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Clinical efficiency of *Nigella sativa* Linn in novel COVID-19: A review study

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Abstract

Objective: To evaluate the efficiency of *N. sativa* in prevention and management of COVID-19.

Background: A novel SARS-CoV-2 which is a severe acute respiratory syndrome, was acknowledged as SARS endemic, started in Asia, with the common of cases occurring in China and the Asia-Pacific countries. According to Ministry of Health and Family Welfare, GOI, since the outbreak, of COVID-19 global pandemic, on March 11, 2020, presently at the end of September 2020, total 940441 cases were active and 5187825 cases were cured, and 97497 were dead. Hence counting the number of cases, including mild cases, is necessary to standardize the epidemic response.

Most drug designs against 2019-nCoV have been focused on immunomodulators (such as corticosteroids and interferons), monoclonal antibody production, and inhibitory agents against viral proteinase, helicase, and polymerases. However, to date, few specific antiviral treatment or vaccine has been approved by the FDA for COVID-19, but not hundred percent effectiveness has been achieved.

Considering the success of AYUSH systems in managing several epidemics and restoring health, AYUSH system recommends some herbs for the treatment of COVID-19. Among them *Nigella sativa* is one which is Known by the common name "black cumin" is a medicinal plant from the Ranunculaceae family.

After an wide-ranging literature review it can be concluded that *N. sativa* and its main constituent's, Thymoquinolol can be used in cases of covid-19 and its complications, due to its anti-inflammatory, antihypertensive, antiatherogenic, antihyperlipidemic, antimicrobial, bronchodilator, Hypotensive, antibacterial and hypoglycemic, Gastroprotective and cardio protective effects.

Keywords: *Nigella sativa* Linn, Covid-19, anti inflammatory, antihypertensive, antimicrobial, bronchodilator, antiatherogenic

Introduction

During the first half of the 20th century, modern medicine has made a incredible evolution in curing and controlling numerous chronic and acute ailments all over the sphere. Currently some of those infections namely malaria, plague and smallpox supposed to have been wiped out are now resurfacing with augmented strength. At the same time, certain new and more deadly diseases are emerging. I.e. COVID-19. Rapid economic progression and consequent suburbanization are wreaking another set of stress environment & behavior related maladies.

Background

an outbreak of pneumonia with unknown origin, commenced in China's Hubei Province, In December 2019, hovering global health alarms due to the deftness of easy transmission and afterwards with the help of abundant studies, a novel severe acute respiratory syndrome corona virus 2 (SARS-CoV-2) was identified as the cause of the disease, and the disease was named "coronavirus-19" (COVID-19) by Chinese Scientists ^[1].

SARS-CoV-2 epidemic originate in Asia, specifically with the preponderance of cases arising in China and the Asia-Pacific region. Henceforth counting the number of cases, including mild cases, is necessary to calibrate the epidemic response ^[2].

It's been estimated that every one of five folks globally could be at greater than before risk of severe COVID-19 disease if they become infected, due to comorbid health conditions ^[3].

Subsequently high-risk or moderate-risk exposure to Covid-19, hydroxychloroquine did not inhibit ailment companionable with Covid-19 or confirmed infection when used as post exposure prophylaxis within 4 days after exposure. To date, no any perfect medication has been revealed that can thwart SARS-CoV-2 spread ^[4].

Quite a few drugs ^[5], like ribavirin, interferon, lopinavir-ritonavir, corticosteroids, remdisvir, tocilizumab etc have been used in patients with SARS or MERS and now for covid 19;

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although the efficacy is poorly understood as a gold standard randomized clinical trial has not been conducted [5]. Archaeologically, plant life have often been designated for drug development and procurement programmes for the reason that they encompass specific classes of chemical and physical compounds, like alkaloids and terpenoids, which are recognized to be biologically active, or because of their customary therapeutic usages [6]. In many constituencies of the sphere, populaces stagnantly rely on traditional plant-based medicines for their primary healthcare or ailments. Particularly in many rural communities of Africa, Asia, and America, information of vegetation and plant life are feasible and inexpensive as a part of their tradition. Foliage with well-known remedial practices has been a foundation of dynamic therapeutic preparations for the management of many diseases. For example, artemisinin (discovered in *Artemisia annua*) and quinine (from *Cinchona officinalis*), together with their synthetic analogues, remain among the most important weapons in our arsenal against malaria [6].

