



## NIGELLA SATIVA: A MIRACULOUS HEALER

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### ABSTRACT

*Nigella sativa* belonging to Ranunculaceae, is a widely used medicinal plant not only in India but around the globe. It is popularly recommended in various indigenous system of medicine like Ayurveda and Unani. In Islam, It is considered as one of the greatest form of healing medicine. Traditionally, *Nigella sativa* seeds have been used as anti-hypertensive, anti-diabetic, anti-bacterial, analgesics, diuretics, digestive, lactagogue, liver tonic, and in skin diseases etc. The aim of present review is to provide a detailed survey of the literature on pharmacological potential of the seeds of this plant so that more pharmacological studies could be conducted to investigate the unexploited therapeutic potential.

**Key-Words:** Anti-Hypertensive, Anti-Bacterial, *Nigella Sativa*, Medicinal Plant, Pharmacological Potential

### INTRODUCTION

*Nigella sativa* (NS) is an annual herb belonging to Ranunculaceae family. This widely distributed plant is native to Arab countries and other parts of the Mediterranean region <sup>[1]</sup>. It is also cultivated in India and Pakistan. Seeds of *Nigella sativa* have been used for thousands of years as

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a spice and food preservative to a variety of food products as bread, yogurt, pickles, sauces, salads etc. <sup>[2]</sup>. Throughout the world, the seeds and different parts of the plant are in use for medicinal purposes to cure various maladies. Use of NS is appreciated and recommended in religious texts of different religions. *Nigella sativa* was referenced in the book of “Isaiah of the Old Testament” where it was called "ketzah"(Isaiah 28:25, 27 NKJV). Black seed is also identified as the curative black cumin in the Holy Bible and is described as the Gith of Pliny and as the Melanthion of Hippocrates and Discroides <sup>[3]</sup>. In Islam, it is considered as one of the greatest form of healing medicine available, Al-Bukhari <sup>[4]</sup>, the hadith of Islam mentions that the black seed can heal every disease except death. In Ayurveda, *Nigella sativa* or black cumin was appreciated for its many qualities and bitter, stimulant and warming nature. In the Indian system of medicine namely Unani and Ayurveda the seeds are reported to possess immunomodulative <sup>[5, 6]</sup>, anti-bacterial <sup>[7]</sup>, anti-tumor <sup>[8]</sup>, diuretic, hypotensive, hepato-protective, antidiabetic <sup>[9]</sup>, bronchodilator <sup>[5]</sup> and estrogenic potential <sup>[10]</sup>. The oil of black cumin has been shown to be effective in treating skin conditions, earaches and chronic colds <sup>[11, 12, 13]</sup>. The present review aims to assess the pharmacological effects of *Nigella sativa* and its bio-active compounds.

## SCIENTIFIC CLASSIFICATION

Kingdom -Plantae

Subkingdom-Tracheobionta

Super division- Spermatophyta

Division- Magnoliophyta

Class- Magnoliopsida

Subclass -Magnoliidae

Order -Ranunculales

Family -Ranunculaceae

Genus -Nigella

Species- *sativa*

## NAMES IN OTHER LANGUAGE

English: Black cumin; Hindi: Kalonji; Sanskrit: Krishana-Jiraka; Arabic: Habbat-al-Barakah.

## MORPHOLOGY OF THE PLANT

*Nigella sativa* is an annual flowering plant, which grows to about 20-90 cm in height. The leaves are compound, having 2-3 pinnatisect, cut into linear or linear-lanceolate segments, feathery, fine and greyish green in colour. The flowers are delicate and usually coloured pale green when young and light blue on maturity, becoming pale blue or white later with 5-10 petals. The fruit of *Nigella sativa* is a large and inflated capsule having many nectaries, generally 10, pocket like, epicalyx present. The seeds are small, triangular in shape and black in colour with a rough surface and an oily white interior. They are roughly triangulate, 1.5-3 mm long (Fig.1.) [14, 15].

