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***Nigella sativa*: Potent Medicinal Seed of *Unani* Medicine**

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ABSTRACT

Nigella sativa (Black seed) is a plant which has been used for centuries for medicinal and culinary purposes and reported to possess a number of pharmacological properties that include anti-parasitic, antibacterial, antifungal, antiviral, antioxidant and anti-inflammatory activities. Its oil is used as condiment, carminative, food preservative, analgesic and to treat many ailments in different parts of world. It has been extensively used in *Unani* system of medicine as a natural remedy for a number of diseases such as asthma, inflammation, cough, eczema, fever and gastrointestinal disturbances. It also has galactagogue, abortifacient, emmenagogue and uterotonic activity which makes it useful in amenorrhoea, dysmenorrhoea, puerperal sepsis and to improve lactation. Many active principles have been isolated from *Nigella sativa* seed including thymoquinone, nigellone, and fixed oils. This review is an attempt to highlight the therapeutic uses of *Nigella sativa* in *Unani* medicine and pharmacological properties.

Keywords: *Unani*, medicine, pharmacological, phytochemical.

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INTRODUCTION

Nigella is a genus of about 14 species of annual plants in the family Ranunculaceae^{1,2} native to southern Europe, North Africa and Southwest Asia. Common names applied to members of this genus are Devil-in-a-bush or Love in a mist.¹ *Nigella sativa* is one of these species which is an annual herb^{2,3} grows in countries bordering the Mediterranean Sea, Pakistan and India. This widely distributed plant is native to Arab countries and other parts of the Mediterranean region³. *Nigella sativa*, first identified and described by Linnaeus in 1753⁴. The seed is variously called *kalonji*, fennel flower, nutmeg flower, black caraway, and Roman coriander. Other names used, sometimes misleadingly, are black cumin, onion seed and black sesame⁵. It is included in the list of the natural drugs of Al Tibb AL-Nabawi as it was recommended by the prophet Mohammed (PBUH), “The *N. sativa* is the medicine for every disease except death^{6,7}.” Blackseed is also identified as the curative black cumin in the Holy Bible and is described as Melanthion by Hippocrates and Dioscorides and as Gith by Pliny⁸. For thousands of years, this plant has been used in many Asian, Middle Eastern and Far Eastern countries as a spice and food preservative as well as a protective and health remedy in traditional folk medicine for the treatment of numerous disorders including bronchial asthma, gastrointestinal problems, obesity, eczema, headache, dysentery, hypertension, diabetes and rheumatism^{3,9}. Seeds have been reported to exhibit many pharmacological effects that include anti-parasitic, antibacterial, antifungal, antiviral, antioxidant and anti-inflammatory activities. Its oil is used as condiment, carminative, food preservative, analgesic and to treat many ailments in different parts of world¹⁰. Seeds are also have emmenagogue, galactagogue, uterotonic property and are used in small doses in amenorrhoea and dysmenorrhoea whereas it is considered to lead to abortion in large doses¹¹.



Figure 1: *Nigella sativa* seeds

It contains over 100 valuable nutrients including 21 % protein, 38 % carbohydrates and 35 % plant fats and oils. The active constituents of black seed are thymoquinone, nigellone, and fixed oils.

Other ingredients comprise linoleic acid, oleic acid, calcium, potassium, iron, zinc, magnesium, selenium, vitamin A, vitamin B, vitamin B2, niacin, and vitamin C.¹²This review is an attempt to highlight the therapeutic uses of *Nigella sativa* in *Unani* medicine and pharmacological properties.

Scientific classification

Kingdom: Plantae

(Unranked): Angiosperms

(Unranked): Eudicots

Order: Ranunculales

Family: Ranunculaceae

Genus: *Nigella*

Species: *N. sativa*

Botanical name: *Nigella sativa*⁵

Vernaculars:**Arabic:**-Habtus Sauda, Kabudan¹³. **Sanskrit:**-Krishna-jiraka,^{14,15,16} Karavi,¹⁶Upakunchika.^{11,14,16}**English:**-Small Fennel^{14,16} or Black Cumin. **Hindi:**-Kalajira, Kalunji,^{14,15,16} Mangrela.**Bengali:**-Mugrela. **Persian:**-Shoniz, shonuz,¹³Siyahdana.¹⁴**Telgu:**-Nallajilakara.^{14,16}**Tamil:**-Karunjiragam.^{14,15,16}**Kannada:**-Karijirige. **Malayalam:**-Karinchirakam.^{14,16}

