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NIGELLA SATIVA: A MEDICINAL HERB CURING SINCE AGES

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ABSTRACT

Nigella sativa (N. sativa) is an annual herb of the *Ranunculaceae* family, which grows in countries bordering the Mediterranean Sea, Pakistan and India. 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 Acute and chronic toxicity studies have recently confirmed the safety of *N. sativa* oil and its most abundant active component, thymoquinone, particularly when given orally. The extracts of *N.sativa* seeds have shown anti-inflammatory, antioxidant, anticancer, antihypertensive, hepatoprotective, antimicrobial, antiparasitic, antiosteoporotic, antihypercholesterolemic and antidiabetic effects. This review paper describes the seed, its chemical components and popular uses in traditional medicine. The paper also discusses the medicinal potential and therapeutic values of some of the individual components present in the extracts of the seeds.

KEYWORDS: Nigella sativa, Thymoquinone, Antiinflammatory, Antioxidant.

INTRODUCTION

Medicinal plants have been a major source of therapeutic agents since ancient times to cure human diseases. India is considered as “Botanical Garden of the World” and more than 2200 species of medicinal and aromatic plants have been identified after studies (Paarakh, 2010). One such plant is *Nigella sativa*, an annual herb of the Ranunculaceae family, which 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 region (Jansen, 1981). 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 (Chopra *et al*., 1956; Nadkarni, 1976). According to Zohary and Hopf, archeological evidence about the earliest cultivation of *N. sativa* "is still scanty", but they report that *N. sativa* seeds have been found in several sites from ancient Egypt, including Tutankhamun's tomb. Although its exact role in Egyptian culture is unknown, it is known that items entombed with a pharaoh were carefully selected to assist him in the after life (Dwivedi, 2004). In Islam, it is regarded as one of the greatest forms of healing medicine available. 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 "holds 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 (Satish and Ansari, 2013). Black seed is also identified as the curative black cumin in the Holy Bible, and is described as the Melanthion of Hippocrates and Discroides and as the Gith of Pliny. Other names for the seed include black caraway seed, Habbatu Sawda and Habatul Baraka‘‘the Blessed Seed” (Al-Khalaf and Kholoud, 2013).

Scientific Classification
Kingdom: Plantae
Division: Magnoliophyta
Order: Ranunculales
Family: Ranunculaceae
Genus: *Nigella*
Species: *sativa*

Morphology

It is small prostrate annual herb about 45 cm high 2-3 slender leaves pinnatisect, 2-4 cm long cut into linear segment, segments oblong. Flowers pale, blue on solitary long peduncles, seeds trigonous and black in colour. The plant has a rather stiff, erect, branching stem, bears deeply-cut grayish green leaves and terminal grayish blue flowers, followed by odd, toothed seed vessels, filled with small somewhat compressed seeds, usually three-cornered, with two sides flat and one convex, black or brown externally white and oleaginous, strong agreeable aromatic odour, like that of nutmegs, and a spicy, pungent taste. The flowers are delicate, and usually colored pale blue and white, with 5–10 petals. The fruit is a large and inflated capsule composed of 3–7 united follicles, each containing numerous seeds. It has a pungent bitter taste and a faint smell of strawberries (Varghese, 1996; Dwivedi, 2003).

Chemical Composition

Many active compounds have been isolated, identified and reported so far in different varieties of black seeds. The most important active compounds are thymoquinone or TQ (30%-48%), thymohydroquinone, dithymoquinone, p-cymene (7%-15%), carvacrol (6%-12%), 4-terpineol (2%-7%), t-anethol (1%-4%), sesquiterpene longifolene (1%-8%) α-pinene and thymol *etc*. Black seeds also contain some other compounds in trace amounts. Seeds contain two different types of alkaloids; *i.e.* isoquinoline alkaloids *e.g*. nigellicimine and nigellicimine-N-oxide, and pyrazol alkaloids or indazole ring bearing alkaloids which include nigellidine and nigellicine. Moreover, *N. sativa* seeds also contain alpha-hederin, a water soluble pentacyclic triterpene and saponin, a potential anticancer agent (Al Jassir, 1992; Atta-Ur-Rahman, 1995)

