doi:10.30495/MEDHERB.2021.681959

Journal of Medicinal Herbs

journal homepage:**www.jhd.iaushk.ac.ir**

A review on hepatoprotective effects of *Nigella sativa* L.

Mehrdad Ostadpoor[1], Majid Gholami-Ahangaran[2*]

[1] *Graduated of Veterinary Medicine , Shahrekord Branch, Islamic Azad University, Shahrekord, Iran*

[2]*Associate Professor, Department of Clinical Sciences, Faculty of Veterinary Medicine, Shahrekord Branch, Islamic Azad University, Shahrekord, Iran;*

Email:** ***mgholami6@gmail.com

ARTICLE INFO

Type: *Review Article*
Topic: *Medicinal Plants*
Received *December 21th2020*
Accepted *April 16th2021*

Key words:
- ✓ *Black seeds*
- ✓ *Hepatoprotective*
- ✓ *Nigella sativa*
- ✓ *Thymoquinone*
- ✓ *Toxicity*

ABSTRACT

Background & Aim: *Nigella sativa* L. (Black seeds) which is a member of the *Ranunculaceae* family, grows in Southwestern Asia, Europe, and Northern Africa. The use of *N. Sativa* seeds and oil in traditional remedies goes back more than 2000 years, and the herb is described as 'the Melanthion' by hippocrates and dioscorides.

Experimental: In the current literature review, key words including *N. Sativa*, thymoquinone, black seeds, toxicity, protection of hepatocellular were searched in scientific websites such as Science Direct, PubMed, Google Scholar etc. to compile the protective effects of *N. Sativa* against hepatocellular damage.

Results: Many active components of *N. Sativa* have been identified, including thymoquinone, dithymoquinone, thymohydroquinone, nigellone, melanthin, nigilline, nigelamine, damascenone, *p*-cymene and pinene. *N. Sativa* is a medicinal plant with antifungal, anti-viral, anti-bacterial, anti-parasite, anti-oxidant, analgesic, antipyretic, anti-tussive, and anti-inflammatory properties. Thymoquinone could prevent many disorders such as neurobehavioral kidney and liver disorders. *N. Sativa* was also found to be able to relieve the symptoms of patients with several diseases, such as hypertension, dyslipidemia, metabolic syndrome, diabetes and natural and chemical toxicities.

Recommended applications/industries: According to literature, *N. Sativa* treatment will decrease the elevated lipid peroxidation, liver enzyme levels and increase antioxidant enzyme levels. *N. Sativa* administration can also protect hepatic tissue from deleterious effects of toxic metals.

1. Introduction

Nigella sativa L. (Black seeds) is a member of the family *Ranunculaceae* grows in western Asia like Iran and Turkey, Europe, and Northern Africa. *N. sativa* is a 20-30 cm long flowering plant. Sensitive flowers have 5-10 leaves and the colors are usually yellow, white, pink, pale blue or pale purple (Ezergan *et al*., 2020). The use of *N. Sativa* seeds and oil in traditional remedies dates back more than 2000 years ago, and the herb is described as 'the Melanthion' by hippocrates and discroides (Darakhshan *et al*., 2015). Black seeds and their oil have a long history of folklore usage in the Indian and the Arabian civilizations as food and medicine and have been commonly used as treatment for a variety of health conditions pertaining to the respiratory system, digestive tract, kidney and liver functions, cardiovascular system, and immune system support, as well as for general well-being (Ahmad *et al*., 2013; Mollazadeh and Hosseinzadeh, 2014).

