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## Articles

### Effect of Black Seeds (*Nigella Sativa*) on Some Parasitic Diseases: A Review

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#### Abstract

Parasitology is a branch of biology that studies the interaction of two microorganisms, one of whom benefits and the other threatens. Previously include Bacteria, Fungi and viruses, now are limited to parasitic protozoa, helminths, arthropods and species of arthropods serve as a vector for parasite. Six important human tropical illnesses are known and five are parasitic diseases. Parasitic diseases are high prevalence in developing countries where poverty and poor hygiene are predominant. As a result, using chemical drugs is costlier.

For thousands of years humans used herbal plants for treatment as a science named herbal medicine (botanical medicines or phytomedicine). Because of their efficacy, safety, low cost, and lesser side effects, traditional herbal medicine is often used as the first line of protection in disease treatment by 80 percent of the world's population.

*Nigella sativa* has been used for medicinal purposes and food from ancients, both as a herb and oil. *N. sativa* belong to the genus *Nigella*.

This review aims to investigate the possibility of using black seeds as a therapeutic agent in protozoal and helminthic disease based on published data.

**Keywords:** *Nigella sativa*, Protozoa, Helminth.

#### 1. Introduction

Phytomedicine, also known as herbal medicine, refers to the use of plant parts for medical purposes (Bhardwaj et al., 2018). Numerous modern medications are obtained mainly from plants, such as aspirin (willow bark), digitoxin (foxglove), morphine (opium poppy), quinine (cinchona bark), and pilocarpine (jaborandi) (Bulter, 2004).

*Nigella sativa* is a comments herbal plant that really has stimulated the interest of researchers. It is often known as black seed (capsulated plant seed), black cumins, Love-in-a-mist, Habatut, Barakah, Sonez, Habatut, Sauda, Kalonji, Krishana, Jiraka, and Sidadanah (Ijaz et al., 2017).

#### Classification of the plant (Ijaz et al., 2017)

Kingdom: Plantae.

Subkingdom: Tracheobionata that is, vascular plant.

Supervision: Spermatophyte.

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Order: Ranunculales.

Family: Ranunculaceae Butter cup family.

Genera: *Nigella*.

Species: *sativa*.

### **Plant Morphology**

*Nigella* is a genus of about 14 species of annual plants in the family Ranunculaceae, native to southern Europe, North Africa and Southwest Asia.

*Nigella sativa* Linn grows to 20-30 cm tall with finely divided, linear leaves. Flow *Nigella sativa* *ers* are pale blue and white in colour with 5-10 petals with a variable number of sepals and are characterized by the presence of nectaries. The gynoeceum is composed of a variable number of multiovule carpels, developing into a follicle after pollination. Terminal fruit is a capsule having many rectories, pocket like epicalyx present. Seeds are small, dicotyledonous, trigonous black, rugulose-tubercular (Jabbar et al., 2006).

### **Chemical Composition (Ali, Blunden, 2003; Boskabady, Shirmohammadi, 2002):**

Seeds of the herbal is the common part used in cooking and for medical purpose. It is contain total ash (4.8 %), carbohydrates (24.9 %), crude fiber (8.4 %) fat (28.5 %), protein (26.7 %). and a good amount of various vitamins and minerals like Cu, P, Zn, and Fe.

Also contain fatty oil rich in unsaturated fatty acids, constituting dihomolinoleic acid (10 %), eicosadienoic acid (3 %), linoleic acid (50-60 %) and oleic acid (20 %), and saturated fatty acids (palmitic and stearic acids) constitute up to 30 %.  $\alpha$ -Sitosterol is the major sterol, accounting for 44-54 % of the total sterols in *N. sativa* oils, followed by stigmasterol (6.57-20.9 %).

The most important active compounds of *N. sativa* are thymoquinone (TQ) (30-48 %), *t*-anethole (1-4 %), carvacrol (6-12 %), *p*-cymene (7-15 %) thymohydroquinone, dithymoquinone (nigellone), 4-terpineol (2-7 %), sesquiterpene longifolene (1-8 %),  $\alpha$ -pinene, and thymol.