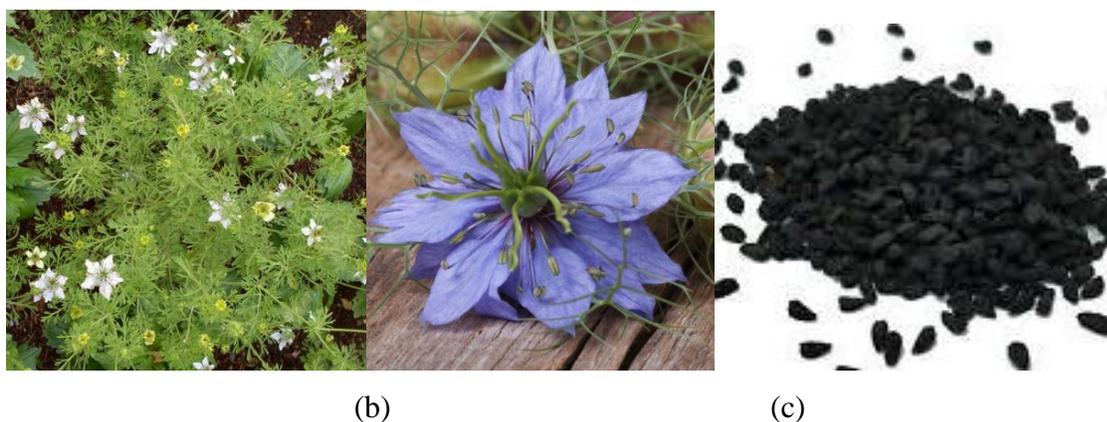


Fig.1. (a) *Nigella sativa* plant (b) its flower and (c) seeds

## CULTIVATION AND DISTRIBUTION

The plant is cultivated and distributed all over India particularly in Himachal Pradesh, Punjab, Gangetic Plains, Bihar, Assam, Bengal and Maharashtra. Besides India, the plant is also cultivated in Israel, Syria, Turkey, Lebanon, South Europe, Bangladesh, as well as in Middle East and Mediterranean basin [16].

## CHEMICAL COMPOSITION AND ACTIVE INGREDIENTS OF NIGELLA SATIVA

*Nigella sativa* seeds are an important spice possessing fat (22.0–56.4%), protein rich seeds (18.59–31.2%) with good amount of crude fibre (3.7–4.7%) [17,18,19]. Moisture content of the seeds have not been found to exceed beyond 7% which is good attribute for longer shelf life of seed as moisture is known to be a major causative factor behind deterioration of seed. Total ash

value of *Nigella sativa* usually ranges between (5.5–15.0%) which indicate presence of minerals in seeds [20]. Al-Jassir in 1992, have reported that *Nigella sativa* seeds are rich in minerals like Cu, P, Zn, Fe etc. The seeds also contain beta-carotene, which is converted to vitamin A in liver [21]. The seed oil of *Nigella sativa* was found to be rich in polyphenols and tocopherols [22, 23]. The seeds contain 36–38% fixed oils, 0.4–2.5% essential (volatile) oil, alkaloids and saponins [24]. The fixed oil is composed mainly of fatty acids, namely, linoleic (C18:2), oleic (C18:1), palmitic (C16:0) and stearic (C18:0) acids [25]. Several active compounds were isolated and identified in *Nigella sativa* (Fig.2). Chief constituents reported in *Nigella sativa* are thymoquinone (TQ), dithymoquinone (DTQ), thymohydroquinone (THQ), thymol (THY), 4-terpineol t-anethol and p-cymene and these functional ingredients are predominantly present in its fixed and essential oils [26, 27].

