REVIEW

Nigella sativa (Prophetic Medicine): A Review

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Abstract: The present report is a significant effort to explore detail description of *N. Sativa,* its pharmacognostic characteristics, morphological characteristics, and mechanism of actions, doses and medicinal uses*. Nigella sativa (N. Sativa*) is greatest form of healing medicine. It is also known as Prophetic Medicine as its use has been mentioned in Prophetic Hadit, as natural remedy for all the diseases except death. It is recommended on daily basis in Tibb-e-Nabwi (Prophetic Medicine). Hazrat Abu Hurairah States *''I have heard from Rasool Allah (PBUH) that there is cure for every disease in black seeds except death and black seeds are shooneeze''*. Salim Bin Abdullah narrates with reference to his father Hazrat Abdullah Bin Omar that Rasool Allah (PBUH) said*, 'Let all the black seed upon you, these contain cure of all diseases except death'. N. sativa* claimed to have anti-inflammatory, analgesic, hepato-protective, neuro-protective, gastro-protective and other useful properties. Biological and pharmacological effects are attributed to its two important constituents Thymoquinone (TQ) and *Nigella sativa* oil (NSO). TQ has interaction with human serum albumin. Seeds containing volatile oils mainly Melanthin showed toxicity at larger doses. This report is a reference for all pharmaceutical researchers, physicians and biologists researching on *N.Sativa* and will open a door towards novel agent.

Keywords: *Nigella sativa*, Ranunculaceae, Prophetic Medicine, Thymoquinone (TQ) and *Nigella sativa* oil (NSO).

INTRODUCTION

Natural compounds have found their applications in the treatment of refractory diseases, a new trend in modern clinical medicine. Because of their satisfactory clinical efficacy and low toxicity, natural products are being used as alternative treatments for various diseases. *Nigella sativa* is one of them and is also known as black seed (seed of capsulated plant), black cumins, Love-in-a-mist, Habatut, Barakah, Sonez, Habatut, Sauda, Kalonji, Krishana, Jiraka, Sidadanah (Sultan, *et al*., 2009; Ismail, 2009). *Nigella sativa* has historical as well as religious background. Prophet Mohammad (PBUH) referred to black seed as healing power. Black cumin is also mention in Holy Bible as "Curative black cumin" and is described as 'Melancthon of Hippocrates and Dioscorides' and as 'Glitch of Pliny' (Al-Ghamdi, 2001).

Pharmacognostic characteristics

It belongs to butter-cup or crowfoot family (Ranunculaceae). *Nigella sativa* is herbaceous annual plant ranging from 30-60 cm in height. Plant has 2-3 pinnatisect leaves, cut into linear-lanceolate segments; leaves are greyish, green, and fine (Cheikh *et al*., 2008). Flowers are bluish white, pale, yellow and solitary. Terminal fruit is capsule having many rectories, pocket like epicalyx present. Seeds are small, dicotyledonous, trigonous black, rugulose-tubercular. (Jabbar *et al*., 2006).

Scientific classification of the plant

Kingdom: Plantae
Subkingdom: Tracheobionata that is, vascular plant.
Supervision: Spermatophyte.
Order: Ranunculales.
Family: Ranunculaceae Butter cup family.
Genera: *Nigella.*
Species: *sativa*.

Chemical constituents

Phytochemical analysis of *Nigella sativa* demonstrated the presence of volatile oil, fatty acids, which are accountable for its pharmacological action (Al-Ghamdi *et*

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Table 1: Chemical composition

