

Natural therapeutic approach of *Nigella sativa* (Black seed) fixed oil in management of Sinusitis



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ABSTRACT

Sinusitis is associated with inflammation and infections of air-filled cavities of sinuses. The aim of this study was to evaluate the potential efficacy of *Nigella sativa* seed fixed oil in management of sinusitis. The information was extracted from accessible international databases, traditional books, electronic resources, and unpublished data.

Results: The results of investigations on *N. sativa* seed fixed oil showed its therapeutic potential in treatment of sinusitis by its anti-inflammatory, antioxidant, antihistaminic, immune-modulator, antimicrobial and analgesic effects. The use of *N. sativa* seed fixed oil can inhibit the inflammation of sinuses and respiratory airways, microbial infections and finally help the patients suffering from clinical symptoms of sinusitis such as coryza, nasal congestion, headache, neck pain, earache and toothache. Clinical studies are required to evaluate its efficacy in patients with sinusitis in future.

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1. Introduction

The air-filled cavities of sinuses is one of host defense system, which act by classical, pseudostratified and ciliated columnar epithelium. When one or more of paranasal sinuses become inflamed, sinusitis occurs. Classically, there are four types of sinusitis including acute, sub-acute, chronic and recurrent ones. The infection of paranasal sinuses, which occur 10 days and less than 4 weeks is defined as acute sinusitis. The inflammatory diseases of sinuses, much similar to asthma is chronic sinusitis. Viral upper respiratory infection leads to inflammation of sinuses, damaging the mucosa and defective performance of cilia, which prone the environment to bacterial infections¹. Rhinoviruses, *Streptococcus pneumonia*, *Haemophilus influenza*, and *Moraxella catarrhalis* are the major-

ity pathogens of acute sinusitis^{2,3}. In spite of inflammatory nature of acute sinusitis, the involved bacterial pathogens of acute sinusitis, *Staphylococcus aureus*, coagulase negative *Staphylococci* are found in chronic sinusitis⁴. Postnasal drip, greenish nasal discharge, nasal congestion, tenderness of the face under the eyes or at the bridge of the nose, frontal headaches, pain in teeth, cough and fever are common symptoms of sinusitis. Antibiotics (amoxicillin, doxycycline, cephalexin and cefadroxil, etc.) are prescribed for 85-98% of patients with acute sinusitis⁵⁻⁷. Nasal corticosteroids, and anti-histamines are used in patients with sneezing or rhinitis. Corticosteroids and antibiotics are used in chronic sinusitis⁸. The appearance of antibiotic resistant pathogens to chemical agents along with the adverse effects of drugs encourage the scientists to search among the medicinal plants. One of popular plants in traditional medicines for management of sinusitis and clinical symptoms is *Nigella sativa* seeds.

Nigella sativa, a member of Ranunculaceae family is commonly known as black seed. *N. sativa* seed with a rich historical and religious background is the miracle curative herb for all

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ailments, except the death. *N. sativa* seeds are used widely for extraction of fixed oil. *N. sativa* seeds were used by Dioscorides as diuretic, emmenagogue, galactopoietic. Avicenna in the "Canon of Medicine" used the black seed for stimulating the body's energy and helping recovery from fatigue and dispirit- edness. It was a remedy for coryza. Frying the seeds in oil and putting in the lint and putting on forehead, relieves the headache. Soaking the seeds in the vinegar for one night and crushing them and smelling was a remedy for chronic headache⁹. In Middle East countries, *N. sativa* seed oil is used as antiseptic, local analgesic and for treatment of asthma, bronchitis, rheumatism and other inflammatory diseases¹⁰. Algerians take the roasted seeds with butter for cough, and with honey for colic, Arabians use its seed as lactagogue, soaking in rose oil as eye drops for eye infections. Indian people use the seed tincture for anorexia, diarrhea, dyspepsia and fever or seed fixed oil in sesame oil for dermatosis. *N. sativa* is anthelmintic, carminative, emmenagogue and stim- ulant in Ayurvedic. Sniffing the cloth containing the mixture of *N. sativa* seed with melted butter is used by Ethiopians for headache. Indonesians combine *N. sativa* seed with astrin- gent medicines for abdominal disorders. The seed extract is used for treatment of liver ailments. The poultice seeds is used by Malaysians for treatment of abscesses, headache, nasal ulcers, orchitis and rheumatism. In North Africans, mixture of *N. sativa* seed with honey is used as morning aperitif. Unani Medicine consider the plant as abortifacient, diuretic, anthelmintic and emmenagogue and good treat- ment for cough, fever, jaundice, pulmonosis and sore eyes. In Yemen, the seeds are used for hemorrhoids¹¹.

