ACTA SCIENTIFIC NUTRITIONAL HEALTH (ISSN: 2582-1423)

Volume 3 Issue 8 August 2019

Review Article

Black Cumin (*Nigella sativa* L.): Auspicious Natural Therapy for Extensive Range of Diseases

Tahreem Javaid, Shahid Mahmood*, Wajiha Saeed and Muhammad Qamrosh Alam

Institute of Food Science and Nutrition, University of Sargodha, Pakistan

***Corresponding Author:** Shahid Mahmood, Institute of Food Science and Nutrition, University of Sargodha, Sargodha, Pakistan.

Received: June 18, 2019; **Published:** July 24, 2019

DOI: 10.31080/ASNH.2019.03.0377

Abstract

Black cumin is deliberated as herbal medicine for a number of diseases in Unani traditional medicine. Except death and aging, black cumin has been named as a cure for all diseases by a Hadith of the Holy Prophet Muhammad P.B.U.H in Islamic medicine. Not only in Islam but in the Bible and other religious sources the black cumin has been recommended of therapeutic use well. Black cumin has been traditionally used in the treatment of several diseases as a herbal medicine such as infertility, fever, chronic headache, migraine, dizziness, chest congestion, paralysis, dysmenorrhea, cough, bronchitis, asthma, obesity, diabetes, infection and inflammation, rheumatism, hemiplegia, back pain hypertension and gastrointestinal disorders such as dyspepsia, flatulence, diarrhea and dysentery. In accumulation, black cumin oil has been used as a balm for aid from nasal ulcers, orchitis, eczema, abscesses and swollen joints. Black cumin has also been conventionally used to treat respiratory disorders such as bronchospasm, asthma and chest congestion in combination with honey.

Keywords: Black Cumin; *Nigella sativa*

Introduction

Black cumin known as kalonji belongs to family Ranunculaceae. It is cultivated and used in different parts of the world, such as the southern Europe, Mediterranean countries and North Africa. It is an annual flowering plant and is inherent to Southwest Asia and South [1,2]. It is an annual grassy plant with black trigonal seeds and green to blue colored flowers. The seeds taste like oregano and have bitterness to them like mustard-seeds. The active ingredients of the plants source is seeds [3]. Siah-Daneh in Persian, Habbat al-barakah in Arabic and black seed or black cumin in English are the different common (folkloric) name known all over the world by this plant. Black cumin is deliberated as herbal medicine for a number of diseases in Unani traditional medicine. Except death and aging, black cumin has been named as a cure for all diseases by a Hadith of the Holy Prophet Muhammad P.B.U.H in Islamic medicine [2]. Not only in Islam but in the Bible and other religious sources the black cumin has been recommended of therapeutic use well [4]. Black cumin has been traditionally used in the treatment of several diseases as a herbal medicine such as infertility, fever, chronic headache, migraine, dizziness, chest congestion, paralysis, dysmenorrhea, cough, bronchitis, asthma, obesity, diabetes, infection and inflammation, rheumatism, hemiplegia, back pain hypertension and gastrointestinal disorders such as dyspepsia, flatulence, diarrhea and dysentery [5,6]. In accumulation, black cumin oil has been used as a balm for aid from nasal ulcers, orchitis, eczema, abscesses and swollen joints. Black cumin has also been conventionally used to treat respiratory disorders such as bronchospasm, asthma and chest congestion in combination with honey [6].

Bioactive compound

The seed extract of black cumin have been categorized with organic compounds comprising of alkaloids, non-essential and essential fatty acids, carbohydrates, flavonoids, steroids etc. The supercritical extraction techniques (SFE) and microwave assisted extraction (MAE) are the new extraction techniques. Hydrodistillation (HD) is the classical method generally, laboring for the trans-

mission and separation of unrecognized new compounds. The essential oil of black seed comprises a lipid portions containing essential fatty acids, fats soluble vitamins and special amount of volatile compounds [7]. The bioactive compounds of Nigella sativa are thymoquinone, carvacrol, and p-cymene. These bioactive compounds have an expansive antimicrobial band. The study objective was to consider the resistance modifying and antimicrobial activity of N. sativa essential oil. These bioactive compounds (thymoquinone, carvacrol, and p-cymene) are in contradiction of one methicillin inclined and one methicillin resistant. Thymoquinone, carvacrol, and p-cymene were considered for antimicrobial activity, inhibition of antimicrobial efflux, modulation of antimicrobial resistance, relative expression of *mepA* gene, membrane disrupting effect and finally antibiofilm activity [8].

