

Review Article

PHARMACOLOGICAL ACTIONS OF NIGELLA SATIVA (KALONJI)

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ABSTRACT

Nigella Sativa (Kalonji) is extensively grown in many countries including Pakistan. These have been used for therapeutic purposes for centuries.

Its effects are due to its constituent's thymoquinone and thymohydroxyquinone. Thymoquinone reduces the duration of tonic-clonic seizures. Nigella Sativa possesses anxiolytic and neuroprotective effects. Its seeds extract reduces systolic and diastolic blood pressures and blood lipids. Reduction in blood glucose, leucocyte and platelet counts has been reported. Thymoquinone has gastroprotective and hepatoprotective effects. Its seeds are potential immunosuppressive, cytotoxic, antibacterial and antiproliferative agents. Aqueous extract of Nigella Sativa increases weight of reproductive organs, spermatogenesis, and secretion of seminal vesicles and prostate. This extract also has anti-inflammatory, analgesic, antipyretic and antioxidant effects.

To conclude, the seeds of Nigella Sativa in addition to their use as spices possess a variety of Pharmacological actions.

KeyWord: Nigella Sativa, Blood platelets, Spermatogenesis, Prostate

INTRODUCTION:

Nigella sativa is extensively grown all over the world including Pakistan, India, Iran, Afghanistan, and many Arab countries. Its seeds are used as a condiment in Middle Eastern and South Asian cuisine. The seeds impart flavor to curries, vegetable stews, and pulses. The scientific name, Nigella Sativa, is a derivative of the Latin "niger" (black). It is known by a variety of names in English such as black cumin, fennel flower or Roman coriander. It is called "siyahdaneh" in Persian, "habbat-ul-barakah" in Arabic and "kalonji" in Urdu.¹

Numerous references to kalonji seeds can be found in ancient medical texts and religious scriptures. Prophet Muhammad (peace be upon him) said, "Use this Black Seed regularly, because it is a cure for every disease, except death." An Assyrian Herbal book has described black seed as a remedy for stomach related problems and also as a medicine for external problems like those of ears, eyes, mouth, and skin (e.g. herpes, sores, and rashes).

Nefertetes and Cleopatra used it for its healthy and rejuvenating qualities. Pliny described its myriad of uses like therapy for scorpion stings, snake bites, skin rashes, abscesses and tumors.³⁻⁴

TRADITIONAL USES:

Nigella sativa was used for therapeutic purposes both in herb and oil-pressed forms for centuries, in Middle East, Asia, and Africa. Traditionally, it was used as a remedy for a number of conditions related to respiratory, gastrointestinal, renal and hepatic functions, and as circulatory and immune system support apart from generalized health.

It was usually consumed with food or in combination with honey. In the 'UnaniTibb', Nigella sativa was considered as a useful cure for various ailments. A suspension made from its seeds was considered useful in the treatment of dyspepsia, anorexia, diarrhea, amenorrhea, parasitic infestations, and skin lesions. Ingestion of roasted seeds provided anti-emetic effect.¹⁻⁵

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PLANT MORPHOLOGY:

Nigella Sativa is a member of the Ranunculaceae family with about 14 species in its genus. Amongst these species, *Nigella sativa* is extensively investigated for medicinal properties.^{6,7}

It is an annual flowering plant, found in southwest Asia. The average height of this plant is 20-30 cm, and its leaves are finely divided (Fig. 1). It has a range of colorful flowers. The fruit is a capsule comprising of many unified follicles, containing abundant seeds. It has a pungent taste and smells faintly of strawberries. The seeds contained in the fruit are used for medicinal purposes.⁸



Fig. 1: The seeds (right) and flowering plant (left) of Kalonji.

The majority of the studies involved the seeds of the plant. Phytochemical studies have been done on the essential oil⁹, fixed oil¹⁰, methanolic extract¹¹, aqueous extract¹², ethanolic extract^{13,14} and n-hexane extract¹⁴ obtained from the seeds.

