Black Cumin SAP

Potent anti-inflammatory and antioxidant nutraceutical

Black cumin (*Nigella sativa*) is an herb native to the Middle Eastern and South-Asian regions of the world, and has long been used in traditional healing systems for a variety of treatments. Ayurvedic medicine as well as Unani practices demonstrate the uses of black cumin seed against diseases and conditions related to inflammation, obesity, and hypercholesterolemia. When following a supplemental dose of *N. sativa* daily, patient trials have resulted in lowered levels of total cholesterol and LDL-C, as well as higher levels of HDL-C, providing measurable verification of the herb's therapeutic qualities. Today, many practitioners are finding black cumin to be a potent herb in adjunctive cancer treatment. Recent studies and clinical experimentation have demonstrated the positive effects of black cumin in the prevention of cancer via free-radical scavenging and promotion of apoptosis. In addition, Black cumin has been found to improve thyroid status and ameliorate disease severity in patients with Hashimoto's thyroiditis. These seeds contain a number of substances attributed to their healing potential, including thymoquinone, saponins, alkaloids, and high levels of beneficial fatty acids including linoleic acid and oleic acid.

ACTIVE INGREDIENTS

Each softgel contains:

Organic black cumin (*Nigella sativa*) seed oil . . . . . 500 mg
50% linoleic acid — 20% oleic acid

Other ingredients: Vitamin E (mixed tocopherols from non-GMO sunflower) in a softgel made of bovine gelatin, glycerin, and purified water.

This product is non-GMO.

Contains no: Gluten, soy, wheat, eggs, dairy, yeast, citrus, preservatives, artificial flavor or color, starch, or sugar.

Black Cumin SAP is available in bottles of 60 capsules.

DIRECTIONS OF USE

Adults: Take 2 softgels twice daily before a meal or as directed by your healthcare practitioner. Take a few hours before or after taking supplements containing iron, zinc, calcium or copper. Consult a healthcare practitioner for use beyond 4 weeks. Use for a minimum of 2 weeks.

INDICATIONS

Black Cumin SAP may support:

- Healthy cholesterol levels, mitigate or manage signs and symptoms of metabolic syndrome,[4, 14, 15, 16, 17] and improve hepatic function.[4, 5]
- Reducing the size of some tumours
- The prevention of cancer.[6, 9, 12]
- Improving thyroid status and ameliorating disease severity in patients with Hashimoto's thyroiditis.[18]
- Treatment of seasonal allergies and skin conditions such as eczema.[26,27]

SAFETY, CAUTIONS, AND WARNINGS

Consult a healthcare practitioner prior to use if you have a known immune disorder. Discontinue use if you experience gastrointestinal upset.

Contraindications: Do not take if you are pregnant, breast-feeding, or trying to conceive.

Known adverse reactions: May cause gastrointestinal upset when taken on an empty stomach.

PURITY, CLEANLINESS, AND STABILITY

All ingredients listed for all **Black Cumin SAP** lot numbers have been tested by a third-party laboratory for identity, potency, and purity.

Scientific Advisory Panel (SAP): adding nutraceutical research to achieve optimum health

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BLACK CUMIN (*Nigella sativa*) SEED

Black cumin seed (*Nigella sativa*) is an herb native to the Middle-Eastern and South-Asian regions of the world, and has long been used in traditional healing systems for a variety of treatments. Asian and Ayurvedic medicine as well as Unani practices historically demonstrated the uses of black cumin seed for the promotion of good health, and against diseases and conditions related to inflammation, obesity, and hypercholesterolemia. The most well-studied active ingredient in *N. sativa* is thymoquinone, a component found in the fixed and essential oils of the seed, which has been investigated most rigorously for its antioxidant, free-radical scavenging, anti-inflammatory, and anticancer activities in both in vitro and in vivo studies.[1, 2, 3]

METABOLIC SYNDROME AND CARDIOVASCULAR BENEFITS

Black cumin seed supplementation (2 g *N. sativa* per day for 4 weeks) was seen to be associated with significant decreases in total cholesterol (4.78%), LDL (7.6%), and triglycerides (16.65%) in a randomized, placebo-controlled trial (n = 88).[4]