The ICMR efforts assume special significance in the light of multifaceted use of medicinal plants, and the need of better drugs and remedies for various diseases [7]. Moreover, the ethnic system of medicine, and the herbal drugs, could potentially work together to provide both concepts of therapy, as well as healing agents in the extents, where modern system of medicines has few answers. These ingenuities are also in courtesy of the World Health Organization promoting herbal medications as effective alternate system of therapy in the form of phytomedicines or herbal drugs or herbal drug preparations or herbal medicinal products [7]. W.H.O Expert Committee has recommended that traditional medicinal herbs be further investigated [7]. These herbal remedies are in different physical form like powders, extracts, concentrates, decoctions, emulsions, oils, ointments, and creams will be a sure Panacea for many disorders. Hence there is a need to evaluate the effects of these herbs in infectious diseases too [7].

AYUSH (Ayurveda, Siddha, Unani, and Homeopathy) are Indian medicinal systems that use natural medicines of plant, animal, and mineral origin for management of diseases. Currently in this pandemic, AYUSH has endorsed that the Homeopathy, Unani and Ayurveda system therapies has potential as immune-boosters to avert and treat COVID-19. Bearing in mind the success of AYUSH systems in managing numerous epidemics and reinstating well-being, AYUSH commends certain preparations including Chyavanprash, diffusions and concoctions, Herbal tea, and Turmeric mix milk and many other preparations as immune boosters and has suggested some herbal formulations for treating COVID-19 [8].

Other examples of herbal medicine used in COVID-19 treatment include: Ginseng (*Panax ginseng*) regulates the activity of immune cells including T cells, and B cells, macrophages, dendritic cells, natural killer cells; Ginger (*Zingiber officinale*) has anti-apoptotic, anti-inflammatory, anti-tumor activities, anti-tumourigenic, anti-hyperglycaemic, antioxidant, and analgesic properties; garlic (*Allium sativum*) product is a strong immune stimulator; Echinacea extract (*Echinacea purpurea* (L.) Moench) with antimicrobial and antioxidant activities is used to improve the immune system and to treat pulmonary symptoms caused by bacterial infections [9].

Narrated Khalid bin Sa'd: "Ibn Abi 'Atiq said, "Treat him with black cumin, for 'Ayesha ^{pbh} has narrated to me that,

she heard the Prophet ^{SAW} saying, 'This black cumin is healing for all diseases except As-Sam.' { 'يقول رسول الله - صلى الله عليه وسلم إن في الحبة السوداء شفاء من كل داء إلا السام } 'Ayesha ^{pbh} said, 'What is As-Sam?' He said, 'Death'" [10-12]

After searching its authenticity, this Hadith have been appear in front as *SEHATMAND* (Healthy hadith)) [11, 12] not *MODUA* (self made) for its existence [13].

Because of the pharmacological properties of *Nigella sativa* linn : i.e. Carminative [14-20], appetizer [14], detergent [21], coctive [21], stimulant [14, 18], Diuretic [14, 16, 17, 19, 20, 22], anthelmintic [14, 17-20, 22], Anti-inflammatory [14, 17, 18, 19, 20, 23], Antineoplastic activity [17, 22, 24], Anti fertility [22], antimicrobial [24, 25, 26] bronchodilator [22], Hypotensive [22], antibacterial [22], Anti spasmodic [22], insect repellent [22], immune system support [17, 22], analgesic [22, 23, 24, 27] Antipyretic [22, 23, 27]. The oil decreases blood pressure and cough, increases respiration [17, 23] useful in liver disease, joints, eczema, rheumatism, and colic [17] and It ceases the connective tissue disease [15], antioxidant [28], anticancer [23] and antimicrobial activities [23], protective against nephrotoxicity and hepatotoxicity [15]. *Nigella sativa* can be used in prevention and management of COVID 19.

Study Objectives

To define the *Nigella sativa* is effective as preventive and curative herbal drug of COVID-19 disease.