Actions and Therapeutic Uses Mentioned In *Unani* Medicine

Actions: *Mudirr-e-baul wa Mudirr-e-haiz* (diuretic and emmenagogue), *Mukhrije janeen wa mashema*(abortifacient, expulsive for placenta and foetus, oxytocic), *Muqawwi bah wa Aasab*, *Dafe dard* (analgesic)^{17,18} *Jali* (detergent), *Muhallile riyah*(carminative),^{19,20}*Munaffise balgham* (expectorant),²⁰ *Dafe bukhar* (Antipyretic), *Mukhrije deedan*.²¹

Therapeutic uses

Seeds have a decided action as a galactagogue and are therefore given to recently delivered females in combination with a few other medicines. In a dose of 10 to 20 grains, they have a well marked emmenagogue effect, useful in dysmenorrhoea and in large doses cause abortion.¹⁴It can be applied locally to dissolve swelling^{18,21}. It can be applied either alone or in combination with vinegar to relieve headache^{13,21}. It is helpful in cold cough, chest pain and ascitis. Along with ghee it causes blushing of face and also fairness of skin. It is also used in case of dog bite in the dose of 4g to 10g with water. In case of fever it can be given with *sikanjabeen*. 7grains of black seeds grind in human milk is used as nasal drop in jaundice patients. It is also effective in nausea, vomiting, splenomegaly and breathlessness. Local application of burnt seeds mixed with wax and oil is effective in alopecia even its long term application will start growing new hairs.¹⁸ Along with vinegar it can be applied over the warts and acne with benefit^{13,18}. Grind seeds with water and mix

honey is helpful in removing kidney and bladder stones by oral intake.^{18,21} It is effective in corrhyza. Local application over abdomen act as wormicide. It is also effective in renal colic as well as dysmenorrhoea. After grinding mix in *roghane irsa* and is used with benefit as nasal drop in initial stage of cataract. It can be applied in the eye by mixing in *surma* to remove cataract. It is used with boric powder in case of breathlessness. It can be applied locally to remove joints pain.¹³

Mizaj (Temperament): Hot and Dry.^{17,19}

Miqdare Khurak (Dose): 1g to 2g^{19,20} 3g.¹⁸

Muzir (Adverse effect): For kidney,¹⁷ vertigo,*Khanak*.^{17,18,20}

Musleh (Correctives): soaking in vinegar, *Kateera* (Tragacanth).¹⁷

Badal (Substitute): *Anisoon* (Aniseed),^{18,19,20} seeds of *Soya*.¹⁸

Murakkabat (Formulations): Habbe Hiltet, Jawarishe Shoneez, Majoone Kaklanj.²⁰

Phytochemical Constituents

Seeds have been reported to yield esters of unsaturated fatty acids with C₁₅ (esters of dehydrostearic and linoleic acid) and higher terpenoids, carvone, d-limonene, cymene, nigellone, thymol, citronellyl acetate, (+) citronellol, aliphatic alcohols, and α , β -unsaturated hydroxyl ketone, alkaloids, steroids and hederagenin glycoside, α -hederin (a triterpene saponin), thymoquinone, dithymoquinone, thymohydroquinone.^{10,15}

Pharmacological Properties

Antibacterial activity

The effect of *Nigella sativa* seed (1% and 3%) and oil (0.3% and 1%) on some food poisoning and pathogenic bacteria as well as on the total bacterial count TBC (cfu/g) in soft white cheese prepared from raw ewe's milk and laboratory pasteurized ewe's milk inoculated with *Staphylococcus aureus*, *Brucella melitensis* and *Escherichia coli* at a concentration of 1×10^6 cfu/ml were carried out. Results showed that there was Significant decrease ($P < 0.05$) in TBC, *Staphylococcus aureus*, *Brucella melitensis* and *Escherichia coli* count in cheese samples treated with *N. sativa* seed (1% and 3%) and oil (0.3% and 1%) with pronounced concentration dependent inhibition in contrast to control cheese samples which exerted significant increase in bacterial counts²². The ethanolic extracts of *N. sativa* was investigated against Methicillin resistant *Staphylococcus aureus*. Disc diffusion and in agar dilution methods were performed to assess the antibacterial activity. *Staphylococcus aureus* ATCC 25923 was used as the standard reference strain. All tested strains were sensitive to *N. sativa* extract at a concentration of 4 mg/disc¹⁰. The two main components of black seed essential oil, thymoquinone (TQ) and thymohydroquinone (THQ) were investigated for their antibacterial activity against *Escherichia coli*, *Pseudomonas*