There were no significant changes in fasting blood sugar levels or HDL in this study; however, in another study, black cumin was shown to modulate fasting, postprandial blood glucose levels, and HbA_{1c}.[15] A study showed statistically significant reduction in systolic and diastolic blood pressure compared to placebo, while also showing reduction in total cholesterol and LDL.[14]

In another study, 1.5 g/d black cumin seed over three months demonstrated an ability to aid in weight management, reducing body weight, waist circumferences, as well as systolic blood pressure measures.[16] Another study showed similar impact of crushed black cumin seed as compared to placebo, reporting a "favorable impact on almost all variables" of metabolic syndrome, including, but not limited to, body mass index, waist-hip ratio, blood pressure, fasting blood sugar, and serum lipids.[17]

Black cumin has shown an antidiabetic effect via modulation of insulin sensitivity in animal models, where diabetic rodents treated in randomized trials benefited from progressive normalization of glycemia comparable to the effects of metformin, including decreased OGTT. These studies suggest insulin-sensitizing action by enhancement of GLUT4 expression, activation of the AMPK pathway, and ACC phosphorylation.[6, 7]

ANTIBACTERIAL, ANTIFUNGAL, AND ANTIPARASITIC

Crude alkaloid extracts and water extracts have shown the most promising results for black cumin seed as antimicrobial, though alcohol extracts have also shown efficacy. In vitro studies show effect for black cumin seed extract against isolates of methicillin-resistant *Staphylococcus aureus, Helicobacter pylori,* and other bacteria, most prominently against Gram-positive cocci, as well as anti-yeast activity against *Candida albicans* and antischistosomiasis effectiveness.[8] Another in vitro study showed *N. sativa* oil and its bioactive components inhibited strains of *S. aureus* via increased ethidium bromide accumulation (indicating antimicrobial efflux) and membrane integrity disruption. Reductions of *S. aureus* levels in biofilm by 28% to 40% were observed, indicating potential efficacy of *N. sativa* oil against methicillin susceptible and methicillin resistant *S. aureus* (MRSA) strains.[19] Activity against antibiotic resistant pathogens has been tested against human salivary bacteria, where *N. sativa* oil killed more than 60% of pathogens.[20] Other studies have further established the antiviral and antibacterial activity of thymoquinone, the principal active ingredient of *N. sativa* seeds, with both studies showing an anti-biofilm effect.[21, 22] A dose of *N. sativa* (450mg 3 times a day) for 3 months to hepatitis C patients significantly reduced hepatitis C viral load and oxidative stress, and improved glycemic control (n=30).[23] Furthermore, doses of 1g and 3g of *N. sativa* seeds for 4 weeks, given in addition to an antibiotic reduced *H. pylori* load significantly more than an antibiotic treatment alone, in 88 *H. pylori* patients with non-ulcerative dyspepsia.[24] Future clinical trials will help support the anti-microbial and anti-biofilm activity of *N. sativa*.

ANTI-INFLAMMATORY, ANTIOXIDANT, AND ANTICANCER

The various actions of thymoquinone, including antioxidant, free radical–scavenging, and superoxide-mitigating effects, are supported by noted preservation of activity of various antioxidant enzymes, including catalase, glutathione peroxidase, and glutathione-S-transferase. This supplement seems to exhibit anti-inflammatory and anticancer effects via antiproliferation, apoptosis induction via p53 pathways, cell-cycle arrest, and antimetastatic or antiangiogenesis mechanisms. These include the modulation of TNF-α, NF-κB, PTEN, and STAT3 regulation, and the mitigation of T_h1 cytokines including IL-4, IL-5, and IL-13, while inhibiting 5-lipoxygenase enzyme activity.[6, 9]