Methodology

Published research papers during the period of 2000 to 2020 have been reviewed for the antiviral, antipyretic, antitussive, immunomodulatory activities of *Nigella sativa* Linn. and SARS CoV-2, COVID-19, through various search engines like PubMed, Science Direct, ncbi, nlm, stat pearls, Elsevier, springer nature, Google Scholar, Research Gate, Springer nature, Academia etc. research strategy was followed as the key- words employed were i.e. epidemic fever, COVID-19, SARS CoV- 2, antiviral and immunomodulator Unani drugs, *Nigella sativa* Linn, antiviral, antipyretic, antitussive, immunomodulatory effect of Nigella, kalonji, Shooneez, black seeds etc. A total of 255 kinds of literature were reviewed, of them, 46 were selected as references for this manuscript.

Literature Review

According to Ministry of Health and Family Welfare, GOI, since the outbreak, of COVID-19, global pandemic, on March 11, 2020, presently at the end of September 2020, total 940441 cases were active and 5187825 cases were cured, and 97497 were dead [29].

Ever since the outbreak of COVID-19, at Maharashtra, at present at the end of September 2020, total 260789 cases were active and 1069159 cases were treated and 36181 were deceased [29].

It has been estimated that about one in five individuals worldwide could be at increased risk of severe COVID-19 disease if they become infected, due to underlying health conditions [31].

Transmission of Covid-19: The basic itineraries of human-to-human spread of Covid 19 amid folks, not only consist of direct inhalation of contaminated droplets released into the environment by sneezing or coughing, but also by contact of mucosa of oral, nasal, and eye. Granting a 6-ft distance is highlighted to protect against the blowout of the illness, is

also not enough. Microbes in droplets $< 5 \mu\text{m}$ in diameter can stay in the air for a long time and can be transmitted to others over distances of more than 1 m [32].

WHO has declared the outbreak as a Public Health Emergency of International Concern (PHEIC), In a meeting on January 30, 2020, as per the International Health Regulations (IHR, 2005), as it had feasted to 18 countries with four countries reporting human-to-human transmission, as they are a large family of single-stranded RNA viruses (+ssRNA) that can be isolated in different animal species [31, 33].

It's inexplicable that how these viruses can cross species barriers and can cause, illness in humans such as MERS and SARS but Interesting fact is this that, these viruses have most likely instigated from bats and then moving into other mammalian hosts - the Himalayan palm civet for SARS-CoV, and the dromedary camel for MERS-CoV-before jumping to humans [31].

Etiopathogenesis: [34] COVID-19 is caused by SARS-CoV-2, a betacoronavirus. It is comprised of a single-stranded ribonucleic acid (RNA) structure that belongs to

the Coronaviridae subfamily, part of the Coronaviridae family. Sequence analysis of SARS-CoV-2 has shown a structure typical to that of other corona viruses, and its genome has been likened to a previously identified coronavirus strain that caused the SARS outbreak in 2003. Structurally, the SARS coronavirus (SARS-CoV) has a well-defined composition comprising 14 binding residues that directly interact with human angiotensin-converting enzyme 2. Of these amino acids, 8 have been conserved in SARS-CoV-2. In humans, corona viruses were thought to cause mild respiratory infections until the identification of SARS-CoV and MERS coronavirus (MERS-CoV). Although the exact pathophysiological mechanisms underlying the emergence of SARS-CoV-2 are unknown (due to pending laboratory trials), genomic similarities to SARS-CoV could help to explain the resulting inflammatory response that may lead to the onset of severe pneumonia. Until these laboratory trials are initiated, the precise mechanism of SARS-CoV-2 remains hypothetical [34].