aeruginosa, Shigella flexneri, Salmonella typhimurium, Salmonella enteritidis and Staphylococcus aureus. Both TQ and THQ exerted antibacterial activity against gram-positive and gram-negative bacteria regardless to their susceptibility to antibiotics²³. The antibacterial activity of Thymoquinone (TQ) and its biofilm inhibition potencies were investigated on 11 human pathogenic bacteria. The growth and development of the biofilm were assessed using the crystal violet (CV) and the 2, 3-bis [2-methoxy-4-nitro-5-sulfohenyl]-2H-tetrazolium-5-carboxanilide (XTT) reduction assay. TQ exhibited a significant bactericidal activity against the majority of the tested bacteria (MICs values ranged from 8 to 32 µg/ml) especially Gram positive cocci (Staphylococcus aureus ATCC 25923 and Staphylococcus epidermidis CIP 106510). Crystal violet assay demonstrated that the minimum biofilm inhibition concentration (BIC50) was reached with 22 and 60 µg/ml for Staphylococcus aureus ATCC 25923 and Staphylococcus epidermidis CIP 106510 respectively²⁴. Different extracts of successive stages of *Nigella sativa* Linn. was studied for antibacterial activity against various bacteria resistant to a number of antibiotics, in varying concentrations by Agar well diffusion technique on nutrient agar plates. The extracts showed pronounced dose or day dependent antibacterial activity against Gram positive and Gram negative bacteria⁷. The antibacterial activities of the extracts were investigated by the agar dilution method against Gram-positive bacteria (*Bacillus cereus* F 4810 and *Staphylococcus aureus* FRI 722) and Gram-negative bacteria (*Escherichia coli* MTCC 108 and *Yersinia enterocolitica* MTCC 859). SCCO2-1 (120 bar/40°C) extract showed effective growth inhibition than conventional solvent extracts against all the tested bacteria.²⁵The antibacterial activity of the essential oil was determined against a panel of strains bacteria, using a broth microdilution method. The GC-MS analysis showed that the major constituents of the oil were monoterpene hydrocarbons and phenolic monoterpenes, and results of antibacterial activity confirmed the possibility of using *Nigella sativa* essential oils or some of their components in biology and pharmaceutic preparations². Antibacterial activity of *Nigella sativa* seed extract against some pathogenic bacterial strains (*Streptococcus pyogene*, *Pseudomonas aeruginosa*, *Klebseilla pneumoniae* and *Proteus vulgaris*) was evaluated. Methanol extract at the concentration of 100 mg/mL had a remarkable sensitivity towards all tested bacteria in this study.²⁶Several seed extracts from *Nigella sativa* L. have been tested for antibacterial activity. Ether extract has found effective against Gram-positive bacteria²⁷.

Antifungal activity

Antifungal activity of methanolic and ethanolic extracts of the seeds of *Nigella sativa* was investigated on different pathogenic fungal strain such as *Aspergillus*, *Candida*, *Cryptococcus* and

Issatchenkia species. Methanolic extract of plant exhibits potent inhibition of fungus growth against Candida Parapsilosis, and Issatchenkia Orientalis with IC₅₀ Value 4.846 µg/ml, and 6.795 µg/ml, respectively and ethanolic extract also shows significant anti-fungal activity against fungus strain Issatchenkia Orientali with IC₅₀ value 5.805 µg/ml.²⁸ Nigella seed oil has a strong antifungal activity compared to the conventional fungicides.²⁹

Antidiabetic activity

One study was conducted to investigate antidiabetic efficacy of extracts of *Nigella sativa* Linn. seeds (NS). Serum glucose, triglyceride (TG), total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C) and very low-density lipoprotein cholesterol (VLDL-C) were measured by kit methods. NS demonstrated hypoglycaemic and hypolipidaemic activities. Although NS treatments decreased blood glucose, TC, TG and LDL-C and increased HDL-C in diabetic groups³⁰. The effects of *Nigella sativa* L. and Cinnamomum zeylanicum Blume oils on some physiological parameters were investigated in streptozotocin (STZ)-induced diabetic male Wistar rats. Administration of the tested oils to diabetic rats resulted in a significant decrease in blood glucose, triglycerides, cholesterol, LDL-cholesterol and ALT while HDL-cholesterol level was markedly increased after three weeks compared to untreated diabetic rats³¹. Experimental study was carried out to investigate the blood glucose lowering effect of *Nigella sativa* in alloxan induced diabetic rats. Significant differences were observed for blood glucose among groups on different days. The blood glucose was low in *Nigella sativa* compared with alloxan (p=0.001), however, it was more compared to glimepiride group (p=0.001).³²

