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CHEMICAL CHARACTERIZATION AND POTENTIAL HEALTH BENEFITS OF NIGELLA SATIVA

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ABSTRACT

Nigella Sativa, commonly known as black seed or black cumin, holds a storied history dating back millennia, with its medicinal use documented in ancient Egyptian, Greek, and Islamic texts. This review provides a historical overview, chemical characterization, and potential health benefits of N. sativa, shedding light on its enduring significance in traditional medicine and its modern therapeutic potential. Chemical characterization reveals that N. sativa contains a diverse array of bioactive compounds, including thymoquinone, thymohydroquinone, and dithymoquinone, which exhibit potent antioxidant, anti-inflammatory, antimicrobial, and anticancer properties. These compounds are primarily found in the essential oil fraction of N. sativa seeds. *Nigella Sativa*, with its diverse array of bioactive compounds, presents several notable health benefits. Research indicates its effectiveness in managing diabetes, cardiovascular diseases, respiratory ailments, and neurological disorders. Moreover, it demonstrates hepatoprotective and nephroprotective effects while also modulating the immune system. These findings underscore its potential as a versatile natural remedy for addressing a range of health issues. The black seeds are used for reducing adverse effects of arthritis, asthma, inflammation, liver and gastro disorders besidesthe irpotentialrolei ndiabetes andcancers. Thefocusof thisreview istohighlight themedicinal significance of N. sativa in traditional medicine and opportunities for exploitation in contemporary medicine.

❖ **KEYWORD:** N. Sativa, Thymoquinone, Thymohydroquinone, Anticancer.

1. INTRODUCTION

- The history of plants as medicines is extensive, spanning thousands of years and encompassing diverse cultures and civilizations across the globe. From 3000 BCE to 500 CE, humanity's understanding of medicine was rooted in the natural world, with cultures like Egypt, Mesopotamia, China, and Greece harnessing the healing power of plants through herbal remedies. These ancient civilizations laid the groundwork for sophisticated healing systems such as Ayurveda in India, Traditional Chinese Medicine (TCM) in China, and Hippocratic medicine in Greece, which emphasized holistic approaches to health and the balance of bodily humors. The efficacy of different plants such as Coriandrum sativum, Acroptilon repens, Berberis lyceum, Alium sp., Opuntia sp., Lepidium sativum and Prosopis sp., among many others has been well established in the literature for treating different diseases.

- *Nigella Sativa* also well known as the Kalonji, Kalojeera, Black Caraway or Black seed. It belongs to the family Ranunculaceae. It is a short plant with average height of 20-30 cm. this plant has a branched stem with fine and deeply segmented leaves. It bears pale blue or white flower with 5-10 petals. It’s leaves are long and straited. It is not frost tender and flowers in summer month of June and July. It’s seeds ripen in spring around the month of August and September.

- In Unani literature it is described in the name of Habat-ul Sauda.

- N. Sativa has a broad spectrum of positive pharmacological effects, including antiviral, anti-inflammatory, hypotensive, hypoglycaemic and antitumor effects. These biological properties are related to the abundance of several phytochemicals, including

thymoquinone, terpenes, saponins, flavonoids, and essential oils. These promising active ingredients and their biological properties make N. sativa a powerful natural candidate for the prevention and control of diseases.

- The evolutionary origins of Nigella species are presumably in the Aegean and the adjacent Western-Irano-Turanian region; its centre of species diversity. The genus is found as wild in southern Europe, Russia, northern Africa, Asia Minor, Turkey, Middle-East, India, Pakistan, and Bangladesh.

- Today, the seed powder of N.sativa is recommended at 0.5–4 g in the Pharmacopoeia of India, which is used as a stimulant to ease bowel and indigestion problems and as carminative. It has also been administered to manage pain during menstruation and diabetes in India and Bangladesh. Similarly, N. sativa is widely used in traditional medicine of Algeria for the treatment of diabetes and also to treat high blood pressure (BP). Moreover, according to the Bedouins (Egypt), the wooden stem is used to treat jaundice, while seeds are used to treat BP as before, as well as heart diseases, etc. Similar uses have been reported in Iranian traditional medicine.

- The seeds of *Nigella Sativa* and their oil have been widely used for centuries in the treatment of various ailments throughout the world and it is an important drug in the Indian traditional system of medicines like unani and ayurveda. Among Muslims it is considered as one of the latest forms of healing medicines available due to it was mentioned that black seed is the remedy for all disease except that death in one of the prophetic hadith. It is also recommended for use on regular basis in Tibb-r-Nabwi.