Clinical Manifestation: [35]

Table 1: The authors of the Chinese CDC report divided the clinical manifestations of the disease by their severity [35]

Mild Disease	Severe Disease	Critical Disease
non-pneumonia and mild pneumonia	dyspnea, respiratory frequency $\geq 30/\text{min}$, blood oxygen saturation (SpO_2) $\leq 93\%$, $\text{PaO}_2/\text{FiO}_2$ ratio or P/F [the ratio between the blood pressure of the oxygen (partial pressure of oxygen, PaO_2) and the percentage of oxygen supplied (fraction of inspired oxygen, FiO_2)] < 300 , and/or lung infiltrates $> 50\%$ within 24 to 48 hours;	respiratory failure, septic shock, and/or multiple organ dysfunction (MOD) or failure (MOF)

- Mild disease: non-pneumonia and mild pneumonia; this occurred in 81% of cases.
- Severe disease: dyspnea, respiratory frequency $\geq 30/\text{min}$, blood oxygen saturation (SpO_2) $\leq 93\%$, $\text{PaO}_2/\text{FiO}_2$ ratio or P/F [the ratio between the blood pressure of the oxygen (partial pressure of oxygen, PaO_2) and the percentage of oxygen supplied (fraction of inspired oxygen, FiO_2)] < 300 , and/or lung infiltrates $> 50\%$ within 24 to 48 hours; this occurred in 14% of cases.
- Critical disease: respiratory failure, septic shock, and/or multiple organ dysfunction (MOD) or failure (MOF); this occurred in 5% of cases [35].

Treatment: The results of epidemiological and clinical studies show that most of the infected individuals who are asymptomatic or show mild symptoms have good body capacity for protective responses to activate the body's antiviral defense mechanisms including immune cell defense and interferons induction. But, such supportive and immune responses are weak in most elderly people or patients with immunodeficiency, lung problems such as fibrosis, chronic obstruction and asthma, cardiovascular and hypertension problems, diabetics, or obesity. Such infected people may encounter more severe symptoms of the disease, severe respiratory problems, and even death. Weak immune responses and inability to fight the virus increase the viral load, leading to increased secretion of inflammatory cytokine in the bronchoalveolar lavage fluid and severe inflammatory/oxidative stress response, followed by severe lung damage. Considering acute respiratory distress

syndrome, antiviral therapy, antibiotics, corticosteroids, and anti-inflammatory drugs are commonly used in treatment protocols [32]. Most drug designs against 2019-nCoV have been focused on immunomodulators (such as corticosteroids and interferons), monoclonal antibody production, and inhibitory agents against viral proteinase, helicase, and polymerases. However, to date, no specific antiviral treatment or vaccine has been approved by the FDA for COVID-19 [32].

In this Scenario the Author emphasizes here the Hadith "Narrated Khalid bin Sa'd: 'Ibn Abi 'Atiq said, "Treat him with black cumin, for 'Ayesha has narrated to me that she heard the Prophet SAW saying, 'This black cumin is healing for all diseases except As-Sam.

يقول رسول الله - صلى الله عليه وسلم إن في الحبة السوداء شفاء من كل داء إلا السأم

'Ayesha said, 'What is As-Sam?' He said, 'Death' [10-12]. After searching its authenticity, this Hadith have been appear in front as *SEHATMAND* (Healthy Hadith)) [11, 12] not *MODUA* (self-made) for its existence [13].

Pharmacological Actions Of *Nigella sativa* L.: [13]

According to Unani system of medicine the *Nigella sativa* poses several pharmacological actions. i.e. Kasire riyah (Carminative) [14-20], Mushtahi-e-toam (appetizer) [14], Jali (detergent) [21], Munzij (coctive) [21], Muharrik (stimulant) [14, 18], Mudir-e-baul(Diuretic) [14, 16, 17, 19, 20, 22], Mudir-e-laban (galactagogue) [14-20, 22], Qatil-e-deedan-e-ama (anthelmintic) [14, 17-19, 20, 22], useful in scorpion stings [22, 23], Mudir-e-haiz (Emmenagogue) [14-20, 22], Musquit-e-junain

(abortifacient) [14-20, 22], , Muhallil-e-awram (Anti-inflammatory, [14, 17-20, 23], treatment for skin eruption, eruption fever, eczema), Antineoplastic activity [17, 22, 24], Anti fertility [22], antimicrobial [24, 25, 26], bronchodilator [22], Hypotensive [22], antibacterial [22], Dafe Tashannuj (Anti spasmodic) [22], insect repellent [22], immune system support [17, 22], Musakkin-e-waja (analgesic) [22, 23, 24, 27], Daf-e-Humma (antipyretic) [22, 23, 27], beneficial for cold [17, 23], Antidermatophyte activity [22], insect repellent [22]. The oil decreases blood pressure and cough, increases respiration [17,23], useful in Nifas (puerperium) [17], liver disease, joints, eczema, rheumatism, and colic [17], It ceases the Khilt-eBalgham [15]. Dafa-e-Sara (Antiepileptogenic) [22] and antioxidant [23], anticancer [23] and antimicrobial activities [23], protective against nephrotoxicity and hepatotoxicity [15, 22].