Groups	Concentration	Subgroups	Components	Reference
Fixed Oil	32-40%	Saturated fatty acids	Palmitic acid (12.5%), Stearic and Myristic acid (30%).	(Tembhurne *et al*., 2014)
		Unsaturated Fatty Acids	Arachidonic, Eicosadienoic acid (3%), Linoleic (50-60%), Linolenic, Oleic Acid (20%), Almitoleic acid, β-Sitosterol, α-Sitosterols (44-54%), Cycloeucalenol, Cycloartenol, Sterol Esters and Sterol Glucosides	(Tembhurne *et al*., 2014).
Volatile Oil	0.4-0.45%	-	Nigellone, Thymoquinone (30-48%), Thymohydroquinone, Dithymoquinone, Thymol, Carvacrol, α & β-Pinene, D-limonene, D-citronellol, P-cymene (7-15%) and 2-(2-Methoxypropyl)-5-Methyl-1,4-Benzenediol	(Tembhurne *et al*., 2014)
Proteins	16-19.9%	Amino Acids	Arginine, Glutamic acid, Leucine, Lysine, Methionine, Tyrosine, Proline And Threonine	(Tembhurne *et al*., 2014)
Alkaloids		Isoquinoline Alkaloids	Nigellicimine, Nigellidine, Nigellimine-N-oxide	(Ahmad *et al*., 2013)
		Pyrazole Alkalods	Nigellidine Nigellicine	(Benkaci *et al*., 2007).
Coumarins			6-Methoxy-Coumarin, 7-Hydroxy-Coumarin, 7-Oxy-Coumarin	(Ahmad *et al*., 2013)
Saponins		Triterpenes and Steroidals	α-Hedrin, Steryl-glucosides, Acetyl-steryl-glucoside	(Ahmad *et al*., 2013)
Minerals	1.79-3.74		Cu, P, Zn, Fe Etc	(Ahmad *et al*., 2013).
Carbohydrates	33.9%			(Tembhurne *et al*., 2014)
Fiber	5.5%			(Ahmad *et al*., 2013)
Water	6%			(Ahmad *et al*., 2013)
Others Reported Chemicals			Nigellone, Avenasterol-5-Ene, Avenasterol- 7c-Ycelnoee, Egrroalm, Isctheorolel, S Tleorpohle, N Coilt, R O2l4--7m-Eetnhey, Gvloulactoipley Roainl Osyl(1→6)-B-D- Oil (0.5-1.6%), Fatty With(3 C5.6-41.6%), Oleic Acid, Esters Of Unsaturated Fatty Acids Linoleic1 5a Caindd, N Tiann Ngilny,C Oressidine, Hriend, Ngilny, N2o3--Dihydroxy-28-Methy-Lolean-12-Enoate,Stigma-5, 22-Dien- 3-B-D-Gluco-Pyranoside, Cycloart-Triene- 23-Methyl-7, 20, 22- A 3β, 25-Diol, Nigellidine-4-O-Sulfite.	(Gali-Muhtasib,*et al*., 2006)

Table 2: Various mechanisms responsible for *N. sativa* Effects

Activity of *Nigella sativa*	Mechanism	Reference
Anti-inflammatory	Anti-inflammatory activity is attributed to inhibition of cytokine, eicosanoids generation and measure lipid peroxidation through inhibition of cyclo-oxygenase and 5-lipoxygenase pathway of arachidonate metabolism. In addition, T cell- and natural killer cell-mediated immune responses are also accountable to its immune-modulatory activity.	(Marsik, *et al*., 2005; Chehl, *et al*., 2009)
Cardiovascular actions	Cardiovascular depressant effects are mediated centrally via indirect and direct mechanisms that involved both 5-hydroxytryptaminergic and muscarinic mechanisms. Direct mechanism is virtue of volatile oil (TQ) which processes potent antihypertensive potential.	(Demir *et al*., 2006)
Anti-hyperlipidemic	Anti-hyperlipdemic effect is owing to significant reduction in hepatic HMG-COA reductase activity. In addition, this effect is attributed to blockage of the *ex-vivo* basal and *in-vitro* maximal formation of conjugated diene and malondialdehyde, and lengthened the lag times of low density lipoprotein, small dense low density lipoprotein and large buoyant low density lipoprotein. Methanolic extract possessing ω-6 linoleic acid along with palmitic acid is more effective than volatile extract containing thymol and isothymol phenolic antioxidant compounds. Thymoquinone has anti-hyperlipidemic as well as antioxidant activity	(Ahmad *et al*., 2013; Kanter, 2008)
Hypoglycemic effects	*N.sativa* has non-insulin-mediated mechanism for the demonstration of hypoglycemic activity. However, petroleum ether extract exerts an insulin-sensitizing action by enhancing the activity of the two major intracellular signal transduction pathways of the hormones receptor.	(Al-Hader *et al*., 1993; Kaleem *et al*., 2006).
Antinociceptive effects	Antinociceptive effects of *N. sativa* oil and thymoquinone are mediated by indirect activation of the supraspinal μ_1- and κ-opioid receptor subtypes.	(Aboul , 2002)

