the controls, G1 and G3. Yield of milk was significantly ($P < 0.01$) higher for ewes suckling twins than those suckling single lambs. The study also showed that dietary supplementation with *Nigella sativa* Linn. seeds significantly ($P < 0.01$) increased the percentage of milk fat, protein, and milk energy. In addition, the fat percentage, protein percentage, and milk energy gradually increased with advancement in lactation until the lactation period ended.⁴⁴

Immunomodulatory action

A study was conducted by Opeyemi *et al.*, in which 96 mice, weighing 20–25 g, were divided into 12 groups of

eight animals each. The mice were infected with a standard inoculum of the strain NK65 *Plasmodium berghei* (chloroquine sensitive), and the percentage parasitaemia suppression was measured. The absolute effect of black seed-supplemented diet and its combinatory effect with chloroquine were investigated on reactive oxygen species (ROS), glutathione peroxidase, reduced glutathione, glutathione-S-transferase and serum immunoglobulins (IgG and IgM), and the haematological parameters (haemoglobin, packed cell volume, and red blood cell count) in *P. berghei*-infected mice were studied. The serum levels of inflammatory cytokines, tumour necrosis factor (TNF- α), interleukin (IL-6 and IL-10), IgG, and IgM were assayed. The temperature and behavioural changes in the mice were observed. Infected mice were treated with dietary supplementation of black seed with a percentage inclusion (2.5%, 5%, and 10%) and showed significantly decreased parasitaemia and ROS levels ($p < 0.05$) compared with untreated mice. The results showed a significant suppression of pro-inflammatory cytokines (TNF- α and IL-6) and a significant elevation of the anti-inflammatory cytokine (IL-10), as well as antioxidant markers and immunoglobulin levels, in *P. berghei*-infected mice treated with black seed. The study revealed that black seed enhanced host body antioxidant levels and modulated inflammatory and immune responses by regulating and controlling inflammatory cytokines and immunomodulatory mediators.⁴⁶

Majdalawieh *et al.* suggested that *Nigella sativa* Linn. constituents may serve as potent immunomodulators of splenocyte responses, Th1 versus Th2 immune reactions, macrophage inflammatory responsiveness, and NK activity against tumour formation and progression using BLAB/c and C57BL/6 primary cells. They demonstrated that the aqueous extract of *Nigella sativa* Linn. significantly enhanced splenocyte proliferation in a dose-dependent manner and promoted the secretion of Th2, Th1, and cytokines by splenocytes. The secretion of IL-6, TNF- α , and NO, key pro-inflammatory mediators, by primary macrophages was significantly suppressed by the aqueous extract, indicating that *Nigella sativa* Linn. exerts anti-inflammatory effects in vitro. Experimental evidence indicated that the aqueous extract significantly enhanced NK cytotoxic activity against YAC-1 tumour cells.⁴⁶

Antihistaminic effect

Gunel *et al.* conducted a study to investigate the anti-inflammatory activity of thymoquinone (TQ) in a rat model of allergic rhinitis. Allergic rhinitis was induced in 42 rats, which were divided into six groups: healthy controls, allergic rhinitis (AR) group, AR group treated with corticosteroid, healthy rats administered TQ at 10 mg/kg, AR group treated with TQ at 3 mg/kg, and AR group treated with TQ at 10 mg/kg. Serum levels of interferon-gamma (IFN- γ), interleukin-4 (IL-4), IL-10, and ovalbumen-specific immunoglobulin E (IgE) were measured. The level of ovalbumin-specific IgE was

increased by sensitisation but significantly reduced in the TQ10+AR and corticosteroid-treated groups. IL-4 levels were significantly increased in the AR group, but were inhibited by TQ administration at both 3 and 10 mg/kg doses. IFN- γ -levels did not differ significantly among the groups but tended to decrease in the treatment groups. IL-10 levels significantly decreased in the TQ group at both doses. Histopathological examination of the nasal mucosa showed normal findings in the control group, whereas the AR group exhibited oedema, eosinophilic infiltration, and increased goblet cell count. Eosinophil count in the nasal mucosa was significantly higher in the AR group compared to the control group, but significantly decreased in the TQ3+AR and TQ10+AR groups. Oedema was significantly greater in the AR group, but significantly decreased with TQ administration at both doses. The goblet cell counts did not differ significantly between the groups. TQ at a dose of 10 mg/kg was more effective than TQ at a dose of 3 mg/kg. Thus, TQ may potentially be considered a supplemental agent in the treatment of AR.⁴⁷

