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Black Cumin Seed

Updated: April 27, 2023.

OVERVIEW

Introduction

Black cumin also known as black seed and *Nigella sativa* is a flowering plant native to Eastern Europe and the Middle East that produces black seeds which are used to produce spice and flavoring of food and have been used in traditional medicine as therapy for a wide variety of conditions. Black cumin is well tolerated, is generally recognized as safe and has not been associated with serum enzyme elevations during therapy nor implicated in cases of clinically apparent liver injury.

Background

Black Cumin (*Nigella sativa*) is a flowering annual plant native to Eastern Europe and the Middle East that is now cultivated in many areas of world and produces a black seed, extracts of which are used as a spice and for flavoring foods. In addition to its culinary uses, black cumin seeds and their extracts have also been used extensively in traditional medicine for multiple conditions including constipation, dyspepsia, ulcer disease, fever, cough, bronchitis, headaches, hypertension, gout, arthritis, heart disease, toothache, back pain, skin disease, and wounds. Claims have been made that black cumin seed extracts and oils have antioxidant, antiinflammatory, antineoplastic, antihypertensive, antidiabetic, cholesterol lowering, immunomodulatory, cardioprotective, neuroprotective, nephroprotective, and even hepatoprotective properties. Indeed, a famous comment is: "the black cumin is healing for all diseases except death." These purported effects, while shown in vitro in cell culture and in vivo in animal experiments have not been consistently demonstrated in clinical trials in humans. Black cumin seeds have multiple phytoconstituents including a high concentration of elemental oils such as linoleic acid, oleic acid, palmitic acid and several volatile oils such as thymoquinone, the suspected major bioactive component. In small, placebo controlled clinical trials in patients with hyperlipidemia, black cumin extracts and thymoquinone were associated with a slight decrease in LDL cholesterol and triglyceride levels and increase in HDL cholesterol levels. In trials in patients with type 2 diabetes, black cumin extracts and oils have been found to have a modest salutary effect on hemoglobin A1c and postprandial blood glucose levels. Similarly, in trials in patients with systemic arterial hypertension, black cumin extracts had a modest favorable effect on systolic and diastolic blood pressure. The overall evidence for clinical benefit of these effects, however, is not very convincing. Neither black cumin seed extracts nor concentrated thymoquinone oils have been approved as therapy for hyperlipidemia, diabetes, hypertension or any other medical disease or condition by the FDA. Black cumin extracts remain available over-the-counter as a dietary supplement in multiple forms including liquid, powders and capsules purported to be helpful for digestive health and to boost energy. The typical recommended dose is 300 to 1000 mg taken one to two times daily. Extracts and oils from black cumin seeds have consistently been found to be well tolerated and safe and the FDA lists black cumin spice as "generally recognized as safe" (GRAS).

Side effects can include abdominal discomfort, bloating, dysgeusia, diarrhea, and headache, but these effects are generally transient and mild. Rare, potentially severe adverse events include rash and hypersensitivity reactions.

Hepatotoxicity

In multiple, largely short term clinical studies of different preparations and concentrations of black cumin seed powdered extracts and oils, adverse side effects were usually described as uncommon and mild with either no change or slight improvement in serum aminotransferase and alkaline phosphatase levels. Furthermore, black cumin products have been used to treat liver diseases including nonalcoholic fatty liver and chronic hepatitis C without evidence of disease worsening during therapy. Despite widespread use, there have been no published reports of serum enzyme elevations or clinically apparent liver injury attributable to products containing black cumin seed.

Likelihood score: E (unlikely cause of clinically apparent liver injury).

Mechanism of Injury

The mechanism by which black cumin seed extracts might cause liver injury is unknown.

Outcome and Management

Hepatotoxicity from extracts of black cumin seeds has not been reported.

Drug Class: Herbal and Dietary Supplements

Other names: Black seed, Black caraway, Small fennel, Fennel flower, Roman Coriander, Nigella, *Nigella sativa*.

