Nigella sativa

Nigella sativa (NS) is a promising nutraceutical plant and is used to remedy various ailments.

From: Nutraceuticals (Second Edition), 2021

Related terms:

Antiinfective Agent, Lipid, Antioxidant, Vegetable Oil, Inflammation, Interleukin 2, Essential Oil, Thymoquinone, Diabetes Mellitus

Subchronic and Chronic Toxicities of African Medicinal Plants

Adejuwon Adewale Adeneye, in Toxicological Survey of African Medicinal Plants, 2014

6.7.11 *Nigella sativa* Linn. (Ranunculaceae)

Nigella sativa Linn. is an annual flowering plant, native to South and Southwest Asia. The seeds of *Nigella sativa*, commonly known as black seed or black cumin, are used in folk medicine worldwide in the local treatment and prevention of bronchial asthma, cough, diarrhea, abdominal pain, and dyslipidemia [141,142]. The plant seed is known to be rich in both fixed and essential oils, proteins, alkaloids, and saponin [143]. However, much of the biological activity of the seeds (including antihypertensive, nephroprotection, hepatoprotection, analgesic, antipyretic, antimicrobial, and antineoplastic activities) has been attributed to its thymoquinone, the major component of the essential oil (although present in lower quantity in the fixed oil) of *Nigella sativa* [143,144]. Toxicological studies of the acute oral toxicity of thymoquinone component of the volatile oil of *Nigella sativa* by Badary et al. [145] showed its LD_{50} value to be 2.4 g/kg, while the immediate behavioral toxicity signs of 2 and 3 g/kg of the compound were hypoactivity and difficulty in respiration. Delayed toxicities of the acute oral toxicity of thymoquinone include a significant reduction in the relative organ weight and glutathione concentrations of the liver, kidneys, and heart. Plasma urea and creatinine concentrations and the enzyme activities of alanine aminotransferase, lactate dehydrogenase, and creatine phosphokinase were significantly increased [145]. In the subchronic study, mice treated with 30, 60, and 90 mg/kg/day of thymoquinone in drinking water at concentrations of 0.01%, 0.02%, and 0.03% (translating to 30, 60, and 90 mg/kg/day, respectively) for 90 days resulted in no mortality or signs of toxicity but significant lowering of fasting blood glucose [145]. There were no changes of toxicological significance in body and organ weights, food and water intake, or urine and feces output. Tissue-reduced glutathione contents, plasma concentrations of total protein, urea, creatinine, and triglycerides, and enzyme activities of alanine aminotransferase, lactate dehydrogenase, and creatine phosphokinase also were not affected. Histological examination revealed no gross or microscopic tissue damage [145]. Similarly, oral treatment of Wistar rats with the seed extract for 12 weeks significantly improved the hemogram (packed cell volume and hemoglobin) and decreased the plasma concentrations of cholesterol, triglycerides, and glucose [141]. In human subjects, topical administration of the seed oil has been reported to cause contact dermatitis [141]. Another clinical trial conducted recruited patients in Karachi reported that oral

administration of powdered *Nigella sativa* seed in capsule induced weight loss in 25% of the subjects administered *Nigella sativa* capsule through reduction in appetite [146].

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Anti-inflammatory and Anti-nociceptive Activities of African Medicinal Spices and Vegetables

J.P. Dzoyem, ... U. Bakowsky, in Medicinal Spices and Vegetables from Africa, 2017

3.5 *Nigella sativa*

Nigella sativa L. (Ranunculaceae), commonly known as black seed or black cumin, has been used for medicinal purposes for centuries. It originated from Southeastern Asia and was also used in ancient Egypt, Greece, Middle East, and Africa. It is a flowering plant which has been used for centuries as a spice and food preservative (Khan et al., 2011).The seeds have been added as a spice to a variety of Persian foods such as bread, yoghurt, pickles, sauces, and salads (Hajhashemi et al., 2004). In Northern Africa, it has been used traditionally for thousands of years to treat headache, asthma, bronchitis, rheumatism, fever, cough, influenza, and eczema. Several therapeutic effects have been attributed to the *N. sativa* seed crude extract as well as its purified components (Al-Ghamdi, 2001; Ali and Blunden, 2003; Majdalawieh and Fayyad, 2015; Amin and Hosseinzadeh, 2016). A large number of recent scientific reports have highlighted the biological activities of *N. sativa*. Particularly, *N. sativa* seeds and its oil have been extensively studied for in vivo antinociceptive and antiinflammatory effects (Hajhashemi et al., 2004; Ghannadi et al., 2005; Pichette et al., 2012). In addition, the active ingredients dithymoquinone, thymol, thymohydroquinone, saponins, alkaloids, and vitamins as well as oligo elements contribute to the health benefits associated with black cumin seeds. In particular, thymoquinone has been extensively studied and shown to possesss antinociceptive and antiinflammatory effects (Abdel-Fattah et al., 2000; Cheh et al., 2009; Woo et al., 2012; Alemi et al., 2013). Furthermore, many studies have been conducted to unfold the molecular mechanisms underlying the antiinflammatory effect of *N. sativa* (Houghton et al., 1995; El Mezayen et al., 2006; Taka et al., 2015).