Antidiabetic activity

Antidiabetic activity, as conducted by Rabey *et al.*, divided 40 male Albino rats into four groups to investigate the effects of *Nigella sativa* and propolis methanol extracts on streptozotocin-induced diabetes. The first group served as the negative control and received a standard diet, whereas the other three groups were injected with streptozotocin to induce diabetes. Group 2 received streptozotocin and a normal basal diet, Group 3 was treated with *Nigella sativa* Linn. methanol extract, and Group 4 was treated with propolis methanol extract. The treatment lasted for 4 weeks. Results showed that the serum fasting blood sugar levels were significantly higher in the positive control group than in the negative control group. However, treating diabetic rats with either *Nigella sativa* Linn. or propolis methanol extract for 4 weeks led to a significant reduction in fasting blood sugar levels. Propolis extract was found to be more effective than *Nigella sativa* Linn. in lowering blood sugar levels. Histological examination of the kidney sections revealed that the *Nigella sativa* Linn. extract appeared to restore the normal appearance of glomeruli and regenerate tubules, accompanied by interstitial haemorrhage. The propolis extract, on the other hand, nearly restored the normal cortical tissue in the kidneys. Haematological examinations revealed that diabetic rats in group 2 had elevated glucose levels and lipid peroxide, along with reduced enzyme activities of superoxide dismutase, catalase, and glutathione-S-transferase, compared to the negative control group. Hyperglycaemia also led to increased levels of carboxymethyl lysine, interleukin-6, and immunoglobulins. Renal function parameters were elevated, whereas potassium and sodium levels were decreased. Kidney and pancreatic tissues exhibited severe histopathological changes. Treating diabetic rats with either *Nigella sativa* Linn. or propolis methanol extracts in Groups 3 and 4, respectively, resulted in improvements in all altered biochemical and

pathological examinations. Overall, this study demonstrates that both *Nigella sativa* Linn. and propolis methanol extracts have beneficial effects on streptozotocin-induced diabetes in rats, leading to a reduction in fasting blood sugar levels and the restoration of normal kidney appearance and function.⁴⁸

Abdelmeguid *et al.* studied the effects of *Nigella sativa* Linn. aqueous extract and oil, as well as thymoquinone, on serum insulin and glucose concentrations in streptozotocin-induced diabetic rats. Serum insulin and glucose concentrations and pancreatic tissue malondialdehyde (MDA) were determined. Electron microscopy was used to identify any subcellular changes. Diabetes was associated with increased tissue MDA levels and serum glucose levels, and decreased insulin and SOD levels. Treatment of rats with *Nigella sativa* Linn. extract and oil, as well as thymoquinone, significantly decreased diabetes-induced increases in tissue MDA and serum glucose and significantly increased serum insulin and tissue SOD.⁴⁹

Gastro-protective activity

The study conducted by Magdy *et al.* aimed to investigate the gastroprotective effect of thymoquinone (TQ). Male Wistar rats were divided into 7 groups, with different treatments administered before undergoing pyloric ligation and ischemia/reperfusion (I/R) procedures. The control group received the vehicle only, while the positive control group received 1% Tween 80. The other groups were treated with different doses of Thymoquinone (TQ) (10 mg/kg; TQ10), TQ (20 mg/kg; TQ20), omeprazole (10 mg/kg; omeprazole10), omeprazole (20 mg/kg; omeprazole20), or a combination of omeprazole10 and TQ10. The results showed that I/R led to an increase in acid concentration, acid output, pepsin, and proton pump activity, while reducing mucin content when compared to the sham control group. However, all pretreatment regimens using TQ, especially TQ20, significantly hindered the alterations caused by I/R, similar to the effect observed with omeprazole20. These findings suggest that TQ has a comparable gastroprotective effect to omeprazole in inhibiting acid secretion and preserving mucin content. Histological examination revealed that I/R caused mucosal sloughing, haemorrhage, vacuolated parietal cells, vascular congestion, inflammatory cell infiltration, and submucosal oedema. However, rats pretreated with TQ showed reduced congestion in submucosal blood vessels and mild inflammatory cell infiltration. TQ20-treated rats exhibited a normal histological structure, similar to that of the control group, while omeprazole-treated rats showed effects similar to TQ10, with congested submucosal blood vessels, inflammatory cell invasion, and oedema. The combination treatment of TQ10 and omeprazole10 resulted in dilated gastric pits and mild inflammatory cell infiltration.