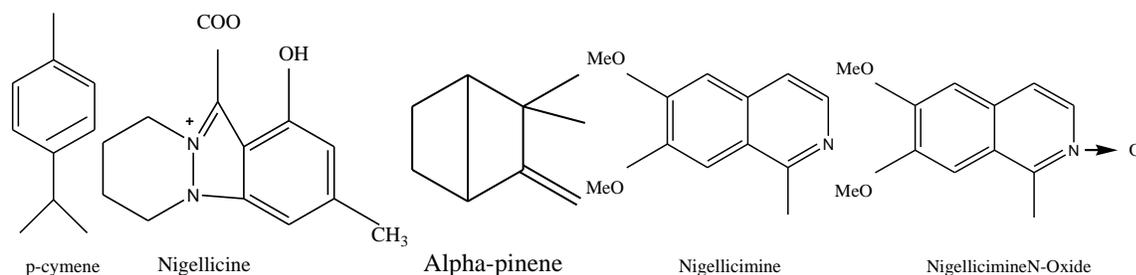


Fig.2. Chemical structure of some active compounds of *Nigella sativa* seed

## TRADITIONAL USES OF FOLK REMEDIES

*Nigella sativa* seeds and its oil have been traditionally used for the ailment of various diseases (Fig.3). The seeds are used as appetizer, diuretic, galactagogue, anthelmintic, thermogenic, deodorant, abortifacient etc. They were also used against cough, cold, fever, jaundice, paralysis,

flatulence, skin diseases, diarrhoea, dysentery and amenorrhoea. Seed oil is used as local anesthetic agent and antiseptic [28, 29, 30].

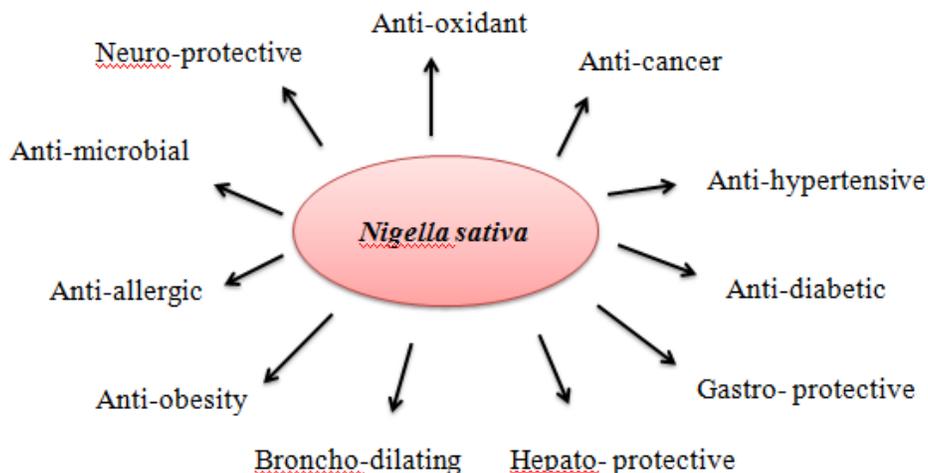


Fig.3. Traditional uses of *Nigella sativa*

## PHARMACOLOGICAL POTENTIAL OF *NIGELLA SATIVA*

### Anti-microbial activity

Topozada et al. studied the anti-bacterial effect of *Nigella sativa* in its oil in 1965 [31]. The extract and the oil have been reported to have a broad spectrum of activity against a number of microbes including *E. coli*, *Vibrio cholera*, *Staphylococcus albus* and *Salmonella typhi*. The oil inhibited gram positive bacteria more than gram negative ones. The oil has also been reported for anti-fungal activity particularly against *Aspergillus* species. Using murine *cytomegalovirus* as a model intraperitoneal administration of oil substantially decreased the viral load both in liver and spleen [32, 33].

Anti-microbial effects of methanol, ethanol and n-Hexane and aqueous extracts of *Nigella sativa* were investigated against three pathogenic fungal strains (*C. albicans*, *A. flavus* and *A. niger*) and four bacterial strains (*P. syringica*, *B. subtilis*, *E. coli* and *Staphylococcus* sp.). Among different extracts of *Nigella sativa* screened, the methanol extract showed the highest anti-fungal potential against all the tested fungi. Aqueous extract showed marked. Ethanol extract showed significant

decrease in bacterial growth whereas aqueous extract depicted marked anti-bacterial and anti-fungal activity<sup>[34]</sup>.