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Dietary Spices in the Prevention of Rheumatoid Arthritis

Manjeshwar Shrinath Baliga, ... Faizan Kalekhan, in Foods and Dietary Supplements in the Prevention and Treatment of Disease in Older Adults, 2015

5.2.4 Black Cumin

Nigella sativa, a plant originally native to Southern Europe, North Africa, and Southwest Asia, is today cultivated in many countries in the world, including the Middle Eastern Mediterranean region, Southern Europe, India, Pakistan, Syria, Turkey, and Saudi Arabia [25]. The seeds are the most important plant part, and have been used since time immemorial in various traditional systems of medicine, such as Unani-Tibb, Ayurveda, and Siddha, to treat various ailments [25]. The seeds and oil have a long history of folklore usage, being widely used as an antihypertensive; as a liver tonic, diuretic, digestive, antidiarrheal, appetite stimulant, and antibacterial; for skin disorders; and as an analgesic [25]. Scientific studies carried out in the recent past have validated the ethnomedicinal uses, and reports indicate it to possess antidiabetic, anticancer, immunomodulatory, analgesic, antimicrobial, anti-inflammatory, spasmolytic, bronchodilator,

hepatoprotective, renal-protective, gastroprotective, antioxidant, and anticancer properties [25,26]. Studies have also shown that thymoquinone, which is the major bioactive component of the essential oil of the seed, possesses myriad benefits and is pleiotropic in its action [25–29].

With respect to its antiarthritic effects, studies have shown that thymoquinone was effective in reducing the inflammation and arthritis induced by incomplete Freund's adjuvant (IFA)-induced arthritis in rats, as evaluated by the clinical and radiological gradings [30]. Detailed studies showed that, when compared to placebo-treated cohorts, administering thymoquinone caused decreases in the levels of TNF-α and IL-1β [30]. Subsequent studies have shown that oral administration of thymoquinone to arthritic rats caused a decrease in arthritis scoring and bone resorption, as well as bone turnover markers such as alkaline phosphatase and tartrate-resistant acid phosphatase [31].

Additionally, cell culture studies with human RA fibroblast-like synoviocytes have also shown that thymoquinone inhibited lipopolysaccharide (LPS)-induced proliferation of the synoviocytes, generation of H_2O_2-induced 4-hydroxynonenal, and levels of IL-1β, TNF-α, metalloproteinase-13, cyclooxygenase-2, and prostaglandin E2 [31]. Thymoquinone blocked LPS-induced phosphorylation of p38, MAPK, ERK1/2, and NF-κB p65 in a time-dependent manner [31]. Additionally, studies have shown that oral administration of thymoquinone to arthritic rats reduces the serum levels of HNE, IL-1β, and TNF-α [31].

Clinical studies have also shown that consumption of 500-mg capsules of *Nigella sativa* oil twice daily significantly decreased the disease activity score (DAS-28) in people with RA when compared with before and after placebo [32]. Similarly, the number of swollen joints and the duration of morning stiffness improved. A marked improvement in disease activity was shown by both the ACR20 and EULAR response criteria in 42.5% and 30% of the patients, respectively, after intake of *Nigella*[32]. Together, these observations clearly indicate that supplementation with *Nigella sativa* during DMARD therapy in RA may be considered an affordable potential adjuvant biological therapy [32].

