

The importance of medicinal herbs and the effective substances they contain in facing the emerging coronavirus (COVID-19) and their uses in our daily life

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Abstract: Coronavirus disease 2019 (COVID-19), caused by severe acute respiratory coronavirus-2 (SARS-CoV-2), is extremely infectious and has already infected nearly seven million people and caused more than 402,852 deaths in the world. Based on our current knowledge of this virus and in the absence of a vaccine, this article is an attempt to propose ways to prevent treat, and control the COVID-19 virus, using medicinal plants such as *Eucalyptus globulus* Labill, *Cymbopogon citratus*, *Mentha*, citrus, *Zingiber officinale*, *Syzygium aromaticum* that are effective. Ginger (*Zingiber officinale* Roscoe) is a common and widely used spice. It is rich in various chemical constituents, including phenolic compounds, terpenes, polysaccharides, lipids, organic acids, and raw fibers. The health benefits of ginger are mainly attributed to its phenolic compounds, such as gingerols and shogaols. Accumulated investigations have demonstrated that ginger possesses multiple biological activities, including antioxidant, anti-inflammatory, antimicrobial, anticancer, neuroprotective, and cardiovascular protective, respiratory protective, antiobesity, antidiabetic, antinausea, and antiemetic activities. In this review, we summarize current knowledge about the bioactive compounds and bioactivities of ginger, and the mechanisms of action are discussed. We hope that this updated review paper will attract more attention to ginger and its further applications, including its potential to be developed into functional foods or nutraceuticals for the prevention and management of chronic diseases. An effective vaccine to prevent the SARS-CoV-2 causing COVID-19 is yet to be approved. Further, no drug is specific to treat COVID-19. In line with the proposed use of chloroquine, *Nigella sativa* (black seed) could be considered as a natural substitute that contains several bioactive components such as thymoquinone, dithymoquinone, thymohydroquinone, and nigellimine. Among the general and important benefits of those herbs used in this paper and this research are the merging of herbs together, obtaining general benefits for the human body, strengthening the immune system, improving the properties of the digestive system and blood circulation, general tonics, antioxidants and some other benefits that benefit the person in the face of any disease or bacterial infection or Viral infection.

Keywords: anti-inflammatory; anticancer; antinausea; anti-obesity; antioxidant; phytochemicals (COVID-19)

Introduction

The new Coronavirus epidemic (SARS-CoV-2) (COVID-19) started in the city of Wuhan in Hubei Province in China on December 8, 2019. It was spreading quickly in China, causing deaths by ten

circles and then exported to other Asian countries (South Korea etc.). It will ravage the old continent in turn by Italy, Spain, the United Kingdom, France, Belgium etc. infecting the environment of individuals and causing more than 100,000 deaths in the space of two months. The United

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States will not be spared with more than 100,000 dead in record time. The virus has managed to thwart the prognoses even of those who wrongly said that Covid-19 would be a disease affecting only the white race. Ironically, we too are paying the cost today (Africa) (**Ashok Kumar Marwah et al., 2020**).

The COVID-19 (SARS-CoV-2) pandemic is spreading as rapidly as uncontrolled bushfires. It can infect the respiratory, gastrointestinal, hepatic, and central nervous systems of humans, livestock, birds, bats, mice, and many other wildlife (**Ashok Kumar Marwah et al., 2020; Jin X, L.J.S. et al., 2020**) It has been declared as a pandemic by the World Health Organization (WHO) since March 11, 2020 (**J. Tummers, C.C., et al., 2020**). The most common mode of transmission of Covid-19 encountered is the inhalation of infectious aerosols and contact with saliva droplets or nasal secretions from a positive person (**Balachandar Vellingiri, et al., 2020**). Its incubation period remains in the range of 3 to 14 days, but researchers have been able to demonstrate that its median incubation period was 5 days, as was the case with SARS (**Hussin A. Rothan, et al., 2020; Alessandro Repici, et al., 2020**). The Covid-19 can cause illness ranging from asymptomatic to life-threatening.

