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A REVIEW ON ANTIVIRAL EFFECTS OF *NIGELLA SATIVA* L.

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Abstract

Nigella sativa seeds have wide therapeutic effects and have been reported to have significant effects against many ailments such as skin diseases, jaundice, gastrointestinal problems, anorexia, conjunctivitis, dyspepsia, rheumatism, diabetes, hypertension, intrinsic hemorrhage, paralysis, amenorrhea, anorexia, asthma, cough, bronchitis, headache, fever, influenza and eczema. Thymoquinone (TQ) is one of the most active constituent and has different beneficial properties. Focus on antimicrobial effects, different extracts of *N. sativa* as well as TQ, have a broad antimicrobial spectrum, including Gram-negative, Gram-positive bacteria, viruses, parasites, schist soma and fungi. The effectiveness of *N. sativa* seeds and TQ is variable and depends on species of target microorganisms. The present review paper tries to describe some antiviral activities of *N. sativa*. Such as murine cytomegalo virus infection, avian influenza (H9N2), Chistosoma Mansoni Infection, PPR virus, Broad bean mosaic virus, HIV virus, Hepatitis C Virus, Zucchini Yellow Mosaic Virus, and Papaya Ring Spot Virus.

Keywords: *Nigella sativa; antiviral effects; HIV; thymoquinone*

Introduction

Nigella sativa, a dicotyledon of the Ranunculaceae family, has been employed for thousands of years as a spice and food preservative, as well as a protective and curative remedy for numerous disorders, and is known to have many medicinal properties in traditional medicine (Chopra et al., 1956, Nadkarni et al., 1976). It is the black seed referred to by the prophet Mohammed (PBUH) as having healing powers. Black seed is also identified as the curative black cumin in the Holy Bible, and is described as the Melanthion of Hippocrates and Discroides and as the Gith of Pliny (Attar-ur-Rahman et al.,1985).

Most of studies on biological effect of *N. sativa* have dealt with its crude extracts in different solvents, however, some studies used its active principles. Haq et al. (1999) fractionated whole *N. sativa* seeds using SDS-PAGE, which showed a number of protein bands ranging from 94 to 10 kDa molecular mass. Quinones thymoquinone and dithymoquinone are also important constituents of *N. sativa* (Daba et al.,1998; Nagi et al.,1999).

N. sativa has been reported to have various biological activities (Islam et al., 2019). It exhibited antioxidant properties by suppressing chemiluminescence (Daba et al., 1998; Nagi et al.,1999). Black seed preparations have also demonstrated significant *in vivo* antineoplastic activity against Erlich ascites carcinoma (Worthen et al.,1998), and *in vitro* against murine Dalton's ascites lymphoma and sarcoma, and human pancreatic adenocarcinoma, uterine sarcoma and leukemic cell lines (Salomi et al., 1991). The active components of black seed also showed antihel-minthic effects against nematodes, cestodes, tapeworms and earthworms (Agarwal et al.,1979; Akhtar et al., 1991). Extracts of *N. sativa* also showed antimicrobial activity against *Escherichia coli, Bacillus subtitles, Streptococcus faecalis, Staphylococcus aureus, Pseudomonas aeruginosa* and the pathogenic yeast *Candida albicans* (Saxena et al.,1986; Hanafy et al.,1991). Black seed has also been evaluated in clinical and animal studies for its choleretic and cytotoxic action (Mahfouz et al., 1962; Tennekoon et al., 1991).

In this review, we have sketched a current scnario on the anti-viral effects of *N. sativa* and its derived compounds on the basis of database information.

Methods

An up to date (May 2019) search was made in the following databases: PubMed, Science direct and google scholar with the key word 'Nigella sativa' and/or 'Virus' and 'Anti-virus effect'.

Findings

N. sativa against murine cytomegalovirus infection

N. sativa oil was found to act against murine cytomegalovirus (Messerle et al., 1992; Reynolds et al., 1993; Smith et al., 1994). In another study, *N. sativa* oil was also found to act against cytomegalovirus, where an increase in macrophage number and function, and interferon gamma (IFN-γ) production was also reported (Salem et al., 2000).

N. sativa against avian influenza (H9N2)

Avian influenza virus (AIV) subtype H9N2 is becoming a serious threat to poultry birds. H9N2 AIV is an emerging respiratory problem, isolated from different birds from a number of countries and has been reported to have zoonotic potential (Swayne, 2012; Ahad et al., 2013; Umar et al., 2016a,b). Currently, the feed industry is focusing on various substitutes for antimicrobial drugs (Al-Mufarrej, 2014). Antimicrobial agents of plant origin, such as essential oils, plant extracts, and complete plant substances are considered as alternatives to the traditional antimicrobial feed additives. *N. sativa* oil is one of such alternatives that could be used as feed additives in order to reduce the pathogen load in poultry. Thymoquinone (TQ) has been found as the main bioactive constituent of the volatile oil of *N. sativa* seeds. In a study, *N. sativa* was found to exert an anti-influenza virus activity (Umar et al., 2016).