Fig. 1

Fixed oils is extracted for edible purposes, flavoring foods, preservatives in confectioneries, stabilizing of edible fats and pharmaceutical applications. According to traditional uses of *N. sativa* seed for treatment of headache, fever, cough and coryza, *N. sativa* seed fixed oil has a good potency for treatment of sinusitis. In this review article, we evaluate the therapeutic potency of *N. sativa* fixed oil in management of sinusitis and its symptoms.

2. Chemical composition of *N. sativa* seed fixed oil

The therapeutic effects of herbal medicines has direct correla- tion with their chemical compositions. Before everything, we evaluate the chemical composition of *N. sativa* seed oil in this section.

The seeds contain amino acids, proteins, carbohydrates, 0.4-1.49% essential oil, 30-44.21% fixed oil, sterols (choles- terol, campesterol, stigmasterol, α -spinasterol, β -sitosterol)¹², alkaloids (nigellidine, nigellimine, nigellicine), saponins and crude fiber, minerals (calcium, iron, sodium, potas- sium)¹³. Thymoquinone (26.8-54.8%), *p*-cymene (14.7-38.0%), longifolene (1.2-10.2%), α -thujene (1.3-10.1%), carvacrol (0.5-4.2%), α -cubebene (0.4-3%), α -pinene (0.2-2.4%), limonene (0.7-2.3%), β -pinene (0.4-3.0%), sabinene (0.2-1.6%) were the main components of *N. sativa* seed essential oil¹⁴. Linoleic acid make up 50% of fixed oil, followed by oleic acid (25%), palmitic acid (18%). Thymoquinone

(2-isopropyl-5-methyl-1,4-benzoquinone) is present at con- centration of 3.5-8.7 mg/g in fixed oil^{15,16}.

3. The potential efficacy of *N. sativa* fixed oil in treatment of sinusitis

3.1. The anti-histaminic, anti-oxidant and anti-inflammatory effects of *N. sativa* seed fixed oil

Sinusitis is associated with inflammation of sinus cavi- ties as the result of an irritant or triggering the body's histamine responses. Therefore, the anti-inflammatory, anti- histaminic and antioxidant effects of *N. sativa* seed fixed oil may explain one of mechanisms related to its efficacy in reducing the inflammation of sinuses and respiratory airways.

In animal model of allergic asthma, cyclooxygenase and 5-lipoxygenase pathways of rat peritoneal leukocytes inhibited by *N. sativa* fixed oil, by inhibition of thrombox- ane B₂ and leukotriene B₄ metabolites¹⁷. Lung inflammation was improved and peripheral blood eosinophil count was decreased by *N. sativa* fixed oil¹⁸. Oral administration of fixed oil in animal models significantly decreased the leukocyte, platelet counts¹⁹.

The anti-inflammatory effects of *N. sativa* seed fixed oil is related to thymoquinone, nigellone, thymohydroquinone. Low concentration of Nigellone has been proved to inhibit the histamine release²⁰. 500mg *N. sativa* seed fixed oil in the form of capsule is used as anti-histamine agent²⁰. *N. sativa* seed fixed oil, thymoquinone and nigellone dose dependently inhibited the formation of 5-lipoxygenase prod- ucts and 5-hydroxy-eicosa-tetra-enoic acid (5-HETE) from polymorphonuclear leukocytes²¹. Thymoquinone has exhib- ited anti-histaminic, anti-inflammatory and immunoboosting effects²².

Rather than, the anti-inflammatory effects of *N. sativa* seed fixed oil in mice and rat animal models, *N. sativa* seed fixed oil reduced the serum levels of TNF- α and high sensi- tivity C-reactive protein in calorie restricted obese women²³. Furthermore, oral administration of 1g *N. sativa* seed fixed oil in patients suffering from rheumatoid arthritis for 8 weeks increased the serum levels of IL-10 without any changes in TNF- α ²⁴. The anti-inflammatory effects of daily administration of 0.5ml *N. sativa* seed fixed oil for 30 days were associated with significant suppression of nasal mucosal congestion, turbinate hypertrophy, nasal itching, mucosal pollar and sneezing attacks of patients suffering from aller- gic rhinitis²⁵. In nasal congestion, the mucosa of nose and para-nasal sinuses becomes swollen, and this condi- tion is associated with edema, mucus secretion and difficult breathing. The inflammatory disorders like sinusitis, otitis, bronchitis or asthma may be the reason of nasal congestion. Therefore, the significant suppression of nasal congestion may improve the clinical sign of sinusitis. The clinical evi- dence about preventive and bronchodilatory effects of *N. sativa* seed fixed oil on obstructive respiratory diseases are attributed to its anti-inflammatory, and antioxidant effects of its oil or oil components²⁶. This beneficial effects of *N. sativa* seed fixed oil in sinusitis could be attributed to