### **Hepato-protective activity**

Hepatotoxicity is associated with alteration in the levels and activities of certain enzymes as serum glutamic oxaloacetic transaminase (SGOT), serum glutamic-pyruvic transaminase (SGPT), oxidant scavenger enzymes system including glutathione (GSH), superoxide dismutase (SOD) and catalase (CAT). Ibrahim et al. in 2008 reported that oral administration of *Nigella sativa* oil (1ml/kg body weight) every day for one week prior to carbon tetrachloride (CCl<sub>4</sub>) injection has a protective effect against the CCl<sub>4</sub>-mediated suppression of hepatic cytochrome P450 (CYP) enzymes, which may be due to the down-regulation of NO production and up-regulation of the anti-inflammatory IL-10<sup>[35]</sup>. Al-Ghamdi in 2003 studied the effect of the aqueous suspension of *Nigella sativa* on CCl<sub>4</sub>-induced liver damage. Aspartic transaminase (AST), L-alanine aminotransferase (ALT), lactate dehydrogenase (LDH) were determined in liver cells in rats with CCl<sub>4</sub> induced hepatotoxicity and reported protective against CCl<sub>4</sub> induced hepatotoxicity<sup>[36]</sup>. The protective effects of thymoquinone, the active ingredient of *Nigella sativa*, against tamoxifen-induced hepatotoxicity in female rats were evaluated. Thymoquinone (orally, 50 mg per kg body mass per day for 20 consecutive days) significantly prevented the elevation in serum activity of the hepatic enzymes<sup>[37]</sup>.

### **Anti-cancer activity**

Cancer has been reported to be the second common cause of death in the United States after cardiovascular disorders<sup>[38]</sup>. Many naturally occurring compounds have been reported to possess cancer-preventive effects<sup>[39]</sup>. *Nigella sativa* have been shown in a number of studies to have chemo-preventive potential. Its components are effective in mediating inflammation and cancerous cell growth side by side. Sayed in 2008 observed that thymoquinone (TQ) decreased NF-kappa B activation in a dose dependent manner with a maximum inhibitory effect at a concentration of 500 nM<sup>[40]</sup>. Moreover, one more study also supported the use of thymoquinone for the treatment of colon cancer<sup>[41]</sup>. Rahmani et al. in 2014 also reported that *Nigella sativa* and TQ have beneficial effect in the prevention of cancer through the activation or inactivation of molecular cell signaling pathways<sup>[42]</sup>. One of its constituent, especially  $\alpha$ -Hederin, shows some extent of significant effects in mitigating the cancerous cell growth<sup>[43, 44]</sup>. *Nigella sativa* volatile

oil containing thymoquinone and other antioxidants could also be considered as a potential immunosuppressive cytotoxic agent [44, 45, 46].

In another study, aqueous and alcoholic extracts of NS seeds were found to be effective in vitro in inactivating MCF-7 breast cancer cells [47]. *Nigella sativa*, in combination with retinoic acid and melatonin showed anti-carcinogenic effects of DMBA (7, 12-di-methyl benz(a)anthracene) in mammary carcinoma of rats [48].

Recently, an in vivo study was conducted to investigate the efficacy of thymoquinone on N-nitrosodiethylamine (NDEA) (0.01% in drinking water for 16 weeks) -induced hepatocarcinogenesis in experimental rats. At the end of experimental period, the hepatic nodules, liver injury marker and tumor marker levels were significantly enhanced in NDEA induced liver tumors in rats. However, thymoquinone supplementation (20 mg/kg body weight) significantly reduced liver injury markers and decreased tumor markers and prevented hepatic nodule formation and reduced tumor multiplicity in NDEA induced hepatic cancer bearing rats [49]. In one more study, thymoquinone was tested for investigating the effect on survival, actin cytoskeletal reorganization, proliferation and signal transduction in multiple myeloma cells. It was revealed that thymoquinone decreases F-actin polymerization and the proliferation of human multiple myeloma cells by suppressing STAT3 phosphorylation and Bcl2/Bcl-XL expression [50]. *Nigella sativa* oil might be useful as nutritional supplement to complement surgery and chemoprevention in familial adenomatous polyposis [51].