Some other compounds *e.g.* carvone, limonene, citronellol were also found in trace amounts. Most of the pharmacological properties of *N. sativa* are mainly attributed to quinone constituents, of which TQ is the most abundant. On storage, TQ yields dithymoquinone and higher oligocondensation products. The seeds of *N. sativa* contain protein (26.7%), fat (28.5%), carbohydrates (24.9%), crude fibre (8.4%) and total ash (4.8 %). The seeds are also containing good amount of various vitamins and minerals like Cu, P, Zn and Fe *etc*. The seeds contain carotene which is converted by the liver to vitamin A. Root and shoot are reported to contain vanillic acid (Al Jassir, 1992; Nickavar *et al*., 2003)

The seeds reported to contain a fatty oil rich in unsaturated fatty acids, mainly linoleic acid (50-60%), oleic acid (20%), eicodadienoic acid (3%) and dihomolinoleic acid (10%). Saturated fatty acids (palmitic, stearic acid) amount to about 30% or less. α-sitosterol is a major sterol, which accounts for 44% and 54% of the total sterols in Tunisian and Iranian varieties of black seed oils respectively, followed by stigmasterol (6.57-20.92% of total sterols) (Cheikh-Rouhou *et al*., 2008; Mehta *et al*., 2008, Bourgou *et al*., 2008)

Examples of various other reported chemical components includes nigellone,avenasterol-5-ene, avenasterol-7-ene, campesterol, cholesterol, citrostadienol, cycloeucalenol,, gramisterol, lophenol, obtusifoliol, stigmastanol, stigmasterol-7-ene, β-amyrin, butyro-spermol, cycloartenol, 24-methylene-cycloartanol, taraxerol, tirucallol, 3-O-[β-D-xylopyranosyl(1→3)-α-L-rhamnopyranosyl(1→2)-α-L-arabino-pyranosyl]-28-O-[α-L rhamnopyranosy l(1→4)-β-D-glucopyranosyl (1→6)-β-D-gluco-pyranosyl] hederagenin, volatile oil (0.5-1.6%), fatty oil (35.6-41.6%), oleic acid, esters of unsaturated fatty acids with C15 and higher terpenoids, esters of dehydrostearic and linoleic acid, aliphatic alcohol, β-unsaturated hydroxy ketone, hederagenin glycoside, melanthin, melanthigenin, bitter principle, tannin, resin, protein, reducing sugar, glycosidal saponin, 3-O-[β-D-xylopyranosyl-(1→2)-α-L-rhamno-pyranosyl-(1→2)-β-D-glucopyranosyl]-11-methoxy-16, 23-dihydroxy-28-methy-lolean-12-enoate, stigma-5,22-dien-3-β-D-gluco-pyranoside, cycloart-23-methyl-7, 20, 22-triene-3β, 25-diol, nigellidine-4-O-sulfite, N. mines A3, A4, A5, C, N. mines A1, A2, B1, and B2 (Nickavar *et al*., 2003; Morikawa *et al*., 2004; Morikawa *et al*., 2004; Mehta *et al*., 2009).