Many active components of *N. Sativa* have been identified, including thymoquinone, dithymoquinone,

thymohydroquinone, nigellone, melanthin, nigilline, nigelamine, damascenone, *p*-cymene and pinene. *N. Sativa* contain minerals such as magnesium, calcium, phosphorus, potassium, iron, cobalt, zinc and manganese and vitamins A, B, C, D and E. *N. Sativa* are rich in both fixed and essential oils, proteins, alkaloids, saponins, polyphenols and flavonoids (Cherif *et al*., 2018; Tabassum et al., 2018). Thymoquinone (TQ) is the most abundant constituent in the volatile oil of NS seeds, and most properties of the herb are related to the TQ. Cell culture studies and animal models have indicated several therapeutic potentials such as anti-cancer activities (Khan *et al*., 2011; Banerjee *et al*., 2010; AbuKhader, 2013). *N. Sativa* is a medicinal plant with anti-fungal (Aljabre *et al*., 2015; Nadaf *et al*., 2015; Forouzanfar *et al*., 2014), anti-viral (Aljabre *et al*., 2015; Forouzanfar *et al*., 2014), anti-bacterial (Aljabre *et al*., 2015; Forouzanfar *et al*., 2014; Manju *et al*., 2016; Hariharan *et al*., 2016), anti-parasite (Aljabre *et al*., 2015; Forouzanfar *et al*., 2014; Simalango and Utami, 2014), anti-oxidant (Karna, 2013; Amin and Hosseinzadeh, 2016; Hosseinzadeh *et al*., 2012; Hosseinzadeh *et al*., 2007; Hosseinzadeh *et al*., 2007), analgesic (Amin and Hosseinzadeh, 2016; Amin *et al*., 2014), antipyretic (Ali and Blunden, 2003), anti-tussive (Hosseinzadeh *et al*., 2008) and anti-inflammatory properties (Ahmad *et al*., 2013; Gholamnezhad *et al*., 2015). TQ utilization could prevent many disorders such as neurobehavioral (Javidi *et al*., 2016), kidney (Havakhah *et al*., 2014; Hosseinzadeh and Montahaei, 2007), and liver disorders (Mollazadeh and Hosseinzadeh, 2014). *N. Sativa* was also found to be able to relieve the symptoms of patients with several diseases, such as hypertension, dyslipidemia, metabolic syndrome, diabetes (Cherif *et al*., 2018; Shabana *et al*., 2013; Razavi and Hosseinzadeh, 2014) and natural and chemical toxicities (Pourbakhsh *et al*., 2014; Mehri *et al*., 2014).

2. Materials and Methods

In the current literature review, key words including *N. sativa*, thymoquinone, black seeds, toxicity, protection hepatocellular were searched in scientific websites such as Science Direct, PubMed and Google Scholar to compile the literature related the effects of *N. Sativa* on protection against hepatocellular toxicity.

3. Results and discussion

Liver is a vital organ and play an important role in detoxification of variety of drugs and xenobiotics. A study was performed based on rat model to evaluate the hepato protective effects of *N. Sativa* alcoholic extract against D-Galactosamine (D-galn)/Lipo polysaccharide (LPS) induced hepatotoxicity and it was found that D-galn/LPS caused significant rise in serum aspartate aminotransferase (AST), alanine transaminase (ALT) and alkaline phosphatase (ALP) while *N. Sativa* alcoholic extract maintained the levels of AST, ALT and ALP close to normal (Gani and John, 2013). Another study based on carbon tetrachloride (CCL4) induced rats has shown that CCL4 treatment increased the lipid peroxidation and liver enzymes, and decreased the antioxidant enzyme levels. Furthermore, *N. Sativa* treatment decreased the lipid peroxidation, and liver enzyme levels. Also, it increased the antioxidant enzyme levels (Kanter *et al*., 2005).

An important study was performed to show the protective role of *N. Sativa* and bees' honey on hepatotoxicity induced by sodium nitrite and sunset yellow in rat and found that NANO2 and sunset yellow caused various biochemical abnormalities while administration of black seed and bees' honey caused fully recovery of most of biochemical abnormalities (EL-Kholy *et al*., 2009).