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Activity of *Nigella sativa*	Mechanism	Reference
Anti-oxytocic potential.	The volatile oil of *Nigella sativa* seeds inhibit the spontaneous uterine smooth muscle contractions induced by oxytocin stimulation. These effects are concentration-dependent and reversible by tissue washing.	(Aqel *et al*., 1996)
Gastro- protective effects	*N. sativa* cause significant reduction in acidity and glutathione level while it produced a significant increase in mucosal histamine content	(Rajkapoor *et al*., 2002; Abdel-Sater, 2009).
Neuroprotective action	Neuro-protective action of NSO is correlated to its ability to inhibit not only excessive reactive oxygen species (ROS) formation but also seizure generation	(Ilhan *et al*., 2005)
Nephro-protective effect	NSO acts in the kidney as a potent scavenger of free radicals	(Yaman *et al*., 2010 ; Yildiz, *et al*., 2010)
Anti-schistosomiasis	TQ were considered as protective agents against the chromosomal aberrations induced as a result of schistosomiasis	(Aboul, 2002; Shenawy *et al*., 2008)
Anxiolytic effect	*N. sativa* oil increased brain levels of 5-HT but the levels of brain 5-HIAA decreased significantly. Brain and plasma levels of tryptophan also increased significantly following oral repeated administration of *N.sativa* oil. Based on this, it may be suggested that *N.sativa* oil is a useful choice for the treatment of anxiety.	(Perveen *et al*., 2009)

Table 3: Effectiveness of *N. Sativa*

Experimental Drug Constituents	Uses	Combined Medication	Disease Type/ Indication	Efficacy	Reference
Thymoquinone (TQ)	Antibacterial activity (Effective against *MRSA, Staphylococcus aureus, H. pylori, Staphylococcus aureus*, *Staphylococcus epidermidis*	Melanin	Ulcer	Seed of *Nigella sativa* has good antimicrobial activity against *H. Pylori* as compare to triple therapy (clarithromycin, amoxicillin, omeprazol). H. pylori eradication was 82.6, 47.6, 66.7 and 47.8% with TT, 1 g NS, 2 g NS and 3 g NS, respectively. Eradication rates with 2 g NS and TT were statistically not different from each other, whereas *H. pylori* eradication with other doses was significantly less than that with TT ($P < 0.05$). Azithromycin was used as positive control.	(Salem *et al*., 2010; Kanter, 2008).
Thymoquinone (TQ)	Antifungal against *Trichophyton rubrum species* including *Trichophyton interdigitale, Trichophyton mentagrophytes, Epidermophytone Floccosum,* and *Microsporum canis*	Thymohydroquinone, Quinines, Dithymoquinone	Anti-dermatophyte, Vaginal candidiasis	A cream containing different concentrations of TQ (from 1% to 10%) was used to treat the infected mice and the effectiveness was compared with that treated with miconazole nitrate (2%). So it was strongly recommended (Ahmed *et al*., 2013) to use TQ for treatment of Vaginal candidiasis. Griseofulvin and miconazole were used as positive control.	(Azeiz *et al*., 2013; Morsi, 2000)
Thymoquinone (TQ)	Antioxidant, Anti-arthritic	None	Arthritis, Treating Broiler chicks	The effects of treatment in the rats were assessed by glutathione (articular elastase, myeloperoxidase (MPO), LPO, mediators [(IGLS-H), catalase (CAT), SOD and NO), inflammatory mediators and histological studies. TQ significantly changed theses parameters.	(Meral *et al*., 2011)
α-lipoic acid, L-carnitine, *N.sativa* alone or in combination	Anti-diabetic	Experimental drug use alone or in combination	Diabetes	Combination of α-lipoic acid, L-carnitine, *N.sativa* oil helps in significant reduction of carbohydrate metabolism, glucose level thereby causing significant increase in insulin levels in diabetic rats,. Dose of 2gm/day is effective in oral hypoglycaemic patients for treatment of Type 2 DM Diabetes. Streptazocin was used as positive control.	(Hawsawi *et al*., 2011, El-Dakhakhny *et al*., 2002; Meddah, *et al*., 2009; Najmi, *et al*., 2008).