Anti-tumor activity

In vitro and *in vivo* anti-cancer effect of *Nigella sativa* L. seed extracts was evaluated. The essential oil (IC₅₀ = 0.6%, v/v) and ethyl acetate (IC₅₀ = 0.75%) extracts were more cytotoxic against the P815 cell line than the butanol extract (IC₅₀= 2%). Similar results were obtained with the Vero cell line. Although all extracts had a comparable cytotoxic effect against the ICO1 cell line, with IC₅₀ values ranging from 0.2 to 0.26% (v/v), tests on the BSR cell line revealed a high cytotoxic effect of the ethyl acetate extract (IC₅₀ = 0.2%) compared to the essential oil (IC₅₀ = 1.2%)⁸. Ethanolic extracts of *Nigella sativa* (ENS) was evaluated for its potentials on tumor progression during the initiation and post initiation phases of Dimethylhydrazine-induced colon carcinogenesis in a rat model. ENS treatment during the initiation phase unveiled chemopreventive effect manifested by significant reductions in tumor incidence, multiplicity and tumor volumes. Histopathological findings and modified Duke's classification of tumors provided evidence that

ENS, administered in the initiation phase, is capable of delaying progression, restricting invasion and attenuating aggressiveness of colon tumors.⁴In another study the *Nigella sativa* was used as a pharmaceutical agent in the hepatocarcinogenesis of rats which induced by Diethylnitrosamine (DEN). Rats treated with diethyl nitrosamine and protected with *Nigella sativa* extract, showed hepatocytes with normal nuclei, large number of mitochondria and well developed RER indicating liver regeneration.⁹

Antioxidant activity

One study was done to estimate the antioxidant activity of various extracts prepared from *Nigella sativa* seeds, methanolic extract (ME), chloroformic extract (CE), hexanic extract (HE : fixed oil), ethyl acetate extract (EAE) water extract (WE). CE and HE showed the most scavenging activity against superoxide radical generated in the PMS-NADH-NBT system with respective IC₅₀ values of 361.86 µg/ml and 371.80 µg/ml, which is comparable to the activity of the standard antioxidant BHT (344.59 µg/ml)³³. Another study was done to investigate phenolic content and antioxidant activity in extracts obtained from seeds of *N. sativa*, using Soxhlet and ultrasound extraction techniques. All examined samples showed prominent antioxidant activity, except p-cymene³⁴. Another study was done to evaluate the possible protective role of *Nigella sativa* oil with potent antioxidant/anti-inflammatory properties, on a rat model of EG-induced toxicity. Administration of *Nigella sativa* oil completely prevented the acute toxic effect of Ethylene Glycol overdose-toxicity. *Nigella sativa* oil supplementation also significantly protected the bone marrow, blood, and brain tissues from the toxic effects of Ethylene Glycol³⁵.

Antiuro lithiatic effect

One study was done to investigate the effects of the ethanolic extracts of *Nigella sativa* seed on kidney calculi in rats. Thirty-two Wistar rats were randomly divided into 4 groups: group A received tap drinking water for 30 days (intact control). Groups B, C, and D received 1% ethylene glycol for induction of calcium oxalate calculus formation. As the preventive, and treatment subjects, rats in groups C and D received ethanolic extract of NS, 250 mg/kg, in drinking water since day 0 and day 14, respectively. Calcium oxalate concentrations in the urine on days 14 and 30 increased significantly in group B and were higher than those in group C (P = .006 and P = .002, respectively). Urine oxalate concentration in group D decreased on day 30 and was lower than that in group B (P = .04). Treatment of rats with ethanolic extract of NS reduced the number of calcium oxalate deposits in a group of rats that received ethanolic extract of NS³⁶.

Wound healing activity

An experiment was conducted in order to compare the effects of *Nigella sativa* (NS) and silver sulfadiazine (SSD) cream on healing of burn wounds in rats. A burn was generated on the backs of all the rats. The burned areas in the first, second and third groups were covered with daily cold cream (control), SSD cream and NS cream (50% NS oil + 50% cold cream), respectively. Histopathological evaluations on the 4th, 9th and 14th days showed burn healing to be better in the NS and SSD groups with respect to the control group. Wound healing was significantly different among the groups at 4th, 9th and 14th days ($P < 0.001$)³⁷.