PRODUCT INFORMATION

REPRESENTATIVE TRADE NAMES

Black Cumin – Generic

DRUG CLASS

Herbal and Dietary Supplements

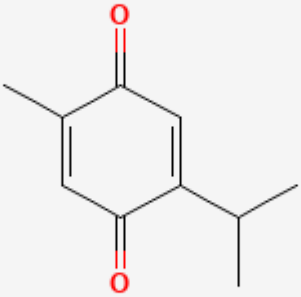
SUMMARY INFORMATION

Fact Sheet at MedlinePlus, NLM

CHEMICAL FORMULA AND STRUCTURE

DRUG	CAS REGISTRY NUMBER	MOLECULAR FORMULA	STRUCTURE
Black Cumin	90064-32-7	Herbal	Not Applicable

Table continued from previous page.

DRUG	CAS REGISTRY NUMBER	MOLECULAR FORMULA	STRUCTURE
Thymoquinone	490-91-5	Volatile Oil	

ANNOTATED BIBLIOGRAPHY

References updated: 27 April 2023

Abbreviations: HDS, herbal and dietary supplements.

Zimmerman HJ. Unconventional drugs. Miscellaneous drugs and diagnostic chemicals. In, Zimmerman, HJ. Hepatotoxicity: the adverse effects of drugs and other chemicals on the liver. 2nd ed. Philadelphia: Lippincott,1999: pp. 731-4.

(Expert review of hepatotoxicity published in 1999; several herbal medications are discussed, but not black cumin seed oils or extracts).

Liu LU, Schiano TD. Hepatotoxicity of herbal medicines, vitamins and natural hepatotoxins. In, Kaplowitz N, DeLeve LD, eds. Drug-induced liver disease. 2nd ed. New York: Informa Healthcare USA, 2007, pp. 733-54.

(Review of hepatotoxicity of herbal and dietary supplements [HDS] published in 2007; no mention of black cumin).

Qidwai W, Hamza HB, Qureshi R, Gilani A. 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. J Altern Complement Med. 2009;15:639–44. PubMed PMID: 19500003.

(Among 123 Pakistani adults with hypercholesterolemia treated with black cumin powdered extract [1 gm] or placebo twice daily for 6 weeks, only 73 completed the trial in whom there were minimal changes in LDL cholesterol or triglycerides levels and no changes in serum ALT; no mention of adverse events).

Jacobsson I, Jönsson AK, Gerdén B, Hägg S. Spontaneously reported adverse reactions in association with complementary and alternative medicine substances in Sweden. Pharmacoepidemiol Drug Saf. 2009;18:1039–47. PubMed PMID: 19650152.

(Review of 778 spontaneous reports of adverse reactions to herbals in a Swedish Registry does not list black cumin among products associated with 5 or more reports).

Reuben A, Koch DG, Lee WM; Acute Liver Failure Study Group. Drug-induced acute liver failure: results of a U.S. multicenter, prospective study. Hepatology. 2010;52:2065–76. PubMed PMID: 20949552.

(Among 1198 patients with acute liver failure enrolled in a US prospective study between 1998 and 2007, 133 [11%] were attributed to drug induced liver injury of which 12 [9%] were due to herbals, including several herbal mixtures, usnic acid, Ma Huang, black cohosh, and Hydroxycut, but not black cumin).

Teschke R, Wolff A, Frenzel C, Schulze J, Eickhoff A. Herbal hepatotoxicity: a tabular compilation of reported cases. Liver Int. 2012;32:1543–56. PubMed PMID: 22928722.

(A systematic compilation of all publications on the hepatotoxicity of specific herbals identified 185 publications on 60 different herbs, herbal drugs and supplements, but does not mention or list black cumin extracts or oils).

Barakat EM, El Wakeel LM, Hagag RS. Effects of *Nigella sativa* on outcome of hepatitis C in Egypt. World J Gastroenterol. 2013;19:2529–36. PubMed PMID: 23674855.

(Among 30 Egyptian adults with chronic hepatitis C treated with black cumin [450 mg] or placebo oil thrice daily for 3 months, fasting blood glucose levels improved [104 to 92 mg/dL], but ALT levels did not [35 to 41 U/L], and HCV RNA levels decreased slightly [5.6 to 5.2 log_{10} copies/mL], while adverse events included gastritis [n=1] and hypoglycemia [n=5] but no acute liver injury or hepatic decompensation).

Bunchorntavakul C, Reddy KR. Review article: herbal and dietary supplement hepatotoxicity. Aliment Pharmacol Ther. 2013;37:3–17. PubMed PMID: 23121117.

