



# Nigella sativa and Non-Alcoholic Fatty Liver Disease: A Review of the Current Evidence

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## Abstract

**Context:** *Nigella sativa* (NS) has been used as an herbal remedy for the treatment and prevention of a variety of diseases. In this review, we aimed to summarize the current evidence on the effects of NS consumption on non-alcoholic fatty liver disease (NAFLD) characteristics.

**Evidence Acquisition:** We reviewed the existing literature published by the end of 2017 using the following key words: "Nigella sativa", "black seeds", "black cumin", "thymoquinone", "NAFLD", "NASH", and "diabetes". Papers used in this study were collected by searching the PubMed, Google Scholar, Science Direct and Scopus databases. Our search was limited to English-language articles. All the articles published between 2000 and 2017 meeting the inclusion criteria were included in the study.

**Results:** The results of current studies indicate that NS has many biological effects such as anti-inflammatory, anti-hyperlipidemic, anti-microbial, anti-cancer, anti-oxidative, anti-diabetic, anti-hypertensive and wound healing activities. In summary, it can be used as a valuable plant for designing therapeutic strategies in NAFLD.

**Conclusions:** Results from available studies indicate that NS can ameliorate the main metabolic disturbances related to NAFLD including hyperglycemia, hyperlipidemia, and overweight. These effects are mainly attributed to the anti-oxidative and anti-inflammatory properties of thymoquinone. Clinical trials on human subjects are highly essential to confirm the results found in *in vivo* and *in vitro* studies.

**Keywords:** *Nigella sativa*, NAFLD, NASH, Fatty Liver

## 1. Context

Non-alcoholic fatty liver disease (NAFLD) is among the most common causes of liver disorders worldwide ([1-5](#)), which may progress to nonalcoholic steatohepatitis (NASH) and hepatic cirrhosis ([6-11](#)). NAFLD usually develops due to the accumulation of fatty acids in hepatocytes, which can progress to steatohepatitis through rise in oxidative stress in the body ([6, 12, 13](#)). Due to the rising prevalence of obesity and sedentary life, NAFLD has become the most common cause of chronic liver disease ([14-16](#)).

*Nigella sativa* (NS), also known as black seed, is from Ranunculaceae family that is cultivated in Asia ([17-20](#)). The main components of NS are thymoquinone (TQ), unsaturated fatty acids, flavonoids, nigellone, p-cymene and carvone ([19, 21-27](#)).

It has been shown that nutrition and dietary supple-

ments play a pivotal role in the treatment of NAFLD ([28-40](#)). Recently, some studies have evaluated the effects of medicinal herbs such as NS on some risk factors for NAFLD such as insulin resistance, hyperlipidemia, oxidative stress and inflammation in experimental models ([41-44](#)). In this study, we sought to review the results of these studies and find the future direction in this field of science.

## 2. Evidence Acquisition

We searched the literature published until 2017 using the following key words: "Nigella sativa", "thymoquinone", "black seeds", "NAFLD", NASH, and "diabetes". Papers used in this study were collected by searching the PubMed, Google Scholar, Science Direct and Scopus databases and journals. To avoid the use of duplicate studies, titles and abstracts were screened. Then, compatibility of the selected

articles was assessed according to our inclusion criteria. All the articles published between 2000 and 2017 meeting the inclusion criteria were included in the study. Review articles, case reports, conference abstracts and symposium publications were excluded.

### 3. Results

#### 3.1. In Vitro and In Vivo Studies

*In vitro* and *in vivo* studies have shown some mechanisms for hepato-protective effects of TQ as the main effective component of NS. Bai et al. demonstrated the antifibrotic effects of TQ in their *in vitro* study. They found that these anti-fibrotic effects are attributed to the inhibition of apoptosis through attenuation in the expression of CD14, Toll-like receptor 4 (TLR4),  $\alpha$ -SMA, collagen-I, X-linked inhibitor of apoptosis protein (XIAP), and expression of cellular FLIP (c-FLIP) and other genes related to the regulation of apoptosis. Furthermore, these properties of TQ have been shown in *in vivo* studies (45). It has been proposed that TQ improves survival against LPS challenge in D-galactosamine (D-GlaN)-sensitized mice through the inhibition of TLR4 expression and PI3K phosphorylation. Therefore, it seems that TQ may be a potential candidate for hepatic fibrosis treatment (45).