- The pharmacologically significant constituent of *Nigella Sativa* is thymoquinone, a bioactive compound found in the seeds of the plant. Thymoquinone is a potent antioxidant and possesses a wide range of therapeutic properties, including anti-inflammatory, antimicrobial, antiviral, and anticancer effects. It exerts its pharmacological actions by modulating various cellular pathways and molecular targets involved in inflammation, oxidative stress, and immune response. Thymoquinone has been extensively studied for its potential health benefits and has shown promise in the treatment and prevention of various diseases and conditions, including asthma, allergies, diabetes, cardiovascular disorders, and cancer. Its multifaceted pharmacological activities make thymoquinone a valuable natural compound with diverse therapeutic applications.

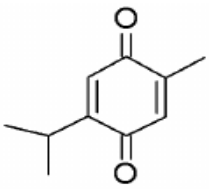
❖ **Table no. 1: General properties.**

Properties	Information
● Genus	● Nigella
● Family	● Ranunculaceae
● Species	● *Nigella Sativa*,Linn
● Common name	● Black cumin, Black seed, Black caraway
● Parts used	● Seeds
● Main chemical constituents	● Thimoquinone, thymol, thymohydroquinone
● Other Bioactive compounds	● Alpha-haderin, carvacrol, T-anethole,4-terpineol

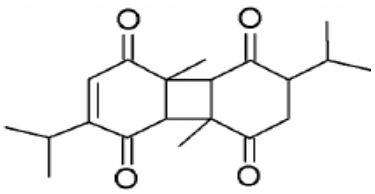
❖ **Table No. 2: Chemical constituents with their pharmacological use.**

Chemical constituents	Pharmacological uses
● Thymoquinenae	● Anti-oxidant, Anti-inflammatory, Anti-microbial, Anti-cancer.
● Thymohydroquinona	● Anti-oxidant, Anti inflammatory
● Thymol	● Anti-microbial, Anti-oxidant
● p-cymene	● Anti-oxidant, Anti inflammatory
● Alpha-hederin	● Anti-cancer, Anti-microbial
● Cavacrol	● Anti-inflammatory, Anti-microbial
● T-anethole	● Antimicrobial, Antioxidant
● 4-terpineol	● Antioxidant, Antimicrobial
● Linoleic acid	● Anti-inflammatory, Skin health
● Oleic acid	● Cardiovascular health, Skin health
● Palmitic acid	● Skin health, Anti-inflammatory
● Stearic acid	● Skin health, Anti-inflammatory
● Nigellone	● Antioxidant, Anti-inflammatory, Immunomodulatory
● Beta-pinene	● Anti-inflammatory, Antimicrobial
● Alpha-pinene	● Anti-inflammatory, Antimicrobial

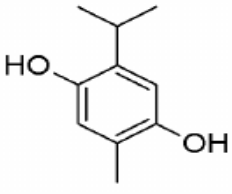
1.1 Structure of chemical constituents



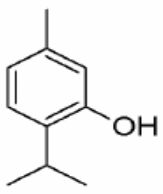
Thymoquinone



Dithymoquinone



Thymohydroquinone



Thymol

❖ **Methods of extraction of nigella sativa**

1. **Cold pressing -** Oil can be extracted from *Nigella Sativa* seeds by using the is suitable for extracting *Nigella Sativa* oil from different methods. The cold pressing method seeds. In this method, mechanical pressing was used for the pressing of seeds at a temperature of 25 °C. Furthermore, the separation of oil and crushed seed fiber has been performed by soaking the solution for one night at a 25 °C temperature. After that, filtered oil was obtained by using a glass funnel and Watman #4 filter paper (0.45 µm, Vivascience AG, Hannover, Germany).

2. **Supercritical fluid extraction** - Another innovative method for the extraction of *Nigella Sativa* oil from seeds was used by Mohammed et al. The supercritical fluid extraction equipment (FeyeCon Development B.V. Weesp, Netherlands) was used for *Nigella Sativa* seed oil extraction, by using a stainless steel grinder (Waring Commercial, Torrington, CT, USA) for 3–4 min; the crushed dried seeds were obtained, placed the material in a 50-L container of extractor, and sealed tightly. The system used an automatic back pressure regulator for maintaining the temperature at 40 °C for 1 h; the pressure was 600 bar, and the flow rate of injected liquid carbon dioxide (CO_2) was 150 L/h.