In elderly patients, COVID-19 infects the lower respiratory tract and can lead to fatal pneumonia (**Hussin A. Rothan, et al., 2020**), even children are not spared from this pandemic (**Ping Wu, et al., 2020**). Other non-specific symptoms include fever, cough, myalgia, dyspnea with or without diarrhea (**Yuan Tian, et al., 2020; Shilei Wang, Y.Z., et al., 2020**); but usually patients have gastrointestinal

symptoms (nausea, vomiting, diarrhea, abdominal pain), shortness of breath, headache, sore throat, colds, breathing problems, myalgia, nasal congestion and inflammation of the mucous membranes that cover the inside of the sinuses and a runny nose (**Jin X, L.J.S., et al., 2020; Qiuhong Wang et al., 2019; Shihua Luo, et al., 2020**). It can also affect the central nervous system in some cases (**Juan Wang, et al., 2020**). According to Trisha Greenhalgh *et al.*, (**Trisha Greenhalgh, et al., 2020**), the best clinical signs to predict acquired pneumonia in an adult are a temperature higher than 38°C, a respiratory rate higher than 20 breaths/minute and a heart rate higher than 100 beats/minute; low urine flow is also a worrying symptom. Two of the major symptoms of Covid-19 include anosmia (loss of smell) and ageusia (loss of taste) (**Carol H. Yan, F.F., et al., 2020**). Coronaviruses (Co.Vs) are so-called because of their crown-like appearances under an electron microscope.

In the last few decades, two major groups of CoVs namely severe acute respiratory syndrome coronavirus (SARS-CoV) and Middle East respiratory syndrome coronavirus (MERS-CoV) have caused epidemics with high mortality (**Hui et al., 2014**). Another member of the coronaviridae family - SARS-CoV-2 is responsible for the ongoing pandemic of Coronavirus Disease 2019 (COVID-19). On March 11, 2020, World Health Organization (WHO) declared the COVID-19 outbreak as a pandemic. The SARS-CoV-2 primarily infects cells of the small air sacs known as alveoli, consisting of alveolar cells (also known as pneumocytes) and alveolar macrophages. Infection by the SARS-CoV-2 augments

inflammatory conditions in the lungs, causing pneumonia with symptoms like dry cough, chest pain, fever, and difficulty in breathing (Huang *et al.*, 2020; Lescure *et al.*, 2020). The pneumonic condition in COVID-19 is severe and is associated with its high mortality rate (Mallapaty, 2020).

The critical challenges to manage the current COVID-19 pandemic are due to a lack of a preventive vaccine as well as an effective drug against the SARS-CoV-2. Furthermore, there is an unprecedented rate of spread of the virus and mortality on a global scale. Researchers and clinicians around the world are competing to find an effective treatment for COVID-19. The current opinion paper will highlight the potential of using *Nigella sativa* (commonly known as black seed) and Zn salt as a supplement to treat COVID-19 patients.

Black seed from *Nigella sativa*: a natural alternative to Chloroquine.

Black seed from an annual flowering plant *Nigella sativa* of *Ranunculaceae* family has been reported for its range of medicinal applications. The use of black seeds and its oil has been recommended

for rheumatoid arthritis, asthma, inflammatory diseases, diabetes, and digestive diseases (Ahmad *et al.*, 2013; Butt and Sultan, 2010; Ijaz *et al.*, 2017; Kooti *et al.*, 2016; Padhye *et al.*, 2008). *N. sativa* seeds contain unsaturated fatty acids (26%–38%), proteins, alkaloids, saponins (melanin), and essential oil (0.4%–2.5%). A GC-MS analysis has revealed a mixture of eight fatty acids and 32 volatile terpenes in the seed extract (Nickavar *et al.*, 2003). Thymoquinone, dithymoquinone (nigellone), thymohydroquinone, and thymol are considered the main active constituents. Thymoquinone is the major component (28%–57%) of the volatile essential oil (Kiralan, 2012; Liu *et al.*, 2012). The major alkaloids that have been isolated from *N. sativa* seeds are nigellidine, nigellidine (indazoles), nigellimine and nigellimine N-oxide (isoquinolines). Other constituents include palmitic, glutamic, ascorbic, and stearic acids; arginine; methionine; lysine; glycine; leucine; and phytosterols (Avula *et al.*, 2010). It can be noted that several bioactive components such as nigellimine share structural similarities with chloroquine and hydroxychloroquine.