Galactagogue Property

One study showed that serum prolactin level, of lactating female mice kept on *Nigella sativa* containing diet, was significantly higher ($P < 0.01$) than that of mothers switched on to control diet. The weight of the litter of the females kept on *Nigella sativa* containing diet was significantly ($P < 0.01$) higher than those of female given control diet. In comparison with control group, the sections of the breast tissue of mothers kept on *Nigella sativa* containing diet showed large acini with an increase in the proliferation and thickness of the epithelium. The majority of the acini in the breast tissue showed more secretory activity³⁸.

Gastroprotective effect

One study was done to investigate the possible effects of *Nigella sativa* aqueous extracts (NS) on gastric acid secretion in isolated rat stomach. Gastric acid secretion was measured in the isolated rat stomach preparation. The results obtained in vitro experiments showed that doses of 2 mg/100 ml DMSO and 5 mg/100 ml DMSO of NS aqueous extracts reduced gastric acid secretion stimulated by histamine and 5 mg/100 ml DMSO of NS aqueous extracts reduced gastric acid secretion stimulated by bethanechol, but none of the doses of NS did affect pentagastrin-induced acid secretion³⁹.

Antihyperlipidemic effect

The effect of *Nigella sativa* seeds was assessed in the diet on lipid profile in albino rats. Albino rats fed on low fat diet containing 3% sunflower oil supplemented with *Nigella sativa* showed significant reduction in TC and LDL cholesterol and rise in HDL cholesterol. Those on high fat diet containing 20% sunflower oil with *Nigella sativa* seeds showed significant reduction in TG and LDL cholesterol and increase in HDL cholesterol. While in those given high fat diet with 20% sunflower oil, along with 1% cholic acid and 0.5% propylthiouracil with the addition of *Nigella sativa*, there was significant reduction in TC and LDL cholesterol and rise in HDL cholesterol⁴⁰.

Hepatoprotective activity

The effect of *N. sativa* oil was investigated on carbon tetrachloride (CCL₄) induced liver damage using 35 adult Wistar rats. Histopathological or biochemical changes were not evident following administration of *N. sativa* alone. Serum levels of aspartic transaminase (AST) was significantly increased in animals treated with CCL₄ when compared to the control group while L-alanine aminotransferase (ALT) and alkaline phosphatase (ALP) was significantly decreased in animals treated with CCL₄ when compared to the control group. This increase and decrease in liver enzymes was almost restored to normal in animals treated with *N. sativa* and CCL₄ has that of the control⁴¹.

Clinical studies

One clinical trial was done to evaluate the effect of combination of *Nigella sativa* and Trigonella foenum-graecum seeds with Glibenclamide on serum triglyceride, HDL, and creatinine levels in type-2 diabetes mellitus patients. This study provides evidence that the combination therapy of *N. sativa* and T. foenum graecum with Glibenclamide is beneficial for type-2 diabetic patients as it increases serum HDL level in these patients⁴². In another clinical study *Nigella sativa* seeds were used as an adjuvant therapy in patients with diabetes mellitus type 2 added to their anti-diabetic medications. A total of 94 patient were recruited and divided randomly into three dose groups. Capsules containing *Nigella sativa* were administered orally in a dose of 1, 2 and 3 gm/day for three months. *Nigella sativa* at a dose of 2 gm/day caused significant reductions in fasting blood glucose, 2 hours postprandially, and HbA1c without significant change in body weight. Fasting blood glucose was reduced by an average of 45, 62 and 56 mg/dl at 4, 8 and 12 weeks respectively. HbA1c was reduced by 1.52% at the end of the 12 weeks of treatment ($P < 0.0001$)⁴³. A randomized clinical trial was conducted in 70 healthy subjects referring to Bagiatallah hospital. The subjects were randomly selected and enrolled in to two groups of 35 each. One group received 2.5 ml Black seed oil and the other group received similarly 2.5 ml mineral oil two times a day. The fasting blood glucose, HbA1c, liver and renal function test was determined at the baseline and after two months. Results showed that significant decrease in fasting blood glucose and HbA1c levels in Black seed oil treated patients as compared to control group at the end of the study⁴⁴.

CONCLUSION

Nigella sativa contains a number of phyto constituents, which are the key factors in the medicinal value of this plant. It is quite evident from this review that it is an important medicinal herb of *Unani* system with several pharmacological properties. This review also throws the attention to set

the mind of the researchers to carry out the work for developing the new formulations which can ultimately beneficial for the human being.

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