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Safe African Medicinal Plants for Clinical Studies

Theophine Chinwuba Okoye, ... Emeka K. Okereke, in Toxicological Survey of African Medicinal Plants, 2014

18.2.24 *Nigella sativa* L. (Ranunculaceae)

The seeds of *Nigella sativa* (commonly known as black seed or black cumin) are used in folk medicine for the treatment and prevention of a number of diseases which include asthma, diarrhea, and dyslipidemia. Much of the biological activity of the seeds has been shown to be due to thymoquinone. Thymoquinone has been reported to possess anticonvulsant as well as anticancer effects [77]. Reported pharmacological actions of the seeds and some of its active constituents include protection against nephrotoxicity and hepatotoxicity, as well as antiinflammatory, analgesic, antipyretic, antimicrobial, antineoplastic, immunological, antihypertensive, respiratory stimulating, hematinic, and trypanocidal activities [78,79]. The seeds extract has exhibited a low degree of toxicity and has been shown not to induce significant adverse effects on liver or kidney functions. It would appear that the beneficial effects of the use of the seeds and thymoquinone might be related to their cytoprotective and antioxidant actions, and to their effect on some mediators of inflammation [78].

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Insomnia

Jane Buckle PhD, RN, in Clinical Aromatherapy (Third Edition), 2015

Black Cumin

Khanna et al (1993) found that black cumin *(Nigella sativa)* essential oil had a sedative effect more powerful than the drug chlorpromazine (Largactil) and was also an analgesic. The study suggested that black cumin contained an opioid-like component. More recent studies on animals have concentrated on anxiolytic effects (Gilhotra & Dhingra 2011) and anticonvulsant effects (Hosseinzadeh & Parvardeh 2004) in mice. It would be interesting to study inhaled black cumin on human insomnia. Because black cumin has a strong, pungent aroma, it would probably need to be "softened" with another calming aroma such as lavender, clary sage, or Roman chamomile.

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Herbal antilithiatic biomolecules

Shubhadeep Roychoudhury, ... Subhash C. Mandal, in Herbal Biomolecules in Healthcare Applications, 2022

23.3.4.1 Sources

Thymoquinone is the main biologically active component of *Nigella sativa* oil belonging to the family Ranunculaceae. Dithymoquinone, thymohydroquinone, and thymol are also the important active quinones found in *N. sativa* [98,99]. Thymoquinone is also found in *Nigella arvensis* seeds; *Thymus* spp., *Thymbra* spp., *Satureja* spp., *Monarda* sp., *Mosla* spp., *Origanum* spp., *Agastache* spp., and *Coridothymus* spp. belonging to the family Lamiaceae; *Tetraclinis* sp., *Juniperus* spp., and *Cupressus* spp. belonging to the family Cupressaceae in glycosidic form [100].

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Kiwifruit

P. Padmanabhan, G. Paliyath, in Encyclopedia of Food and Health, 2016

Fruit Morphology

Botanically, *Actinidia* fruits are berries with numerous black seeds embedded in a juicy pericarp. *Actinidia deliciosa* (A. Chev.) 'Hayward' ('green' kiwifruit), a green fleshed kiwifruit, is the most common commercial variety with superior flavor. It is an oval berry about the size of a hen's egg with a light brown hairy skin and emerald-green flesh with numerous tiny black seeds embedded in a juicy pericarp. *Actinidia deliciosa* fruits have persistent long, hard, bristlelike hairs, which are partially removed during grading and packaging. The green color of the flesh of *A. deliciosa* is due to the presence of chlorophyll, which is retained during fruit maturation and ripening. The flesh has a combination of tangy, sweet, and sour flavors. The most common yellow-fleshed kiwifruit is *A. chinensis*, 'Hort16A'. *A. chinensis* fruits are usually covered with soft, downy hairs that are shed early in fruit development. Fruits of *A. chinensis* have a characteristic 'beak,' which is a protrusion of stylar end. Fruit flesh of *A. chinensis* is yellowish due to partial or complete loss of chlorophyll.

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Alkaloid Chemistry

Seneca, in Alkaloids - Secrets of Life, 2007

2.9.3.3 Seed colour method

The simple observation that white seeds are sweeter that black seeds was used in the construction of a practical method of judging lupine seeds qualitatively. This method cannot be used with confidence, because, especially in white lupine, even very white seeds can have a high alkaloid content. On the other hand, plants from the same species are "sweet". In some species, for example in the case of L. *angustifolius* or L. *luteus*, the tendency of white seeds to be "sweet" is more likely but not absolutely certain.

