



Black Seed (*Nigella sativa*) As Antimicrobial Drug: A Mini-Review

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Abstract

In the last decades, the antibiotics-resistance phenomenon has become a global health crisis, due to the rapid emergence of multi-drug resistant pathogens. Novel approaches in designing drugs able to overcome these resistant microbes are persistent need. With the suggestion of looking at nature for solutions, exploring medicinal plants may lead to develop new antimicrobial drugs. Seeds of *Nigella sativa* are mentioned and used since ancient great civilizations and until now in many regions as a part of their traditional health care systems. This mini-review highlights the potential use of this distinguished plant product as an effective antimicrobial drug.

Keywords: *Nigella sativa*; Antibacterial; Antifungal; Antiviral; Antibiotics resistance

Abbreviations: HCV: Hepatitis C virus; CER: Chicken Embryo Rough Cells; MCMV: Murine cytomegalovirus; ILTV: Laryngotrachietis Virus

Introduction

Undoubtedly, antibiotics, the marvelous drugs of the 20th century, have successively reduced the human mortality and morbidity during their golden period (from 1950s to 1970s) [1]. However, pathogens have gradually developed resistance to these miracle drugs. Recently, the antibiotics resistance has become a serious global health concern, with a huge economic burden on the community by increasing the cost of the treatment and raises the rates of hospitalization, particularly in the developing countries which already suffers from economic crises, poor sanitation and misuse of antibiotic drugs [2]. So far, it turns out that the development of new antibiotics, which are costly and time-consuming process, has become useless, as pathogens rapidly develop resistance to these new antibiotics. This has led to an increasing interest in searching for effective alternatives for the current antibiotics with different mode of action on microbes. Hence, medicinal plants appeared to be the best alternative source for new antimicrobial drugs [3]. In literature, numerous studies reported that some plant's photochemical compounds have potent antimicrobial activity, such as Phenolics, flavonoids, alkaloids, terpenoids, saponins, tannins, anthraquinones, among others; which may kill the bacteria or fungal cells by inhibiting the growth, affect on cellular membrane permeability, interference with some metabolic processes and modulating the signal transduction or gene expression [4]. Accordingly, with the urgent need for new

antimicrobial drugs, the efforts toward innovate new antibiotics must behaves different approaches and get benefit from the hidden treasures of medicinal plants. A plethora of scientific research has been published on the bioactivity and medicinal properties of the seeds of *Nigella sativa*, This mini-review highlights the significance of this plant product as an alternative and promising source for new antimicrobial drugs.

Seeds of *Nigella sativa*



Figure 1: Seeds of *Nigella sativa*.
Source: https://en.wikipedia.org/wiki/Nigella_sativa

Nigella sativa Linn., is an annual herbaceous plant, belong to family Ranunculaceae, it is grown in many parts of the world,

particularly the Mediterranean region, North Africa, Middle East and some parts of Asia [5]. The seeds of *Nigella sativa* (Figure 1) are known as black seed or black cumin (English), black-caraway seeds (US), Al-habba Al-sawda (Arabic), shonaiz (Persian), kalonji (India and Pakistan), kalajira (Bangladesh) and krishnajirika (Southeast Asia) [6]. Seeds of *Nigella sativa* are initially considered as spices, it has a distinctive aroma and taste and used in some bread recopies in some regions such as Pakistan [7].

Interestingly, these tiny seeds are rich in bioactive compounds. In general, it contains about 32-40% fixed oils, 0.4-0.45% volatile oil 8-9 types of essential amino acids beside some vitamins, and carbohydrates [8]. In addition, some interesting derivatives of alkaloids, steroids, saponins, terpenes, monoterpenes and phenolic compounds were isolated from the black seed [5]. Among these pure compounds of pharmacological benefits isolated from the black seed are nigellicine, nigellicimine, nigellicimine N-oxide, carvone, thymoquinone, thymol and many more [9]. The wealth, complex, and diverse chemical compounds involved in the seeds of *Nigella sativa* may provide exceptional opportunity for development and innovation of new health-promoting medication including antimicrobial drugs.

Black seed in traditional medicine and current studies

Table 1: Some investigated therapeutic properties of the seeds of *Nigella sativa*.