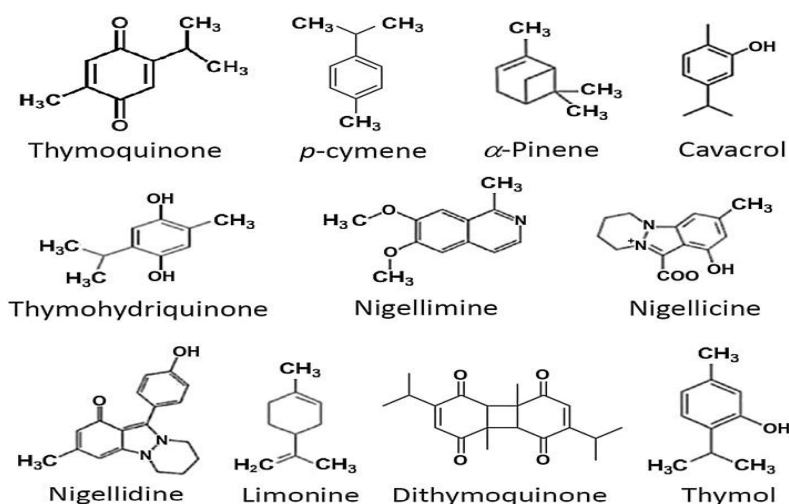


Figure 2: Major bioactive terpenes of black seed oil extract.

Among the active medicinally bioactive constituents from *N. sativa*, thymoquinone has been given more emphasis (Gholamnezhad *et al.*, 2016; Houghton *et al.*, 1995). For example, *N. sativa* oil and thymoquinone were found to produce antinociceptive effects through indirect activation of the supraspinal μ 1- and κ -opioid receptor subtypes (Abdel-Fattah *et al.*, 2000). Furthermore, brain endogenous angiotensin II was suggested to be involved in central nociceptive mechanisms by its antagonistic interaction with the endogenous opioid system (Takai *et al.*, 1996). In addition, opioid

active peptides such as hemorphins were shown to have an inhibitory effect on ACE (Lantz *et al.*, 1991). These lines of evidence suggest that opioid receptors and ACE share similar inhibitory molecules. Hence thymoquinone might also block ACE2. In other words, thymoquinone may block the SARS-CoV-2 entry via ACE2 in pneumocytes. Therefore, both nigellimine and thymoquinone from *N. sativa* might be considered as potential medicinally bioactive components to treat COVID-19 patients.