Its chemical composition reveals that *Nigella Sativa* has: fixed oil (35.6-41.6%), volatile oil (0.5-1.6%), amino acids, proteins (22.7%), alkaloids, saponins, toxic glycosides, amongst many other compounds. These also contain minerals like iron, sodium, copper, calcium and zinc and vitamins e.g. ascorbic acid, folic acid, thiamine, niacin, and pyridoxine. They also yield fatty acids esters (e.g. dehydrostearic acid, palmitic acid and oleic acid,) and unsaturated hydroxy ketones, steryl esters, sterylglucosides, acylated sterylglucosides, lipase, phytosterols, and β -sitosterols.¹

Ghoshehet al.¹⁵ after carrying out HPLC (high-performance liquid chromatography) analysis of *Nigella sativa* concluded that the concentration of thymoquinone and thymohydroquinone (THQ, termed 'Nigellone' by earlier workers) and some other constituents depended upon the conditions of storage of the seeds.

PHARMACOLOGICAL

ACTIONS OF NIGELLA SATIVA:

Nigella sativa possesses a large number of pharmacological actions and numerous studies have been done so far on various properties of this plant.

Thymoquinone shortened the time span of tonic-clonic fits.¹⁶ Aqueous and methanolic extracts produced significant alteration in the general behavioral patterns and reduction in spontaneous motor activity and body temperature, suggesting a central nervous system (CNS) depressant action of *Nigella sativa*.¹¹ *Nigella sativa* was also found to possess anxiolytic and neuroprotective effects in rats.^{17,18}

In an eight weeks study, systolic blood pressure (SBP) values in patients with hypertension receiving *Nigella sativa* seed extract supplementation were found to be significantly lower when compared with the control group. In addition, the reduction in blood pressure was found to be dose-dependent. A significant decrease in total cholesterol and LDL-cholesterol were also seen.¹⁹ Another study revealed that *Nigella sativa* also possessed blood pressure-lowering properties which were similar to nifedipine. A *Nigella sativa* extract given orally had significantly increased diuresis after 15 days of treatment in spontaneously hypertensive rats. Thymol, one of its active ingredients, reduced blood pressure by blocking calcium channels.⁷ Supplementation of the diet with seed extract, caused homogenous cardiac hypertrophy and enhanced cardiac contractility in normal rats.²⁰

In one study, *Nigella sativa* fixed oil was administered orally to rats for 12 weeks.

Total cholesterol, total leukocyte count (TLC), platelets and serum glucose were found to be decreased.²¹ In another study, Thymoquinone resulted in a significant decrease in blood cholesterol, low-density lipoprotein (LDL) levels and triglycerides.²² In hamsters, a significant reduction in serum glucose and an increase in insulin level was noted following treatment with oil of *Nigella Sativa*.²³ El-Mahmoudy et al. demonstrated β -cell conserving function of thymoquinone using diabetic rat model. The hyperglycemia was significantly diminished in thymoquinone treated rats.²⁴ Recently, in a Pakistani study also, *Nigella sativa* was found to possess hypoglycemic properties.²⁵ In minute concentrations, cells sensitized by the secretagogues antigen demonstrated reduced histamine release with Nigellone.²⁶ Effects of thymoquinone and nigellone were investigated on the trachea (antispasmodic effect) in rats. Thymoquinone minutely modified the ciliary clearance rate whereas nigellone markedly increased it.²⁷ In another study, intraperitoneal injection of thymoquinone resulted in a significant reduction of allergen-induced eosinophilic lung inflammation while decreasing the activity of goblet cells.²⁸ Thymoquinone and oil of *Nigella sativa* also showed gastroprotective activity.²⁹ The gastroprotective activity of *Nigella sativa* was also established against alcohol-induced gastric injury, acidity of the stomach and experimentally induced colitis.³⁰⁻³² Significant protection was exhibited against carbon tetrachloride mediated hepatotoxicity by Thymoquinone given orally.³³ When comparing hepatoprotective effects of Thymoquinone and Silybin against the toxicity produced by tetra-butyl hydroperoxide (TBHP) in rat hepatocytes, it was found out that even though both compounds prevented TBHP-induced toxicity, thymoquinone resulted in lesser enzyme leakage than silybin.³⁴ In another study, hepatic ischemia was induced in rats, followed by reperfusion. *Nigella sativa* was administered intraperitoneally, both before inducing ischemia and before reperfusion.