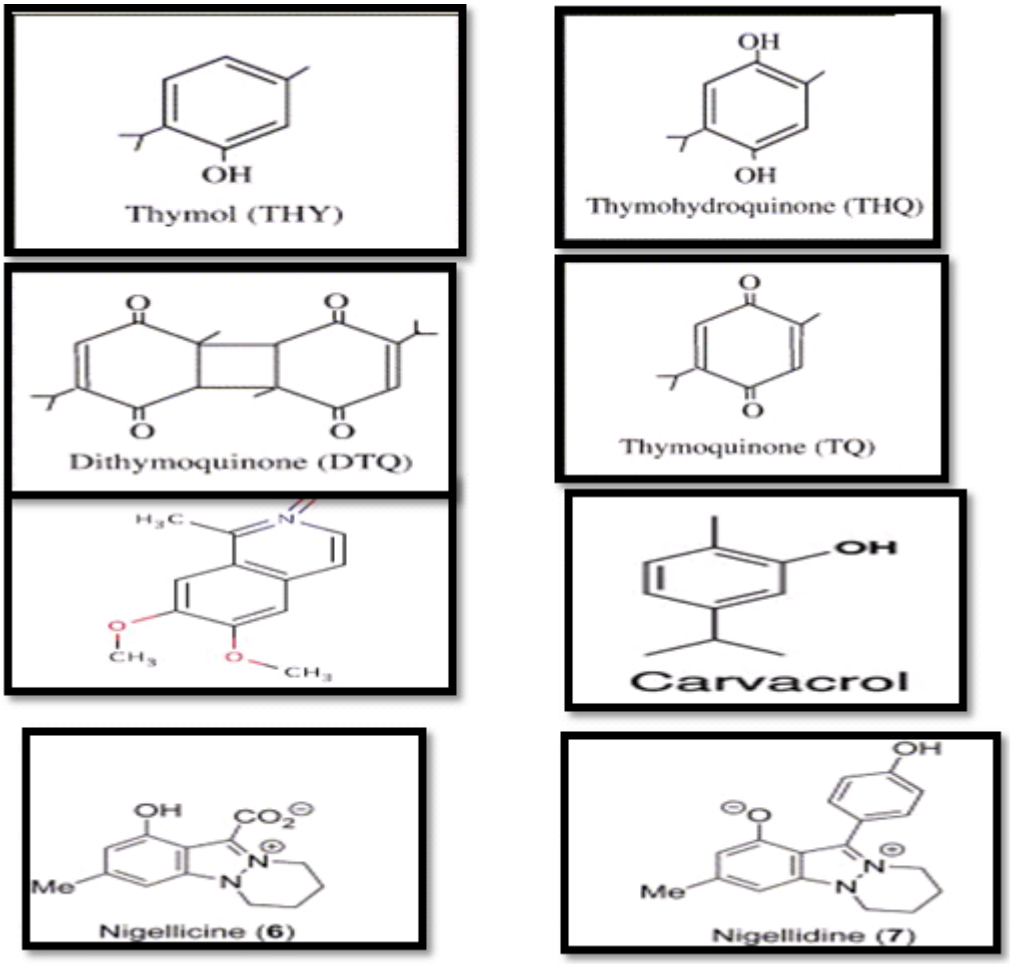

Fig. 1: The chemical Structure of the compound Present in Essential Oil from the Quinone Family (Al-Khalaf and Kholoud, 2013).