In human breast-cancer studies, *N. sativa* extracts have been shown to be effective in vitro for influencing the survival of MCF-7 breast-cancer cells.[10] *N. sativa* oil or thymoquinone administration has been shown to lower cyclophosphamide toxicity via antioxidant mechanisms and suggests a potential adjunctive role in current conventional cancer therapies. Thymoquinone has also been shown benefit in pancreatic ductal adenocarcinoma cells via reduction of MCP-1 activity.[11] Other cancers that have received attention regarding treatment with thymoquinone or extracts of *Nigella sativa* include blood, colon, hepatic, lung, skin, renal, prostate, fibrosarcoma, and cervical cancers.[12] In a randomized trial conducted with 80 children suffering from febrile neutropenia (FN), administration of 5g per day of *N. sativa* seeds for 3-9 months decreased the incidence of FN in children suffering from brain tumors, and shortened their hospital stay.[25]

HASHIMOTO'S THYROIDITIS BENEFITS

A common cause of hypothyroidism is Hashimoto's thyroiditis, an autoimmune disorder. A clinical study investigated the effects of *N. sativa* on thyroid function, serum vascular endothelial growth factor (VEGF) – 1, Nesfatin-1 and anthropometric features in 40 patients with Hashimoto's thyroiditis. In this placebo controlled randomized study, participants either received powdered *N. sativa* or a placebo daily for 8 weeks. *N. sativa* powder significantly reduced body weight and body mass index (BMI). In addition, serum concentrations of thyroid stimulating hormone (TSH) and anti-thyroid peroxidase (anti-TPO) antibodies, serum VEGF concentrations were observed to be decreased compared to the placebo. In addition, significant reductions in body weight and BMI were observed. Although more studies are required to validate these findings, *N. sativa* can be regarded as a useful therapeutic approach in the management of Hashimoto's thyroiditis.

SEASONAL ALLERGIES AND SKIN CONDITIONS

Traditional medicine has used *N. sativa* for the treatment of certain skin conditions. Clinical trials have studied this therapeutic effect. In a trial conducted with 60 patients, application of *N. sativa* twice a day for 4 weeks produced the same effect as a steroidal medication in alleviation of hand eczema.[26] Administration of *N. sativa* oil in a dose of 40-80mg/kg/day to 152 participants decreased the perceived symptoms in patients, with slight reduction in plasma triglycerides and increase in HDL cholesterol, indicating potential benefits of N. *sativa* as a supportive treatment for allergic diseases such as allergic rhinitis, bronchial asthma and atopic eczema.[27]

SAFETY CONSIDERATIONS

Acute toxicity of *N. sativa* fixed oil from seeds has been investigated in mice. LD_{50} values were 28.8 ml per kg of body weight. This high LD_{50} value suggests a wide margin of safety for therapeutic dosages although hemoglobin and hematocrit levels were observed to have increased over 12 months of exposure.[6, 13]