El-Gharieb *et al.* (2010) have investigated the hepatoprotective effect of Ns in isoniazid (INH)-induced hepatotoxicity and it was concluded that *N. Sativa* has hepatoprotective effects against INH-induced hepatotoxicity in rabbits. Furthermore, no histopathological or biological abnormalities were observed (Hassan *et al*., 2012). Another important study has shown that human and animal exposure to malathion (organ phosphorus insecticide) leads to a significant increase in biochemical parameters such AST, ALT, and lipid peroxidation and decrease in albumin, albumin/globulin ratio, and total protein. Also, *N. Sativa* oil or vitamin E administration caused improvement of liver function, lipid peroxidation, and antioxidant enzymes alteration induced by malathion (El-Gharieb *et al*., 2010).

Hepatoprotective studies showed that Thymoquinone (TQ), chief constituents of *N. Sativa* (12.5 mg/kg, i.p.) has a vital role as antioxidant and may efficiently act as a protective agent against chemically-induced hepatic damage (Mansour *et al*., 2001). The relation between

thymoquinone and hepatic diseases illustrated in figure 1. In vitro studies using isolated rat hepatocytes have shown that preincubation of hepatocytes with TQ or silybin had protective effect on isolated hepatocytes against tert-Butyl hydroperoxide (TBHP) induced toxicity evidenced by decreased leakage of ALT and AST (Daba and Abdel-Rahman, 1998). Another study finding showed that TQ and desferrioxamine are efficient cytoprotective agents against CCL4-induced hepotoxicity, possibly via inhibition of the production of oxygen free radicals that cause lipid peroxidation (Mansour, 2000).

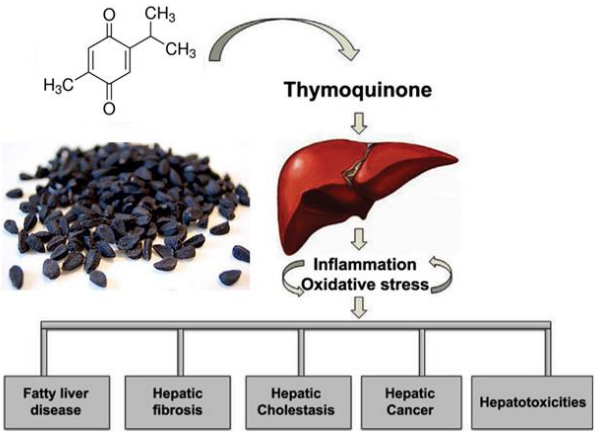

Figure 1. The relation between thymoquinone and hepatic diseases (Noorbakhsh *et al.*, 2018)

Hagag *et al.* (2015), reported that Ns oil (80 mg/kg per day) administration for one week after each methotrexate treatment could reduce hepatotoxicity and improve the survival rate in all children. It is reported that Ns (0.2 mL/kg) intraperitoneally relieves the deleterious effects of ischemia reperfusion injury on liver. Biochemical parameters like the serum aspartate aminotransferase, alanine aminotransferase lactate dehydrogenase levels and total antioxidant capacity (TAC), CAT, total oxidative status (TOS), oxidative stress index (OSI) and Myeloperoxidase (MPO) were determined in hepatic tissue in rats with hepatic ischemia. Results of studies suggested that Ns treatment protects the rat liver against hepatic ischemia reperfusion injury (Yildiz *et al.*, 2008).