Physiological Effects of *Nigella sativa* (NS) and Its Component TQ

The oil extract of black seed has been shown to exert effects on various systems including the respiratory, cardiovascular, gastric and uterine and smooth muscle. The effects of intravenous administration of volatile oil and of TQ were investigated on the respiratory system of the guinea pig. The latter compounds were found to increase the intratracheal pressure in the dose range of 4–32 ml/kg and 1.6–6.4 mg/kg, respectively. Although *Nigella sativa* oil (NSO) significantly increased the discovery and new trends respiratory rate of guinea pigs, TQ was without any effect. The effects of NSO were significantly antagonized by treatment of the animals with antihistamines such as atropine and reserpine, suggesting that the oil-induced respiratory effects were mediated via the release of histamine and indirect activation of muscarinic and cholinergic mechanisms. This also suggested that the removal of TQ from black seed oil might provide a potential centrally acting respiratory stimulant (El-Tahir *et al.*, 1993[a]). This same group demonstrated that the intravenous administration of NSO (4–32 ml/kg) or TQ (0.2–1.6mg/kg) to rats decreased the arterial blood pressure and the heart rate in a dose dependent manner (El Tahir *et al.*, 1993[b]) suggesting that the oil may possess antihypertensive effects. The cardiovascular depressant effects of the oil were significantly antagonized by atropine and cyproheptadine, suggesting that these effects were mediated mainly centrally via indirect and direct mechanisms that involved both 5-hydroxy tryptaminergic and muscarinic mechanisms. NSO has also been shown to increase bile secretion in dogs and uric acid in rats as well as protect guinea pigs against histamine-induced bronchospasm (El-Dakhakhany *et al.*, 2002). The fatty and petroleum extracts shortened bleeding time and inhibited fibrinolytic activity in rabbits. In a recent study, the crude extract of *Nigella sativa* seeds was found to exhibit spasmolytic and bronchodilator activities mediated possibly through calcium channel blockade and this activity was concentrated in the organic fraction of the extract (Gilani *et al.*, 2001). Traditionally *Nigella sativa* plant has been in use in many Middle Eastern countries as a natural remedy for diabetes. Significant reduction in blood glucose and cholesterol levels in humans following the use of the plant was reported. The oil of this plant has a great potential in the treatment of diabetic animals because of its combined hypoglycemic (Zaoui *et al.*, 2002) and immunopotentiating properties (Haq *et al.*, 1999). A plant extract mixture comprising *Nigella sativa*, myrrh, gum Olibanum, gum asafetida and aloe was found to lower blood glucose in streptozotocin

diabetic rats. In an attempt to elucidate the mechanism of this antidiabetic action, the rate of gluconeogenesis in isolated hepatocytes as well as the activity of pyruvate carboxylase and phosphoenol pyruvate carboxykinase in rat liver homogenates was examined. It was found that the plant extracts significantly decreased hepatic gluconeogenesis, suggesting that it may prove to be a useful therapeutic agent in the treatment of non-insulin-dependent diabetes mellitus.Similar insulin tropic effects of NSO were recently observed in streptozotocin plus nicotinamide-induced diabetes mellitus in hamsters (a model of type 2 diabetes) orally fed with the oil (Fararh *et al*., 2002). In this study, positive immune reactivity for the presence of insulin was observed in the pancreases from oil-treated vs.non-treated hamsters using immune histochemical staining, suggesting that the hypoglycemic effect of NSO resulted, partly, from a stimulatory effect on beta cell function with consequent increase in serum insulin level.The ability of NSO to lower blood glucose concentrations was later confirmed in streptozotocin diabetic rats following 2, 4 or 6weeks of treatment (El-Dakhakhny *et al*., 2002). In addition, the effects of NSO, nigellone and TQ were studied on insulin secretion of isolated rat pancreatic islets. The blood glucose-lowering effect of NSO was not paralleled by a stimulation of insulin release. The data indicated that the hypoglycemic effect of NSO might be mediated by extrapancreatic actions, to be elucidated, rather than by stimulated insulin release (El-Dakhakhny *et al*., 2002). *Nigella sativa* and its derived products are consumed abusively for traditional treatment of blood homeostasis abnormalities and as a treatment for dyslipidemia (Zaoui *et al*., 2002). Several studies support the use of NSO extract for the treatment of thrombosis and dyslipidemia (Zaoui *et al*., 2002). The purified components (2-methoxypropyl-5-methyl- 1, 4-benzenediol, thymol and carvacrol) obtained from the methanol-soluble portion of NSO showed inhibitory effects on arachidonic acid-induced platelet aggregation and blood coagulation. Interestingly, some aromatic compounds present in the extract were found to be more potent than aspirin,which is well known as a remedy for thrombosis (Enomoto *et al*., 2001). In addition, an aqueous suspension of *Nigella sativa* seeds was found to decrease the serum total lipids and body weight in Psammomys obesus sand rat. Analogous results, accompanied by decreases in serum lipid levels have also been observed in rats chronically treated with *N. sativa* fixed oil (Zaoui *et al*., 2002). Animals were treated daily with an oral dose of 1 ml/kg body weight of the *Nigella sativa* seed fixed oil for 12 weeks. The serum cholesterol, triglycerides and the count of leukocytes and platelets decreased significantly by15.5%, 22%, 35% and 32%, respectively, compared to the control values. Haematocrit and hemoglobin levels increased significantly by 6.4% and 17.4%, respectively (Zaoui *et al*., 2002), suggesting that the oil influences blood homeostasis. *Nigella sativa* is also used in Arab folk medicine as a diuretic and hypertensive plant. In an attempt to experimentally support the above traditional uses of the plant, a study was conducted on the diuretic and hypertensive effects of the dichloromethane extract of *Nigella sativa* seeds in the spontaneously hypertensive rat. An oral dose of either *Nigella sativa* extract (0.6mL/kg/day) or furosemide (5mg/kg/day) significantly increased diuresis by 16% and 30%, respectively, after 15 days of treatment. The urinary excretions of Cl-, Na+, K+ and urea were also increased after 15 days of treatment. In the same rat study, a comparison between *Nigella sativa* and nifedipine found mean arterial pressure to be decreased by 22% and 18% in the *Nigella sativa* and nifedipine-treated rats, respectively, suggesting that *Nigella sativa* extract may play a role in decreasing blood pressure. Evidence indicates that NSO has a protective role against gastric ulcers (El-Dakhakhny *et al*., 2002).