In the supercritical fluid extraction method for *Nigella Sativa* seed oil extraction. In its instrumentation, it contained a syringe pump with 260 mL capacity, controller system (ISCO 260D), and ISCO series 2000 SCF extraction system (SFX 220), consisting of a dual chamber extraction module with two 10 mL stainless steel vessels. Hence, about 5 g of ground black seeds were added in a stainless steel cell (10 mL). Then, the standard quantity of supercritical carbon dioxide (SC CO_2) (50–400 mL) was flushed into the cell at a 1 mL/min flow rate. The

final concentration of the extract was collected in the cold trap. After optimization of supercritical fluid extraction conditions, the lower yield of 0.84% (508 °C, 400 bar, and 100 mL) and higher yield of 31.7% (508 °C, 100 bar, and 200 mL) were obtained at optimum levels.

3. **Soxhlet extraction** - The soxhlet apparatus for *Nigella Sativa* oil extraction from black seeds. For this purpose, *Nigella Sativa* seeds were collected from different regions of India, including Tamil Nadu, Triplicane, and Chennai. During the sieving process, the small and contaminated seeds were removed at room temperature. In this process, the seeds were first ground using a tabletop mixture, hexane was used for extraction of seed oil for approximately 2 h in a soxhlet apparatus, and the extracted oil was stored at room temperature in a selected amber glass bottle until use. *Nigella Sativa* seed has 28–35% fixed oil, which mainly consists of unsaturated fats. Through gas chromatography–mass spectrometry (GC-MS) analysis, 32 different compounds were found in black seeds.

4. **Hydro Distillation (HD) Method** - The hydro distillation (HD) method for the extraction of oil from *Nigella Sativa* seeds. In the first step, the seeds were ground at 25 °C. Then, they weighed the 70 g sample to be used for further analysis. The average yields were achieved and figured on a dry weight basis. For attaining essential oil through the HD method, they used a water holding flask for placing the material. It is called a Clevenger-type apparatus because the flask is directly connected to the condenser. After 2 h of continuous processing, a yield of 0.29 wt/wt of pale-yellow oil was obtained.

Burits and Bucar also chose the same technique for oil isolation, and an Austrian pharmacopoeia (Clevenger apparatus) was used as standard apparatus in the whole process. The results were not satisfactory because the oil extracted had lower quantities of essential oil, with only 3% thymoquinone content, while Soxhlet extraction yielded 48% thymoquinone content.

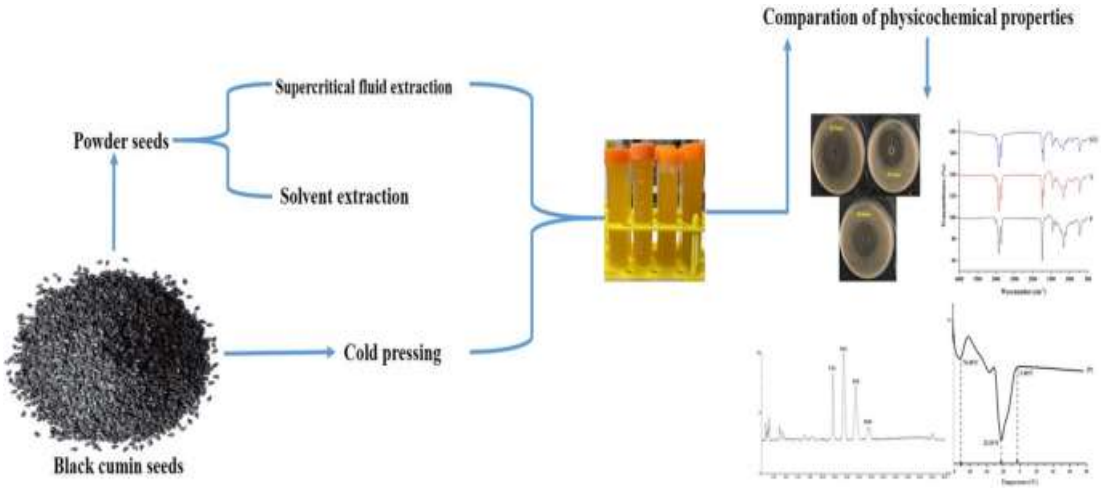
5. **Microwave Assisted Extraction (MAE) -** IN this method performed the oil extraction through a domestic microwave oven (Daewoo Electronics KOC-154KWR Microwave Oven) with a frequency of 2450 MHz. Initially, they took 50 g of ground seeds and selected a 500 mL round-bottomed flask for the soaking of seeds in 50 mL of water for about half an hour. After that, the Clevenger apparatus was fixed with a flask and utilized 450 W of power for heating (30 min). However, the essential oil was leached out in the n-

hexane solvent. Only 0.33% essential oil yield was achieved by using MAE extraction conditions (power 450 W, moisture content 50%, and time 30 min).