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Experimental Drug Constituents	Uses	Combined Medication	Disease Type/ Indication	Efficacy	Reference
Thymoquinone (TQ)	Anticancer, Antitumor, Anti-angiogenic effect	None	Cervical squamous carcinoma, Brest cancer	TQ is more effective in treatment of squamous carcinoma as compare to cisplastin. Cisplatin was used as positive control here.	(Kumara & Huat, 2001; Alenzi *et al*., 2010; Thomas *et al*., 2002).
Thymoquinone (TQ)	Anti-inflammatory Analgesic	None	Use to treat inflammation and pain	TQ contents of callus leaf have higher anti-inflammatory activity than seed of *N.sativa*. Studies on inflamed rat mix glial cell showed significant reduction in NO at concentration of 0.2-0-1.6mg/ml (TQ from Callus leaf) and at concentration of 1.25-20µl/ml(TQ from *N.sativa* seed)	(Landa *et al*., 2009)
N.sativa oil	Anti-tumor activity Immunomodulatory activity	None	Immunosuppresive , cytotoxic agent	Two groups of mice were immunocompromised with cyclophosphamide, the one treated with black seed show (P<0.01).Treatment of *N.sativa* oil show 2 fold decrease in antibody production in response to typhoid vaccine in Long-Evans rats.	(Khan *et al*., 2011)
Thymoquinone (TQ)	Cardiovascular effects include decrease in platelet numbers, prothrombotic events, but not platelet aggregation in-vitro	None	Decrease in blood pressure, leucocytosis, increase IL-6 concentration	The acute effect of diesel exhausted particles (DEP) and TQ on cardiopulmonary parameters were evaluated. Pre-treatment with TQ in mice reduce DEP induce increase in blood pressure, leucocytosis, increase IL-6 concentration. Saline DEP was used as positive control here.	(Dehkordi, & Kamkhah, 2008).
Thymoquinone (TQ)	Gastroprotective	None	Decrease acid output, improve gastric mucosa	Male wistar rats were injected with NO (2.5-5 mL/Kg) or TQ (5, 20, 50, 100 mg/kg p.o). Results showed both TQ and NSO are effective in treating ulcer and has good gastro-protective activity. Omeprazole was used as positive control here.	(Al-Mofleh *et al*., 2008 ; Terzi *et al*., 2010)
Thymoquinone (TQ)	Hepatoprotective activity	None	Effective against heptic perfusion injury and hepatotoxicity	Total asparatate aminotransferase, alanine aminotransferase, lactate dehydrogenase level, total antioxidant capacity, oxidative stress index (OSI), total antioxidant capacity(TAC) and MPO were determined in hepatic tissues Results show *N.sativa* has hepatic activity.,	(Daba & Abdel-Rahman,.1998 ; Abdel-Daim, *et al.*, 2015).
NSO	Nephro-protective activity	None	Nephroprotective activity	NSO shows significant reduction in blood urea nitrogen, creatinine, urea. Gentamicin was used as a positive control.	(Ahmed *et al*., 2013)
Nigellone and TQ	Pulmonary protective and anti-asthmatic activity, anti-spasmodic effect	Combination of Nigellone and TQ	Asthma	The broncho-dilatory effects achieved at a dose of 50 and 100 mg/kg of boiled extract in comparison with 6 mg/kg theophylline were studied on 15 asthmatic patients. Extract caused significant increases in all measured pulmonary function tests (PFTs), in most time intervals (p<0.05 to p<0.001). Theophylline was used as positive control.	(Boskabady *et al*., 2010)
TQ	Testicular protective activity	None	Testicular injury	Thymoquinone treatment decreased total antioxidant capacity and prevented the increase in the myeloperoxidase activity. Methotrexate was used as positive control.	Gökçe *et al*., 2010)
Curcumin, NSO	Anticonvulsant activity	None	Anti-epileptics	The protective effect of thymoquinone against lethality was 45% and 50% in the respective doses	(Hosseinzadeh, *et al*., 2005)
TQ	Contraceptive and Anti-fertility activity	None	Contraceptive	Ethanolic extract of N.Sativa has anti-fertility activity. This effect is attributed to its anti-estrogen activity.	(Ahmad *et al*., 2013)

al. 2001). Eight fatty acids are reported which constitute 99.5% of fatty acids however volatile oil constitute 0.5%. Fatty acids include four saturated (17.5%), four unsaturated (82.5%) fatty acids (Cheikh *et al*., 2008).