Anticancer Effects of Nigella sativa

The active principles in NSO have been found to exert antineoplastic effects both in vitro and in vivo using various models of carcinogenesis. Black seed preparations (TQ and TQ2) have been demonstrated to have significant antineoplastic activity against various tumor cells in vitro. (Jafri *et al*., 2010). The active principles of N.sativa showed 50% cytotoxicity against Ehrlich ascites carcinoma, Dalton's lymphoma ascites and Sarcoma-180 cells at a concentration of 1.5,3 and 1.5 mg, respectively, with little activity against lymphocytes (El-Najjar *et al*., 2010). *In vitro* cytotoxicity was also demonstrated against human pancreatic adenocarcinoma, uterine sarcoma and leukemic cell lines. The growth inhibitory activity was found to be related to the extract's ability to inhibit DNA synthesis as measured by the incorporation of tritiated thymidine into cells. These findings were later confirmed by (Worthier *et al*., 1998) who assayed the in vitro cytotoxicity of a crude gum, a fixed oil and two purified components of *Nigella sativa* seed, TQ and TQ2, on several parental and multidrug resistant human tumor cell lines. Although as much as 1% w/v of the gum or oil was devoid of cytotoxicity, both TQ and TQ2 were cytotoxic for all of the tested cell lines (IC50: 78 to 393 mM). Interestingly, the multidrug resistant cell variants that are over 10-fold more resistant to the standard antineoplastic agents doxorubicin and etoposide were sensitive to TQ and TQ2. The ethyl acetate fraction of *Nigella sativa* seeds (identified as CC-5) was later found to exhibit significant growth inhibition on a variety of cancer cell lines without inhibiting the growth of normal human endothelial cells (Swamy and Tan, 2000). The ED50 values of the extract showed increased sensitivity towards Hep G2, LL/2 and Molt4 cell lines compared with SW620 and J82 cell lines. Badary and Gamal El-Din, 2001 also showed that TQ inhibited the survival of fibrosarcoma cells with IC50 of 15 mM by inhibiting the incorporation of 3H thymidine into cells. The cellular mechanism of antineoplastic activity of TQ was only recently investigated (Shoieb *et al*., 2003). In this study, the cellular mechanisms of TQ-induced cytotoxicity in parental and cisplatin-resistant osteosarcoma human breast adenocarcinoma, human ovarian adenocarcinoma and Madin–Darby canine cell