The levels of various liver enzymes were significantly lower in *Nigella sativa* treated group compared to control group.³⁵

It was found that in the diabetic rabbit model, treatment with *Nigella sativa* increased the red blood cells, neutrophil percentage, and leukocyte counts.³⁶ Anti-angiogenic activity on endothelium of aorta in rats was also observed.³⁷

Nigella sativa oil possesses immunomodulatory and immunotherapeutic properties.^{38,39} It is able to improve age-related decline in functions of T cells. Supplementation with the *Nigella sativa* oil in healthy elderly people has been shown to enhance immune response.⁴⁰ It could be regarded as potential cytotoxic and immunosuppressive agent.⁴¹

Thymoquinone's concentration-dependent anti-proliferative actions were investigated in neoplastic and normal cell lines. It was found to impede proliferation.⁴² In osteosarcoma and human colon neoplastic cells it also induced G1 phase cell-cycle arrest.⁴³⁻⁴⁵ Thymoquinone also offers some protection against human neuroblastoma and androgen-dependent human prostate cancer.^{46,47}

Treatment of rats with ethanolic extract decreased deposits of Calcium oxalate.⁴⁸ Aqueous extract of *Nigella sativa* significantly increased the size of reproductive organs, sperm motility, spermatogenesis and secretions of seminal vesicle and prostate.⁴⁹

In *S. aureus* and *E. coli* infected mice, both essential oils and crude extracts of *Nigella sativa* exhibited anti-bacterial effects.⁵⁰ Similarly, thymohydroquinone (THQ) and thymoquinone (TQ) were also found to possess antibacterial effects against *Pseudomonas aeruginosa*, *Escherichia coli*, and other bacteria.⁵¹

Nigella sativa oil showed a strong anti-viral action against infection with cytomegalovirus.⁵² In another study, antiviral activities against laryngotracheitis virus were exhibited by both *Nigella sativa* and green tea.⁴⁰ Chloroform and Methanol extracts of the *Nigella sativa* showed strong

anti-fungal actions against the hospital and standard *Candida albicans* strains. Aqueous extract of *Nigella sativa*, however, showed no effect.⁵³ *Nigella sativa* oil also produced significant effects on parasitemia in *Trypanosomabrucei*-infected rats.⁵⁴

Antioxidant properties of thymoquinone have been explained through different mechanisms in several studies.⁵⁵⁻⁵⁶

Nigella sativa significantly declined the paw edema induced with carrageenan. Analgesic activity was also tested in mice. The extract produced a significant analgesic effect in mice as seen by the increase in reaction time when exposed to hot plate. However, its crude suspension showed no effect on pyrexia induced by yeast.¹²

The effect of methanolic and aqueous extracts of black cumin seeds was investigated on pain response in albino mice. Methanolic and aqueous extracts were injected intraperitoneally to the mice and hot plate reaction time was estimated. The observations suggested that both the extracts possessed analgesic and CNS depressant effects.¹¹

Effectiveness of thymoquinone and *Nigella sativa* oil against rheumatoid arthritis was evaluated in rats. Oral thymoquinone was given to rats in a dose of 2.5mg/Kg. The control group received only the normal saline while the reference group was given standard drug methotrexate. Thymoquinone was found to suppress adjuvant-induced arthritis clinically and radiologically, significantly, as compared with the control and reference groups.⁵⁷

It can be concluded that seeds of *Nigella Sativa* in addition to their use as spice possess a variety of Pharmacological actions.

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