N. sativa against PPR virus

Peste des petits ruminants (PPR), is an acute, highly contagious and economically important transboundary viral disease of sheep and goats associated with high morbidity and mortality (Balamurugan et al., 2014). It is caused by PPR virus, a morbillivirus of the Paramyxoviridae family. Disease severity depends on species infected, breed

or virus strain (Wernike et al., 2014). As PPR is a viral disease, there exists no particular treatment for the disease and post-exposure therapeutic approaches for infection are not described much in the literature (Balamurugan et al., 2014). Numerous studies report the use of *N. sativa* as liver tonics, anti-diarrheal, analgesics, and anti-bacterial. Extensive studies on the herb have explored a wide spectrum of its pharmacological actions, including immunomodulatory, antimicrobial and antiinflammatory, properties, etc. Because of its miraculous power of healing, *N. sativa* has got the place among the top ranked evidence based herbal medicines (Ahmad et al., 2013). Current story describes the immunomodulatory and therapeutic effect of this herb against the PPR virus in experimentally infected goats. *N. sativa* prevented the occurrence of clinical signs and significant decrease in clinical signs, gross and histopathological abnormalities.

N. sativa against broad bean mosaic virus

Broad bean (*Vicia faba* L.) is one of the major legumes crops. Broad bean mottle disease is one of the world's main virus diseases in broad bean producing areas. Broad bean mottle virus (BBMV) has spread worldwide wherever broad bean plants are grown. Broad bean mottle virus (BBMV) was classified as a member of the bromovirus group (Hashim and El-Kiey, 1962; El-Alfy et al., 1975). *N. sativa* is also found to act against MCMV (Nafez et al., 2009; Mehdi et al., 2010).

N. sativa against human immunodificency virus (HIV)

Since 1980's when the human immunodeficiency virus (HIV) was isolated from patients with opportunistic infections and Kaposi sarcoma, there aremillions of people living with this dreadful virus (Barre-Sinoussi et al, 1983; Gallo et al, 1983; UNAIDS, 2010). It was estimated that no infectious organism has claimed more lives in history than HIV (UNAIDS, 2010). Although the prevalence of HIV infection is reducing globally, many factors had been associated with this gain. The advent of highly active antiretroviral therapy (HAART) and vigorous campaign on sexual behavior considerably have reduced the loss of lives to HIV infection. However, HIV infection is still believed to be incurable and can only be managed with HAART. *N. sativa* was found to act against HIV in a number of reports (Onifade 2011,2012,2013).

N. sativa against hepatities C virus

Acute hepatitis C virus (HCV) infection is rarely associated with life-threatening disease, with 15–45% of infected persons recovering within 6 months without any treatment (WHO, 2015). However, chronic infection develops in the remaining 55-85% out of which 15-30% eventually progress to liver cirrhosis after many years of persistent virus carriage. Persistent HCV infection has been a major risk factor for hepatocellular carcinoma (HCC) development (about 2-6% per year) in patients with cirrhosis, mainly through indirect pathways, which include chronic inflammation, cell death, cell proliferation, and induction of free radicals (Sangiovanni et al., 2004; Farinati et al., 2007). Treatment of hepatitis C for virus eradication and non-progression to decompensated liver diseases is achievable and highly recommended for all with chronic infection. The recovery rate however is determined by the strain of the infecting virus, the type of treatment and its early institution (WHO, 2015). An earlier treatment for hepatitis C which combined interferon and ribavirin effectively resolved the infection leading to a cure in 50% of the treated individuals; though frequently associated with life threatening adverse reactions (WHO, 2015). *N. sativa* was found to act against HCV (Olufunmilayo et al., 2016).

N. sativa against Zucchini yellow mosaic virus

Watermelon (*Citrullus lanatus* L.; family Cucurbitaceae) crop is infected by a dozen of viruses of which Zucchini yellow mosaic virus (ZYMV) that belongs to the genus Potyvirus (family: Potyviridae), is regarded as one of the most destructive viruses. Watermelon infected plants exhibit symptoms that vary from mild to server mosaic, mottling and bubbling followed by leaf deformation and blister (Lisa et al.,1984). ZYMV has a positive single-stranded RNA and flexuous filamentous particles. The antiviral activity of the products including plant extracts, and synthetic chemicals is connected to their components which may act directly by interaction with virus particles in the early stage of infection and block the liberation of its nucleic acid

that could finally lead to stopping the virus multiplication (Abdel-Shafi et al., 2013). Nigella decoction was found to act against ZYMV (Essam et al., 2017).

***N. sativa* against Newcastle disease virus**

Newcastle disease virus (NDV) has different strains *viz*, lentogenic less virulent, velogenic and intermediate virulent mesogenic. The disease has high morbidity and mortality with marked decrease in eggs production in laying birds (Alexander, 2000). *N. sativa* is also found to act against NDV (Al-Garib et al., 2003). The velogenic NDV strains kill the embryo within 48 hours, while lentogenic take 5 to 7 days to affect the embryos (Lam et al., 1995). The active component is crystalline nigellone and thymoquinone that has potent anti-bacterial, anti-inflammatory immune stimulator, anti-parasitic, anti-histamine and anti-hypertensive are the main effects of these seeds (Sultan et al., 2009; Umar et al., 2017). The antiviral drug Ribavirin is well known for the treatment of different diseases like hepatitis. But high dosage produced different types of organ toxicity and was also one the causes of death. Ethanolic extract of the *N. sativa* is markedly effective against NDV in term of decreased viral load and mortality in embryonated chicken eggs (Khan et al., 2017).

In summary, *N. sativa* and its derived compounds have been seen to act against a number of human, animals, birds and plant pathogenic viruses. *N. sativa* may be one of the best sources of anti-viral drugs.

Conflict of Interest

None declared.

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