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PHARMACOGNOSY AND PHARMACOLOGY OF *NIGELLA SATIVA* - A REVIEW

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ABSTRACT
The importance of natural flora is well known by the scientific community. The medicinal plant gifted by nature have by explored by the humans to find out there respective values in the medical field. Times to time there have been report regarding the medicinal plants having huge possibilities for use. In the above article a similar kind of plant have been described, which have been reported of having many medicinal uses. The plant *Nigella sativa* have been reported to have significant activity agnist many diseased condition such as pancreatic cancer, asthma, bronchitis, and coughing, antitumor (tumors of the abdomen, eyes, and liver), opioid dependence. The potency of the above plant can be stated with a simple statement that six patent of the use of above plant have been granted for different countries. Various part of the plant has been used in traditional medicine, such as seeds, fruits. The above article is a sincere effort to describe the pharmacology and pharmacognosy of the above important plant.
Key words: *Nigella sativa,* Kalonji, Pharmacology, Pharmacognosy.

INTRODUCTION

The plant *Kalonji* or *Nigella sativa* is an annual flowering plant, native to south west Asia and cultivated in countries like Middle Eastern Mediterranean region, South Europe, Syria, Turkey, Saudi Arabia, Pakistan, India. The above plant is a small annual herb distributed all over India[1,2]. In the religion of Islam, the plant has been given a great importance because of its number of uses. As per the religion it is one of the greatest healing plants. The Islamic prophet Muhammad once stated that the black seed can heal every disease except death. Avicenna, most famous for his volumes called The Canon of Medicine, refers to *Nigella* as the seed that stimulates the body's energy and helps recovery from fatigue and dispiritedness. It is also included in the list of natural drugs of 'Tibb-e-Nabavi', or "Medicine of the Prophet (Muhammad)", according to the tradition "hold onto the use of the black seeds for healing all diseases. In the Unani Tibb system of medicine, *N. sativa* is regarded as a valuable remedy for a number of diseases. In the Indian system of medicine, the seeds are used as astringent, bitter, stimulant, diuretic, emmenagogue, anthelmintic, jaundice, intermittent fever, dyspepsia, paralysis, piles and skin diseases and many more [3-5]. The present article is an effort to present out the pharmacology, traditional uses, and chemical constituent of the above plant.

Figure no 01. *Nigella sativa*.

Figure no 02. Seeds of *Nigella sativa*.

Classification

Kingdom: Plantae
Division: Magnoliophyta
Class: Magnoliopsida
Order: Ranunculales
Family : Ranunculaceae
Genus: *Nigella*
Species: *N. sativa*

Pharmacognostical Description of Plant

Annual herb which grows about 45 cm in height. Leaves: 2.5-5.0 cm long, linear-lanceolate. Flower pale blue, 2.0-2.5 cm across, solitary on long peduncles; capsule 1.2 cm long; seeds flattened, oblong, angular, funnel shaped, small, 0.2 cm long and 0.1 cm wide, black in colour. Flowering and fruiting occur from January to April. It is generally cultivated on dry soil between November to April and seeds take about 10-15 days to germinate. It can also be propagated from the callus culture *in vitro* from leaf, stem and root explants from aseptically grown seedlings. The seed are small dicotyledonous, trigonus, angular, regulose-tubercular, 2-3.5 × 1-2 mm, black externally and white inside; odor slightly aromatic and taste bitter [6-11].

Character of seed

They are small dicotyledonous, trigonus, angular, regulose-tubercular, 2-3.5 × 1-2 mm, black externally and white inside. Odor slightly aromatic and taste bitter. Transverse section of seed shows single layered epidermis consisting of elliptical, thick walled cells, covered externally by a papillose cuticle and filled with dark brown contents. Epidermis is followed by 2-4 layers of thick walled tangentially elongated parenchymatous cells, followed by a reddish brown pigmented layer composed of thick walled, rectangular elongated cells. Inner to the pigment layer, is present a layer composed of thick walled rectangular elongated or nearly columnar, elongated [10-11].

Traditional Uses

Traditionally the seeds and its oil are used in several diseases. The seeds are considered as bitter, pungent, aromatic, appetizer, stimulant, diuretic, emmenagogue, galactagogue, anthelmintic, acrid, thermogenic, carminative, anodyne, deodorant, digestive, constipating, sudorific, febrifuge, expectorant, purgative, abortifacient. They are used in ascites, cough, jaundice, hydrophobia, fever, paralysis, conjunctivitis, piles, skin diseases, anorexia, dyspepsia, flatulence, abdominal disorders, diarrohoea, dysentery, intrinsic hemorrhage and amenorrhea. Seed oil is a local anesthetic [5,7,12].