REFERENCES

1. Randhawa, M.A. and M.S. Alghamdi. "Anticancer activity of *Nigella sativa* (black seed) — a review." *The American Journal of Chinese Medicine* Vol. 39, No. 6 (2011): 1075–1091.
2. Shabana, A., et al. "Cardiovascular benefits of black cumin (*Nigella sativa*)." *Cardiovascular Toxicology* Vol. 13, No. 1 (2013): 9–21.
3. Ali, B.H. and G. Blunden. "Pharmacological and toxicological properties of *Nigella sativa*." *Phytotherapy Research* Vol. 17, No. 4 (2003): 299–305.
4. Sabzghabaee, A.M., et al. "Clinical evaluation of *Nigella sativa* seeds for the treatment of hyperlipidemia: a randomized, placebo controlled clinical trial." *Medicinski Arhiv* Vol. 66, No. 3 (2012): 198–200.
5. Qidwai, W. "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." *Journal of Alternative and Complementary Medicine* Vol. 15, No. 6 (2009): 639–644.
6. Vanamala, J., et al. "Mitigation of obesity-promoted diseases by *Nigella sativa* and thymoquinone." *Plant Foods for Human Nutrition* Vol. 67, No. 2 (2012): 111–119.
7. 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* Vol. 2011 (2011): 538671.
8. Ahmad, A., et al. "A review on therapeutic potential of *Nigella sativa*: A miracle herb." *Asian Pacific Journal of Tropical Biomedicine* Vol. 3, No. 5 (2013): 337–352.
9. Woo, C.C., et al. "Thymoquinone: potential cure for inflammatory disorders and cancer." *Biochemical Pharmacology* Vol. 83, No. 4 (2012): 443–451.
10. Farah, I.O. "Assessment of cellular responses to oxidative stress using MCF-7 breast cancer cells, black seed (*N. sativa* L.) extracts and H_2O_2." *International Journal of Environmental Research and Public Health* Vol. 2, No. 3–4 (2005): 411–419.
11. Motaghed, M., F.M. Al-Hassan, and S.S. Hamid. "Cellular responses with thymoquinone treatment in human breast cancer cell line MCF-7." *Pharmacognosy Research* Vol. 5, No. 3 (2013): 200–206.
12. Khan, M.A., et al. "Anticancer activities of *Nigella sativa* (black cumin)." *African Journal of Traditional, Complementary, and Alternative Medicines* Vol. 8, No. 5 Suppl. (2011): 226–232.
13. Zaoui, A. "Acute and chronic toxicity of *Nigella sativa* fixed oil." *Phytomedicine* Vol. 9, No. 1 (2002): 69–74.
14. Dehkordi, F.R. and A.F. Kamkhah. "Antihypertensive effect of *Nigella sativa* seed extract in patients with mild hypertension." *Fundamental & Clinical Pharmacology* Vol. 22, No. 4 (2008): 447–452.
15. Bamosa, A.O., et al. "Effect of *Nigella sativa* seeds on the glycemic control of patients with type 2 diabetes mellitus." *Indian Journal of Physiology and Pharmacology* Vol. 54, No. 4 (2010): 344–354.
16. Datau, E.A., et al. "Efficacy of *Nigella sativa* on serum free testosterone and metabolic disturbances in central obese male." *Acta Medica Indonesiana* Vol. 42, No. 3 (2010): 130–134.
17. 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." *Journal of Alternative and Complementary Medicine* Vol. 15, No. 6 (2009): 639–644.
18. Farhangi, M.A., et al. The effects of *Nigella sativa* on thyroid function, serum Vascular Endothelial Growth Factor (VEGF) – 1, Nesfatin-1 and anthropometric features in patients with Hashimoto's thyroiditis: a randomized controlled trial. BMC Complementary and Alternative Medicine, 2016; 16:471.
19. Mouwakeh A., et al. Nigella sativa essential oil and its bioactive compounds as resistance modifiers against Staphylococcus aureus. Phytother Res, 2019, 33(4):1010-1018.
20. Vlachojannis C., et. al. Activity of preparations from Spilanthes oleracea, propolis, Nigella sativa, and black garlic on different microorganisms involved in oral disease and on total human salivary bacteria: a pilot study. Phytother Res, 2018, 32(10):1992-2001.
21. Shi C., et. al. Thymoquinone inhibits virulence related traits of Cronobacter sakazakii ATCC 29544 and has anti-biofilm formation potential. Front Microbiol, 2017, 8:2220.
22. Chaieb K., et. al. Antibacterial activity of Thymoquinone, an active principle of Nigella sativa and its potency to prevent bacterial film formation. BMC Complement Altern Med, 2011, 11:29.
23. Barakat E.M., et. al. Effects of Nigella sativa on outcome of hepatitis C in Egypt. World J Gastroenterol, 2013, 19(16):2529-36.
24. Salem E.M., et. al. Comparative study of Nigella sativa and triple therapy in eradication of Helicobacter pylori in patients with non-ulcer dyspepsia. Saudi J Gastroenterol, 2010, 16(3):207-14.
25. Mousa H.F.M., et. al. Effect of Nigella sativa seed administration on prevention of febrile neutropenia during chemotherapy among children with brain tumors. Childs Nerve Syst, 2017, 33(5):793-800.
26. Yousefi M., et. al. Comparison of therapeutic effect of topical Nigella with Betamethasone and Eucerin in hand eczema. J Eur Acad Dermatol Venereol, 2013, 27(12):1498-504.
27. Kalus U., et. al. Effect of Nigella sativa (black seed) on subjective feeling in patients with allergic diseases. Phytother Res, 2003, 17(10):1209-14.

For healthcare professional use only.