### **Immunomodulatory effects**

The immunomodulatory effects of *Nigella sativa* were investigated on human peripheral blood mononuclear cells (PBMCs) on a Phytohemagglutinin (PHA) and a non- Phytohemagglutinin (non-PHA) stimulated proliferation. Cells isolated from human PBMCs, which were treated with methanolic extract of NS for 48 h into two separate environments (PHA and non-PHA stimulated). Flow cytometry (for T helper/inducer cells and natural killer cells) and real time-polymerase chain reaction (PCR) assays for a few selected proinflammatory gene expressions were performed. Extracts from NS had an immunostimulating effect on non-PHA-stimulated proliferation of human PBMCs. In contrast, immunosuppressive activity was observed on PHA-stimulated proliferation of human PBMCs. This in vitro study revealed the effects of NS plant extract on nonspecific cellular immune responses [52].

Ghonime in 2011 studied the immunomodulatory effect of medicinal plants including *Nigella sativa* and demonstrated that the methanolic extract enhances the total white blood cells count (up to  $1.2 \times 10^4$  cells/mm<sup>3</sup>) in a dose-responsive manner. Bone marrow cellularity also increased significantly ( $P < 0.01$ ) after the administration of the extract [53]. In another study, immunopotentiating effects of *Nigella sativa* oil in streptozotocin-induced diabetic hamsters were investigated. Results suggested that the immunopotentiating effect of *Nigella sativa* oil is mediated through stimulation of macrophage phagocytic activity either directly or via activation of lymphocytes [54].

### **Anti-diabetic effect**

Diabetes mellitus is a metabolic disorder with multiple etiologies characterized by chronic hyperglycemia with disturbances of carbohydrate, protein and fat metabolism resulting from defects in insulin secretion, insulin action or both. It occurs when the body cannot produce enough or effectively use insulin [55]. Several pathogenic processes are involved in the development of diabetes. These range from autoimmune destruction of the b-cells with consequent insulin deficiency to abnormalities that result in resistance to insulin action.

Ethanol extract of *Nigella sativa* (300 mg/kg body weight per day) significantly reduced the elevated levels of blood glucose, lipids and improved altered levels of antioxidant enzymes like catalase, superoxide dismutase, lipid peroxidation products (TBARS and hydroperoxides), reduced glutathione and glutathione peroxidases in liver and kidney. The study confirms the anti-diabetic activity of *Nigella sativa* seeds extract possibly due to its antioxidant effects as observed in experimental diabetic rats [56].

The effect of *Nigella sativa* against  $\beta$ -cell damage from streptozotocin-induced diabetes in rats was investigated by Kanter et al. in 2004. Single dose of streptozotocin (50 mg/kg body weight) was injected intraperitoneally to induce diabetes. However, *Nigella sativa* extract (0.2 ml/kg/day, i.p.) for 30 days caused reductions in lipid peroxidation and serum NO and increasing antioxidant enzyme activity. Islet cell degeneration and weak insulin immunohistochemical staining was observed in rats with STZ-induced diabetes. Increased intensity of staining for insulin, and preservation of  $\beta$ -cell numbers were apparent in the NS-treated diabetic rats. These findings suggest that NS treatment exerts a therapeutic protective effect in diabetes by decreasing oxidative stress and preserving pancreatic  $\beta$ -cell integrity. Consequently, NS may be clinically