Ultrasound-Assisted Extraction Moghimi et al. used an ultrasound-assisted extraction method for oil extraction. For one treatment, a sample of 500 g was transferred to the 1.5-l container that was placed in the ultrasonic bath. Several optimization conditions were selected, including the time (30, 45, and 60 min) and ultrasound pretreatment power (30, 60, and 90 W) at a fixed frequency of 25 kHz. After completing this process, the oil was isolated by using a screw press at 33 rpm speed. The maximum results of 39.93% extraction efficiency were achieved at power of 90 W and time of 60 min, while the minimum results of 27.29% extraction efficiency were achieved at power of 30 W and time of 30 min.

6. **Steam distillation** - For the prevention of the side effects of degradation, steam distillation was performed at a low temperature. In 100 mL of distilled water, 10 g of seeds were added and mixed. This mixture was quantitatively transferred into the separatory funnel. This process of extraction was performed three times; a total of 10 mL of diethyl ether was added at every step, and the funnel was shaken vigorously. Sodium sulfate was used to dry the organic layer, and 0.4% was the obtained yield after evaporation in the water bath. A glass column-containing material was interpolated between the condenser and flask. The yield of oil that was extracted by steam distillation was 0.39%, and the color of the oil was pale yellow.

7. **Accelerate Solvent Extraction (ASE)** - A 1 g sample of black seeds in powdered form was taken in a stainless steel cell with a 34 mL capacity. The conditions were set: 100 atm pressure, 10 min static time, 20% rinse volume, 2 extraction cycles, 30 s purge time, and 26 mL of solvent volume. P1-P9 black seed samples from Pakistan, Indian, and Saudi Arabian were treated with n-hexane as P1-P3, methanol (MeOH), and dichloromethane (DCM) at 40 °C, P4-P6 with MeOH, DCM, and n-hexane at 50 °C; the same procedure was performed for P7-P9 at 70 °C. The results reveal that the solvent with high yield, following n-hexane, was MeOH, whereby the yield and recovery observed was 2.5 g (12.5%) for Saudi Arabia, 2.2 g (11%) for Pakistan, and 2.04 g (10.2%) for Indian black seed sample.



Process of extraction

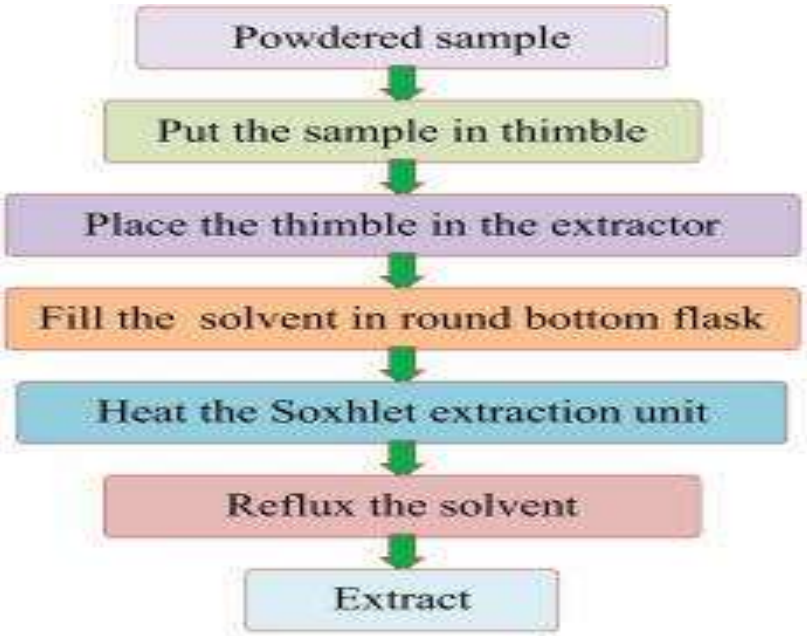


Table No. 3: Different extraction methods of nigella seeds oil.