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INDICATION-SPECIFIC DOSAGE SUMMARY BASED ON HUMAN CLINICAL RESEARCH#

#Please note these suggestions are guidelines based on the clinical studies. Evidence for efficacy and safety has been qualitatively (study quality in terms of study design, sample size, appropriate methods of analysis, use of appropriate placebo/control, bias etc.) assessed and has been rated using a 5-star ★ rating classification.

Indication	Suggested Black Cumin SAP dosage	Supporting evidence and study outcomes	Study design	Outcomes measures	Safety	Evidence quality rating
RHEUMATOID ARTHRITIS						
Rheumatoid arthritis [1],[2]	2 softgels/day	Significant increase in serum IL-10 levels; significant reduction of malondialdehyde (MDA).	Randomized, double-blind, placebo-controlled study (*n* =42, 8 weeks). 1,000 mg/d of *Nigella sativa* oil.	Serum levels of TNF-α and IL-10, serum total antioxidant capacity, superoxide dismutase, catalase activity, and serum MDA concentration.	No severe adverse effects reported.	★★★
	2 softgels/day	Significant decrease in disease activity score (DAS-28). Effective relief from morning stiffness and improved ACR20 and EULAR response criteria.	Placebo-controlled study (*n* = 40, 1 month). 1,000 mg/d of *Nigella sativa* oil.	Clinical and laboratory parameters of disease activity rheumatoid arthritis, DAS28, CR20 and EULAR response criteria.	No severe adverse effects reported.	★★
CARDIOVASCULAR AND METABOLIC HEALTH						
Cardiovascular health [3],[4],[5],[6],[7]	4 softgels/day	Significant improvement in total cholesterol, mean arterial pressure, and heart rate in type 2 diabetes–affected individuals.	Nonrandomized, single-blind study (*n* = 57, 1 year). 2,000 mg/d of *Nigella sativa* oil.	Lipid parameters; triglycerides (TG), total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), heart rate, systolic and diastolic blood pressure.	No severe adverse effects reported.	★★
	2 softgels/day	Significant improvement in fasting blood-sugar levels (p = 0.03), TC (p = 0.04), BMI, and waist circumference; SBP and DBP.	Randomized, double-blind, placebo-controlled study (*n* = 43, 8 weeks). 1,000 mg/d of *Nigella sativa* oil extract.	Fasting blood sugar (FBS), TC, TG, LDL-C, HDL-C, serum glucose levels, glycosylated hemoglobin (HbA_{1C}).	No severe adverse effects reported.	★★
	6 softgels/day	Significant improvement in TG levels, very-low density lipoprotein (VLDL) levels, weight, and waist circumference.	Randomized, double-blind, placebo-controlled study (*n* = 90, 8 weeks). 3,000 mg/d of *Nigella sativa* oil.	BMI, waist circumference, waist-hip ratio, blood pressure, TC, TG, LDL-C, HDL-C, VLDL.	No severe adverse effects reported.	★★★
	2 to 6 softgels/day	Significant reduction in total cholesterol and LDL after the consumption of *Nigella sativa* powder.	17 randomized, controlled studies (*n* = 1,185, 4 weeks to 3 months). 1,000 mg/d to 2,000 mg/d of *Nigella sativa* powder or 1,000 mg/d to 3,000 mg/d of *Nigella sativa* oil.	BMI, SBP, DBP, TC, TG, LDL-C, HDL-C.	No severe adverse effects reported.	★★★
	10 softgels/day	Significant reduction in SBP; significant fall in DBP, TC, LDL, FBS, HDL, and MDA levels.	Randomized, double-blind, placebo-controlled study (*n* = 55, 8 weeks). 5 ml/d of *Nigella sativa* oil, 6.6 mg/ml of thymoquinone from *Nigella sativa* oil	SBP, DBP, FBS, LDL-C, HDL-C, MDA, Na, K, and creatinine; blood urea nitrogen (BUN), aspartate transaminase (AST), and alanine transaminase (ALT).	No severe adverse effects reported.	★★★