It was reported that Ns administration protects hepatic tissue from deleterious effects of toxic metals such as lead, and attenuates hepatic lipid peroxidation following exposure to chemicals such as carbon tetrachloride (Kapoor, 2009). Cadmium (Cd++) causes alteration of the cellular homeostasis and oxidative damage. The protective role of TQ on the hepatotoxicity of Cd++ with special reference to its protection against perturbation of nonenzymatic and enzymatic antioxidants was investigated. The effect of TQ pretreatment was examined in post-nuclear supernatant prepared from liver of Swiss albino mice under in vitro conditions. CdCL2 treatment (5 mmol/L) resulted in a significant increase in antioxidant enzymatic activities. It also caused a significant ($p<0.001$) increase in protein carbonyls and reduce in glutathione content. Pretreatment with TQ (10 µmol/L) showed a significant protection as manifested by noticed attenuation of protein oxidation and rejuvenation of the depleted antioxidants of cellular fraction. These results support the hypothesis that TQ exerts modulatory influence on the antioxidant defense system subjected to toxic insult (Zafeer *et al.*, 2012). TQ showed a protective effect against AFB1-induced hepatotoxicity in mice by decrease of liver hurt indicators including AST, ALT, and ALP and also via inhibiting degradation and necrosis of liver tissue (Karimi *et al.*, 2019). It was reported that simultaneous administration of TQ and ethanol reduced the severity of lipid peroxidation (Malondialdehyde levels) and increased antioxidant capacity (reduced GSH content) in the liver and kidney tissues in rats. In addition, the protective effect of TQ against ethanol-induced hepatotoxicity has been confirmed by the significant reduction of liver enzymes (AST, ALT and ALP) activity, along with considerable decrease in inflammatory cytokine (IL-6 and TNF-α) in liver tissue (Hosseini *et al.*, 2017). In one study, TQ was used for anti-cadmium toxicity through its antioxidant properities (Karimi *et al.*, 2019).

In a similar study, Abdel-Daim *et al.* (2015) reported that Oxytetracycline (OTC) leads in considerable modifications in serum biochemical renal-hepato hurt markers, and significantly inhibited the tissue antioxidant biomarkers and renal-hepatolipid peroxidation in treated animal. However, combination of *N. Sativa* oil with OTC protects animal against OTC induced serum and tissue biochemical revisions.

Abdel-Wahab *et al.* (2014) reported that administration of TQ greatly normalized suppressed enzymatic and non-enzymatic antioxidants. It also decreased the hepatic biomarkers and lipid peroxidation.

4. Conclusion

Some of the natural herbs and their bioactive components have been used in several studies with the purpose of toxicity prevention in different tissues induced by different chemical and natural toxins especially toxins in food due to daily intake. The accessibility and cost benefit properties and less toxic effects of natural plant constituents compared with synthetic products make them an ideal candidate for inhibition of food and chemical toxicity. This review summarized several *in vivo* and *in vitro* studies in order to realize the role of *N. Sativa* and its bioactive component, TQ, in inhibition of food toxins related hepatocyte toxicities.

5. References

A Hagag, A., M AbdElaal, A., S Elfaragy, M., M Hassan, S. and A Elzamarany, E. 2015. Therapeutic value of black seed oil in methotrexate hepatotoxicity in Egyptian children with acute lymphoblastic leukemia. *Infectious Disorders-Drug Targets (Formerly Current Drug Targets-Infectious Disorders)*, 15(1):64-71.

Abdel-Daim, M.M. and Ghazy, E.W. 2015. Effects of *Nigella sativa* oil and ascorbic acid against oxytetracycline-induced hepato-renal toxicity in rabbits. *Iranian Journal of Basic Medical Sciences*, 18(3):221-227.

Abdel-Wahab, W.M. 2014. Thymoquinone attenuates toxicity and oxidative stress induced by bisphenol A in liver of male rats. *Pakistan journal of biological sciences: PJBS*, 17(11):1152-1160.

AbuKhader, M.M. 2013. Thymoquinone in the clinical treatment of cancer: Fact or fiction? *Pharmacognosy Reviews*, 7(14):117-222.

Ahmad, A., Husain, A., Mujeeb, M., Khan, S.A., Najmi, A.K., Siddique, N.A., Damanhouri, Z.A. and Anwar, F. 2013. A review on therapeutic potential of *Nigella sativa*: A miracle herb. *Asian Pacific journal of tropical biomedicine*, 3(5):337-352.