useful for protecting  $\beta$ -cells against oxidative stress <sup>[57]</sup>. Another study was also carried out by Kanter et al. in 2003 to investigate the effect of *Nigella sativa* on histopathology of pancreatic  $\beta$ -cells, blood insulin and glucose concentrations in streptozotocin-induced diabetic rats and concluded that the hypoglycemic action of *Nigella sativa* could be partly due to amelioration in the  $\beta$ -cells of pancreatic islets causing an increase in insulin secretion <sup>[9]</sup>. Recently, in 2014 Sultan et al. studied the effect of *Nigella sativa* fixed and essential oils on antioxidant status, hepatic enzymes, and immunity in streptozotocin induced diabetes mellitus and concluded that *Nigella sativa* fixed and essential oils significantly ameliorate free radicals and improve antioxidant capacity thus reducing the risk of diabetic complications. *Nigella sativa* fixed and essential oils also reduced the MDA levels by 11.54 and 26.86% and the conjugated dienes levels by 32.53 and 38.39%, respectively. NS oils improved the health and showed some promising anti-diabetic results <sup>[58]</sup>.

### **Gastroprotective activity**

Gastroprotective activity of *Nigella sativa* oil and thymoquinone, against gastric mucosal injury induced by ischaemia/reperfusion in rats was examined. *Nigella sativa* oil and thymoquinone tended to normalize the level of reduced glutathione (GSH) and superoxide dismutase (SOD), lipid peroxide (LPX) and lactate dehydrogenase (LDH) <sup>[59]</sup>. In another study, *Nigella sativa* oil and its constituent, thymoquinone was found to possess gastroprotective activity against acute alcohol-induced gastric mucosal injury in rat. Thymoquinone and *Nigella sativa* oil have been also shown protective effect against gastric mucosal injurious and promote ulcer healing. *Nigella sativa* and thymoquinone prevented alcohol-induced increase in thiobarbituric acid-reactive substances (TBARS), an index of lipid peroxidation, enzymatic activities of gastric superoxide dismutase (SOD), gastric glutathione content (GSH) and glutathione-S-transferase (GST). These gastroprotective effects might be due to their radical scavenging activity, antiperoxidative and antihistaminic effects <sup>[60, 61]</sup>. Thymoquinone has novel gastroprotective mechanisms via inhibiting acid secretion, proton pump and neutrophil infiltration, while enhancing nitric oxide production and mucin secretion <sup>[62]</sup>. The anti-ulcer effect of aqueous suspension of *Nigella sativa* on necrotizing agents (80% ethanol, 0.2 M naoh, 25% nacl and indomethacin)-induced gastric injury in experimental animals were examined. NS significantly prevented gastric ulcer formation induced by various noxious chemicals. It also significantly ameliorated the basal gastric acid secretion and ulcer severity in experimental rats. Furthermore, the suspension

significantly replenished the ethanol-induced depleted gastric wall mucus content levels and gastric mucosal non-protein sulfhydryl concentration. These findings validate the anti-ulcer effect of NS is possibly through its antioxidant and anti-secretory activities <sup>[63]</sup>.

### **Cardiovascular activity**

Protective effect of thymoquinone against acute (at 4 and 18 h) exposure to diesel exhaust particles (DEP) on cardiopulmonary parameters in mice was investigated. Mice were given, intratracheally, either saline (control) or DEP (30 µg/ mouse). At 18 h, DEP caused loss of lung function, lung inflammation and decreased SOD activity. At both 4 and 18 h, DEP caused systemic inflammation characterized by leucocytosis, increased IL-6 concentrations and reduced systolic blood pressure. DEP reduced platelet numbers and aggravated in vivo thrombosis in pial arterioles. In vitro, addition of DEP (0.1-1 µg·mL<sup>-1</sup>) to untreated blood-induced platelet aggregation. Pretreatment of mice with TQ prevented DEP-induced cardiovascular changes <sup>[64]</sup>.