Chemical Constituents

The chemical constituent reported in the above plant is been tabulated under [12].

Table no. 01. Chemical constituent of *Nigella sativa*

Fundamental Oil Composition (1.4%)	*Nigella sativa*
Carvone	21.1%
Alfa-Pinene	7.4%
Sabinene	5.5%
Beta-Pinene	7.7%
P-cymene	46.8%
Fatty Acids	
Myristic Acid (C14:0)	0.5%
Palmitic Acid (C16:0)	13.7%
Palmitoleic Acid (C16:1)	0.1%
Stearic Acid (C18:0)	2.6%
Oleic Acid (C18:1)	23.7%
Linoleic Acid (C18:2)(Omega-6)	57.9%
Linolenic Acid (18:3n-3) (Omega-3)	0.2%
Arachidic Acid (C20:0)	1.3%
Saturated & Unsaturated Fatty Acids	
Saturated Acid	18.1%
Monounsaturated Acids	23.8%
Polyunsaturated Acids	58.1%
Nutritional Value	
Protein	208 ug/g
Thiamin	15ug/g
Riboflavin	1 ug/g
Pyridoxine	5ug/g
Niacin	57 ug/g
Folacin	610 IU/g
Calcium	1.859 mg/g
Iron	105 ug/g
Copper	18 ug/g
Zinc	60 ug/g
Phosphorus	5.265 mg/g
Nutritional Composition	
protein	21%
Carbohydrates	35%
fats	35-38%

PHARMACOLOGICAL PROPERTIES

Analgesic and Anti-inflammatory activity

The above activity have been evaluated using Acetic acid-induced writhing, formalin and light tail flick tests were used for assessment of analgesic activity. Anti-inflammatory activity was evaluated using carrageenan-induced paw oedema in rats and croton oil-induced ear oedema in mice. Steam-distilled essential oil of Iranian black cumin seed (*Nigella sativa* L.) was used. Black cumin seed essential oil (BCSEO) was found to produce a significant analgesic effect in acetic acid-induced writhing, formalin and light tail flick tests. Naloxone, an opioid antagonist, could not reverse the analgesic effect observed in the formalin test. Intra peritoneal injection of the same doses significantly ($p < 0.001$) inhibited carrageenan-induced paw oedema [14].

Antidiabetic activity

Anti diabetic activity was evaluated on human volunteers. *Nigella* seed were used as adjuvant therapy for the treatment. A total of 94 patients 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 FBG, 2hPG, and HbA without significant change in body weight. Fasting blood glucose was reduced, while β-cell function was increased at 12 weeks of treatment [15].

In another study the antidiabetic effect of *N. sativa* seed ethanol extract was assessed in *Meriones shawi* after development of diabetes. At the end of the study, an Oral Glucose Tolerance Test was performed to estimate insulin sensitivity. Upon sacrifice, plasma lipid profile, insulin, leptin, and adiponectin levels were assessed. ACC phosphorylation and Glut4 protein content were determined in liver and skeletal muscle. Animals treated with plant extract showed a progressive normalization of glycaemia, although slower than that of metformin controls. Moreover, *N. sativa* increased insulinemia and HDLcholesterol, compared to diabetic controls. Leptin and adiponectin were unchanged. *N. sativa* treatment decreased OGTT and tended to decrease liver and muscle triglyceride content. *N. sativa* stimulated muscle and liver ACC phosphorylation and increased muscle Glut4. [20].

Anti cancer

The anticancer activity evaluated and documented in an article evidence of using the essential oil of above plant in the study. The essential oil when injected directly into the tumor, in reducing tumor volume, inhibiting metastasis development and delaying mortality of P815 tumor-bearing mice tumor [16]. Thymoquinone shows promising *in* vitro and in vivo antineoplastic growth inhibition against various tumor cell lines and inhibitory activity on cancer cell growth and its capability for inducing apoptosis [17]. It has been found active against many multidrug-resistant variants of different human cancer cell lines. Thymoquinone also exhibited antineoplastic activities in prostate cancer cells have now been evidenced that the compound effectively blocks G1-phase prostate cancer cells from entering the S phase and thus may prove to be useful in treating prostate cancer, particularly in hormone refractory cases [18]. Thymoquinone also produced significant cellular destruction and interference of cellular metabolic functions of SW-626 human colon cancer cells, which was comparable to the effect of 5-fluorouracil.

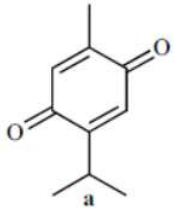

Figure no. 03. (a) Chemical structure of thymoquinone.