(Systematic review of literature on HDS associated liver injury does not mention black cumin).

Navarro VJ, Seeff LB. Liver injury induced by herbal complementary and alternative medicine. Clin Liver Dis. 2013;17:715–35. PubMed PMID: 24099027.

(Review of the epidemiology, regulatory status, diagnosis, pathogenesis and causes of liver injury from herbal products with specific discussion of conjugated linoleic acid, ephedra, germander, green tea, usnic acid, flavocoxid, aloe vera, chaparral, greater celandine, black cohosh, comfrey, kava, skullcap, valerian, noni juice, pennyroyal and traditional herbal remedies).

Navarro VJ, Barnhart H, Bonkovsky HL, Davern T, Fontana RJ, Grant L, Reddy KR, et al. Liver injury from herbals and dietary supplements in the U.S. Drug-Induced Liver Injury Network. Hepatology. 2014;60:1399–408. PubMed PMID: 25043597.

(Among 839 cases of liver injury from drugs collected in the US between 2004 and 2013, 130 were due to HDS products, including 45 from body building agents [probably anabolic steroids] and 85 from diverse HDS products but no case was attributed specifically to black cumin extract).

Mohtashami R, Huseini HF, Heydari M, Amini M, Sadeqhi Z, Ghaznavi H, Mehrzadi S. Efficacy and safety of honey based formulation of *Nigella sativa* seed oil in functional dyspepsia: A double blind randomized controlled clinical trial. J Ethnopharmacol. 2015;175:147–52. PubMed PMID: 26386381.

(Among 70 Iranian adults with functional dyspepsia treated with black cumin oil vs placebo for 8 weeks, index of dyspepsia scores improved more with black cumin that placebo [-12 vs -3] as did quality of life scores, and mild adverse events occurred in similar proportion of the two groups; no mention of ALT levels or hepatotoxicity).

Sahebkar A, Beccuti G, Simental-Mendía LE, Nobili V, Bo S. Nigella sativa (black seed) effects on plasma lipid concentrations in humans: A systematic review and meta-analysis of randomized placebo-controlled trials. Pharmacol Res. 2016;106:37–50. PubMed PMID: 26875640.

(Systematic review identified 17 randomized controlled trials of black cumin formulations for effect of serum lipid levels, the combined results demonstrating differences with placebo in decreases in total cholesterol of -15.6 mg/dL, LDL cholesterol of -14.1 mg/dL and triglycerides of -20.6 mg/dL with little effect on HDL cholesterol levels, the overall effects being more convincing with black cumin oil than with powdered extracts).

Sahebkar A, Soranna D, Liu X, Thomopoulos C, Simental-Mendia LE, Derosa G, Maffioli P, et al. A systematic review and meta-analysis of randomized controlled trials investigating the effects of supplementation with Nigella sativa (black seed) on blood pressure. J Hypertens. 2016;34:2127–35. PubMed PMID: 27512971.

(Systematic review identified 11 randomized controlled trials [in 860 adults] of black cumin for its effects on blood pressure, found differences of -3.3 mmHg in systolic and -2.8 mmHg in diastolic blood pressure between black cumin and placebo or standard therapy after an average of 8 weeks).

Brown AC. Liver toxicity related to herbs and dietary supplements: Online table of case reports. Part 2 of 5 series. Food Chem Toxicol. 2017;107:472–501. PubMed PMID: 27402097.

(Description of an online compendium of cases of liver toxicity attributed to HDS products does not list or discuss black cumin).

Medina-Caliz I, Garcia-Cortes M, Gonzalez-Jimenez A, Cabello MR, Robles-Diaz M, Sanabria-Cabrera J, Sanjuan-Jimenez R, et al; Spanish DILI Registry. Herbal and dietary supplement-induced liver injuries in the Spanish DILI Registry. Clin Gastroenterol Hepatol. 2018;16:1495–1502. PubMed PMID: 29307848.

(Among 856 cases of hepatotoxicity enrolled in the Spanish DILI Registry between 1994 and 2016, 32 were attributed to herbal products, the most frequent cause being green tea [n=8] and Herbalife products [n=6], no mention of black cumin).