lines have been examined. The cisplatin-resistant cells were the most sensitive to TQ treatment, while the canine cell lines were the least sensitive. A dose of 25 mM of TQ induced apoptosis of osteosarcoma cells 6 h after treatment. This dose also decreased the number of cells in S-phase and increased cells in G1-phase, indicating cell cycle arrest at G1.These results suggest that TQ induces cell cycle arrest and apoptosis in cancer cells. Interestingly, noncancerous cells are relatively resistant to the apoptotic effects of TQ (Shoieb *et al*., 2003). The effect of CC-5 (ethyl acetate fraction of NSO) was evaluated for its in vivo antitumor activity against intraperitoneally implanted murine P388 leukemia and subcutaneously implanted Lewis lung carcinoma cells in BDF1 mice (Kumara and Huat, 2001). At doses of 200 and 400 mg/kg b.w., the fraction prolonged the life span of these mice by 153% compared to DMSO-treated control mice. The antitumor activity of a 21-day treatment of CC-5 against subcutaneously implanted LL/2 was tested and found to produce a 60–70% tumor inhibition rate. Atriterpene saponin was isolated from the CC-5 fraction and identified to be a-hederin. This compound was found to exert more potent anticancer effects compared to the commonly used anticancer drug, cyclophosphamide. When a-hederin was given i.p. at doses of 5 and 10 mg/kg b.w. to mice with formed tumors, it produced significant dose-dependent tumor inhibition rate values of 50% and 71%, respectively, on day 15, compared to 42% on day 15 in the cyclophosphamide (CP)-treated group. The underlying mechanism (s) of antitumor activity of a-hederin is not defined yet (Kumara and Huat, 2001). The protective effect of Nigella grains on carcinogenesis induced by methylnitrosourea in Sprague Dawley rats was investigated. When given orally (0.2 g ground Nigella grains) alone or with honey, a 6-month treatment reduced MNU-induced inflammatory reaction in lung and skin and MNU-induced colon adenocarcinomas by 80% (Mabrouk *et al*., 2002). There was an associated elevation of malondialdehyde and nitric oxide in sera obtained from methylnitrosourea-treated animals, which was lowered by ingestion of *Nigella sativa* grains. Interestingly, combined oral treatment of honey and *Nigella sativa* grains protected 100% against methylnitrosourea-induced oxidative stress,carcinogenesis and abolished the nitric oxide and malondialdehyde elevations shown in sera of animals that did not receive these nutrients (Mabrouk *et al*., 2002).

An other study also proved the anti cancer impact of *Nigella sativa* during which treatment with DMBA resulted in the formation of neoplastic nodules, which was evident from the appearance of multiple tumours on greyish white patches on the liver of the carcinogen treated rats. Morphological and histological examination of liver, kidney and pancreases from rats treated with DMBA, revealed damage to the cells, particularly the nuclei. Consistent with morphological and histological examinations, elevated ALP activities of the carcinogen treated rats were also indicative of the severity of liver, lung and kidney carcinogenesis. These untoward changes were significantly prevented by the administration of Black Caraway oil. In concluded, that daily use of Black Caraway oil by normal population will prevent the occurrence of Hepatocarcinogenic as well as initiation and promotion of certain forms of cancer (Thapliyal *et al*., 2012).

Antiinflammatory Effects of Nigella sativa

Nigella sativa and its derived products have been traditionally used as a treatment for rheumatism, liver diseases and related inflammatory disorders. The effect of black seed on the immune system has been investigated by several researchers (Al-Ghamdi, 2001). All studies have shown that the oil and its most abundant component, TQ, inhibit many inflammatory mediators, and, thus, may be useful in ameliorating inflammatory and autoimmune conditions. In rat models of acute lung injury or acute respiratory distress syndrome, thymoquinone (6 mg/kg, administered intraperitoneally) was able to improve lung oxygenation while its coadministration with steroids (thymoquinone 6 mg/kg plus methylprednisolone 10 mg/kg, intraperitoneally) protected lung tissue from the hazardous effects of intratracheal instillation of human gastric juice (pH 1.2) (El Mezayen *et al*.,2006). The anti-inflammatory effects of thymoquinone was supported by its ability to attenuate allergic airway inflammation by inhibiting Th2 cytokines and eosinophil infiltration into the airways and goblet cell hyperplasia (Boskabady *et al*., 2004). Attenuation of airway inflammation occurred concomitant to inhibition of COX-2 (cyclogenase) protein expression and prostaglandin D2 production in a mouse model of allergic airway inflammation induced with ovalbumin (Boskabady *et al*., 2004). Aqueous and macerated extracts of *Nigella sativa* produced relaxant, anticholinergics (functional antagonism) and antihistaminic effects on guinea pig tracheal chains (Gilani *et al*., 2004). The relaxant effect of the extracts, however, was probably not associated with the calcium channel blocking effect of the herb as the extracts did not inhibit KCl-induced contraction of tracheal chains (Gilani *et al*., 2004).