Ali, B.H. and Blunden, G. 2003. Pharmacological and toxicological properties of *Nigella sativa*. *Phytotherapy Research: An international journal devoted to pharmacological and toxicological evaluation of natural product derivatives*, 17(4):299-305.

Aljabre, S.H., Alakloby, O.M. and Randhawa, M.A. 2015. Dermatological effects of *Nigella sativa*. *Journal of dermatology & dermatologic surgery*, 19(2):92-98.

Amin, B. and Hosseinzadeh, H. 2016. Black cumin (*Nigella sativa*) and its active constituent, thymoquinone: an overview on the analgesic and anti-inflammatory effects. *Planta medica*, 82(1-2):8-16.

Amin, B., Taheri, M.M.H. and Hosseinzadeh, H. 2014. Effects of intraperitoneal thymoquinone on chronic neuropathic pain in rats. *Planta medica*, 80(15):1269-1277.

Banerjee, S., Padhye, S., Azmi, A., Wang, Z., Philip, P.A., Kucuk, O., Sarkar, F.H. and Mohammad, R.M. 2010. Review on molecular and therapeutic potential of thymoquinone in cancer. *Nutrition and* cancer, 62(7):938-946.

Cherif, M., Valenti, B., Abidi, S., Luciano, G., Mattioli, S., Pauselli, M., Bouzarraa, I., Priolo, A. and Salem, H.B. 2018. Supplementation of *Nigella sativa* seeds to Barbarine lambs raised on low-or high-concentrate diets: Effects on meat fatty acid composition and oxidative stability. *Meat science*, 139:134-141.

Daba, M.H. and Abdel-Rahman, M.S. 1998. Hepatoprotective activity of thymoquinone in isolated rat hepatocytes. *Toxicology letters*, 95(1):23-29.

Darakhshan, S., Pour, A.B., Colagar, A.H. and Sisakhtnezhad, S. 2015. Thymoquinone and its therapeutic potentials. *Pharmacological research*, 95:138-158.

El-Gharieb, M.A., El-Masry, T.A., Emara, A.M. and Hashem, M.A. 2010. Potential hepatoprotective effects of vitamin E and *Nigella sativa* oil on hepatotoxicity induced by chronic exposure to malathion in human and male albino rats. *Toxicological & Environ Chemistry*, 92(2):391-407.

EL-Kholy, W.M., Hassan, H.A., Nour, S.E., Abe Elmageed, Z.E. and Matrougui, K. 2009. Hepatoprotective effects of *Nigella sativa* and bees' honey on hepatotoxicity induced by administration of sodium nitrite and sunset yellow. *The FASEB Journal*, 23:733-2.

ERDOĞAN, Ü., YILMAZER, M. and ERBAŞ, S. 2020. Hydrodistillation of *Nigella sativa* seed and analysis of Thymoquinone with HPLC and GC-MS. *Bilge International Journal of Science and Technology Research*, 4(1):27-30.

Forouzanfar, F., Bazzaz, B.S.F. and Hosseinzadeh, H. 2014. Black cumin (*Nigella sativa*) and its constituent (thymoquinone): a review on antimicrobial effects *Iranian Journal of Basic Medical Sciences*, 17(12):929.

Gani, M.S. and John, S.A. 2013. Evaluation of hepatoprotective effect of *Nigella sativa* L. *International Journal of Pharmacy and Pharmaceutical Sciences*, 5(4):428-430.

Gholamnezhad, Z., Keyhanmanesh, R. and Boskabady, M.H. 2015. Anti-inflammatory, antioxidant, and immunomodulatory aspects of *Nigella sativa* for its preventive and bronchodilatory effects on obstructive respiratory diseases: A review of basic and clinical evidence. *Journal of Functional Foods*, 17:910-927.

Hariharan, P., Paul-Satyaseela, M. and Gnanamani, A. 2016. In vitro profiling of antimethicillin-resistant Staphylococcus aureus activity of thymoquinone against selected type and clinical strains. *Letters in Applied Microbiology*, 62(3):283-289.