Mineral profile

Nutrient	Unit	Value per 100g
Energy	Kcal	400
Protein	G	16.67
Total Lipids (fats)	G	33.33
Carbohydrates	G	50.00
Dietary fiber	G	0
Calcium (Ca)	Mg	0
Iron (Fe)	Mg	12.00
Sodium (Na)	Mg	0
Vitamin C	Mg	0
Vitamin A	Mg	0

Table 1: Hussain [9].

Anti-inflammatory effects

One of the main pathophysiological features of many chronic and acute diseases is Inflammation. The result in promotion of the force of inflammatory mediators is due to activation of the expression of inflammatory genes by infection and oxidative stress containing cytokines, oxidants, eicosanoids and lytic enzymes. Thus, outline of an anticipatory and multi potential agent is encouraging in the cure of inflammatory syndromes. According to several preclinical studies, *Nigella sativa* and thymoquinone overcome the oxidative stress and inflammatory mediators [10]. The treatment inhibited the synthesis of 5-hydroxyeicosatetraenoic acid production and 5-lipoxygenase products in calcium and ionophore-stimulated polymorphonuclear leukocytes in rats are thymoquinone (0.01 and 6.25 µg/mL), plant oil (12.5–50 mg/mL), and nigellone (6.25 and 50 µg/mL) [11]. Thymoquinone inhibited eicosanoid generation through inhibition of both LTC4 synthase and 5-lipoxygenase pathways in human blood cells [12]. The inhibition of eicosanoid generation in human blood cells needed by the effective concentration of thymoquinone was 0.16–16.4 mg/mL, which is very close to the animal effective concentration range. In a clinical study, the effects of *Nigella sativa* and Phyllanthus niruri (NSPN) extract with acute tonsillopharyngitis were examined in 186 patients. The patients were directed NSPN capsules orally (50 mg Phyllanthus niruri and 360 mg *N. sativa*) t.i.d. for 7 days. Swallowing, inflammation, and pain significantly decreased compared with the placebo group on the first day of medication (14.4 mg/kg/day *N. sativa* and 2 mg/kg/day Phyllanthus niruri) [13]. Although, more randomized clinical trial (RCT) is needed to Meta-analyze such findings by applying effective practice and assessing the wellbeing of therapy in this study. In a placebo-controlled study, the rheumatoid arthritis was examined in patients by anti-inflammatory effect of *N. sativa* oil. In addition, the duration of morning stiffness and the number of swollen joints decreased and European League against Rheumatism (EULAR) show that there was a manifest improvement in the disease activity by response criteria after *N. sativa* treatment.

Immunomodulatory effects

Nigella sativa and its constituents can improve immune response in humans [10]. In human volunteers, the effect of the plant seed therapy on cellular immunity was investigated. For 4 weeks, Subjects were treated with *N. sativa* of a dosage of 1 g (twice daily). *N. sativa* (26.7 mg/kg/day) received in most of the subjects, the CD4þ/CD8þ T cell ratio and natural killer (NK) cell function were increased [14]. On Scientific Miracles of Quran and Sunnah, the result of this study was presented in the 1st International Conference but there is no data about the methodology. In addition, on human peripheral blood mononuclear cell (PBMC) responses to different mitogens were investigated by the immunomodulatory effects of the whole and soluble fractions of *N. sativa* seeds (0.1–10 mg/mL). The influence of the whole plant and its purified proteins on mixed lymphocyte culture (MLC) was inhibitory as well as stimulatory (in different donors). Though, an inhibitory effect of *Nigella sativa* and all its four peaks at a concentration of 10 mg/mL was observed in pokeweed mitogen (PWM)-stimulated lymphocytes [15]. Cytokine secretion was also evaluated by the effect of *N. sativa* proteins. On