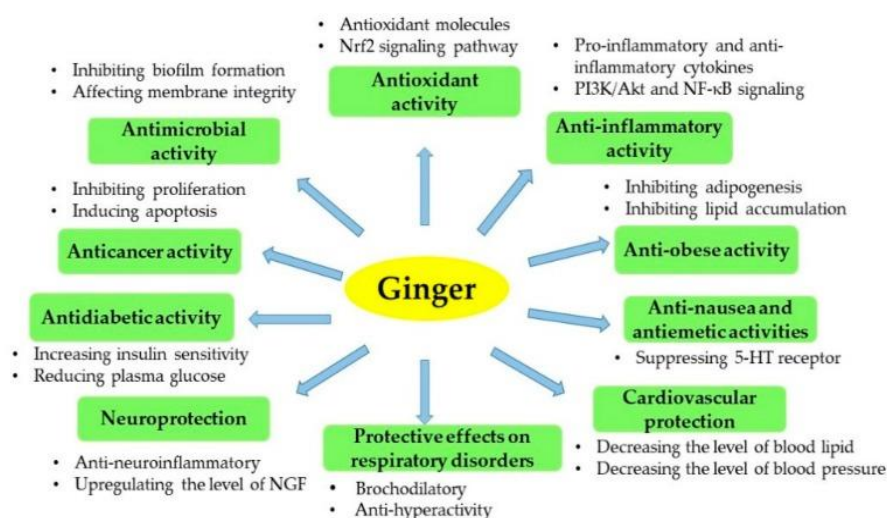


Figure 1: An overview of the bioactivities

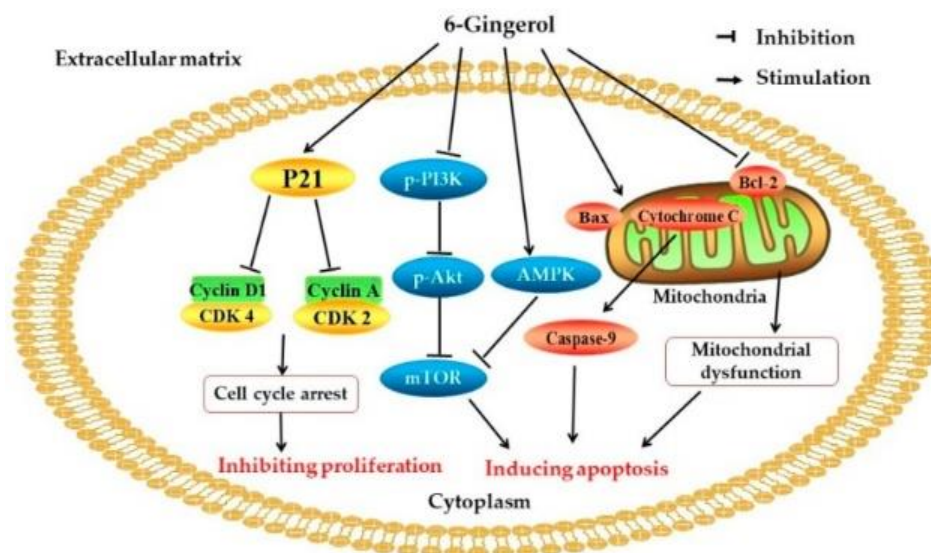


Figure 2: Several signaling pathways are involved.

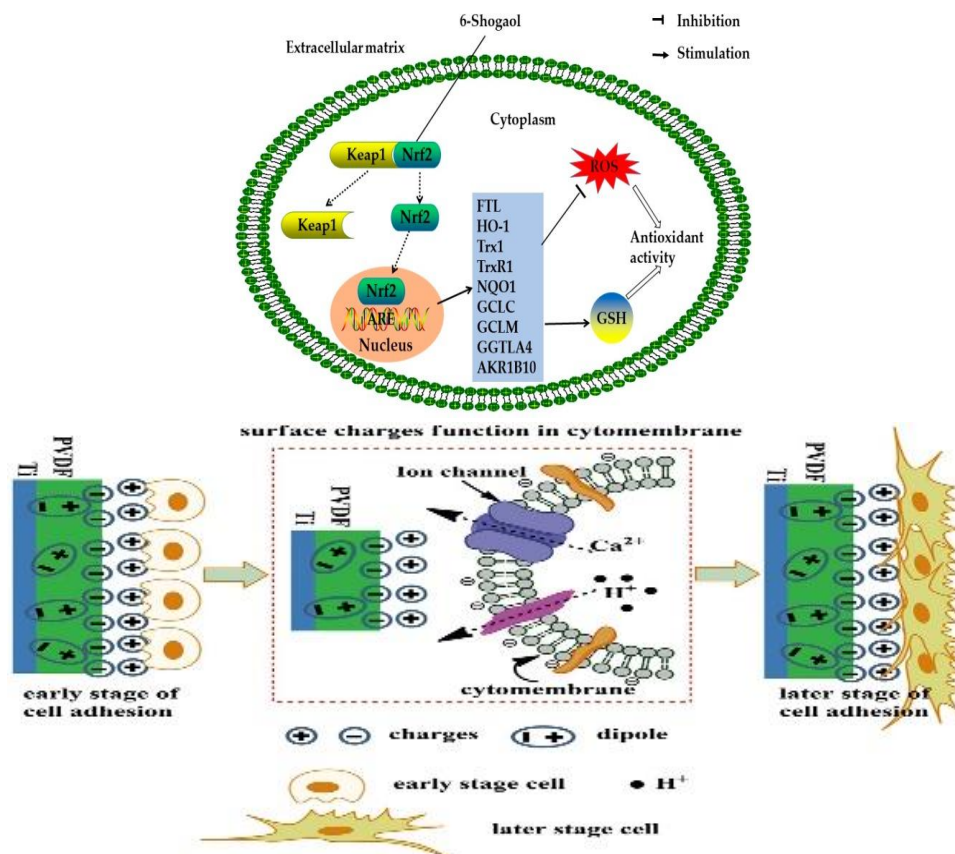


Figure 3: The potential mechanism for the polarization of an electroactive functional film on titanium for inducing osteogenic differentiation Schematic illustration of a potential mechanism for the enhanced cellular response of the PPTi.