Khonche A, Huseini HF, Gholamian M, Mohtashami R, Nabati F, Kianbakht S. 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. J Ethnopharmacol. 2019;234:106–111. PubMed PMID: 30639231.

(Among 120 Iranian adults with nonalcoholic fatty liver disease treated with black cumin or a placebo oil twice daily for 3 months, the decrease in ultrasound hepatic steatosis scores was greater in the black cumin than placebo groups as were changes in serum ALT [-29 vs -12 U/L], cholesterol [-14 vs -9 mg/dL] and triglyceride levels [-10 vs -0.2 mg/dL], while patients "did not report any adverse drug effect").

Darand M, Darabi Z, Yari Z, Saadati S, Hedayati M, Khoncheh A, Hosseini-Ahangar B, et al. *Nigella sativa* and inflammatory biomarkers in patients with non-alcoholic fatty liver disease: results from a randomized, double-blind, placebo-controlled, clinical trial. Complement Ther Med. 2019;44:204–209. PubMed PMID: 31126557.

(Among 50 adults with nonalcoholic fatty liver disease treated with black cumin powdered extract [2 gm daily] vs placebo for 12 weeks, changes in serum aminotransferases were similar in the two groups while the change in hepatic steatosis was greater with black cumin, but the differences were not statistically significant).

Azizi N, Amini MR, Djafarian K, Shab-Bidar S. The effects of *Nigella sativa* supplementation on liver enzymes levels: a systematic review and meta-analysis of randomized controlled trials. Clin Nutr Res. 2021;10:72–82. PubMed PMID: 33564654.

(Systematic review of randomized controlled trials of black cumin vs placebo identified 8 published studies [n=560 patients] that included serum aminotransferase levels, found a found difference in the weighted mean change in ALT levels of -7 U/L and AST of -8.1 U/L with black cumin vs placebo).

Hossain MS, Sharfaraz A, Dutta A, Ahsan A, Masud MA, Ahmed IA, Goh BH, et al. A review of ethnobotany, phytochemistry, antimicrobial pharmacology and toxicology of Nigella sativa L. Biomed Pharmacother. 2021;143:112182. PubMed PMID: 34649338.

(Review of the phytochemistry and antimicrobial activities of black cumin seeds; thymoquinone, the major volatile oil of cumin seeds, showed no evidence of hepatotoxicity in several animal species even when given in high doses).

Hannan MA, Rahman MA, Sohag AAM, Uddin MJ, Dash R, Sikder MH, Rahman MS, et al. Black Cumin (*Nigella sativa* L.): a comprehensive review on phytochemistry, health benefits, molecular pharmacology, and safety. Nutrients. 2021;13:1784. PubMed PMID: 34073784.

(An extensive review of the phytochemistry of black cumin and its use in traditional medicine for a wide array of diseases and conditions, toxicity studies have shown that thymoquinone toxicity occurs only with very high doses [above 500 mg/kg] when given orally).

Shoaei-Hagh P, Kamelan Kafi F, Najafi S, Zamanzadeh M, Heidari Bakavoli A, Ramezani J, Soltanian S, 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. Phytother Res. 2021;35:4388–4400. PubMed PMID: 33957004.

(Among 60 Iranian adults with hypertension treated with black cumin oil vs sunflower oil twice daily for 8 weeks, systolic and diastolic blood pressure decreased more with black cumin [-8 and -6.5 vs -3 and -1 mm/Hg], as did fasting blood glucose [-6.5 vs +4.0 mg/dL] and LDL cholesterol levels [-14 vs -4 mg/dL], and while 20% of patients on black cumin oil had mild gastrointestinal side effects, there were no changes in serum ALT, AST or alkaline phosphatase levels).

Ballotin VR, Bigarella LG, Brandão ABM, Balbinot RA, Balbinot SS, Soldera J. Herb-induced liver injury: Systematic review and meta-analysis. World J Clin Cases. 2021;9:5490–5513. PubMed PMID: 34307603.

(Systematic review of the literature on herb induced liver injury identified 446 references describing 936 cases due to 79 different herbal products, the most common being He Shou Wu [91], green tea [90] Herbalife products [64], kava kava [62] and greater celandine [48]; black cumin was not listed among the 79 implicated products).