Antimicrobial activity

The antimicrobial activity has been evaluated by using disc diffusion method. The volatile oil of concentration 20µg for the test was applied to the discs. The results of the antimicrobial activity of the *N. sativa* volatile oil were compared with the standard and accordingly, the efficacy of volatile oil was far better than the standard [21].

In a study the evaluation of antimicrobial study was done using minimal bactericidal concentrations of the isolated compound were determined by the broth dilution method. The data obtain from the above study that the compound isolated and used for the activity is of high antimicrobial activity against gram-positive bacteria and yeasts, but has no sporicidal activity. Thus, the use of the oil as flavoring agent in food and as antiseptic agent in topical pharmaceutical preparations can be recommended [22].

Table no. 02. Antimicrobial spectrum of the volatile oil of N. sativa seeds.

Organism	Oil	1:25 Dilution in 95% alcohol
Escherichia coli	+	−
Salmonella typhi	+	−
Pseudomonas aeruginosa	+	−
Bacillus subtilis	+	−
Staphylococcus aureus	++	+
Micrococcus lysodeikticus	++	+
Sarcina lutea	++	+
Candida albicans	+	−

[a] The disk method was used. Symbols: + and ++, relative inhibition zones; −, no inhibition zone.

Table No. 03. MIC and MBC of the isolated antimicrobial principle

Microorganism	MIC (μg/ml)	MBC (μg/ml)
Escherichia coli	125	125
Salmonella typhi	125	125
Pseudomonas aeruginosa	125	125
Bacillus subtilis	4	—[b]
Staphylococcus aureus	8	8
Micrococcus lysodeikticus	8	8
Sarcina lutea	16	16
Candida albicans	125	125

[a] MIC, minimal inhibitory concentration; MBC, minimal bactericidal concentration.
[b] —, No activity.

Anoxia tolerance test, swimming endurance, cold induced stress and Immobilization

The above tests have been evaluated using estimation of various biochemical parameters in cold, Immobilization stress like glucose, cholesterol, triglycerides and blood urea nitrogen (BUN), and by determining the weight of organ such as, liver, spleen, testes, adrenal gland, blood cell count (WBC). The administration of the extract was done at different dose of 200mg/kg and 400 mg/kg body weight per oral. It was found that the ethanolic extract of *Nigella sativa* significantly ($p<0.001$) increases swimming time and anoxia tolerance time. The extract also showed significant ($p<0.001$) decrease in blood glucose, cholesterol, triglyceride and BUN and also decreased the weight of organs. It also showed a significant ($p<0.05$) decrease in weight of adrenal gland. A significant ($p<0.01$) decrease in WBC count, polymorphs and monocytes and decrease in lymphocytes ($p<0.05$) and eosinophils was observed, compared to control group. Thus the obtained results revealed that the *Nigella sativa* has got a significant anti stress activity [23].

Antiepileptogenic and Antioxidant

This above study was used to evaluate the anticonvulsant and antioxidant activities of NSO on pentylenetetrazol (PTZ) kindling seizures in mice. *Nigella sativa* oil was tested evaluated by animal study determine the suppressive, convulsive and the lethal effects of PTZ in kindled mice (anti-epileptogenic effect). The study also aimed to attenuate the PTZ-induced oxidative injury in the brain tissue (antioxidant effect) when given as a pretreatment prior to each PTZ injection during kindling acquisition. Valproate, a major antiepileptic drug, was also tested for comparison. Both the test and the standard used for study significantly decreased oxidative injury in the mouse brain tissue in comparison with the PTZ-kindling group. *Nigella sativa* oil was found to be the most effective in preventing PTZ-induced seizures relative to valproate. *Nigella sativa* oil showed anti-epileptogenic properties as it reduced the sensitivity of kindled mice to the convulsive and lethal effects of PTZ. The standard drug valproate was ineffective in preventing development of any of these effects. The data obtained support the hypothesis that neuroprotective action of NSO. The result of the study may also used to correlate with its ability to inhibit not only excessive reactive oxygen species (ROS) formation but also seizure generation [24].