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URL: https://www.sciencedirect.com/science/article/pii/B9780444527363500040

Thymoquinone

Bhanushree Gupta, ... Ramesh C. Gupta, in Nutraceuticals, 2016

Abstract

Thymoquinone (TQ) is a chief bioactive constituent of black seed oil (*Nigella sativa*). TQ holds promising pharmacological properties against several diseases. It exhibits outstanding antioxidant, anti-inflammatory, anticancer, and other important biological activities. TQ effectively transforms cancer progression signaling pathways. It not only improves anticancer activity of chemotherapeutic drugs but also attenuates their side effects. Considering the extraordinary activity of TQ, this chapter accounts for the origin of TQ and its pharmacological characteristics. The recent advances in the form of chemical modifications and no formulations for the design of TQ analogs have been discussed. Finally, the present status of adjuvant potency of TQ and its *in vivo* toxicity are summarized.

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Therapeutic Potential of Thymoquinone in Treatment of Rheumatoid Arthritis and Related Autoimmune Diseases

Arzoo Pannu, ... Mukesh Nandave, in Bioactive Food as Dietary Interventions for Arthritis and Related Inflammatory Diseases (Second Edition), 2019

2 Thymoquinone Against Rheumatoid and Autoimmune Diseases

Thymoquinone is a phytochemical compound obtained from the plant *Nigella sativa*. It has been reported for its analgesic, anticancer, antioxidant, antiinflammatory, and antipyretic activity. In the literature, it has shown its curative action against RA because of its strong antiinflammatory activity. Thymoquinone inhibits the severe clinical signs and symptoms of RA, namely joint pain, swelling, etc. It shows its action by various mechanisms, including: (i) inhibits the COX and LOX enzymes, resulting in inhibition of the synthesis of the inflammatory mediators' prostaglandins, thromboxane, and leukotrienes from eicosanoids. Reduced levels of inflammatory mediators lead to a decrease in joint inflammation [20]; (ii) the blockage of proinflammatory cytokines IL-1β, TNF-α, IFN-γ, IL-6, and PGE2 will result in a reduction of disease severity. These proinflammatory cytokines are abundantly expressed in the arthritic joints of rats with collagen-induced arthritis, leading to joint inflammation. On the other hand, IL-4 and IL-10 have protective actions and suppress bone erosion in RA. Hence, it is plausible to suggest that thymoquinone shows a protective effect through inhibition of harmful

proinflammatory cytokines such as IL-1β, TNF-α, IFN-γ, IL-6, and PGE2 and raises the level of IL10, showing a protective effect. Decreased production of these harmful proinflammatory cytokines by thymoquinone also leads to a reduction in the production of free radicals; (iii) the inhibition of elastase and myeloperoxidase activity, the enzyme responsible for the accumulation and activation of polymorphonuclear leukocytes released from the injured tissue. These in-filtered cells cause inflammation by releasing nitrogen and oxygen species. Thymoquinone is found to be a sound antioxidant, having a free radical scavenging property that aids in curing RA; and (iv) inhibition of lipid peroxidation and nitric oxide.[21] Thymoquinone increases the activity of antioxidant enzymes by suppressing lipid peroxidation and boosting the antioxidant defense system. Lipid peroxidation is found to be a critical mechanism of injury. Thiobarbituric acid reactive substances also relate to oxidative damage by free radicals. Damage of the joint cell can be prevented by detoxification or removal of these free radicals, which leads to lipid peroxidation. In an animal model of collagen-induced arthritis, a significant increase in lipid peroxidation was found to be associated with a decrease in the level of antioxidants such as glutathione in the body. An increase in free radicals leads to a disruption of the homeostasis of the joint. In the study, after treatment with thymoquinone, the activity of the antioxidant enzyme was found to be increased in the animal model of collagen-induced arthritis. Thymoquinone inhibits nitric oxide production from activated cells and macrophages which increase inflammatory responses. Inflammatory cytokines produce excessive NO and their production leads to apoptosis. Therefore, the inhibition of the production of excessive NO has a beneficial effect by blocking cartilage damage in RA. Hence, all these mechanisms reflect the protective action of thymoquinone in RA (Figure 33.3).