human PBMC stimulated with phytohemagglutinin and concanavalin as mitogens were investigated by the immunomodulatory effects of Nigella sativa extracts (0.1–5 mg/mL). In this study, two immunobiochemical pathways are tryptophan degradation and neopterin production and they were induced by pro-inflammatory cytokine interferon-γ have been assessed. The production of neopterin and mitogen-enhanced degradation of tryptophan are suppressed by Incubation of nigella sativa. All these well-designed in vitro studies showed T-cell-mediated immunity is a potent potentiating effect by lipid-soluble components of the plant, while B-cell-mediated immunity was affected by water-soluble components. These effects could also alternating the provisional on the type of immune system stimulation. An adjuvant therapy in patients with allergic diseases is the influence of *Nigella sativa* oil (40–80 mg/kg/day). The allergic diseases includes allergic rhinitis, atopic eczema, and bronchial asthma in both adults and children. 152 patients were assessed (for 8 weeks) for subjective severity of target symptoms as well as biochemical parameters in four studies (two RCT and two open label). Treatment of *Nigella sativa* oil decreased scores of subjective feeling. A discrete increase in high-density lipoprotein-cholesterol (HDL-C) and a mild decrease in plasma triglycerides occurred, but the lymphocyte subpopulations and adrenocorticotropic hormone (ACTH) released. Endogenous cortisol concentration remains same. There is no side effect was reported with the exception of receiving a high dose of 80 mg/kg in children. Nigellone and TQ may be responsible for the immunological effects of the plants was suggested according to previous rudimentary studies [16]. *Nigella sativa* oil consumption twice a day for six months reduces the size of lesions in patient with vitiligo lesions.

Antimicrobial effects

Various clinical isolates of bacteria resistant to a number of antibiotics was evaluated as against by the antibacterial effect of *N. sativa* essential oil (4 µl in pure or 1:200 dilution). The oil demonstrated a persuasive dose-dependent antibacterial activity, which was more patent against Gram-positive than Gram-negative bacteria. Gram-positive bacteria such as Enterococcus faecalis and Streptococcus agalactiae were resistant, while *Staphylococcus aureus* S*. epidermidis*, other coagulase-negative staphylococci, and *Streptococcus* pyogenes were sensitive to the oil. However, among the Gram-negative bacteria tested are Acinetobacter baumannii, Vibrio cholerae, Proteus mirabilis, Klebsiella pneumoniae, *P. vulgaris*, and Citrobacter freundii were resistant and only *Pseudomonas aeruginosa* was sensitive to oil [17]. In clinical settings, methicillin-resistant *Staphylococcus aureus* (MRSA) is one of the commonest pathogens encountered was investigated by the antibacterial inhibitory effect of *Nigella sativa*. The treatment of skin infection is a natural remedy by the traditional use of plant.

In a clinical study, the effects of ethanolic extracts of *N. sativa, Zingiber officinale* and their mixture in patients with hepatitis C virus (HCV) infection were evaluated. Patients were divided into healthy subjects; (HCV) as HCV control; HCVþ a capsule containing 500 mg *Z. officinale* extract administered twice daily; HCVþ a capsule containing 500 mg of the plant extract administered twice daily and HCVþ a capsule containing 500 mg of each extract administered twice daily. The ethanolic extracts of *N. sativa* (13.3 mg/kg/day) and *Z. officinale* had a potent effect in HCV patients, as it altered the liver function and decreased the viral load showed as a result [18]. In another study, patients with HCV decreased the viral load and improved oxidative stress, clinical condition and glycemic control by the administration of Nigella sativa oil (16.88 mg/kg/day for 3 months). *Nigella sativa* administration was safe in all patients, and only one patient reported hypoglycemia and epigastric pain [19].

Antitumor effects

The incubation of *Nigella sativa* seed oil (0.1, 0.25, 0.5, and 1 mg/mL) and *Nigella sativa* seed extract (0.25, 0.5, and 1 mg/mL) considerably reduces the viability and changes the cellular morphology of A-549 cells in a concentration dependent manner shown by the antitumor activity of *Nigella sativa* seed extract and oil against a human lung cancer cell line [20]. Regulatory effect in cell growth and differentiation in human monocyte and monocyte-derived macrophages in *nigella sativa* oil [21]. Besides, the lipid fraction of nigella seed extract effects the cytotoxicity of aqueous extract at high concentration and hormetic effect at low concentrations in human MCF-7 breast cancer cells. It also increases the antitumor activity of doxorubicin in human MCF-7 breast cancer cells by the adjuvant therapy of oil nanoemulsion [22].