CONCLUSION

The use of *N. sativa* is increasing tremendously in therapy of many diseases. Chemical refinement in Thymoquinone (TQ) and NSO may lead to more effectual drugs which help in treatment of various other diseases.

RECOMMENDATION

Both TQ and NSO have potential for treatment of various diseases due to their anti-oxidant and cyto-protective properties. Clinical studies can be conducted further to assess their effectiveness. Further studies can define various techniques as well as targets to heal other alarming diseases.

REFERENCES

Abdel-Daim, MM & Ghazy (2015). Effects of Nigella sativa oil and ascorbic acid against oxytetracycline-induced hepato-renal toxicity in rabbits. *: Iran J Basic Med Sci.,* 18(3): 221-227

Abdel-Sater KA (2009). Gastro protective effects of *Nigella sativa* oil on the formation of stress gastritis in hypothyroidal rats. *Int. J. Physio. patho and Pharmacoly.*, **1**(2): 143-147.

Aboul-Ela EI (2002). Cytogenetic studies on *Nigella sativa* seeds extract and thymoquinone on mouse cells infected with schistosomiasis using karyotyping. *Mutat. Res. Genet Tox.*, **516**(1): 11-17.

Ahmad A, Husain A, Mujeeb, M Khan, Najmi, Siddique and Anwar (2013). A review on therapeutic potential of *Nigella sativa*: A miracle herb. *Asian. Pac. J. Trop. Med.*, **3**(5): 337-352.

Al Mofleh IA, Alhaider, Mossa, Al-Sohaibani, Al-Yahya, Rafatullah S and Shaik SA (2008). Gastro protective effect of an aqueous suspension of black cumin *Nigella sativa* on necrotizing agents-induced gastric injury in experimental animals. *Saudi. J. Gastroenterology*, **14**(3): 147-155.

Alenzi FQ, El-Bolkiny YS and Salem ML (2010). Protective effects of *Nigella sativa* oil and thymoquinone against toxicity induced by the anticancer drug cyclophosphamide. *Brit. J. Biomed. Sci.,* **67**(1): 20-28.

Al-Ghamdi MS (2001). The anti-inflammatory, analgesic and antipyretic activity of *Nigella sativa*. *J. Ethnopharmacol.*, **76**(1): 45-48.

Al-Hader A, Aqel M and Hasan Z (1993). Hypoglycemic effects of the volatile oil of *Nigella sativa* seeds. *Pharm. Bio.*, **31**(2): 96-100.

Aqel M and Shaheen R (1996). Effects of the volatile oil of *Nigella sativa* seeds on the uterine smooth muscle of rat and guinea pig. *J. Ethnopharmacol,* **52**(1): 23-26.

Azeiz AZ, Saad AH and Darweesh MF (2013). Efficacy of Thymoquinone against Vaginal Candidiasis in Prednisolone-induced Immunosuppressed Mice. *J. Am. Sci.,* **9**(4): 155-159.

Benkaci-Ali F, Baaliouamer A, Meklati BY and Chemat F (2007). Chemical composition of seed essential oils from Algerian *Nigella sativa* extracted by microwave and hydro distillation. *Flavour. Frag. J.,* **22**(2): 148-153.

Boskabady MH, Mohsenpoor N and Takaloo L (2010). Antiasthmatic effect of *Nigella sativa* in airways of asthmatic patients. *Phytomedicine*, **17**(10): 707-713.

Chehl N, Chipitsyna G, Gong Q, Yeo CJ and Arafat HA (2009). Anti-inflammatory effects of the *Nigella sativa* seed extract, thymoquinone, in pancreatic cancer cells. *HPB*, **11**(5): 373-381.

Cheikh-Rouhou S, Besbes S, Lognay G, Blecker C, Deroanne C and Attia H (2008). Sterol composition of black cumin (*Nigella sativa L.)* and aleppo pine *(Pinus halepensis Mill)* seed oils. *J. Food. Compos. Anal.*, **21**(2): 162-168.