Therapeutic potential studied	Reference
Antioxidant and anti-arthritis	Umar [13]
Anti-diabetic	Salama [14]
Anticancer	Salem [15]
Anti-inflammatory and analgesic	Alemi [16]
anti-anxiety	Perveen [17]
In treatment of different respiratory diseases	Wienkotter [18]
Hepato-protective	Yildiz [19]
Nephroprotective	Abul-Nasr [20]
Anti-gastric ulcers (Gastro-protective)	Magdy [21]
Immunomodulatory	Majdalawieh [22]

The black seed is well known since the ancient civilizations such as ancient Egyptian and Greek to promote menstruation and increase milk production beside its use to treat headache, toothache, nasal congestion and many more [10]. It is also famous drug from the Islamic civilization and well known in the Islamic heritage, in what is called Prophetic medicine, as Muslims believe that the black seed is an effective remedy for all diseases except death, based on some Prophetic statements (Haddith) in the Islamic religion. Ibn Sina (Avicenna) mentioned the black in his distinguished book "Al-Kanon fit-tib" or the canon of medicine, he prescribed it to stimulate the body's energy and for treatment of fatigue and dispiritedness [11]. Black seed also prescribed in the Indian traditional system of medicine (Ayurveda and Siddha) which used to treat jaundice, fever,

dyspepsia, paralysis, piles, and skin diseases [9]. It is also widely used in different traditional health systems as antihypertensive, appetite stimulant, analgesic, anthelmintic, liver tonic, diuretic, and anti-diarrheal [12]. On the other side, huge number of studies has been carried out revealing the medicinal, pharmacological, and therapeutic properties of the seeds of *Nigella sativa* and a wide spectrum of its curative power have been explored. Table 1 pointing to some of these findings.

Black seed as antibacterial agent

A large number of scientific articles refers to the antibacterial activity of the black seed have been published in journals of PubMed/Medline, Science Direct, Scopus and Google Scholar; and many publishers. In summary, Oils extracted from showed significant antibacterial effect against multidrug-resistant *Staphylococcus aureus* isolated from wounded diabetic patients from Southeast Nigeria [23]. Oil of *Nigella sativa* revealed effective antibacterial activity against considerable number of methicillin resistant and coagulase negative *Staphylococcus aureus*, safety of that oil was examined, and there was no cytotoxic influence on the proliferation of gingival fibroblasts [24]. The black seed oil was recommended to be used as an antimicrobial agent in food production to prevent spoilage. Based on the results that showed that this oil at 2.0% concentration was able to inhibit the growth of twenty-four pathogenic, spoilage and lactic acid bacteria [25]. Ethanol and n-hexane extracts of the black seeds recorded remarkable dose dependant antibacterial effects against different gram-positive and gram-negative strains, namely *Bacillus cereus*, *Bacillus subtilis*, *Escherichia coli*, *Staphylococcus epidermidis*, *Klebsiella pneumonia* and *Salmonella typhimurium*. However, no antibacterial activity detected against *Pseudomonas aeruginosa* and *Enterobacter aerogens* [26]. The black cumin seeds exhibited antibacterial activity against *Salmonella typhi* [27]. Methanol and water extract of the black seed reported remarkable antibacterial efficacy towards *Streptococcus pyogenes*, *Pseudomonas aeruginosa*, *Klebsiella pneumonia*, and *Proteus vulgaris*, the greater antibacterial effect was against the gram-positive bacteria [28]. An active principle isolated from seeds of *Nigella sativa* called thymoquinone showed a broad spectrum of activity against different gram-positive and gram-negative bacteria, namely *Bacillus cereus* ATCC 14579, *Listeria monocytogene* ATCC 19115, *Enterococcus faecalis* ATCC 29212, *Micrococcus luteus* NCIMB 8166, *Staphylococcus aureus* ATCC 25923, *Staphylococcus epidermidis* CIP 106510, *Pseudomonas aeruginosa* ATCC 27853, *Escherichia coli* ATCC 35218 *Salmonella enteric*, serovar typhimurium ATCC 14028, *Vibrio liginolyticus* ATCC 33787 and *Vibrio paraheamolyticus* ATCC 17802, thymoquinone was able to prevent bacterial biofilm formation [29]. The potential antibacterial activity of the black seed was also evaluated in-vivo, a groups of male mice were infected with *Staphylococcus aureus* and *Escherichia coli*, and subjected to varied doses of methanol, chloroform and essential oil of the black seed. All extracts and oil revealed significant

dose dependant antibacterial effects compared with the positive control group which administered gentamicin [5].