Diabetes [8]	2 to 3 softgels/day	Significant improvement in weight loss, waist circumference, and BMI in *Nigella sativa* oil group when compared to the metformin group.	Randomized, open-label, prospective study (*n* = 44, 3 months). 1,350 mg/d of *Nigella sativa* oil.	Weight, height, BMI, waist circumference, AST, ALT, creatinine, TC, LDL, HDL, TG, and total antioxidant capacity (TAC).	No severe adverse effects reported when compared to metformin.	★★
Obesity [9],[10]	6 softgels/day	Significant reduction of body weight and red blood cell superoxide dismutase levels in the obese population.	Randomized, double-blind, placebo-controlled study (*n* = 50, 8 weeks). 3,000 mg/d of *Nigella sativa* oil.	Dietary intake, anthropometric indices, physical activity levels, serum TAC, MDA, superoxidase dismutase (SOD), and glutathione peroxidase (GPx).	No severe adverse effects reported.	★★★
	6 softgels/day	Significant decreases in tumour necrosis factor (TNF-α) levels in serum were observed when *Nigella sativa* oil was combined with a low-calorie diet.	Randomized, double-blind, placebo-controlled study (*n* = 84, 8 weeks). 3,000 mg/d of *Nigella sativa* oil.	Anthropometric indices, physical activity, dietary intake, BMI, IL-6, TNF-α, and hs-CRP.	No severe adverse effects reported.	★★★
Anthropometric indices [11]	4 softgels/day	Significant decline in weight-related parameters: weight, BMI, waist circumference, hip circumference, SBP, and DBP.	Randomized, double-blind, placebo-controlled study (*n* = 60, 8 weeks). 2,000 mg/d of *Nigella sativa* oil.	Serum TG, HDL-C, TC, and FBS levels, body weight, height, BMI, WC, HC, WHR, SBP, and DBP.	No severe adverse effects reported. One reported stomach pain and one nausea.	★★★
Hypertension [12],[13]	1 to 6 softgels/day	Significant drop in SBP and DBP levels in *Nigella sativa* powder was higher than in *Nigella sativa* oil group when compared to baseline values of individual.	11 randomized, controlled studies (*n* = 860, 8 to 12 weeks); 500 mg/d to 1,600 mg/d of *Nigella sativa* powder or 200 mg/d to 3,000 mg/d of *Nigella sativa* oil or 5 ml/d of *Nigella sativa* oil.	SBP and DBP.	No severe adverse effects reported. Two studies reported mild nausea.	★★★★
	1 to 2 softgels/day	Significant drop in SBP and DBP levels when compared to baseline after *Nigella sativa* oil treatment.	Randomized, double-blind, placebo-controlled study (*n* = 70, 8 weeks). 5 ml/d of *Nigella sativa* oil.	SBP; DBP; BMI; and blood levels of AST, ALT, ALP, BUN, and creatinine.	No severe adverse effects reported. Ten individuals reported mild nausea.	★★★
Fatty liver [14]	10 softgels/day	Significant reduction in the grade of hepatic steatosis, levels of ALT and AST, and triglycerides and HDL-C.	Randomized, double-blind, placebo-controlled parallel-group study (*n* = 120, 3 months); 5 ml/d of *Nigella sativa* oil (thymoquinone = 0.987 ± 0.07 mg/ml of *Nigella sativa* oil).	BMI, hepatic steatosis ultrasound grade, TG, LDL-C, HDL-C, ALT, AST, blood urea, nitrogen, creatinine, and complete blood cell count.	No severe adverse effects reported.	★★★★
RESPIRATORY HEALTH						
COPD [15]	4 softgels/day	Significant improvement in pulmonary function after receiving *Nigella sativa* oil. Significant decrease in protein carbonyl content posttreatment, significant changes in TNF-α, IL-6, catalase, SOD, GPx, GSH, and plasma inflammatory markers.	Randomized, double-blind, controlled, prospective study (*n* = 100, 3 months). 2,000 mg/d of *Nigella sativa* oil.	Lung function tests; TNF-α; IL-6; catalase (CAT); GPx; SOD; and reduced glutathione (GSH), and vitamins E and C levels.	No severe adverse effects reported.	★★★