Daba MH and Abdel-Rahman MS (1998). Hepatoprotective activity of thymoquinone in isolated rat hepatocytes. *Toxicol. Lett.,* **95**(1): 23-29.

Dehkordi FR and Kamkhah AF (2008). Antihypertensive effect of *Nigella sativa* seed extract in patients with mild hypertension. *Fundam. Clin. Phar.,* **22**(4): 447-452.

Demir H, Kanter M, Coskun O, Uz YH, Koc A and Yildiz A (2006). Effect of black cumin (*Nigella sativa*) on heart rate, some hematological values, and pancreatic β-cell damage in cadmium-treated rats. *Biol. Trace. Elem. Res.,* **110**(2): 151-162.

El-Dakhakhny M, Mady N, Lembert N and Ammon HP (2002). The hypoglycemic effect of *Nigella sativa* oil is mediated by extra pancreatic actions. *Planta. Med.,* **68**(5): 465-466.

Fararh KM, Atoji Y, Shimizu Y, Shiina T, Nikami H and Takewaki T (2004). Mechanisms of the hypoglycaemic and immunopotentiating effects of *Nigella sativa L*. oil in streptozotocin-induced diabetic hamsters. *Res. Vet. Sci.*, **77**(2): 123-129.

Gali-Muhtasib H, El-Najjar N and Schneider-Stock R (2006). The medicinal potential of black seed (*Nigella sativa*) and its components. *Adv. Phytomed.,* **2**(4): 133-153.

Gökçe A, Oktar S, Koc A, Gonenci R, Yalcinkaya F, Yonden Z and Duru M (2010). Protective effect of thymoquinone in experimental testicular torsion. *Urol. Int.,* **5**(4): 857-866.

Hawsawi ZA, Ali BA and Bamosa AO (2001). Effect of *Nigella sativa* (black seed) and thymoquinone on blood glucose in albino rats. *Annal. Saudi Med*., **21**(4): 242-244.

Hosseinzadeh H, Parvardeh S, Nassiri-Asl M and Mansouri MT (2005). Intra cerebroventricular administration of thymoquinone, the major constituent of *Nigella sativa* seeds, suppresses epileptic seizures in rats. *Int. J. Exp. Clin. Res.*, **11**(4): 102-106.

Ilhan A, Gurel A, Armutcu F, Kamisli S and Iraz M (2005). Antiepileptogenic and antioxidant effects of *Nigella sativa* oil against pentylenetetrazol-induced kindling in mice. *Neuropharmacol.,* **49**(4): 456-464.

Isik AF, Kati I, Bayram I and Ozbek H (2005). A new agent for treatment of acute respiratory distress

syndrome: Thymoquinone. An experimental study in a rat model. *Eur. J. Cardio-Thorac.,* **28**(2): 301-305.

Ismail MYM (2009). Therapeutic Role of Prophetic Medicine Habbat El Baraka (*Nigella sativa* L.)-A Review. *World Appl. Sci. J.*, **7**(9): 1203-1208.

Jabbar A, Raza MA, Iqbal Z and Khan MN (2006). An inventory of the ethnobotanicals used as anthelmintics in the southern Punjab (Pakistan). *J. Ethnopharmacol.*, **108**(1): 152-154.

Kaleem M, Kirmani D, Asif M, Ahmed Q and Bano B (2006). Biochemical effects of *Nigella sativa* L seeds in diabetic rats. *Indian J. Exp. Biol.,* **44**(9): 745.

Kanter M (2008). *Nigella sativa* and derived thymoquinone prevents hippocampal neuro-degeneration after chronic toluene exposure in rats. *Neurochem. Res.*, **33**(3): 579-588.

Khan MA, Ashfaq MK, Zuberi HS, Mahmood MS and Gilani AH (2003). The *in vivo* antifungal activity of the aqueous extract from *Nigella sativa seeds. Phytother. Res.,* **17**(2): 183-186.

Khan A, Chen HC, Tania M and Zhang DZ (2011). Anticancer activities of *Nigella sativa* (black cumin). *Afr. J. Comp. Clin. Exp. Med.,* **8**(5): 143-149.

Kumara SS and Huat BT (2001). Extraction, isolation and characterisation of antitumor principle, α-hederin, from the seeds of *Nigella sativa*. *Planta. Med.*, **67**(1): 29-32.