Yang et al. ascribed that TQ has hepato-protective effects via AMP- activated protein kinase (AMPK) signaling in hepatic stellate cells (HSCs). They reported that TQ inhibits fibrogenic agents such as collagen-I and TGF- $\beta$ , while inducing peroxisome proliferator activated receptor- $\gamma$  (PPAR- $\gamma$ ) expression. Moreover, TQ (20 or 40 mg/kg) attenuated the rise in hepatic enzymes and triglycerides in an experimental model of alcoholic fatty liver disease (46). Moreover, there are some reports that supplementation with NS oil in experimental models of diabetes ameliorated serum sugar, oxidative stress, and hyperlipidemia after eight weeks and that essential oils were more effective than fixed oils (47, 48). Moreover, Awad et al. showed that TQ improves hepatic steatosis, oxidative stress, inflammatory and apoptotic status (49). Oguz et al. demonstrated that two weeks of supplementation with TQ (50 mg/kg) improved antioxidant enzyme activity in hepatic tissues (50). Furthermore, Kong et al. evaluated the effects of two dosages of TQ, low-dose (25 mg/kg) and high-dose (50 mg/kg); they observed that TQ reduced hepatic hydroxyproline (HP) and malondialdehyde (MDA) levels and increased antioxidant enzyme activity. Thus, TQ reduced oxidative stress injury and fibrosis in the liver (51).

#### 3.2. Human Studies

Although there are some studies that have shown that NS consumption ameliorates some NAFLD risk factors such

as fasting blood glucose and lipid profile (52), we could find only one study that evaluated the effects of NS on human subjects with NAFLD (53). This study evaluated the effects of 12 weeks of supplementation with 2 g/day of NS on body weight and liver enzymes. Although the study suffered from several limitations, it showed promising effects. Further well-designed studies are required in this regard to draw any conclusions.

#### 3.3. Possible Mechanism of Action

It seems that NS improves lipid profile and glycemic indices through its anti-oxidative and insulin sensitizer properties. The main antioxidant components of NS are TQ and dithymoquinone (54). TQ can scavenge free radicals in different body tissues such as the liver (55). Moreover, NS contains other antioxidant agents such as tocopherols, phytosterols, and polyunsaturated fatty acids, which can protect cholesterol molecules from oxidation and inhibit the process of atherosclerosis (1). Anti-oxidative action of NS induces pancreatic beta cell regeneration and rise in their integrity, which result in more insulin secretion and less insulin resistance (56, 57).

Moreover, NS reduces glucose absorption by the inhibition of sodium-glucose co-transporter (58). All of these lead to reduction in insulin resistance and its related metabolic disturbances. Furthermore, it has been shown that NS can decline gluconeogenesis through reduction in gluconeogenic enzymes gene expression by TQ (59). Moreover, it has been shown that TQ up-regulates LDL-C receptors on hepatocytes to reduce the uptake of LDL-C; it also reduces the production of cholesterol by the inhibition of 3-hydroxy-3-methylglutaryl-coenzyme A (HMG-CO-A) reductase (60).

Another proposed mechanism for the beneficial effects of NS on NAFLD risk factors is through its effects on weight management. One-month supplementation of NS extract caused a significant reduction in food consumption and body weight in experimental models and human studies (61).

### 4. Conclusions

Results from available studies indicate that NS can ameliorate the main metabolic disturbances related to NAFLD including hyperglycemia, hyperlipidemia and overweight. These effects are mainly attributed to anti-oxidative and anti-inflammatory properties of TQ. Clinical trials on human subjects are highly essential to confirm the results found in *in vivo* and *in vitro* studies.

## Footnotes

**Authors' Contribution:** Mina Darand and Azita Hekmatdoost conceptualized and designed the study and wrote the manuscript; Seyed Moayed Alavian and Azita Hekmatdoost critically revised the manuscript for intellectual content and data accuracy, and Azita Hekmatdoost was responsible for the final content.

**Conflict of Interests:** None of the authors had any conflicts of interest to report.

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