After polarization, the dipoles of the PTi become aligned, resulting in the distribution of negative charges on the surface. Among the ionic/biological constituents present in the growth medium, cations adhere strongly to the negatively charged surfaces due to electrostatic interactions between charged entities. The proteins and negatively charged cytomembrane are then attracted to one another. Consequently, the PPTi enhances cell adhesion and proliferation due to the presence of a greater surface charge compared with the NPTi. The health-promoting perspectives of ginger are well known. It can treat a wide range of diseases via immune nutrition and anti-inflammatory responses. As a result of anti-inflammatory effect of ginger, it can

reduce muscle pain after intense physical activity. Likewise, the anticancer potential of ginger is well documented and its functional ingredients like gingerols, shogaol, and paradols are valuable ingredients, which can prevent various cancers, angiogenesis and metastasis, induction of apoptosis, and inhibition of cell-cycle progression. Besides these, it improves cardiovascular disorders, diabetes mellitus, and gastrointestinal health. Botanical material we used different plants namely *Eucalyptus globulus* Labill) or its essential oil, lemongrass leaves or its essential oil (*Cymbopogon citratus*), mint leaves (*Mentha*) or its essential oil, lemon (*Citrus*), ginger (*Zingiber officinale*), cloves (*Syzygium aromaticum*), wild honey (*Apis*

mellifera). The leaves of Eucalyptus are traditionally used for the treatment of asthma, bronchitis, as a herbal tea but recently its antimicrobial, antifungal, anthelmintic, and anti-diabetic properties have been demonstrated (HMPC, C.o.H.M.P., 2014); but also for its antioxidant properties (Elena Gonzalez-Burgos *et al.*, 2018). Lemongrass is used in the manufacture of certain drugs, it is commonly taken orally, applied directly to the skin, or inhaled as aromatherapy; its essential oil has antifungal properties. Mint leaves and ginger are used for their antioxidant properties (Aouacheri, *et al.*, 2020). Lemon is used as a powerful antioxidant; it contains biologically active compounds such as mono- and triterpenoids, coumarins, alkaloids, phytosterols, pectin, and polymethoxy flavones (Bhimanagouda S. Patil, *et al.*, 2017). The clove is used as a spice in many culinary preparations but contains several properties such as antibacterial, antimicrobial, anti-inflammatory, antifungal, and antioxidant, its knowledge to treat diarrhea, digestive problems, cough, anticancer, anti-amnesiac, and diabetes (Deepanjeet Kaur *et al.*, 2017).

Traditionally honey is used in the treatment of wounds as antimicrobial, pharyngitis, cough, insect bites, burns, skin problems, and boils. In pediatrics, it is used in the control of skin lesions near stomas. It relieves gastrointestinal disorder, gastroenteritis, gastro-esophageal reflux and in oral, it is used to treat periodontal diseases, stomatitis, and halitosis. He treats dyspepsia, gastritis, peptic ulcer, constipation, and diarrhea. It is also effective against liver and pancreatic diseases. Natural wild honey

exerts cardio protective and therapeutic effects against cardiac disorders and vasomotor dysfunctions induced by epinephrine [38]. Ginger has been suggested to be effective against inflammation, osteoarthritis, and rheumatism (Reginster *et al.*, 2000). The most common and well-established use of ginger throughout history is probably its utilization in alleviating symptoms of nausea and vomiting. The benefits and dangers of herbal treatment of liver and gastrointestinal distress have been reviewed (Langmead and Rampton 2001), The effectiveness of ginger as an antiemetic has been attributed to its carminative effect, which helps to break up and expel intestinal gas. This idea was supported by the results of a randomized, double-blind trial in which healthy volunteers reported that ginger effectively accelerated gastric emptying and stimulated antral contractions (Wu *et al.*, 2008). Previously, [6]-gingesulfonic acid, isolated from ginger root, was showed to be effective against HCl/ethanol-induced gastric lesions in rats (Yoshikawa *et al.*, 1992). This compound showed weaker pungency but more potent antiulcer activity than [6]-gingerol or [6]-shogaol (Yoshikawa *et al.*, 1994).