Research Works on Nigella

- Neuropharmacological activity of *Nigella sativa* L. extracts, suggest that the two extracts of *Nigella sativa* possesses a potent CNS and analgesic activity (depressant action especially in the case of the methanolic extract) [36]
- Consistent hepatotoxicity of *Nigella sativa* seeds not detected. [37]
- Effect of *Nigella sativa* on blood hemostatic function in rats, seems to induce transient changes in the coagulation activity of rats [38].
- The effect of *Nigella sativa* oil against the liver damage induced by Schistosoma mansoni infection in mice, may play a role against the alterations caused by S. mansoni infection [39].
- A study on the possible protective and curative effects of ketotifen, *Nigella sativa* oil, allo-purinol with dimethyl sulphoxide and prednisolone on trinitrobenzene sulphonic acid induced colitis in rats [40].
- Gastroprotective activity of *Nigella sativa* oil and its constituent, thymo quinone, against gastric mucosal injury induced by ischaemia in rats [41].
- protective Effect of thymoquinone and *Nigella sativa* seeds oil on lipid per oxidation level during global cerebral ischemia-reperfusion injury in rat hippocampus [42].
- *N. sativa* and its main constituent's, TQ showed antihypertensive, antiatherogenic, antihyperlipidemic, hypoglycemic and cardio protective effects [43].
- *N. sativa*, through inhibition of acetylcholinesterase enzyme and particularly due to its antioxidative effects improves nervous system diseases. It is also suggested that NS has interactions with the GABA, opioid and NO system [44].
- Methanol extract OF NS has a moderate antioxidant activity [45].

Quantitative Analysis Of The *Nigella sativa* Linn [13, 22]: Approximate composition of black seeds is: moisture 4.64; protein 20.85; fat 38.20; crude fibre 7.94; total carbohydrate 31.94; and ash 4.37%. Total lipid contents are 31.08% . Seeds contain 1.5% volatile oil, while 37.5% Non-volatile oil.

Quantitative Analysis Of The *Nigella sativa* Linn:

Temperament: Hot ¹⁵; Hot 2°: Dry 2° ^{19, 20}; Hot 3°: Dry 3°

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Taste: Sharp bitter¹⁴, slightly bitter and peppery, crunchy texture [18, 19]. Tasteless but slight bitter and spicy with little oiliness (Chipchipa)

Method of Processing: No processing is required, as the herb is free from any toxic effect [18, 21].

Substitute (Badal): Aneeson [22, 46, 47]

Corrective (Musleh): Kateera, sirka [22, 46, 47], cold things [22, 46, 47]. and Bans-alochan [21, 22].

Advers Effects (Muzir): The seeds are characterized by a very low degree of toxicity [20]. May cause pharyngitis (Khunaque) and giddiness [46].

Contra Indications: Should be use with precaution in pregnancy, due to its abortifacient effect [14 - 20, 22]

Important Formulations: Unani system of medicines, Habbe Hilteet, Majoon Kalonji [19], Majoon Fanjanosh, Jawarish Shoonnee, Majoon kalkalanj [46, 22], Shifa drops.

Doses: 2-4gm [20]; 3-7 gm [19, 21]; 1-2 masha (grams) [46].

Conclusion

After reviewing different articles and various studies, it can be concluded that *N. sativa* and its main constituent's, TQ revealed anti-inflammatory, antihypertensive, antiatherogenic, antihyperlipidemic, antimicrobial, bronchodilator Hypotensive' antibacterial and hypoglycemic, Gastroprotective and cardio protective effects.

However, further detailed investigations ie. Systematic reviews, randomized controlled trials, and metaanalysis studies are required to illustrate the exact perspectives of molecubiological and cellular basis of *N. sativa* and its constituent's effects on covid-19 and its complications.

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