Asthma[16]	2 softgels/day	Significant improvement in Asthma Control Test score; blood eosinophil levels; and forced expiratory volume in 1 second.	Randomized, double-blind, placebo-controlled study (*n* = 80, 4 weeks); 1,000 mg/d of *Nigella sativa* oil.	Asthma Control Test score, pulmonary function test, blood eosinophils, total serum, and immunoglobulin E.	No severe adverse effects reported.	★★★
HASHIMOTO'S THYROIDITIS						
Hashimoto's thyroiditis[17]	4 softgels/day	Significant decrease in serum levels of thyroid-stimulating hormone (TSH) and antithyroid peroxidase (anti-TPO) antibodies; increase in serum T3 concentrations; and reduction of anthropometric indices.	Randomized, double-blind, placebo-controlled study (*n* = 47, 8 weeks). 2,000 mg/d of *Nigella sativa* powder.	Thyroid function, serum vascular endothelial growth factor (VEGF)–1, nesfatin-1, and anthropometric features.	No severe adverse effects reported. Three individuals reported itching and nausea.	★★★
RENAL HEALTH						
Diabetic nephropathy[18]	5 softgels/day	Significant improvement in hemoglobin levels, blood urea, serum creatinine, fasting glucose, postprandial glucose, glomerular filtration rate, and urinary protein levels.	Prospective, comparative, open-label study (*n* = 68, 12 weeks). 2.5 ml/d of *Nigella sativa* oil.	Blood glucose, hemogram, serum electrolytes, and kidney function test.	No severe adverse effects reported. Nausea, diarrhea, rashes, and altered taste were reported.	★★