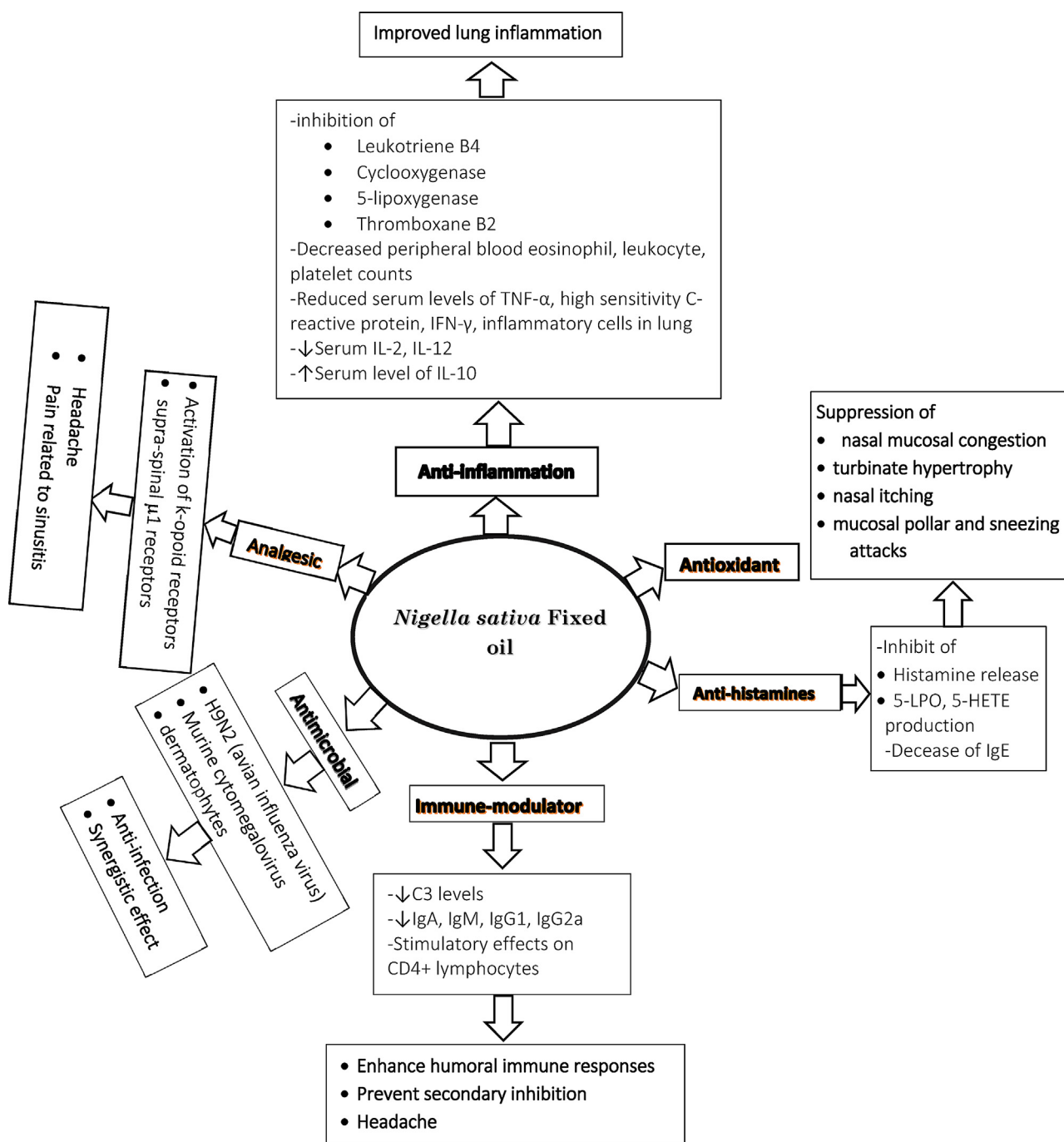


Fig. 1 – Nigella sativa fixed oil in management of clinical symptoms of sinusitis.

these anti-inflammatory and antioxidant effects. The anti-inflammatory effects of *N. sativa* seed fixed oil is attributed to its antioxidant activity. The antioxidant effects of *N. sativa* seed fixed oil were confirmed^{16,26}. Therefore, the antioxidant, anti-histaminic and anti-inflammatory effects of *N. sativa* seed fixed oil and main components decrease the inflammation of sinuses and respiratory airways, and inhibit the nasal congestion, edema, coryza as the clinical signs of sinusitis.