*Nigella sativa* also contains other compounds such as carvone, citronellol, limonene, in trace amounts, and two varieties of alkaloids, i.e. isoquinoline alkaloids (e.g. nigellicimine and nigellicimine-*N*-oxide) and pyrazole alkaloids (e.g. nigellidine and nigellicine).

### **Medical Important of *Nigella stevia*:**

*Nigella sativa* has both historical and religious roots. The healing power of black seed was mentioned by Prophet Mohammad (PBUH). Black cumin is also referred to as "Curative black cumin" in the Holy Bible (Al-Ghamdi, 2001). Black seeds are used to treat a variety of ailments such as airway disorders, chronic headaches, back pain, diabetes, paralysis, infection, inflammation, hypertension, and digestive tract problems. It is also applied topically to blisters, nasal abscesses, orchitis, eczema, and swollen joints (Yimer et al., 2019).

## **2. Methods**

Searching on "PubMed" database for the Keyword *Nigella sativa* gives 1,524 results, and searching with the keyword *Nigella sativa*, Parasitic disease results in 30 results and most of these searches are cited in this review.

## **3. Discussion and results**

### **Parasitic disease**

The cause of the parasitic disease is the infection by parasites (a eukaryotic microorganism) living in or on the host (another organism). Parasites of humans are divided into two groups: Endoparasite (inside the host) and Ectoparasite (on the skin). Endoparasites include protozoa usually single cell and Helminths they are multicellular (Paniker, 2013).

Humans become infected either directly through ingestion of contaminated food or water, or passively through vector bites. Parasitic diseases are ubiquitous throughout the world, especially in developing nations, causing around 3 billion human infections. The infection's major risk factors include parasite pathogenicity, host immunity, the environment, and social settings (Paniker, 2013).

Chemotherapy is necessary for clinical management and disease control; however, drug resistance has emerged in some parasites; in addition, high costs, poor compliance, and side effects encourage researchers to develop drugs that are safer and less toxic; thus, more interest has been placed on herbal remedies such as black seeds.

All information regarding the parasite and sickness is based on this references (Paniker, 2013).

### **Effect of *N. sativa* on Protozoa parasite**

Protozoal parasite divided in Four groups depending on the locomotion organs, this include: amoeba, Flagellates, Sporozoa and Ciliates.

#### ***Acanthamoeba* Species**

This type of *Entamoeba* is Opportunistic free-living, Parasite exists in active trophozoite and resistant cyst, humans get infection by inhalation of cyst or trophozoite, ingestion of cysts, or through traumatized skin or eyes. The parasite can produce granulomatous amoebic encephalitis (GAE) or *Acanthamoeba* keratitis (AK), an infection of the eye that typically occurs in healthy persons and develops from the entry of the amoebic cyst through abrasions on the cornea. The development of resistance and failure of the currently used drugs represent a therapeutic predicament. Using the aqueous extract of the black seed and chitosan nanoparticles against experimentally induced AK, on the 5<sup>th</sup> day post infection the medications were applied, on 10<sup>th</sup> day clinical examination of the cornea and cultivation of the corneal scraps indicate a 100 % cure, followed in the 15<sup>th</sup> and 20<sup>th</sup> day the result of these agents (singly or combined) show potential for the development of new, effective, and safe therapeutic alternatives (Elkadery et al., 2019).

Another search, study the *in vitro* effect of Thymoquinone of *Nigella sativa* on two important parasitic diseases that transmitted through the oral-faecal route to humans. The parasites are *Entamoeba histolytica* and *Giardia lamblia*, these diseases causing diarrhoea leading to anaemia and malabsorption. The result indicates that Thymoquinone is more potent against *E. histolytica* than *G. lamblia* (Sheikh et al., 2016).

Flagellates are a group of parasite moving by Flagellate, they includes *Leishmainaspp.*, *Trypanosomaspp.*, *Trichomonas spp.* and *Giardia lamblia*.