This study proved that TQ has a gastroprotective effect against I/R-induced gastric injury in rats. The pretreatment with TQ, especially TQ20, significantly inhibited acid secretion and preserved mucin content. The histological findings also supported the protective

effects of TQ on the gastric mucosa. These findings provide valuable insights into the potential therapeutic use of TQ for gastric protection.⁵⁰

The anti-ulcer activity of *Nigella sativa* Linn. aqueous extract on experimentally induced gastric ulcers and basal gastric secretion in rats was examined by Mofleh *et al.*, to rationalise its use by herbal and Unani medicine practitioners. Acute gastric ulceration was induced by various noxious chemicals (80% ethanol, 0.2 mol/L NaOH, 25% NaCl, and indomethacin) in rats. Antisecretory studies were performed in a separate group of rats. The gastric wall mucus content was estimated, and the gastric tissue was examined histopathologically. An aqueous suspension of *Nigella sativa* Linn. significantly reduced gastric ulcers induced by ethanol ($P < 0.0001$), NaOH ($P < 0.0001$), and NaCl ($P < 0.006$) at 250 and 500 mg/kg body weight compared with the values obtained in the control. Pretreatment with *Nigella sativa* Linn. suspension (250 and 500 mg/kg body weight) completely protected the gastric mucosa against different histopathological changes (congestion, haemorrhage, oedema, necrosis, inflammatory and dysplastic changes, erosions, and ulceration) in ethanol-treated rats. In addition, treatment with aqueous suspension of *Nigella sativa* Linn. resulted in a significant decrease in the volume of basal gastric secretion and titratable acidity after pyloric ligation for 6 h ($P < 0.0001$ and $P < 0.005$, respectively, at 250 and 500 mg/kg body weight), whereas *Nigella sativa* Linn. treatment did not influence the ulcer index at high doses ($P = 0.57$). Treatment with ethanol (80%) caused a significant ($P < 0.0001$) decrease in the mucus content of the gastric wall in untreated animals. The depleted gastric mucus was significantly replenished ($P < 0.0001$) after pretreatment with the *Nigella sativa* Linn. suspension at both doses. A significant dose-dependent reduction ($P < 0.002$) in stomach ulceration was observed after pretreatment with *Nigella sativa* Linn. suspension at both doses.⁵¹

Hepato-protective activity

In a study conducted by Mushtaq *et al.*, the hepatoprotective activity of 70% methanolic extracts of *Nigella sativa* Linn. (NSE) and *Piper nigrum* (PNE) was investigated at various doses (ranging from 100 to 400 mg/kg body weight) against liver injury induced by concanavalin A (con A) in mice. The study involved qualitative phytochemical analysis of the plant extracts and the induction of acute hepatic injury via intraperitoneal injection of Con A. The extent of liver injury was assessed using serum biochemical parameters, liver antioxidant stress assays, and histopathological analyses. This study found that both NSE extract and PNE exhibited dose-dependent hepatoprotective effects by reducing Con A-induced elevation in liver transaminase levels. Treatment with 400 mg/kg NSE and PNE ameliorated the Con A-induced changes in serum oxidative stress markers, biochemical parameters, liver function markers, and histopathology. These extracts demonstrated antioxidant properties at

both the serum and tissue levels, as they increased total antioxidant capacity (TAC), catalase (CAT), and superoxide dismutase (SOD) levels, while reducing total oxidative status (TOS) and malondialdehyde (MDA) levels in both serum and liver tissue homogenates compared to the Con A group. Furthermore, an acute oral toxicity test revealed that oral administration of NSE and PNE at doses of up to 2 g/kg did not produce any toxic effects in the treated mice. These doses are considered safe. Following toxicity testing, doses of 100–400 mg/kg were selected for assessing hepatoprotective activity. Macroscopic and microscopic analyses of mouse livers showed that Con A induced acute hepatic injury, characterised by changes in colour and tissue structure. However, treatment with NSE and PNE significantly improved liver tissue, reducing inflammation and degenerative effects compared to the Con A-induced group.⁵²