3.2. Immunomodulatory effects of *N. sativa* seed fixed oil

The immunomodulatory effects of *N. sativa* may be another reason for its beneficial effects in sinusitis. Oral *N. sativa* seed fixed oil enhanced humoral immune responses by reduction in IgA, IgM and C3 levels²⁷. The immunomodulatory effects of *N. sativa* seed fixed oil is not related to the effects on Th1 and Th2 cell responsiveness to allergen stimulants²⁸. *N. sativa* seed

fixed oil decreased the serum IgG1, IgG2a, IL-2, IL-12, IL-10, IFN- γ and inflammatory cells in lung tissue of murine model of allergic asthma²⁹. 5 ml/kg/day injected *N. sativa* seed fixed oil for 17 days in CD1 albino mice decreased IgG and serum IL-2 and IL-12²⁹, also 4 ml/kg/day injected *N. sativa* seed fixed oil in OVA sensitized BALB/c mice for 7 days decreased total IgE, IgG1 and OVA IgG1, mRNA expression of IL-4, IL-5, IL-6 and TGF- β 1 from lung cells and nitric oxide, eosinophils, macrophages and lymphocytes³⁰, Thymoquinone decreased leukotriene³¹, OVA IgE & IgG1, IL-4, IL-5, IL-13, IFN-c, eosinophils³², blood IFN- γ ³³ in mice animal models and cell lines. *N. sativa* seed fixed oil can ameliorate the cellular immunological changes due to chloramphenicol³⁴. Weak immune system is the cause of recurrent sinus infections that make the body vulnerable to infections, increase the mucus production, chronic swelling of the mucous membranes, that finally leads to sinus pain. Therefore, the immunomodulatory effects of *N. sativa* seed fixed oil can prevent the secondary infections, headache and other clinical signs of sinusitis.

3.3. Antimicrobial effects of *N. sativa* fixed oil

Sinusitis especially acute ones is associated with viral and bacterial infections. Therefore, the antimicrobial activity of *N. sativa* fixed oil against pathogenic microorganisms can be useful in patients with sinusitis. The antiviral effects of thymoquinone, *N. sativa* seed fixed oil against avian influenza virus (H9N2)³⁵ and murine cytomegalovirus infection model³⁶ were confirmed, respectively. *N. sativa* seed fixed oil had stimulatory effects on CD4+ T lymphocytes in murine BALB/c cytomegalovirus model. It decreased the virus titers in spleen and liver and increased the serum IFN- γ level and M Φ number and function³⁷. The antifungal activity of thymoquinone against *Candida* sp. (*C. albicans*, *C. krusei*, *C. tropicalis*), dermatophytes (*Epidermophyton floccosum*, *Microsporum canis*, *M. gypseum*, *Trichophyton interdigitale*, *T. mentagrophytes* and *T. rubrum*)³⁸ were the subject of some studies. Thymoquinone exhibited strong antimicrobial properties against Gram negative and positive bacteria with MIC values in the ranges of 8-512 μ g/ml³⁹⁻⁴¹, and had synergistic effects with particular antibiotics and act as resistant modifiers³⁹⁻⁴². 0.1% w/w *N. sativa* seed fixed oil is used as potent food preservative²⁰. Although, *in vitro* studies have introduced *N. sativa* seed fixed oil as broad extended antimicrobial agents, but other studies are required to evaluate its antimicrobial effects against the involved pathogens in sinusitis.

3.4. Analgesic effects of *N. sativa* fixed oil

As we noted before, there is a connection between sinusitis and pain in ear, teeth, jaw, throat, neck and so on. Therefore, the analgesic effects of *N. sativa* seed fixed oil can suppress some clinical symptoms in patients suffering from sinusitis.