All members of the genus *Leishmania* are obligate intracellular parasites that pass their life cycle in 2 hosts – the mammalian host and the insect vector (female sandfly). Parasite inside the macrophage of the human appears as Amastigote and inside the vector as promastigote. The disease common in tropic and subtropic area, and occur in three forms: Cutaneous form (usually self-healing disease), Visceral form and mucocutaneous (usually danger and need treatment). Mahmoudvand et al. (2015), mentioned that the Antileishmanial effects of essential oil and methanolic extract of *Nigella sativa* (0-200 µg/mL) and thymoquinone (0-25 µg/mL) on promastigotes of *Leishmania tropica* and *L. infantum* and their cytotoxicity activities against murine macrophages using the MTT assay at 24, 48, and 72 h. and leishmanicidal effects against amastigotes were investigated in a macrophage model, for 48 and 72 h., the result showed a potent leishmanicidal activity of thymoquinone, against both species with an *in vitro* model (Mahmoudvand et al., 2015). Abamor and Allahverdiyev (2016) investigate the antileishmanial activities of *Nigella sativa* oil (NSO) entrapped poly-ε-caprolactone (PCL) nanoparticles on *Leishmania infantum* promastigotes and amastigotes *in vitro*. This process was characterized by scanning electron microscope, dynamic light scattering, Fourier transform infrared, encapsulation efficiency measurements, and release profile evaluations. The PCL nanoparticles released approximately 85 % of entrapped oil molecules after incubation for 288 h. All investigated formulations demonstrated strong antileishmanial effects on *L. infantum* promastigotes. The tested formulations decreased infection indexes of macrophages in a range between 2.4 – and 4.1-fold, in contrast, to control, thus indicating the strong anti-amastigote activities of NSO encapsulated PCL nanoparticles. immunomodulatory effects of NSO-loaded PCL nanoparticles showed an increase in nitric oxide produced amounts within macrophages by 2-3.5-fold in contrast to use of free oil.

Trichomoniasis is the most common sexually transmitted disease caused by the trophozoite of *Trichomonas vaginalis*. The Metronidazole is the best drug for treatment, recently there are reports about drug – resistant so medicinal plants could be a source of new antiprotozoal drugs such as *Nigella sativa* alcoholic extract and oil, as well as *Phaseolus vulgaris*. Aminou et al. (2016) study the *in vitro* activity on the ultrastructure of the parasite in comparison to metronidazole. Both *Nigella sativa* oil and *P. vulgaris* lectin showed ahigh toxic effect on parasite structure, while the effect of *Nigella sativa* alcoholic extract was moderate. This agreement with another result the inhibitory effect of aqueous extract of *N sativa* is dose depended and had a low effect on the parasite growth (Tonkal, 2009).

The fourth group of protozoa is Sporozoa, this group include Malaria, *Toxoplasma gondii*, *Cryptosporidium spp.* and others. All causes serious diseases in human.

Using albino mice infected with *Plasmodium voelli*, and Chloroquine (CQ) as drug in the control group. The antimalarial and antioxidant activities of methanolic extract of *N. sativa* seeds (MENS) were investigated (Okeola et al., 2011). The extract significantly ( $p < 0.05$ ) suppressed the infection in the mice by 94 %, while CQ, the reference drug, produced 86 % suppression when compared to the untreated group after the fifth day of treatment. These results suggest that *N. sativa* seeds have a strong antioxidant property and, maybe a good Phyto therapeutic agent against malaria infection.

Two different isolates of *Blastocystis hominis* were treated with the aqueous extract of *Nigella sativa* then evaluated and compared with metronidazole as active standard drug. *Nigella sativa* at 500 µg/ml concentration has a significant inhibitory effect on both isolates. So, it is considered as the most active concentration of *Nigella* aqueous extract (El Wakil, 2007). The same result of the concentration of 500 mg/of *N. sativa* aqueous extract was improved in another study (Eida et al., 2016).

Toxoplasmosis is an asymptomatic disease in an immunocompetent person, while in immunocompromised causes dangerous complications and in the fetus if it transmitted vertically. The disease is treated by Pyrimethamine which is intolerable by many patients. Mady et al. (2016) assess the therapeutic effects of *Nigella sativa* oil (NSO) alone and combined with pyrimethamine (PYR) compared to a combination of clindamycin (CLN) and (PYR) on one hundred albino mice. Impression smears from the liver and spleen, and histopathological and ultrastructural studies were done. Liver malondialdehyde (MDA) level and total antioxidant capacity (TAC) were determined. Interferon- $\gamma$  and specific IgM were also measured in sera by ELISA. The result showed the combination of NSO with PYR had a potent effect (Synergistic), whereas NSO alone has no direct anti-*Toxoplasma* effect.