An other study was performed to investigate the effect of herbal extract of *Nigella sativa* in Turpentine oil induced acute hyperlipidemia. Herbal extract of *Nigella sativa* was given orally at two doses levels (100 mg/Kg & 150 mg/Kg) for four weeks.Injection of non medicinal turpentine oil (0.2ml) before 6h of sacrificing was given to experimental group. Turpentine oil treated animals showed remarkable changes in inflammation and other lipid biochemical assays when compared to normal control. The 100mg/kg herbal extract treated rats showed significant increase of 25% in total antioxidant activity as compared to control induced hyperlipidemic. In conclusion the extract of *Nigella sativa* appeared to be safe and possibly protective against turpentine oil induced lipid peroxidation (Chauhan *et al*., 2011).

Antioxidant Effects of Nigella sativa

The antioxidant activity of Nigella sativa oil extracted using supercritical CO_2 as the solvent was dependent on thymoquinone and carvacrol but was only 0.14 of the activity of a-tocopherol (Thippeswamy *et al*., 2005). The antioxidant potency of a methanolic extract of *Nigella sativa* was found to be higher than the aqueous extract in soyabean lipoxygenase and rat liver microsomal lipid peroxidation assays, and in the DPPH assay. The phenolic content in both the methanolic and aqueous extracts was about 4.1 mg/g (Al-Saleh *et al*., 2006). Antioxidants present in *Nigella sativa* seeds include selenium, DL-a- and DL-g-tocopherol, all-trans retinol, thymoquinone and thymol with mean concentrations of 0.17,9.02,5.42,0.27, 2224.5 and 169.4 mg/kg fresh weight, respectively (Al-Saleh *et al*., 2006). *Nigella sativa* and thymoquinone partly protected rat gastric mucosa from acute ethanol-induced gastric mucosal damage, with the gastroprotection mediated by their antiperoxidative, antioxidant and antihistaminic effects (Kanter *et al*., 2006). Supplementation of the diet of rats fed oxidised corn oil with *Nigella sativa* led to an improvement in the overall antioxidant capacity as evidenced by a marked reduction in red blood cell hemolysis and plasma AST/ALT activities and a reduction in the formation of thiobarbituric acid reactive substances, indices of peroxidative damage. The antioxidant effects are attributed to thymoquinone, a main constituent of the volatile oil of *Nigella sativa* (Al-Saleh *et al.*, 2006).

Hepatoprotective Effects of Nigella sativa

In an attempt to evaluate the hepatoprotective effects of TQ studied its ability to protect against oxidative stress caused by tert-butyl hydroperoxide in isolated rat hepatocytes and compared it to the effects of the known hepatoprotective agent silybin. The toxicity of tert-butyl hydroperoxide was manifested by the loss of cell viability and the progressive depletion of intracellular glutathione and leakage of cytosolic enzymes, alanine transaminase and aspartic transaminase in isolated rat hepatocytes treated with this compound (Ahmed *et al*., 2010). Preincubation of cells with 1mM of either TQ or silybin resulted in protection against tert-butyl hydroperoxide-induced toxicity as evidenced by decreased leakage of alanine transaminase and aspartic transaminase and increased cell viability. Silybin was slightly more potent in preventing loss of cell viability and enzyme leakage, but both compounds prevented tert-butyl hydroperoxide-induced depletion of glutathione to the same extent (Farrag *et al*., 2007). It was shown that *N.sativa* seeds given orally every day for 2 months decreased the lipid peroxidation, increased the antioxidant defense system and prevented the lipid peroxidation-induced liver damage in experimentally induced diabetic rabbits (Uz *et al*., 2008), suggesting that the seed may be used in diabetic patients to prevent lipid peroxidation.