N. sativa seed fixed oil as an opioid principle with an antagonizing effects on naloxone had been the strong antinociceptive actions in hot plate test, tail pinched test, acetic acid Writhing test models of mice and rats⁴³. *N. sativa* seed fixed oil loaded liposomes in hot plate test showed analgesic effects⁴⁴. The dose dependent analgesic response of 50-400 mg/kg *N. sativa* seed fixed oil (p.o) was confirmed in hot plate test,

tail-pinch test, acetic acid induced writhing test and early phase of formalin test, while the systemic administration of thymoquinone showed antinociceptive effects in early and late phase of formalin test. The antinociceptive effects *N. sativa* seed fixed oil and thymoquinone in early phase of formalin test was blocked by naloxone. Also, the antinociceptive effects of thymoquinone in early phase of formalin test was suppressed by naloxone, naloxonazine, while naltrindole had no effects on nociceptive response of thymoquinone. Thymoquinone and *N. sativa* seed fixed oil decreased the antinociceptive effect of morphine, therefore, the antinociceptive effects of *N. sativa* seed fixed oil and thymoquinone is via indirect activation of k-opoid and supra-spinal μ 1 receptor subtypes⁴⁵. The analgesic effects of *N. sativa* seed fixed oil confirm the scientific reason for traditional uses of it in headache and its novel potential in treatment of pain related to sinusitis.

3.5. Safety of *N. sativa* seed fixed oil

According to traditional believes, *N. sativa* had hot and dry temperament, therefore it can cause respiratory complications in hot temperament individuals. Processing the seeds with vinegar according to Iranian Traditional recommendation eliminate the related adverse effects due to its seed. Comparative study on the fixed oil from non-processed or processed *N. sativa* seed showed the same content of fatty acids, while thymoquinone was eliminated in processed seeds⁴⁶. Evaluating the safety of 0.3% oral *N. sativa* seed fixed oil for 8 weeks in rats, showed no significant changes in vital organs (heart, liver, pancreas, lungs, spleen, kidneys) to body weight ratio, red and white blood cells, cardiac enzymes, liver enzymes, urea, creatinine, albumin, A/G ratio and total protein⁴⁷. 200 mg/kg/day of *N. sativa* seed oil for 14 weeks revealed no histopathological changes in liver, kidneys, spleen, lungs, stomach, intestine, testes and accessory organs, and thyroid Gland⁴⁸. The LD₅₀ of *N. sativa* seed fixed oil was 29 mL/kg in mice and rats. Intake of 2 mL/kg *N. sativa* seed fixed oil for 12 weeks had no clear organ damage, no fall in leukocyte and platelet counts¹⁹. Supplementing the rats with 4% *N. sativa* fixed oil was associated with no harmful effects⁴⁷, while feeding female rats with 0.8 ml/daily *N. sativa* fixed oil caused a minor weight loss and through two pregnancies improved pups health⁴⁹. 500-1000 mg of *N. sativa* seed fixed oil, three times a day is recommended as typical dose. Sub-chronic and sub-acute of thymoquinone (10-100 mg/kg body weight) had been no toxicity and death⁵⁰. The LD₅₀ for intraperitoneal and oral thymoquinone were 104.7 mg/kg and 870.9 mg/kg in mice and 794.3 and 57.5 mg/kg in rats⁵¹.

4. Conclusion

N. sativa seed is valuable herbal medicine that is traditionally used for treatment of all diseases except the death. One component of *N. sativa* seed is its fixed oil rich in fatty acid oils and some valuable ingredients such as thymoquinone, nigellone, etc. *N. sativa* seed fixed oil has been used by traditional practitioners Avicenna, Dioscorides as treatment for headache, infections, coryza, and nasal

congestion. Recent investigations on *N. sativa* seed fixed oil have exhibited that it has anti-inflammatory, anti-oxidant, anti-histaminic, antimicrobial, analgesic, and immunomodulator activities. These pharmacological activities make it as suitable candidates for treatment of sinusitis. The inflammatory effects of sinuses and airways inhibit by *N. sativa* seed fixed oil, also, its immunomodulatory and antihistaminic effects of oil prevent from secondary infections of sinuses and respiratory airways. Also, the antiviral and antibacterial effects of oil kill the pathogenic microorganisms. All of these activities along with analgesic effects of *N. sativa* seed fixed oil protect the patients against pain in ear, head, teeth and neck. Although, previous studies introduce *N. sativa* seed fixed oil as a potential treatment in management of sinusitis, large double blind clinical trials are required to compare the efficacy and safety of *N. sativa* seed fixed oil with current treatment in futures.

Conflict of interest

There was no conflict of interest.

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