#### **Effect of *N. sativa* on Helminth parasite.**

The helminthic parasites are multicellular organisms. Helminths, which occur as parasites in humans belong to 2 phyla (Paniker, 2013):

- Phylum Platyhelminthes. It includes 2 classes: Cestoda (tapeworms) and Trematoda (Flukes or digeneans);
- Phylum Nematelminthes (Nematoda). It includes class Nematoda and 2 subclasses: Adenophorea (Aphasmidia) and Secernentea (Phasmidia).

Helminth parasites causing important and serious diseases like Schistosomiasis, Hydatid diseases, Filariasis and so on.

Dog tapeworm or hydatid cysts caused by a cestode worm *Echinococcus granulosus* and *E. multigularus*, The disease is prevalent in most parts of the world, though it is most extensive in the sheep and cattle raising areas of Australia, Africa, and South America. It is also common in Europe, China, and the Middle. The adult worm lives in the digestive system of dogs and other canine carnivora (wolf and fox). While the larval stage (hydatid cyst) is found in humans and herbivores animals (sheep, goat, cattle and horse). Traditionally surgical removal was considered as the best mode of treatment of cysts or giving drugs in conjunction before surgery to kill protoscolices, to avoid anaphylactic shock from leakage of hydatid fluid into the peritoneum and to decrease opportunities for recurrences.

El-Baby et al. (2019) studied the scolical efficacy of hydroalcoholic extract of *Punica granatum* peel and *Nigella sativa* on the protoscolices of CE that collected from infected camels. *N. sativa* showed the highest scolical efficacy at 100 mg/mL and 10 mg/mL concentrations after 30 and 60 min, they concluded that *N. sativa* extract is more potent than *P. granatum* peel extract regarding scolical effect.

Another study, evaluate the in vitro scolical effect of *Ni. sativa* essential oil and also its active principle, thymoquinone, against protoscolices of hydatid cysts (aseptically) aspirated from livers of infected sheep . The results also indicated the potential of *N. sativa* as a natural source for production of a new scolical agent for use in hydatid cyst surgery (Mahmoudvand et al., 2014).

Schistosomiasis is a water-borne disease constituting an important public health problem. It is estimated that over 100 million people are infected with *Schistosoma. haematobium*, *S. mansoni*, and *S. japonicum*. Praziquantel is the drug of choice but the evolving of drug-resistant



by the parasite reduces the effectiveness of this traditional drug. Medhat et al. (2016) studied the effect of two natural products, *Nigella sativa* oil and *Chroococcus turgidus* (separately or in a combination) to explore their effect on *S. mansoni* in infected mice. They concluded that both extract are promising natural compounds that can be used in fighting schistosomiasis. Similar results obtained by Ali et al. (2016).

The antiparasitic effect of *Nigella sativa* on different Helminth infections (Alone or with another plant extract) was studied like *Hymenolepis nana* in mice (Ayaz et al., 2007). *Fasciola gigantica* is economically important global disease of ruminants in the temperate and tropical (Uiih et al., 2017), *Trichinella spiralis* in the experimentally infected rat (EL Ezz, 2005), *Toxocara canis* (Mussa et al., 2011). All results confirmed the powerful of *N. sativa* on both protozoa and helminths, and that the effect is dose and time dependent. Other possible explanations are that plant extracts have an effect on Bacteria or fungi, which have a symbiotic relationship with the parasite, and that several studies have also shown that *N. sativa* has an anti-bacterial and anti-fungal effect (Salem et al., 2010; Azeiz et al., 2013).

### 3. Conclusion

Finally, we can conclude that the black seed is achieving positive results in the treatment and control of parasitic diseases, but still more research is required at the cellular and molecular level to assess the specific mechanisms or effects of the plant. There is indeed a need for further research with large samples, across a longer period of time, and to study the potential side effects for a long time. Investigate several factors that may affect plant quality, such as soil, environmental conditions (temperature, humidity), and extraction technique.

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