Extraction Method	Solvent Used	Advantage	Disadvantage	Yield/Efficiency
Cold pressing	Hexane	Involves no heat or chemical treatments during oil extraction	Provides low yield	27%
Supercritical fluid extraction	SC CO_2	Rich in antioxidants	High cost	31.7%
Soxhlet extraction	Methanol	Low in cost	Residues of solvent has been left behind in the	29.9%

			extracted oil	
Hydro distillation (HD) method	Water	Very simple method and instrument, shorter extraction time, free from organic components, less labor consumption, good in quality, lower cost with good efficiency	High energy is required for extraction	0.29%
Microwave-assisted extraction (MAE)	n-hexane	Free from organic solvent, less time with maximum yield	Additional filtration or centrifugation required to remove the solid residue	0.33%
Ultrasound-assisted extraction	Hexane	Less energy and solvent consumption, reduced time of extraction		39.93
Steam distillation	Sodium sulphate	Performed at a low temperature to prevent from degradation	More time consuming, due to the low pressure of rising steam	0.40%
Accelerated solvent extraction	MeOH, DCM, and n-hexane	A latest and efficient method for extraction		

- **Potential benefits of nigella sativa**

- **Anti-inflammatory properties:** *Nigella Sativa* contains bioactive compounds such as thymoquinone, thymohydroquinone, and dithymoquinone, which have demonstrated significant anti-inflammatory effects in various studies. These compounds inhibit the production of inflammatory mediators such as cytokines and prostaglandins, thereby reducing inflammation in the body. Chronic inflammation is associated with a wide range of health issues, including cardiovascular diseases, autoimmune disorder, and neurodegenerative conditions.

- **Antioxidant activity:** The seeds of *Nigella Sativa* are rich in antioxidants, including flavonoids, phenolic compounds, and vitamins such as vitamin E. These antioxidants scavenge free radicals and reactive oxygen species (ROS) in the body, thereby protecting cells from oxidative damage. By reducing oxidative stress, *Nigella Sativa* may help prevent various chronic diseases such as cancer, cardiovascular disease, and age-related degenerative disorders.

- **Immune system support:** *Nigella Sativa* has been traditionally used to enhance immune function and combat infections. Research indicates that it may modulate the activity of immune cells such as T cells, B cells, macrophages, and natural killer (NK) cells. Thymoquinone, the major active compound in *Nigella Sativa*, has been shown to stimulate the production of cytokines and enhance the activity of immune cells, thereby bolstering the body's defense against pathogens.

- **Antimicrobial properties:** *Nigella Sativa* extracts and essential oil possess potent antimicrobial properties against a wide range of microorganisms, including bacteria, viruses, and fungi. Thymoquinone and other bioactive compounds disrupt microbial cell membranes, inhibit microbial enzymes, and interfere with microbial DNA replication, thereby exerting antimicrobial effects. This antimicrobial activity may be beneficial for treating infections caused by antibiotic-resistant bacteria and combating common pathogens such as Staphylococcus aureus, Escherichia coli, and Candida albicans.

- **Cardiovascular health:** Several studies have investigated the potential cardiovascular benefits of *Nigella Sativa*. It has been shown to lower blood pressure, reduce total cholesterol, LDL cholesterol, and triglyceride levels, and improve HDL cholesterol levels in animal and human studies. These effects may be attributed to the antioxidant, anti-

inflammatory, and vasodilatory properties of *Nigella Sativa*, which help protect against atherosclerosis, hypertension, and other cardiovascular disorders.

- **Pain relief:** *Nigella Sativa* has been used traditionally for pain relief and analgesia. Research suggests that it may modulate pain perception by interacting with opioid receptors and inhibiting inflammatory pathways. Thymoquinone and other bioactive compounds in *Nigella Sativa* exhibit analgesic effects in animal models of pain, including neuropathic pain, inflammatory pain, and visceral pain.

- **Gastrointestinal health:** *Nigella Sativa* has been used in traditional medicine for gastrointestinal ailments such as indigestion, bloating, and gastrointestinal infections. Thymoquinone and other constituents of *Nigella Sativa* exert gastroprotective effects by reducing gastric acid secretion, enhancing mucosal defense mechanisms, and inhibiting the growth of Helicobacter pylori bacteria, which are implicated in gastric ulcers and gastritis.