It was reported that reduces cell viability of ACHN dependent on dose and time More pronounced morphological changes and apoptotic effect of total extract in ACHN cells compared with the GP-293 cells in ACHN (human renal adenocarcinoma) and GP-293 (normal renal epithelial) cell lines by the plant's hydroalcoholic extract (50–2000 mg/mL) of *Nigella sativa* and its n-hexane and ethyl acetate

fractions [23]. There are many reports about the antitumor activity of Thymoquinone (the main lipid constituents of *N. sativa*) in both *in vitro* and *in vivo* studies [24]. The thymoquinone (10–200 mM) on the growth of colon cancer cells were shown by the inhibitory effects. The apoptotic effects of TQ on HCT-116 could be mediated by increaseing Bcl-2 protein and mRNA expression of p53 [25]. Apoptotic effect of TQ reduces the tumor angiogenesis and tumor growth through suppressing NF-κB, on human osteosarcoma cell line (SaOS-2) and blocking the human umbilical vein endothelial cell (HUVEC) tube formation were shown to be dependent on dose [26]. In addition, the cytotoxic effect of TQ (IC (50) ¼10.6770.12 and 9.3370.19 μg/mL) was more pronounced as compared with cisplatin, but it was less cytotoxic towards the normal cells (3T3-L1 and Vero) in human cervical squamous carcinoma cells [27].

Effects on metabolic disorders

Nigella sativa showed antidiabetic and antihyperlipidemic activities with the help of several animal and clinical studies and its effects on other metabolic disorders. The effect of reducing insulin resistance and increasing insulin sensitivity by improving the intracellular pathways of insulin receptors and increasing their sensitivity to insulin is a plant contribution by antioxidant property [28,29]. It has been reported that the effect of *Nigella sativa* on body weight showed a relationship between weight loss and improvement in the lipid profile and glucose status [30]. An agonist of PPAR-γ gene and increase the PPAR-γ activity are acted by nigella sativa [31]. Plant decreases the glucose absorption by inhibiting the sodium-glucose co-transporter was proposed. In addition, its polyphenol ingredients could have brutal effects on glucose concentration [32]. The inhibition of gluconeogenesis by the liver and muscle activation of adenosine monophosphate-activated protein kinase (AMPK) are also by *nigella sativa* [33]. It was revealed that TQ which is the main constituent of *Nigella sativa* reduces the expression of gluconeogenic enzymes and hepatic glucose production (Al-Rasheed., *et al*. 2014; Alimohammadi., *et al*. 2013). By up regulation of hepatic receptors of LDL-C, It also increases the uptake of low-density lipoprotein-cholesterol (LDL-C) [34]. Phytosterols such as polyunsaturated fatty acids, beta-sitosterol (cholesterollowering effect), TQ, polyphenol components (with antioxidant activity), thymol, nigellamine (lowering triglyceride levels in primary cultured mouse hepatocytes), lipase, and tannins were also responsible for *nigella sativa* [34,35].

Anti-diabetic effects

The disorders of carbohydrate and lipid metabolism was the therapeutic effect of *Nigella sativa* was indicated in previous studies. Nigella sativa shows the therapeutic effect on metabolic parameters in diabetes by several animal and clinical studies [35]. Hypoglycemic and hypolipidemic effects of *Nigella sativa* in patients suffering from diabetes and metabolic syndrome have been reported in many clinical studies [36]. In patients with type 2 diabetes resulted in reduction in fasting blood glucose (FBS), glycosylated hemoglobin (HbAlc), 2-h postprandial blood glucose (2hPG), and insulin resistance, but it did not cause any adverse effect on hepatic or renal functions of the diabetic patients by adjuvant therapy of *Nigella sativa* seed (Bamosa., *et al*. 2010). The chronic rise of blood glucose in diabetes may results in the production of reactive oxygen species (ROS) which improves cellular damage and contribute to the progression and development of diabetic complications. Plant supplementation initiated a significant increment in total antioxidant capacity (TAC), catalase (CAT), superoxide dismutase (SOD) and glutathione and a significant reduction in thiobarbituric acid-reactive substances (TBARS). In the results of renal and liver functions between the two groups there were no significant changes and the complete blood count remained normal. Hence, long-term *Nigella sativa* supplementation improved antioxidant balance and enhanced glucose homeostasis in patients with type 2 diabetes receiving oral hypoglycemic drugs [37]. The antihyperglycemic effect of plant oil adjuvant therapy in type 2 diabetes in an RCT was investigated. All the measured parameters were decreased compared with baseline and placebo groups in *Nigella sativa* treated patients and there were no side effect detected. Though, there was some restrictions, such as the high content of linoleic and oleic acid in the oil and its lipase activity, lack of identification of plant constituents were associated in the hypolipidemic effect of *Nigella sativa* [38].