In another study, cardioprotective effect of Thymoquinone against myocardial ischemia/reperfusion (I/R) injury and ventricular arrhythmias in anaesthetized rats was investigated. TQ treatment reduced the infarct size. Pretreatment with TQ decreased arrhythmia scores, as well as the incidence of ventricular tachycardia and the incidence of ventricular fibrillation during the reperfusion period. These results suggest that TQ confers protection against myocardial I/R injury and suppresses reperfusion-induced arrhythmias <sup>[65]</sup>. The effect of *Nigella sativa* seeds powder and oil on atherosclerosis in diet-induced hypercholesterolemic rabbits was examined. Feeding hypercholesterolemic rabbits with *Nigella sativa* either in powder (1000 mg/ Kg bw) or oil (500 mg/ Kg bw) forms was shown to significantly reduce (P < 0.05) total cholesterol and low-density lipoprotein cholesterol levels and enhance high-density lipoprotein cholesterol levels after treatment for 2, 4, 6 and 8 weeks compared to the positive control group. Plaque formation was significantly inhibited while the intima: media ratio was significantly reduced in the *Nigella sativa* powder and *Nigella sativa* oil supplemented groups compared to the positive control group. Treatment of hypercholesterolemic rabbits with *Nigella sativa* seeds powder or oil showed hypocholesterolemic and antiatherogenic cardioprotective properties <sup>[66]</sup>.

A group of herbal plants including *nigella sativa* were examined on biochemical parameters in streptozotocin-induced diabetic rats. Result showed significant difference in the level of total

cholesterol ( $55 \pm 2$  versus  $97 \pm 11$  mg/dl,  $P < 0.01$ ), triglyceride ( $60 \pm 9$  versus  $158 \pm 37$  mg/dl,  $P < 0.01$ ) between treated rats and diabetic control group<sup>[67]</sup>. The effects of a polyherbal mixture containing *Nigella sativa* were tested on biochemical parameters in diabetic rats. At the end of experiment, the levels of triglyceride and total cholesterol in polyherbal mixture supplemented rats were significantly lower than those in diabetic control group ( $P < 0.05$ ). Results demonstrated that polyherbal mixture has beneficial effects on lipid profile and it has the potential to be used for the treatment of cardiovascular diseases<sup>[68]</sup>.

Recently, cardioprotective effect of thymoquinone in isoproterenol- (ISP-) induced myocardial infarction in rats was examined. Treatment with TQ (20 mg/kg) for 21 days prevented the depletion of endogenous antioxidants and myocyte injury marker enzymes and inhibited lipid peroxidation as well as reducing the levels of proinflammatory cytokines. TQ pretreatment also reduced myonecrosis, oedema, and infiltration of inflammatory cells. These results demonstrate that TQ exerts cardioprotective effect by mitigating oxidative stress, augmenting endogenous antioxidants and maintaining structural integrity and indicate that TQ may serve as an excellent agent alone or as adjuvant to prevent the onset and progression of myocardial injury<sup>[69]</sup>.

### **Contraceptive and anti-fertility activity**

Ethanol extract of *Nigella sativa* seeds were found to possess an anti-fertility activity in male rats which might be due to inherent estrogenic activity of *Nigella sativa*<sup>[70]</sup>. In another study hexane extract of *Nigella sativa* seeds prevented pregnancy in Sprague-Dawley rats when treated orally at a dose of 2 g/kg daily on day's 1-10 post-coitum<sup>[71]</sup>.

### **Anti-oxytocic activity**

*Nigella sativa* seeds oil abolish the contractions of rat and guinea pig uterine smooth muscle induced by oxytocin stimulation and also the impulsive movements of rat and guinea pig uterine smooth muscle which suggest the anti-oxytocic prospective of NS seed oil<sup>[72]</sup>.

### **Galactagogue activity**

Effect of aqueous and ethanolic extracts of *Nigella sativa* seeds on milk production in rats were evaluated. Milk production was measured by pup weight during suckling period. The aqueous (0.5 g/kg bw) and ethanolic extracts (1 g/kg bw) significantly increased milk production and

producing about 31.3% and 37.6% more milk than control, respectively. During the study period, the pups gained weight with the aqueous and ethanolic extracts 0.5 g/kg, 1 g/kg body weight respectively. These results indicate that aqueous and ethanolic extracts of *Nigella sativa* can stimulate milk production in rats <sup>[73]</sup>.