Landa P, Kokoska L, Pribylova M, Vanek T and Marsik P (2009). *In vitro* anti-inflammatory activity of carvacrol: Inhibitory effect on COX-2 catalyzed prostaglandin E2 biosynthesisb. *Arch. Pharmacol. Res.*, **32**(1): 75-78.

Meddah B, Ducroc R, El-Abbas, Faouzi M, Eto B, Mahraoui L, Benhaddou-Andaloussi A and Haddad PS (2009). *Nigella sativa* inhibits intestinal glucose absorption and improves glucose tolerance in rats. *J. Ethnopharmacol.*, **121**(3): 419-424.

Meral I, Yener Z, Kahraman T and Mert N (2001). Effect of *Nigella sativa* on glucose concentration, Lipid peroxidation, Anti-Oxidant defence system and liver damage in experimentally-induced diabetic rabbits. *J. Vet. Med. Ser. A.*, **48**(10): 593-599.

Najmi A, Nasiruddin M, Khan RA and Haque SF (2008). Effect of *Nigella sativa* oil on various clinical and biochemical parameters of insulin resistance syndrome. *Int. J. Diabetes Dev. Countries.*, **28**(1): 11-17.

Perveen T, Haider S, Kanwal S and Haleem DJ (2009). Repeated administration of *Nigella sativa* decreases 5-HT turnover and produces anxiolytic effects in rats. *Pak. J. Pharm Sci.*, **22**(2): 143-149.

Rajkapoor B, Anandan R and Jayakar B (2002). Anti-ulcer effect of *Nigella sativa* Linn against gastric ulcers in rats. *Curr. Sci. India,* **82**(2): 177-178.

Randhawa MA and Alghamdi MS (2011). Anticancer activity of *Nigella Sativa* (Black Seed) A Review. *Am. J. Chinese. Med.,* **39**(6): 1075-1091.

Salem EM, Yar T, Bamosa AO, Al-Quorain A, Yasawy MI, Alsulaiman RM and Randhawa MA (2010). Comparative study of *Nigella sativa* and triple therapy in eradication of Helicobacter Pylori in patients with non-ulcer dyspepsia. *Saudi J. Gastroentology*, **16**(3): 12-18.

Shenawy EL, Nahla S, Soliman MF and Reyad SI (2008). The effect of antioxidant properties of aqueous garlic extract and *Nigella sativa* as anti-schistosomiasis agents in mice. *J. Instit. Trop. Med.,* **50**(1): 29-36.

Sultan MT, Butt MS, Anjum FM, Jamil A, Akhtar S and Nasir M (2009). Nutritional profile of indigenous cultivar of black cumin seeds and antioxidant potential of its fixed and essential oil. *Pak. J. Bot.*, **41**(3): 1321-1330.

Tembhurne S, Feroz BH, More DM and Sakarkar (2014). A review on therapeutic potential of *Nigella sativa* (kalonji) seeds. *J. Med. Plants Res.,* **8**(3): 167-177.

Terzi A, Coban S, Yildiz F, Ates M, Bitiren M, Taskin A and Aksoy N (2010). Protective effects of *Nigella sativa* on intestinal ischemia-reperfusion injury in rats. *J. Invest. Surg.,* **23**(1): 21-27.

Thomas TJ, Panikkar B, Subramoniam A, Nair MK and Panikkar KR (2002). Antitumour property and toxicity of *Barringtonia racemosa Roxb* seed extract in mice. *J. Ethnopharmacol.,* **82**(2): 223-227.

Üstun G, Kent L, Cekin N and Civelekoglu H (1990). Investigation of the technological properties of *Nigella sativa* (black cumin) seed oil. *J. Am. Oil Chem. Soc.*, **67**(12): 958-960.

Yaman İ and Balikci E (2010). Protective effects of *Nigella sativa* against gentamicin-induced nephrotoxicity in rats. *Exp. Toxicol. Pathol.,* **62**(2): 183-190.

Yildiz F, Coban S, Terzi A, Savas M, Bitiren M, Celik H and Aksoy N (2010). Protective effects of *Nigella sativa* against ischemia-reperfusion injury of kidneys. *Renal Failure*, **32**(1): 126-131.