Hepatoprotective effects

The metabolic activities of CYP3A4 and CYP2D6 in human liver microsomes was effected by *Nigella sativa* using dextromethorphan as a probe drug in a subject were estimated [39]. Nigellone, TQ, and nigellamine were proposed to have been responsible for these inhibitory effects by the plant constituents. In children, newly diagnosed with acute lymphoblastic leukemia (ALL) was investigated by the protective effect of *Nigella sativa* oil against methotrexate-induced hepatotoxicity. *Nigella sativa* oil (80mg/kg/day) reduces

total, direct and indirect serum bilirubin; serum ALT; AST, and alkaline phosphatase levels; and prothrombin time Methotrexate therapy in all children (Hagag., *et al*. 2013).

Gastrointestinal protective effects

The clarithromycin, amoxicillin, and omeprazole was the triple therapy against H. pylori in patients with non-ulcer dyspepsia, was evaluated by the effect of *Nigella sativa* seed. TQ, dihydrothymoquinone, and terpenes could be responsible for this effect of the plant by the antibacterial activity [10].

Effects on neurological disorders

Aging and memory impairment has been demonstrated in an animal study as it prevented pyramidal cell loss in hippocampus and enhanced association of the recall capability of stored information and spatial memory by the therapeutic effect of *Nigella sativa* [40]. Thus, the effects of the plant on memory, attention, and cognition in clinical studies have been designated [41]. In children suffering from intractable epileptic of antiepileptic drugs by the anti-seizure effect of the plant oil (40–80 mg/kg/day) [42]. Improvement in all neuropsychological tests in healthy elderly volunteers by *nigella sativa* seed (500 mg twice/day for 9 weeks).

Effects on cardiovascular disorders

Diabetes, lipid profile disturbance, metabolic syndrome, atherogenesis, endothelial dysfunction, cardiac mass and contractility abnormality, platelet aggregation, heart rate, blood pressure disorder, and cardiotoxicity was the therapeutic effect of *Nigella sativa* have been reported *in vitro* and *in vivo* animal studies. Antioxidant and anti-inflammatory properties could be used as a preventive and therapeutic agent in cardiovascular disorders potent by the multipotential plant of *Nigella sativa* [43]. No significant decrease in serum lipid levels, blood sugar, blood pressure, and body weight in adult patient by nigella sativa seed [44].

Effects on respiratory disorders

Clinical research has been studied by the preventive or prophylactic effect of *Nigella sativa*. In asthmatic patients, the prophylactic effect of the plant boiled extract was shown. The elements of the essential oil of *Nigella sativa* were evaluated by the HPLC method, but these results were not available in the published paper. All asthma symptoms, chest wheeze, and pulmonary function test (PFT) values in a 3-month treatment period improved was concluded. In addition, the need for inhaled and oral corticosteroid, oral β-agonists, oral theophylline, and even inhaled corticosteroid reduced in Nigella sativa-treated patients [45]. *Nigella sativa* powder and immunotherapy has No effect on the Th17 cell number and Improvement in clinical symptoms in children with mild asthma [46]. Pulmonary index PI decrement in asthmatic patients by *nigella sativa* oil [47].