The seeds of *N. sativa* and their oil have been widely used for centuries in the treatment of various ailments throughout the world. And it is an important drug in the Indian traditional system of medicine like Unani and Ayurveda (Goreja WG. 2003). Among Muslims, it is considered as one of the greatest forms of healing medicine available due to it was mentioned that black seed is the remedy for all diseases except death in one of the Prophetic hadith. It is also recommended

for use on regular basis in Tibb-e-Nabwi (Prophetic Medicine) (Al-Bukhari MI 1976). *N. sativa* has been extensively studied for its biological activities and therapeutic potential and shown to possess wide spectrum of activities viz. as diuretic, antihypertensive, antidiabetic, anticancer and immunomodulatory, analgesic, antimicrobial, anthelmintics, analgesics and anti-inflammatory, spasmolytic, bronchodilator, gastroprotective, hepatoprotective, renal protective and antioxidant properties. The seeds of *N. sativa* are widely used in the treatment of various diseases like bronchitis, asthma, diarrhea, rheumatism and skin disorders. It is also used as liver tonic, digestive, anti-diarrheal, appetite stimulant, emmenagogue, to increase milk production in nursing mothers to fight parasitic infections, and to support immune system (Abel-Salam BK 2012).

Most of the therapeutic properties of this plant are due to the presence of thymoquinone (TQ) which is a major active chemical component of the essential oil. Black seeds are also used in food like flavoring additive in the breads and pickles because it has very low level of toxicity (Al-Ali A, et al., 2008). Antiviral activity 7 Epigallocatechin-3-gallate, administered to Hep2 cells in culture, produced a therapeutic index of 22 and an IC50 of 25 PM. The agent was the most effective when added to the cells during the transition from the early to the late phase of viral infection suggesting that the polyphenol inhibits one or more late steps in virus infection (Davis AL et al., 1997). Antibacterial activity Alcohol extract of black tea, assayed on *Salmonella typhi* and *Salmonella paratyphi*, was active on all strains of *Salmonella paratyphi* A,

and only 42.19% of *Salmonella typhi* strains were inhibited by the extract (Yen GC, et al., 1996). Coronavirus disease 2019 (COVID-19) is an emerging disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) that causing an ongoing pandemic and is considered as a national public health emergency. The signs and symptoms of COVID-19 vary from mild symptoms to a fulminating disease with acute respiratory distress syndrome (ARDS) and multi-organ failure, which may culminate into death with no available vaccines or specific antiviral treatments. God provides us with important medicinal plants. Here I shall shed the light on one of these plants that may help in the treatment of COVID-19 or may even cure it. *Saussurea costus* (*S. costus*) is a popular plant with medical importance, the roots of which are widely used for healing purposes throughout human history with great safety and effectiveness. Previous studies revealed the presence of many bioactive phytochemical molecules that has antiseptic, antibacterial, antifungal, antiviral, anti-inflammatory, antioxidant, anti-lipid peroxidation, immunostimulant, immunomodulating, analgesic, bronchodilator, hepatoprotective and antihepatotoxic properties. *S. Costus* has immunomodulatory effects on cytokine release and has complement inhibitor substances helpful in the treatment of some diseases related to marked activation of the complement system, like respiratory distress. (Mahmoud Saif-Al-Islam 2020).

Conclusion

Through the study of the active substances in herbs and medicinal plants,

it is noted that there are very important active substances in the treatment of some diseases that a person is exposed to in daily life and also helps him to raise the immune system and improve the physiological properties of the human body and make it more immune and resistant against infection with bacterial diseases or viral infections. Therefore, through research studies, carefully scrutinizing the search for natural and healthy alternatives, studying medicinal herbs in-depth in all respects, their effective uses in our daily life and their importance in treating diseases and using them on an ongoing basis in alternative medicine and being keen on improving and increasing the efficiency of the human immune system and relying on these medicinal herbs In the face of diseases and risks to which the human being is exposed continuously and repeatedly. Therefore, one of the important recommendations is to use medicinal herbs continuously at least once or twice a day because of their great effect and important benefit for the human body, eliminating pathogens and raising the efficiency of the immune system.

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