Hassan, A.S., Ahmed, J.H. and Al-Haroon, S.S. 2012. A study of the effect of *Nigella sativa* (Black seeds) in isoniazid (INH)-induced hepatotoxicity in rabbits. *Indian Journal of Pharmacology*, 44(6):678.

Havakhah, S., Sadeghnia, H.R., Mosa-Al-Reza Hajzadeh, N.M., Roshan, S.S., Hosseinzadeh, H., Mohareri, N. and Rad, A.K. 2014. Effect of *Nigella sativa* on ischemia-reperfusion induced rat kidney damage. *Iranian journal of basic medical sciences*, 17(12):986-994.

Hosseini, S.M., Taghiabadi, E., Abnous, K., Hariri, A.T., Pourbakhsh, H. and Hosseinzadeh, H. 2017. Protective effect of thymoquinone, the active constituent of *Nigella sativa* fixed oil, against ethanol toxicity in rats. *Iranian Journal of Basic Medical Sciences*, 20(8):927.

Hosseinzadeh, H., Eskandari, M. and Ziaee, T. 2008. Antitussive effect of thymoquinone, a constituent of *Nigella sativa* seeds, in guinea pigs. *Pharmacologyonline*, 2:480-484.

Hosseinzadeh, H., Moghim, F.F. and Mansouri, S.M.T. 2007. Effect of *Nigella sativa* seed extracts on ischemia-reperfusion in rat skeletal muscle. *Pharmacologyonline*, 2:326-335.

Hosseinzadeh, H. and Montahaei, R. 2007. Protective effect of *Nigella sativa* L. extracts and thymoquinone, its active constituent, on renal ischemia-reperfusion-induced oxidative damage in rats. *Pharmacologyonline*, 1:176-189.

Hosseinzadeh, H., Parvardeh, S., Asl, M.N., Sadeghnia, H.R. and Ziaee, T. 2007. Effect of thymoquinone and *Nigella sativa* seeds oil on lipid peroxidation level during global cerebral ischemia-reperfusion injury in rat hippocampus. *Phytomedicine*, 14(9):621-627.

Hosseinzadeh, H., Taiari, S. and Nassiri-Asl, M. 2012. Effect of thymoquinone, a constituent of *Nigella sativa* L., on ischemia–reperfusion in rat skeletal muscle. *Naunyn-Schmiedeberg's archives of pharmacology*, 385(5):503-508.

Javidi, S., Razavi, B.M. and Hosseinzadeh, H. 2016. A review of neuropharmacology effects of *Nigella sativa* and its main component, thymoquinone. *Phytotherapy research*, 30(8):1219-1229.

Kanter, M., Coskun, O. and Budancamanak, M. 2005. Hepatoprotective effects of *Nigella sativa* L and Urtica dioica L on lipid peroxidation, antioxidant enzyme systems and liver enzymes in carbon tetrachloride-treated rats. *World Journal of Gastroenterology*, 11(42): 6684.

Kapoor, S. 2009. Emerging clinical and therapeutic applications of *Nigella sativa* in gastroenterology. *World Journal of Gastroenterology*, 15(17):2170.

Karimi, Z., Alizadeh, A.M., Dolatabadi, J.E.N. and Dehghan, P. 2019. *Nigella sativa* and its Derivatives as Food Toxicity Protectant Agents. *Advanced Pharmaceutical Bulletin*, 9(1):22-28

Karna, S.K.L. 2013. Phytochemical screening and gas chromatography mass spectrometry and analysis of seed extract of *Nigella sativa* Linn. *Int J Chem Studies*, 1(4):183-188.

Khan, A., Chen, H.C., Tania, M. and Zhang, D.Z. 2011. Anticancer activities of *Nigella sativa* (black cumin). *African Journal of Traditional, Complementary and Alternative Medicines*, 8(5): 100-110.