Effect of infertility

Infertility was evaluated in a randomized, double-blind, placebo-controlled clinical trial was treated by traditional use of *Nigella sativa*. Peak Expiratory Flow Rate (PEFR) Improvement and Improves sperm count, motility, morphology and semen volume, pH, and round cells in infertile men by anti-infertility properties of nigella sativa oil(5mL/12h) for 2 months. The antioxidant activity of selenium, TQ, vitamin E, and unsaturated fatty acid contents of the *N. sativa* oil may be responsible for this effect of the plant [48,49].

Conclusion

The clinical and preclinical effects of *Nigella sativa* and its main constituent, thymoquinone, on various diseases were reviewed. The followings are the pharmacological and clinical effects of the plant and its constituents showed by reviewed papers.

On basic and clinical studies TQ, and nigellone are the anti-inflammatory effects of the plant. Immunoregulatory effects of *Nigella sativa* and its water-soluble (affecting B-cell immunity) fractions, and lipid (affecting T-cell immunity) with TQ and nigellone being involved in the clinical immunoregulatory effects of the plant. Ethanolic and aqueous extract and the fractions as well as its constituent, thymoquinone, in various cancer cell lines is an anti-tumor effect. The whole plant and its constituent, thymoquinone is an antimicrobial effects. Antidiabetic, antihyperlipidemic, metabolic syndrome, and hepatoprotective effects are due to metabolic disorders. Due to, thymoquinone, dihydrothymoquinone, and terpenes. H. pylori are the effect on gastrointestinal. Effect on aging and memory impairment in both animals and humans for the plant and antiepileptic effect for, thymoquinone are the effects of neurological disorders. Effect on hypertension, which was suggested to be due to thymoquinone, polyphenols, flavonoids, and unsaturated fatty acids of the plant are the effects of cardiovascular disorders. Bronchodilatory effect on asthmatic patients, preventive effect on asthma, and prophylactic effect on respiratory disorders of chemical war victims, all respiratory effects being exerted by its constituent, thymoquinone was the effects on respiratory disorders. Effect on infertility.

Bibliography

1. Polat R., *et al.* "Medicinal plants and their use properties of sold in herbal market in Bingoel(Turkey) district". *Biological Diversity and Conservation* 4.3 (2011): 25-35.

2. Tembhurne S V., *et al*. "A review on therapeutic potential of Nigella sativa (kalonji) seeds". *Journal of Medicinal Plants Research* 8.3 (2014): 167-177.

3. El-Tahir., *et al.* "The black seed Nigella sativa Linnaeus-A mine for multi cures: a plea for urgent clinical evaluation of its volatile oil". *Journal of Taibah University Medical Sciences* 1.1 (2006): 1-19.

4. Chevallier, A. "Encyclopedia of Herbal Medicine: 550 Herbs and Remedies for Common Ailments". Penguin (2016).

5. Durmuşkahya C and Öztürk M. "Ethnobotanical survey of medicinal plants used for the treatment of diabetes in Manisa, Turkey". *Sains Malaysiana* 42.10 (2013): 1431-1438.

6. Nasir A., *et al*. "Therapeutic Uses of Shoneez (Nigella sativa Linn.) Mentioned in Unani System of Medicine-A Review" *International Journal of Pharmaceutical and Phytopharmacological Research* 4 (2014): 47-49.

7. Xu L., *et al.* "Recent advances on supercritical fluid extraction of essential oils". *African Journal of Pharmacy and Pharmacology* 5.9 (2011): 1196-1211.

8. Mouwakeh A., *et al*. "Nigella sativa essential oil and its bioactive compounds as resistance modifiers against Staphylococcus aureus". *Phytotherapy Research* 33.4 (2019): 1010-1018.

9. Hussain D A and Hussain M M. "Nigella sativa (black seed) is an effective herbal remedy for every disease except death-a Prophetic statement which modern scientists confirm unanimously: a review". *Advancement in Medicinal Plant Research* 4.2 (2016): 27-57.

10. Salem M L. "Immunomodulatory and therapeutic properties of the Nigella sativa L. seed". *International immunopharmacology* 5.13-14 (2005): 1749-1770.

11. El-Dakhakhny M., *et al.* "Nigella sativa oil, nigellone and derived thymoquinone inhibit synthesis of 5-lipoxygenase products in polymorphonuclear leukocytes from rats". 81.2 (2002): 161-164.