- **Diabetes management:** Studies suggest that *Nigella Sativa* may help regulate blood glucose levels and improve insulin sensitivity in individuals with diabetes or metabolic syndrome. Thymoquinone and other bioactive compounds in *Nigella Sativa* exhibit hypoglycemic effects by stimulating glucose uptake in cells, enhancing insulin secretion from pancreatic β-cells, and improving insulin signaling pathways. Additionally, *Nigella Sativa* may protect against diabetic complications such as nephropathy, neuropathy, and retinopathy due to its antioxidant and anti-inflammatory properties.

- **Skin health:** *Nigella Sativa* oil has been used topically for various skin conditions, including acne, eczema, psoriasis, and wound healing. The anti-inflammatory, antimicrobial, and antioxidant properties of *Nigella Sativa* oil help reduce inflammation, inhibit bacterial growth, and promote tissue repair and regeneration. Thymoquinone and other bioactive compounds in *Nigella Sativa* oil also exert anti-aging effects by protecting against UV-induced skin damage and collagen degradation.

- **Cognitive function:** Preliminary studies suggest that *Nigella Sativa* may have neuroprotective effects and improve cognitive function. Thymoquinone and other bioactive compounds in *Nigella Sativa* exhibit antioxidant, anti-inflammatory, and anti-apoptotic properties in the brain, which help protect neurons from oxidative stress,

neuroinflammation, and cell death. Additionally, *Nigella Sativa* may enhance memory, learning, and cognitive performance by modulating neurotransmitter levels, synaptic plasticity, and neurotrophic factors in the brain.

- **Respiratory health:** *Nigella Sativa* has been traditionally used to alleviate respiratory symptoms such as cough, asthma, and bronchitis. Thymoquinone and other bioactive compounds in *Nigella Sativa* exhibit bronchodilatory, anti-inflammatory, and antispasmodic effects, which help relax airway smooth muscles, reduce airway inflammation, and improve respiratory function. Additionally, *Nigella Sativa* may inhibit the release of histamine and leukotrienes, which are involved in allergic reactions and asthma attacks.

- **Liver protection:** Studies suggest that *Nigella Sativa* may have hepatoprotective effects and help prevent liver damage caused by toxins, oxidative stress, and inflammatory mediators. Thymoquinone and other bioactive compounds in *Nigella Sativa* exert antioxidant, anti-inflammatory, and detoxifying effects in the liver, which help protect hepatocytes from injury, promote liver regeneration, and improve liver function tests. Additionally, *Nigella Sativa* may prevent liver fibrosis, steatosis, and cirrhosis by inhibiting collagen deposition and hepatic stellate cell activation.

- **Bone health:** Preliminary research indicates that *Nigella Sativa* may have beneficial effects on bone health and prevent osteoporosis and bone loss. Thymoquinone and other bioactive compounds in *Nigella Sativa* stimulate osteoblast activity, inhibit osteoclast formation, and enhance bone mineralization, which help maintain bone density and strength. Additionally, *Nigella Sativa* may reduce inflammatory cytokines and oxidative stress in bone tissue, thereby protecting against bone resorption and fractures.

- **Weight management:** Some studies suggest that *Nigella Sativa* may help regulate body weight and reduce obesity-related complications such as insulin resistance, dyslipidemia, and inflammation. Thymoquinone and other bioactive compounds in *Nigella Sativa* exert anti-obesity effects by inhibiting adipogenesis, lipogenesis, and fatty acid synthesis, while promoting lipolysis, thermogenesis, and energy expenditure. Additionally, *Nigella Sativa* may improve leptin sensitivity, suppress appetite, and enhance glucose uptake in adipocytes and skeletal muscle cells.

- **Reproductive health:** *Nigella Sativa* has been traditionally used to enhance fertility, libido, and reproductive function in both men and women. Thymoquinone and other bioactive compounds in *Nigella Sativa* exhibit aphrodisiac, spermatogenic, and ovulation-inducing effects, which help improve sexual performance, sperm quality, and menstrual regularity. Additionally, *Nigella Sativa* may alleviate reproductive disorders such as polycystic ovary syndrome (PCOS), erectile dysfunction, and infertility by balancing hormonal levels, reducing oxidative stress, and improving blood flow to reproductive organs.

- **CONCLUSION**

The review on *Nigella Sativa* revealed its diverse pharmacological properties, including antioxidant, anti-inflammatory, and antimicrobial effects. Its bioactive compounds, notably thymoquinone, demonstrated promising therapeutic potentials. Moreover, findings underscored the safety profile of *Nigella Sativa*, highlighting its potential as a natural remedy for various health conditions.

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