Antimicrobial and Antiparasitic Effects of Nigella sativa Oil

Several investigations have been directed towards *Nigella sativa* antibacterial properties (Suresh *et al*., 2010). The preliminary assessment of the in vitro antimicrobial effects of different germinating stages of *Nigella Sativa* extracts revealed some basic outcomes in the present study. First, the methanol extracts of *Nigella sativa* showed good inhibitory effect against Gram-positive and Gram-negative clinical bacterial strains during germination phases as compared to seed extract, the extracts showed highest activity from 5th day to 11th day of germination (Islam *et al*., 2013). The ethanolic extract of *Nigella sativa* was shown to have outstanding in vitro antibacterial activity against methicillin resistant and sensitive strains of Staphylococcus aureus (Dadgar *et al*., 2006). Salmonella thyphimurium was non-sensitive to the range of concentrations of the extract used in the study (25-400 µg/disc). The extract showed antibacterial synergism with streptomycin and gentamycin. In vivo studies showed that the diethyl ether extract successfully eradicated localized infections of S.aureus in mice. *Nigella sativa* oil may potentially be useful for inhibition of Listeria monocytogenes in food as it showed strong antibacterial activity against 20 strains of the bacteria with the oil producing inhibition zones that were significantly larger than that of gentamicin.

Antiosteoporotic Effects of Nigella sativa

Animal studies have shown that NS and TQ may be used for the treatment of diabetes-induced osteoporosis and for the promotion of fracture healing. The mechanism involved is unclear, but it was postulated that the antioxidative, and anti-inflammatory activities may play some roles in the treatment of osteoporosis as this bone disease has been linked to oxidative stress and inflammation. NS and TQ were shown to inhibit inflammatory cytokines such as interleukin-1 and 6 and the transcription factor, nuclear factor κB. Both NS and TQ have shown potential as antiosteoporotic agent but more animal and clinical studies are required to further assess their antiosteoporotic efficacies (Soelaiman *et al*., 2012).

Anti-hypercholesterolemic effect of Nigella sativa

The ethanolic root extract of *Boerhaavia diffusa* and Black Caraway Oil have potent antihypercholesterolemic activity that reduces plasma lipids and lipoprotein lipids level in DMBA-Induced hypercholesterolemic rats. A study was carried out to investigate antihypercholesterolemic properties of Black Caraway Oil using drugs.Lipid profiles (plasma lipids and plasma lipoproteins) and biomarker enzyme HMG-CoA reductase were evaluated in normal and hypercholesterolemic rats. Supplementation of this extract by gavage significantly reduced the lipid profiles (plasma lipids and plasma lipoproteins) and biomarker enzyme HMG-CoA reductase. Moreover this supplementation significantly increased the lipid profiles level in plasma (510.36 ± 2.23) as compare to normal

control (390.19 ± 1.40) (P<0.001). Elevated plasma enzymatic HMG-CoA reductase was diminished significantly by the treatment of Black Caraway Oil in respect to infected group. All the above mentioned parameters were restored to the control level. (Khan *et al*., 2011)

CONCLUSION

Evidence indicates that *Nigella sativa* seeds have a potential medicinal value and are relatively safe to consume. Future research should focus on the mechanisms by which *Nigella sativa* seeds exert their medicinal effects. With the increased understanding of its mechanism of bioactivity, the incorporation of this medicinal herb as complementary medicine into mainstream medical science can be achieved in the future.

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