12. Mansour M and Tornhamre S. "Inhibition of 5-lipoxygenase and leukotriene C4 synthase in human blood cells by thymoquinone". *Journal of enzyme inhibition and Medicinal Chemistry* 19.5 (2004): 431-436.

13. Dirjomuljono M., *et al.* "Symptomatic treatment of acute tonsillo-pharyngitis patients with a combination of Nigella sativa and Phyllanthus niruri extract". *International Journal of Clinical Pharmacology and Therapeutics* 46.6 (2008): 295-306.

14. El-Kadi., *et al*. "Nigella sativa cell-mediated immunity". *Archives of AIDS Research* 1 (1987): 232-233.

15. Haq A., *et al.* "Immunomodulatory effect of Nigella sativa proteins fractionated by ion exchange chromatography". *International Journal of Immunopharmacology* 21.4 (1999): 283-295.

16. Kalus U., *et al.* "Effect of Nigella sativa (black seed) on subjective feeling in patients with allergic diseases". *Phytotherapy Research: An International Journal Devoted to Pharmacological and Toxicological Evaluation of Natural Product Derivatives* 17.10 (2003): 1209-1214.

17. Salman M T., *et al.* "Antimicrobial activity of Nigella sativa Linn. seed oil against multi-drug resistant bacteria from clinical isolates (2008).

18. Abdel-Moneim., *et al*. "Beneficial therapeutic effects of Nigella sativa and/or Zingiber officinale in HCV patients in Egypt". *EXCLI journal* 12 (2013): 943-955.

19. Barakat E M F., *et al.* "Effects of Nigella sativa on outcome of hepatitis C in Egypt". *World journal of Gastroenterology: WJG* 19.16 (2013): 2529.

20. Al-Sheddi E S., *et al.* "Cytotoxicity of Nigella sativa seed oil and extract against human lung cancer cell line". *Asian Pacific Journal of Cancer Prevention* 15.2 (2014): 983-987.

21. Mat M C., *et al*. "Primary human monocyte differentiation regulated by Nigella sativa pressed oil". *Lipids in health and disease* 10.1 (2011): 216.

22. Mahmoud S S and Torchilin V P. "Hormetic/cytotoxic effects of Nigella sativa seed alcoholic and aqueous extracts on MCF-7 breast cancer cells alone or in combination with doxorubicin". *Cell Biochemistry and Biophysics* 66.3 (2013): 451-460.

23. Shahraki S., *et al.* "Effect of total hydroalcholic extract of Nigella sativa and its n-hexane and ethyl acetate fractions on ACHN and GP-293 cell lines". *Journal of Traditional and Complementary Medicine* 6.1 (2016): 89-96.

24. Woo CC., *et al.* "Thymoquinone: potential cure for inflammatory disorders and cancer". *Biochemical pharmacology* 83.4 (2012): 443-451.

25. Gali-Muhtasib H., *et al.* "The medicinal potential of black seed (Nigella sativa) and its components". *Advances in Phytomedicine* 2 (2006): 133-153.

26. Peng L., *et al.* "Antitumor and anti-angiogenesis effects of thymoquinone on osteosarcoma through the NF-κB pathway". *Oncology reports* 29.2 (2013): 571-578.

27. Ng W K., *et al.* "Thymoquinone from Nigella sativa was more potent than cisplatin in eliminating of SiHa cells via apoptosis with down-regulation of Bcl-2 protein". *Toxicology in vitro* 25.7 (2011): 1392-1398.

28. Le P. M., *et al.* "The petroleum ether extract of Nigella sativa exerts lipid-lowering and insulin-sensitizing actions in the rat". *Journal of ethnopharmacology* 94.2-3 (2004): 251-259.

29. Rchid H., *et al.* "Nigella sativa seed extracts enhance glucose-induced insulin release from rat-isolated Langerhans islets". *Fundamental & Clinical Pharmacology* 18.5 (2004): 525-529.

30. Najmi A., *et al.* "Indigenous herbal product Nigella sativa proved effective as an antihypertensive in metabolic syndrome". *Asian Journal of Pharmaceutical and Clinical Research* 6.1 (2013): 61-64.