Black seed as antifungal agent

A research was conducted to evaluate the potential antifungal effects of different black seed oils on twenty fungi including pathogenic and industrial strains. All oils exhibited varied remarkable degrees of antifungal activity; however, the essential oil was the most influential [30]. A moderate inhibitory effect were recorded with some components of the black seed, oils and extracts *in vivo* and *in vitro* against some pathogenic yeasts like *Candida albicans*, dermatophytes, non-dermatophytes and some aflatoxin producing fungi [31]. Interestingly, *Nigella sativa* seeds exhibited high inhibitory effect against candidiasis in mice *in vivo*, showing 5-fold decrease in *Candida albicans* counts in kidneys, 8-fold in liver and 11-fold in spleen [32]. Thymoquinone that isolated from *Nigella sativa* revealed high antifungal activity against *Aspergillus niger*, *Fusarium solani* and *Scopnlariopsis brevicaulis*; and this activity was comparable to the antifungal drug amphotericin-B [33]. The methanol and ethanol extracts of the black cumin seeds displayed potent inhibition of *Aspergillus flavus*, *Aspergillus fumigates*, *Issatchenkia orientalis*, *Cryptococcus laurentii*, *Cryptococcus albidus*, *Candida parapsilosis*, *Candida albicans* and *Candida tropicalis*, and these extracts were more potent than the standard drug Amphotericin-B [34]. Two novel defensins peptides (Small cysteine-rich cationic proteins) named Ns-D1 and Ns-D2 were isolated and sequenced from the black seed, these defensins peptides revealed high and divergent antifungal activity [35].

Black seed as antiviral agent

Unlike antibacterial medicines, the available anti-viral drugs are less, narrow in spectrum and have limited efficiency. In an interesting study, *Nigella sativa* oil was administered to infected mice with a DNA-virus with host specificity for mice named "Murine cytomegalovirus (MCMV)". Strikingly, the black seed oil showed complete inhibition of the virus titer s in spleen and liver on day 3 of infection, while MCMV virus was detectable in control mice [36]. *Nigella sativa* seeds have suppressed significantly the pathogenicity of influenza virus (H9N2) in turkey poultry and it enhanced the immune responsiveness as well [37]. It was published that, the black seed recorded good antiviral effects when used against Laryngotrachietis Virus (ILTV) at concentration of 35µM using Chicken Embryo Rough Cells (CER) [38]. In a clinical study conducted on Egyptian patients infected with Hepatitis C virus (HCV), including some diabetic and HCV-positive patients who were not eligible for IFN/ribavirin therapy, there were administered with *Nigella sativa* for up to 3 months at a dose of (450mg three times daily). After treatment period, patients relatively revealed varied recovery and decrease in viral load, improvement in the oxidative stress, clinical condition, and glycemic control in diabetic patients [39]. A surprising case study reported that, an adult person diagnosed as HIV-positive, was subjected to treatment with *Nigella sativa* or up to 6 months

(Dose 10ml twice a day), when repeated "EIA Western Bolt" test on day 187th of treatment, the result as sero-negaive, the test was repeated several times and it was confirmed as sero-negative, which confirmed potency of this plant product as anti-HIV agent [40].

Conclusion

Referring to the vast amount of data in the scientific literature, there are many evidences indicate that the black seed has effective antimicrobial properties against many bacteria, fungi, and viruses and are relatively safe drug with long remarkable history in traditional medicine; it was also more potent than many standard anti-microbial drugs. It is recommended to design and develop novel antimicrobial drugs from *Nigella sativa* seeds, To do so, the mechanism and mode of action of the black seed on the microbial cell (Prokaryotic or eukaryotic) and viruses must be well understood, applying new technologies such as nanotechnology may help to reach that goal. The international health authorities must stimulate research and innovation in such promising plant product. Countries and governments are required to provide more financial support and launch research programs for developing new antimicrobial drugs. The Major pharmaceutical industries should change its attitude and strategy and invest in natural products of potent antimicrobial effects. Implement these recommendations could lead to tackle this global threat.

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