Gastroprotective activity

The pharmacological model used for to evaluate above activity were ethanol-induced gastric mucosal lesions on Male Wistar albino rats. The role of reactive oxygen species in the pathogenesis of gastric mucosal lesions was evaluated. The above study resulted that *Nigella sativa* L oil and thymoquinone could protect gastric mucosa against the injurious effect of absolute alcohol and promote ulcer healing as evidenced from the ulcer index (UI) values. NS prevented alcohol-induced increase in thiobarbituric acid-reactive substances (TBARS), an index of lipid peroxidation. *Nigella sativa* L oil also increased gastric glutathione content (GSH), enzymatic activities of gastric superoxide dismutase (SOD) and glutathione-S-transferase (GST). Likewise, thymoquinone protected against the ulcerating effect of alcohol and mitigated most of the biochemical adverse effects induced by alcohol in gastric mucosa, but to a lesser extent than *Nigella sativa* L oil. Neither *Nigella sativa* L oil nor thymoquinone affected catalase activity in gastric tissue. Hence finally stated that *Nigella sativa* L oil and thymoquinone, particularly *Nigella sativa* L oil can partly protect gastric mucosa from acute alcohol-induced mucosal injury, and these gastroprotective effects might be induced, at least partly by their radical scavenging activity [25].

Another study determining gastroprotective activity was evaluated using gastric mucosal injury induced by ischaemia/reperfusion in rats. The above study resulted that that I/R elevated the levels of lipid peroxide (LPX) and lactate dehydrogenase (LDH), while decreased those of reduced glutathione (GSH) and superoxide dismutase (SOD). These biochemical changes were accompanied by an increase in the formation of gastric lesions, which was reduced by the treatment of *Nigella sativa* oils and its constituents [26].

Rheumatoid Arthritis

The evaluation of above disorder was done using Inflammation Induced Oxidative Stress and Tissue Damage model. For the study Wistar rats were used and was immunised with collagen, disease developed after 13±1 days post induction. *Nigella sativa* Linn. aqueous methanolic extract was given. The analysis of inflammation and associated protease activation was evaluated by myeloperoxidase (MPO) and articular elastase (ELA). Post inflammatory generation of various free radicals was checked by evaluating several enzymatic and non enzymatic parameters (GSH, SOD and catalase), including peroxidation of membranes. The study results as decreased MPO and associated elastase activity dose dependently. Moreover, *Nigella sativa* decreased the lipid peroxidation with replenishment of GSH confirming their inverse nature. SOD activity increased significantly, with a parallel increment in catalase activity. Consistent with these findings, articular nitrite content was reduced, which was further confirmed by the histological findings. The finding of the study reviled the fact that the plant have promising potency agnist Rheumatoid arthritis [27].

Human Neutrophil Elastase Activity

The oils extracted from the seed of *Nigella sativa* were used to evaluate the potency on human neutrophil elastase (HNE) activity. Inhibition of HNE activity by essential oil was found to be dose dependent. The highest inhibitory concentration (HIC) of essential oil which caused total inhibition of HNE activity was 5.8 mg/ml. The assay performed to evaluate the inhibitory effect of major components of essential oil on HNE activity revealed that carvacrol (5-isopropyl-2-methylphenol) showed marked HNE inhibitory activity with a very low IC(50) value (12 microM). Concluding on the result obtained from the study the inhibitory effects of essential oil on HNE activity are due to the presence of bioactive molecules, mainly carvacrol this compound is an inhibitor of HNE and could be considered as a natural antielastase agent and possible candidate for phytotherapy in the treatment of injuries that appear in some pathologic cases such as chronic obstructive pulmonary disease and emphysema [28].

Pharmacological Actions in Sickle Cells

For to evaluate above activity Thirty-two patients with sickle cell disease were enrolled obeying the inclusion criteria, aged 7-47 years old. Methord employed for the experiment was, a total of 3 ml of venous blood was collected from each patient and divided into six tubes with heparin. The blood was mixed with 0.5 ml of 0.1 percent, 0.05 percent or 0.01 percent v/v of the oil extract of *Nigella sativa*. A slide was prepared by spreading a drop of treated blood, covered with a cover slide to ensure the complete deoxygenation condition. The separation of irreversibly sickled cells (ISCs) was performed on eight patients by a density gradient (Percoll-Renografin) centrifugation method. The study concluded that, 0.1 percent v/v

concentration of the oil extract of *Nigella sativa* resulted in an approximately 80 percent reduction in the formation of sickle cells[29].

CONCLUSION

The above review is a sincere effort to provide the updated information regarding the black seed. After knowing the wide range of pharmacological activity, the statement is clear that why the plant and its component were called as the "Medicine of the Prophet (Muhammad)". Quoting to the finding and the result of various experiments preformed and the data evaluated, it can be stated clearly that the potent and fruitful activity resides in its volatile oil and a protein component. However, the volatile oil suffers the drawback of the bronho constricting effect of thymoquinone. In the coming days the study on the principal isolation and finding should be done in clinical way so that the plant and its constituent can be used for the well being of the mankind. It's the responsibility to use and bring out the gift for life presented by nature to mankind.

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