31. Benhaddou-Andaloussi A., *et al*. "Multiple molecular targets underlie the antidiabetic effect of Nigella sativa seed extract in skeletal muscle, adipocyte and liver cells". *Diabetes, Obesity and Metabolism* 12.2 (2010): 148-157.

32. Meddah B., *et al.* "Nigella sativa inhibits intestinal glucose absorption and improves glucose tolerance in rats". *Journal of ethnopharmacology* 121.3 (2009): 419-424.

33. Benhaddou-Andaloussi A., *et al.* "The in vivo antidiabetic activity of Nigella sativa is mediated through activation of the AMPK pathway and increased muscle Glut4 content". Evidence-Based Complementary and Alternative Medicine (2011).

34. Ibrahim R M., *et al.* "Protective effects of Nigella sativa on metabolic syndrome in menopausal women". *Advanced pharmaceutical bulletin* 4.1 (2014): 29.

35. Heshmati J., *et al*. "Nigella sativa oil affects glucose metabolism and lipid concentrations in patients with type 2 diabetes: A randomized, double-blind, placebo-controlled trial". *Food Research International* 70 (2015): 87-93.

36. Sabzghabaee A M., *et al.* "Clinical evaluation of Nigella sativa seeds for the treatment of hyperlipidemia: a randomized, placebo controlled clinical trial". *Medical Archives* 66.3 (2012): 198-200.

37. Kaatabi H., *et al.* "Nigella sativa improves glycemic control and ameliorates oxidative stress in patients with type 2 diabetes mellitus: placebo controlled participant blinded clinical trial". *PloS one* 10.2 (2015): e0113486.

38. Hosseini M S., *et al.* "Effects of Nigella sativa L. seed oil in type II diabetic Patients: a randomized, double-blind, placebo-controlled clinical trial". 3.47 (2013): 93-99.

39. Al-Jenoobi F., *et al*. "Effect of black seed on dextromethorphan O-and N-demethylation in human liver microsomes and healthy human subjects". *Drug metabolism letters* 4.1 (2010): 51-55.

40. Azzubaidi M S., *et al.* "Mnemonic effects of fixed oil of black cumin (Nigella sativa) seeds on aged rats with memory impairment". In Malaysia-Australia Research Colloquium on Exercise. Nutrition, Health and Wellness (2011).

41. Sayeed M S B., *et al.* "Nigella sativa L. seeds modulate mood, anxiety and cognition in healthy adolescent males". *Journal of Ethnopharmacology* 152.1 (2014): 156-162.

42. Shawki M., *et al.* "The clinical outcome of adjuvant therapy with black seed oil on intractable paediatric seizures: a pilot study". *Epileptic disorders* 15.3 (2013): 295-301.

43. Shabana A., *et al.* "Cardiovascular benefits of black cumin (Nigella sativa)". *Cardiovascular toxicology* 13.1 (2013): 9-21.

44. Qidwai W., *et al.* "Effectiveness, safety, and tolerability of powdered Nigella sativa (kalonji) seed in capsules on serum lipid levels, blood sugar, blood pressure, and body weight in adults: results of a randomized, double-blind controlled trial". *The Journal of alternative and complementary medicine* 15.6 (2009): 639-644.

45. Boskabady M H., *et al*. "The possible prophylactic effect of Nigella sativa seed extract in asthmatic patients". *Fundamental & Clinical Pharmacology* 21.5 (2007): 559-566.

46. Kardani A K., *et al.* "The effect of house dust mite immunotherapy, probiotic and Nigella sativa in the number of Th17 cell and asthma control test score". *IOSR Journal of Dental and Medical Sciences* 6 (2013): 37-47.

47. Ahmad J., *et al.* "A study of Nigella sativa oil in the management of wheeze associated lower respiratory tract illness in children". *African Journal of Pharmacy and Pharmacology* 4.7 (2010): 436-439.

48. Dwivedi S N. "Herbal remedies among the tribals of Sidhi District of Madhya Pradesh". *Journal of Economic and Taxonomic Botany* 28.3 (2004): 675-687.

49. Kolahdooz, M., *et al.* "Effects of Nigella sativa L. seed oil on abnormal semen quality in infertile men: a randomized, double-blind, placebo-controlled clinical trial". *Phytomedicine* 21.6 (2014): 901-905.

Volume 3 Issue 8 August 2019