Manju, S., Malaikozhundan, B., Vijayakumar, S., Shanthi, S., Jaishabanu, A., Ekambaram, P. and Vaseeharan, B. 2016. Antibacterial, antibiofilm and cytotoxic effects of *Nigella sativa* essential oil coated gold nanoparticles. *Microbial pathogenesis*, 91:129-135.

Mansour, M.A., Ginawi, O.T., El-Hadiyah, T., El-Khatib, A.S., Al-Shabanah, O.A. and Al-Sawaf, H.A. 2001. Effects of volatile oil constituents of *Nigella sativa* on carbon tetrachloride-induced hepatotoxicity in mice: evidence for antioxidant effects of thymoquinone. *Research Communications in*

Molecular Pathology and Pharmacology, 110 (3-4):239-252.

Mansour, M.A. 2000. Protective effects of thymoquinone and desferrioxamine against hepatotoxicity of carbon tetrachloride in mice. *Life Sciences*, 66(26): 2583-2591.

Mehri, S., Shahi, M., Razavi, B.M., Hassani, F.V. and Hosseinzadeh, H. 2014. Neuroprotective effect of thymoquinone in acrylamide-induced neurotoxicity in Wistar rats. *Iranian Journal of Basic Medical Sciences*, 17(12): 1007-1010.

Mollazadeh, H. and Hosseinzadeh, H. 2014. The protective effect of *Nigella sativa* against liver injury: a review. *Iranian journal of basic medical sciences*, 17(12):958.

Nadaf, N.H., Gawade, S.S., Muniv, A.S., Waghmare, S.R., Jadhav, D.B. and Sonawane, K.D. 2015. Exploring anti-yeast activity of *Nigella sativa* seed extracts. *Industrial Crops and Products*, 77:624-630.

Noorbakhsh, M.F., Hayati, F., Samarghandian, S., Shaterzadeh-Yazdi, H. and Farkhondeh, T., 2018. An overview of hepatoprotective effects of thymoquinone. *Recent patents on food, nutrition & agriculture*, 9(1): 14-22.

Pourbakhsh, H., Taghiabadi, E., Abnous, K., Hariri, A.T., Hosseini, S.M. and Hosseinzadeh, H. 2014. Effect of *Nigella sativa* fixed oil on ethanol toxicity in rats. *Iranian Journal of Basic Medical Sciences*, 17(12):1020-1028.

Razavi, B.M. and Hosseinzadeh, H. 2014. A review of the effects of *Nigella sativa* L. and its constituent, thymoquinone, in metabolic syndrome. *Journal of Endocrinological Investigation*, 37(11):1031-1040.

Shabana, A., El-Menyar, A., Asim, M., Al-Azzeh, H. and Al Thani, H. 2013. Cardiovascular benefits of black cumin (*Nigella sativa*). *Cardiovascular Toxicology*, 13(1):9-21.

Simalango, D.M. and Utami, N.V. 2014. In-vitro antihelminthic effect of ethanol extract of black seeds (*Nigella sativa*) against Ascaris suum. *Procedia Chem*, 13:181-185.

Tabassum, H., Ahmad, A. and Ahmad, I.Z. 2018. *Nigella sativa* L. and its bioactive constituents as Hepatoprotectant: a review. *Current pharmaceutical biotechnology*, 19(1):43-67.

Yildiz, F., Coban, S., Terzi, A., Ates, M., Aksoy, N., Cakir, H., Ocak, A.R. and Bitiren, M. 2008. *Nigella sativa* relieves the deleterious effects of ischemia reperfusion injury on liver. *World journal of Gastroenterology*, 14(33):5204-5210.

Zafeer, M.F., Waseem, M., Chaudhary, S. and Parvez, S. 2012. Cadmium-induced hepatotoxicity and its abrogation by thymoquinone. *Journal of biochemical and molecular toxicology*, 26(5):199-205.