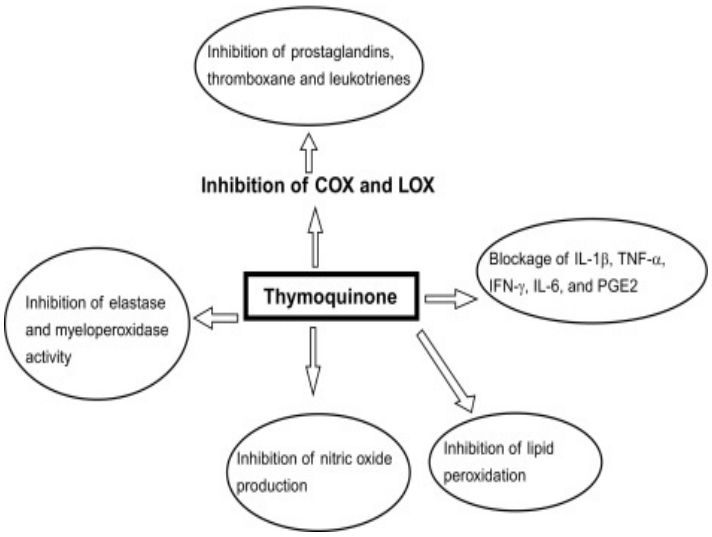

Figure 33.3. Mechanism action of thymoquinone.

The mediation of the inflammatory process is still not understood as it consists of a complex process of cytokines. Nowadays, mitogen-activated protein kinase (MAPKs) p38 has attracted the attention of researchers as a potential therapeutic target because of its ability to suppress the production of key inflammatory mediators. Oxidative stress, calcium overload, and inflammatory cytokines such as tumor necrosis factor α (TNF-α) activate apoptosis signal regulating kinase 1 (ASK1, a member of the MAP3K family), which further activates both the JNK and p38 MAPK pathways. Therefore, ASK1 may serve as a promising therapeutic target in RA as it regulates proinflammatory cytokine release and its activity is controlled by phosphorylation and interactions with other proteins. ROS is one of the factors activating ASK1 by inducing dephosphorylation of ASK1 at Ser967 as well as phosphorylation of Thr845 in the ASK1 activation loop.

Another factor, TNF-α, also enhances the phosphorylation of ASK1 at Thr845 and activates it. Thymoquinone is found to be effective in inhibiting the

phosphorylation of ASK, thereby decelerating the downstream signaling pathway. Upon activation, MAP kinases also transform the stimulus into the pathophysiological responses in mRNA translation by phosphorylating downstream substrates, including transcription factors and cytoskeletal proteins. Thymoquinone is found to be a potent small molecule in inhibiting these stimulation processes.[22]

Phytochemicals reported for lupus act through the same philosophy of inhibiting inflammatory mediators of RA. In lupus, phytochemicals inhibit the level of the inflammatory mediator (PGE2, IL-17a, Th cells, IFN-γ, and IL-6, etc.), the LOX enzyme, and the COX enzyme. Some phytochemicals reduce the production of autoantibodies and inhibit the formation of the immune complex (autoantibodies and autoantigen complex), resulting in the inhibition of tissue damage (Table 33.2).

Table 33.2. Reported phytochemical for lupus[23–25]

Sr. No.	Phytochemical name	Action
1.	Aconitine	Decreased levels of PGE2, IL-17a, and IL-6
2.	Curcumin	Decreased levels of PGE2, IL-17a, and IL-6
3.	Dehyroepiandrosterone	Decreased levels of PGE2, IL-17a, and IL-6
4.	Docosahexaenoic	Inhibition of lipoxygenase, inhibiting NF-κB
5.	Eicosapentaenoic	Inhibition of lipoxygenase
6.	Isofl avones	Inhibiting the production of autoantibodies
7.	l-Canavanine	Suppressor-inductor of T cells
8.	*N*-Acetyl cysteine	Decreased levels of PGE2, IL-17a, and IL-6
9.	Omega 3 fatty acids	Decreased levels of PGE2, IL-17a, and IL-6
10.	Vitamin A	Defects in Th cell activity
11.	Vitamin B	Promote a reduction in homocysteine levels
12.	Vitamin C	Reduces IgG
13.	Vitamin D	Inhibits the proliferation of Th, reduces the secretion of IL-2 and IFN-γ
14.	Vitamin E	Reduction in PGE2, leukotriene B4, and thromboxane B
15.	Ω-3 PUFA	Suppresses the activity of macrophages and the production of cyclooxygenase

Beside these, there are also many undiscovered and unreported phytochemicals, which need to be studied deeply. There are numerous targets in the pathophysiology of RA and lupus that can be targeted in a study of a new phytochemical. Because these drugs only cure the symptoms of inflammation such as pain and swelling in RA and lupus, they don't repair the damage done. So, we need a wide approach in the area of autoimmune diseases (RA and lupus) and have to discover such new phytochemical molecules that restore the damaged tissue integrity.

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