REFERENCES

1. Hadi, V., S. Kheirouri, M. Alizadeh, A. Khabbazi, and H. Hosseini. "Effects of *Nigella sativa* oil extract on inflammatory cytokine response and oxidative stress status in patients with rheumatoid arthritis: A randomized, double-blind, placebo-controlled clinical trial". *Avicenna Journal of Phytomedicine,* Vol. 6, No. 1 (2016): 34–43.
2. Gheita, T.A., and S.A. Kenawy. "Effectiveness of *Nigella sativa* oil in the management of rheumatoid arthritis patients: A placebo-controlled study." *Phytotherapy Research,* Vol. 26, No. 8 (2012): 1246–1248.
3. Badar, A., H. Kaatabi, A. Bamosa, A. Al-Elq, B. Abou-Hozaifa, F. Lebda, A. Alkhadra, and S. Al-Almaie. "Effect of *Nigella sativa* supplementation over a one-year period on lipid levels, blood pressure and heart rate in type-2 diabetic patients receiving oral hypoglycemic agents: Nonrandomized clinical trial." *Annals of Saudi Medicine,* Vol. 37, No. 1 (2017): 56–63.
4. Hadi, S., R. Daryabeygi-Khotbehsara, P. Mirmiran, J. McVicar, V. Hadi, D. Soleimani, and G. Askari. "Effect of *Nigella sativa* oil extract on cardiometabolic risk factors in type 2 diabetes: A randomized, double-blind, placebo-controlled clinical trial." *Phytotherapy Research,* Vol. 35, No. 7 (2021): 3747–3755.
5. Mahdavi, R., N. Namazi, M. Alizadeh, and S. Farajnia. "Effects of *Nigella sativa* oil with a low-calorie diet on cardiometabolic risk factors in obese women: A randomized controlled clinical trial." *Food & Function,* Vol. 6, No. 6 (2015): 2041–2048.
6. Sahebkar, A., G. Beccuti, L.E. Simental-Mendía, V. Nobili, and S. Bo. "*Nigella sativa* (black seed) effects on plasma lipid concentrations in humans: A systematic review and meta-analysis of randomized placebo-controlled trials." *Pharmacological Research,* Vol. 106 (2016): 37–50.
7. Shoaei-Hagh, P., F.K. Kafi, S. Najafi, M. Zamanzadeh, A.H. Bakavoli, J. Ramezani, S. Soltanian, et al. "A randomized, double-blind, placebo-controlled, clinical trial to evaluate the benefits of Nigella sativa seeds oil in reducing cardiovascular risks in hypertensive patients." *Phytotherapy Research,* Vol. 35, No. 8 (2021): 4388–4400.
8. Moustafa, H.A.M., L.M. El Wakeel, M.R. Halawa, N.A. Sabri, A.Z. El-Bahy, and A.N. Singab. "Effect of *Nigella sativa* oil versus metformin on glycemic control and biochemical parameters of newly diagnosed type 2 diabetes mellitus patients." *Endocrine,* Vol. 65, No. 2 (2019): 286–294.
9. Namazi, N., R. Mahdavi, M. Alizadeh, and S. Farajnia. "Oxidative stress responses to *Nigella sativa* oil concurrent with a low-calorie diet in obese women: A randomized, double-blind controlled clinical trial." *Phytotherapy Research,* Vol. 29, No. 11 (2015): 1722–1728.
10. Mahdavi, R., N. Namazi, M. Alizadeh, and S. Farajnia. "*Nigella sativa* oil with a calorie-restricted diet can improve biomarkers of systemic inflammation in obese women: A randomized double-blind, placebo-controlled clinical trial." *Journal of Clinical Lipidology,* Vol. 10, No. 5 (2016): 1203–1211.
11. Tavakoli-Rouzbehani, O.M., M. Abbasnezhad, S. Kheirouri, and M. Alizadeh. "Effects of *Nigella sativa* oil supplementation on selected metabolic parameters and anthropometric indices in patients with coronary artery disease: A randomized, double-blind, placebo-controlled clinical trial." *Phytotherapy Research,* Vol. 35, No. 7 (2021): 3988–3999.
12. Sahebkar, A., D. Soranna, X. Liu, C. Thomopoulos, L.E. Simental-Mendia, G. Derosa, P. Maffioli, and G. Parati. "A systematic review and meta-analysis of randomized controlled trials investigating the effects of supplementation with *Nigella sativa* (black seed) on blood pressure." *Journal of Hypertension,* Vol. 34, No. 11 (2016): 2127–2135.
13. Fallah Huseini, H., M. Amini, R. Mohtashami, M.E. Ghamarchehre, Z. Sadeqhi, S. Kianbakht, and A. Fallah Huseini. "Blood pressure lowering effect of *Nigella sativa* L. seed oil in healthy volunteers: A randomized, double-blind, placebo-controlled clinical trial." *Phytotherapy Research,* Vol. 27, No. 12 (2013): 1849–1853.
14. Khonche, A., H. Fallah Huseini, M. Gholamian, R. Mohtashami, F. Nabati, and S. Kianbakht. "Standardized *Nigella sativa* seed oil ameliorates hepatic steatosis, aminotransferase and lipid levels in non-alcoholic fatty liver disease: A randomized, double-blind and placebo-controlled clinical trial." *Journal of Ethnopharmacology,* Vol. 234 (2019): 106–111.
15. Al-Azzawi, M.A., M.M.N. AboZaid, R.A.L. Ibrahem, and M.A. Sakr. "Therapeutic effects of black seed oil supplementation on chronic obstructive pulmonary disease patients: A randomized controlled double blind clinical trial." *Heliyon,* Vol. 6, No. 8 (2020): e04711.
16. Koshak, A., L. Wei, E. Koshak, S. Wali, O. Alamoudi, A. Demerdash, M. Qutub, P.N. Pushparaj, and M. Heinrich. "*Nigella sativa* supplementation improves asthma control and biomarkers: A randomized, double-blind, placebo-controlled trial." *Phytotherapy Research,* Vol. 31, No. 3 (2017): 403–409.
17. Farhangi, M.A., P. Dehghan, S. Tajmiri, and M.M. Abbasi. "The effects of *Nigella sativa* on thyroid function, serum Vascular Endothelial Growth Factor (VEGF) - 1, Nesfatin-1 and anthropometric features in patients with Hashimoto's thyroiditis: A randomized controlled trial." *BMC Complementary and Alternative Medicine,* Vol. 16, No. 1 (2016): 471.
18. Ansari, Z.M., M. Nasiruddin, R.A. Khan, and S.F. Haque. "Protective role of *Nigella sativa* in diabetic nephropathy: A randomized clinical trial." *Saudi Journal of Kidney Diseases and Transplantation,* Vol. 28, No. 1 (2017): 9–14.