### **Abortifacient activity**

Large oral doses of whole *Nigella sativa* seeds as well as hot water extract of the seeds causes abortion in pregnant women <sup>[74, 75]</sup>.

### **Toxicological studies**

*Nigella sativa* seed extract emerge to have a very low level of toxicity. Several toxicological studies have been done to find the fact. For investigating LD50 value of the aqueous, chloroform and methanol extracts of the seeds, Vahdati et al. in 2005 has given these extracts orally in 4 different doses (6, 9, 14 and 21 g/kg body weight) to mice and no mortality has been found in all groups and with all doses. They were also found significantly decreased in animal weight with methanolic extracts in all doses and chloroform extract in the dose of 21 g/kg body weight. However, degenerative changes in hepatic cells were observed only with aqueous extract of the seeds. These finding suggests that NS extracts are relatively nontoxic in the acute toxicity test, but the possibility of hepatic damage with its aqueous extract should be considered <sup>[76]</sup>.

Zaoui et al. in 2002 also investigated the toxicity of *Nigella sativa* fixed oil in mice and rats through determination of LD50 values and examination of hematological, biochemical and histopathological changes. The LD50 values, obtained by single doses, orally and intraperitoneally administered in mice, were 26.2–31.6ml/kg body wt. and 1.86–2.26 ml/kg body wt., respectively. Chronic toxicity was studied in rats treated daily with an oral dose of 2 ml/kg body wt. for 3 months. The glucose levels, serum triglyceride, cholesterol, count of leukocytes and platelets decreased significantly when compared to control values, while hematocrit and hemoglobin levels increased significantly. This evidence shows a wide margin of safety for therapeutic doses of *Nigella sativa* fixed oil <sup>[7]</sup>. In another study, the LD50 value in mice after intraperitoneal injection of TQ was determined to be 89.7-119.7 mg/kg and after oral ingestion was 647.1-1094.8 mg/kg Whereas, LD50 value in rats after intraperitoneal injection was determined to be 45.6-69.4 mg/kg and after oral ingestion was 469.8-1118.8 mg/kg. The LD50

values presented here after intraperitoneal injection and oral gavages are 10-15 times and 100-150 times greater than doses of thymoquinone reported for its anti-oxidant, anti-inflammatory and anti-cancer effects <sup>[77]</sup>. Tennekoon et al. in 1991 also reported, no toxicity symptoms in male sprague- Dawley rats when aqueous extract of *Nigella sativa* were given orally for 14 days <sup>[78]</sup>. In a recent study, the potential toxicity of a thymoquinone-rich fraction nanoemulsion (TQRFNE) in Sprague Dawley rats was observed. 20 mL TQRFNE (containing 44.5 mg TQ/kg) and distilled water (DW) as a control were administered orally to both sexes of rats for 14 days. General behavior, body weight, food and water consumption, relative organ weight, hematology, histopathology, and other clinical parameters were measured. There was no observed mortality or any signs of toxicity during the experimental period <sup>[79]</sup>. These studies suggest that *Nigella sativa* and its active compounds are safe when given orally to experimental animals.

## CONCLUSION

*Nigella sativa* (Black cumin) is a herb belonging to the family Ranunculaceae. It is grown in Europe, Middle East and Asia, and is most commonly used as traditional medicine in Arabic countries and Europe. It is an important source of protein, essential fatty acids, various vitamins such as A, B<sub>1</sub>, B<sub>2</sub>, B<sub>3</sub>, C and minerals like calcium, iron, magnesium, potassium, selenium and zinc. It also contains considerable quantities of allied bioactive compounds such as thymoquinone, dithymoquinone, thymohydroquinone, thymol, tocopherols and phytosterols which strengthen its hypoglycemic and hypocholesterolemic, gastroprotective hepatoprotective, anti-cancerous perspectives but a number of other pharmacological activities are yet to be explored and further investigations are required to study the mechanism of actions of *Nigella sativa* seeds and its constituents by which they exert their therapeutic effects.

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