Another study conducted by Zafeer *et al.* found that hepatic tissues are protected by the administration of *Nigella sativa* Linn. from the deleterious effects of toxic metals, such as lead, and attenuate hepatic lipid peroxidation following exposure to chemicals like carbon tetrachloride. Cadmium (Cd^{++}) causes alteration of the cellular homeostasis and oxidative damage in the body. The protective role of thymoquinone on the hepatotoxicity of Cd^{++} in the context of its protection against the perturbation of non-enzymatic and enzymatic antioxidants was investigated. The effect of thymoquinone pretreatment was examined in the post-nuclear supernatants prepared from the livers of mice under in vitro conditions. CdCl_2 treatment (5 mmol/L) resulted in a significant increase in antioxidant enzymatic activity in mice. It also caused a significant increase in protein carbonyl content and a reduction in glutathione content. Pretreatment with thymoquinone (10 $\mu\text{mol/L}$) demonstrated significant protection, as evidenced by the rejuvenation of depleted antioxidants in the cellular fraction. These results demonstrate that thymoquinone exerts a modulatory influence on the antioxidant defence system upon exposure to toxic insults.⁵³

Anticancer activity

Salem *et al.* conducted an in vitro study of thymoquinone to determine whether thymoquinone can increase survival and sustain the expression of the homing receptor CD62L in antigen-specific T cells. Stimulation of OT-1 (transgenic CD+) T cells with OVA antigen resulted in activation, as shown by a decrease in the surface expression of CD62L, which coincided with significant apoptosis measured three and five days after antigen stimulation. The addition of lower concentrations of thymoquinone during CD85+ T-cell activation resulted in enhanced survival of activated T-cells and sustained expression of CD62L. These effects are accompanied by an enhancement in the ability of CD8+ T cells to produce the effector cytokine interferon-gamma (IFN gamma). This suggests that thymoquinone

has a beneficial effect on conditioning T-cells in vitro for adoptive T-cell therapy against cancer and infectious diseases.⁵⁴

Dhandapani *et al.* conducted a study in which they developed a new type of gold nanoparticle called CurtoCumin AuNP (CC-AuNP) using a biosynthetic process that involved *Nigella sativa* Linn. seed extract and membrane vesicles from the probiotic strain *Curtobacterium proimmune* K3. They characterized the physical and chemical properties of CC-AuNP using spectroscopic and microscopic analyses. CC-AuNP demonstrated significant cytotoxicity against human gastric adenocarcinoma (AGS) cells, and this cytotoxic effect was linked to the overproduction of reactive oxygen species (ROS) in damaged mitochondria. This study also delineated the molecular mechanisms responsible for the cytotoxic effects of CC-AuNP. In AGS cells treated with CC-AuNP, key apoptotic signalling molecules such as p53, Bcl-associated X protein (Bax), and Caspase 9/Caspase 3 were significantly upregulated, although B-cell lymphoma 2 (Bcl-2) was downregulated. This treatment led to ROS production and disruption of the mitochondrial membrane potential. Additionally, the study confirmed the activation of autophagy-related biomarkers, including LC3b/a, Beclin-1, p62, and Caspase 8, through qPCR and western blotting. However, the autophagy pathway was suppressed in CC-AuNP-treated AGS cells, and it did not progress to the mature state. Overall, these results suggest that CC-AuNP promotes apoptotic signalling while inhibiting autophagy-related pathways, making it a potential candidate for anticancer therapy. The study also suggests that CC-AuNP, incorporating *Nigella sativa* Linn., could be utilised as a novel therapeutic agent against gastric cancer, and that *Nigella sativa* Linn. exhibits anticancer properties.⁵⁵

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Author Contribution:

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