Bessone F, García-Cortés M, Medina-Caliz I, Hernandez N, Parana R, Mendizabal M, Schinoni MI, et al. Herbal and dietary supplements-induced liver injury in Latin America: experience from the LATINDILI Network. Clin Gastroenterol Hepatol. 2022;20:e548–e563. PubMed PMID: 33434654.

(Among 367 cases of hepatotoxicity enrolled in the Latin American DILI Network between 2011 and 2019, 29 [8%] were attributed to herbal products, the most frequent being green tea [n=7], Herbalife products [n=5] and garcinia [n=3], while black cumin is not mentioned).

Thomas JV, Mohan ME, Prabhakaran P, Das S S, Maliakel B. I M K. A phase I clinical trial to evaluate the safety of thymoquinone-rich black cumin oil (BlaQmax®) on healthy subjects: Randomized, double-blinded, placebo-controlled prospective study. Toxicol Rep. 2022;9:999–1007. PubMed PMID: 36518481.

(Among 70 healthy adults treated with a black cumin oil product [200 mg, 5% thymoquinone] or placebo daily for 9 days, LDL cholesterol and triglycerides decreased with therapy, and there were no serious adverse events and only mild gastrointestinal upset with cumin oil [bloating, diarrhea, and dysgeusia], and serum ALT, AST and Alk P levels did not change).

Adam SH, Mohd Nasri N, Kashim MIAM, Abd Latib EH, Ahmad Juhari MAA, Mokhtar MH. Potential health benefits of *Nigella sativa* on diabetes mellitus and its complications: a review from laboratory studies to clinical trials. Front Nutr. 2022;9:1057825. PubMed PMID: 36438767.

(Review of the potential efficacy of black cumin in type 2 diabetes which rests upon data from in vitro and in vivo studies and in small, short term human trials assessing the effects of various oral black cumin preparations on fasting blood glucose and hemoglobin A1c levels; most studies reporting no adverse events, no effects on serum enzyme levels, and no instances of liver injury).

Assaad-Khalil S, Elkafrawy N, Khaled M, Mogeib O, Badr H, Rashwan A, Youssef M, et al. A phase II, randomized, double-blind, double-dummy, active-controlled clinical trial to investigate the efficacy and safety of NW Low-Glu® in patients newly diagnosed with type 2 diabetes mellitus. Evid Based Complement Alternat Med. 2022;2022:9176026. PubMed PMID: 36204125.

(Among 232 adults with newly diagnosed type 2 diabetes treated with 2 or 4 tablets of a combination herbal product [Ficus deltoidei, Cinnamomum cassia and Nigella sativa 250 mg] vs metformin [1000 mg] daily for 90 days, decreases in mean hemoglobin A1c and 2 hour postprandial glucose levels decreased to a similar extend in all 3 arms, while adverse events were more frequent with the herbal product, but there were no severe adverse events or liver related side effects).

Huseini HF, Mohtashami R, Sadeghzadeh E, Shadmanfar S, Hashem-Dabaghian F, Kianbakht S. Efficacy and safety of oral Nigella sativa oil for symptomatic treatment of knee osteoarthritis: A double-blind, randomized, placebo-controlled clinical trial. Complement Ther Clin Pract. 2022 Nov;49:101666. doi: 10.1016/j.ctcp.2022.101666. doiEpub 2022 Sep 17. PubMed PMID: 36150238.

(Among 116 Iranian adults with knee osteoarthritis treated with black cumin seed oil [2.5 mg of thymoquinone] or placebo every 8 hours for 30 days, knee pain, stiffness and function improved with the black seed oil and there were no changes in serum levels of ALT, AST or Alk P, and "no side effect was observed" in either group).

Mohtashamian A, Ebrahimzadeh A, Shamekhi Z, Sharifi N. *Nigella sativa* supplementation and non-alcoholic fatty liver disease: a systematic review of clinical trials. Avicenna J Phytomed. 2023;13:18–33. PubMed PMID: 36698733.

(Systematic review identified four randomized controlled trials of cumin oil vs placebo in a total of 324 patients [3 from Iran, 1 Pakistan] with nonalcoholic steatohepatitis, 3 of which demonstrated a reduction in hepatic steatosis and 3 a decrease in ALT and AST levels; no mention of adverse events).