

Traditional Medicinal Plants and COVID-19

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Abstract

Traditional medicinal plants are used now in all of world countries for remedy from a Numerous diseases, they are considered substituted to biosynthesis drugs that depended on their authority on the effect of herbal in earliest century, the remedy of diseases was discovered with using the hillers some plants to cure disease of breathing, skin diseases, pain diseases and so on, for these reasons called these plants medicinal plants because they did a good work in medicine science. Then the eyes of scientists directed to study the principal ingredients of these plants to know how these plants do their effect for curing. They could to separate this ingredients successfully, and published their effect together or alone, they clarified the mechanism of these ingredients in many articles that published along the hole of world in scientific journals such as photochemistry, pharmaceutical, pharmacy, natural products and so on. Traditional medicinal plants proved a greatest quality in recovery of many diseases with rare side effect of a few of these medicinal plants. The aim this article is to clarification effect of some medicinal plants against COVID-19, as imagine of my suspects to the effect of the chosen plants as a hole or their ingredients, and clarify the bioactivity of these ingredients, I hope to experiment the recommended on the illness people, I will advise by the dosage of these plants which are safe in a safe quantity of some plants considered toxics in high quantity, but the most of medicinal plants in the present article are safe with any quantities.

Medicinal Plants Used for Malaria to Remedy Fever

There are many evidence that COVID-19 virus caused increase of body temperature, so we will refer to some plants that used in Africa from the chapter which presented in the book with the title of African Natural plant products: New Discoveries and Challenges in Chemistry and Quality. Chapter title is traditional medicinal plants and malaria in Africa, chapter is published (Mohammed, 2009).

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The principal medicinal plant in this chapter is *Artemisia annua*, artemisinin, the principal bioactive anti-malarial compound and its derivatives from *Artemisia annua*, a traditional Chinese medicinal plant used against fever and malaria, have yielded a potent new class of anti-malarials. The anti-malaria derived from *A. annua* are considered an integral part of the solution where malaria has become resistant to other medicines and even in areas resistance is not yet problem (De Ridder *et al.* 2008). Artemisinin-based combination therapies (ACTs) have been recommended in the countries where falciparum malaria, the most resistant form of the disease is endemic (RPM plus Program, 2005).

Second important plant in the chapter is *Zanthoxylum tsihanimposa* which contains five alkaloids (γ -fagarine, n-benzoyltyramine, Skimmianine, dictamnine and 4-methoxy-1 methyl-2(IH)-quinoline), which were extracted by decoction, the alkaloids are presented in stem bark. The quinoline γ -fagarine was the most potent five alkaloids. The presence of the methoxy group in positions C4 and C8 appears to be important for bioactive (Milijaona *et al.*, 2003).

The third plant of this chapter is *Aspidosperma quebracho-blanco*, contains aspidospermine, one indole alkaloid that was isolated from bark (Fukamiya, M. O., Lee, K.H. IN., Rahman, A., 1999).

The Recent Published on the Three Plants of Chapter

The recent studies on *Artemisia annua* are cited by many investigators, (Pamela, *et al.* 2011) cited that total chemical synthesis of artemisinin has been achieved, it is not cost effective (Haynes 2006). Current technology for artemisinin production is based on cultivated *A. annua* with best cultivars giving yields of artemisinin of ca. 1.5% of dry plant material and 70kg/ha (Kumar *et al.* 2004). Artemisinin is solvent-extracted from plant material, crystallized, and typically used for semi-synthesis of artemisinin derivatives (Haynes 2006). While *A. annua* is relatively easy to grow in temperate climates, low yields of artemisinin result in relatively high costs for isolation and purification of the useful chemical. The relatively long agricultural timeframe also results in wide swings in supply and price as demand changes. Although scientists at University of York, UK and elsewhere are breeding cultivars of *A. annua* for higher trichome densities and, thus, artemisinin production (Grove *et al.* 2007), and transgenic production schemes are in progress (Arsenault *et al.* 2008), there is still a worldwide shortage of the drug just for treating malaria let alone any other diseases against which artemisinin holds such promise (De Ridder *et al.* 2008). Clearly more low cost production and delivery of artemisinin as WHO recommended Artemisinin Combination Therapy (ACT) are needed.

Rahmatullah *et al.* 2011, published that *Zanthoxylum tsihanimposa* is botanical name, while Tsihanihimposa is common name of the plant that belongs to family *Rutaceae*. A decoction of the leaf and bark is anti-malaria. Milijaona *et al.* 2003, found that traditional healers treat malaria with herbal remedies consisting of one to eight different plants. They identified and listed the medicinal plants commonly used to treat malaria. The plants used included a large number of species from different families. *Zanthoxylum sp* (*Rutaceae*) was frequently cited, and plants from this genus are also used to treat malaria in other parts of Madagascar. From the plant list, *Zanthoxylum tsihanimposa*, bitter plant endemic to Madagascar, was selected and examined. Five alkaloids were isolates from the stem bark of this plant, and tested *in vitro* against malaria parasite. The geometric mean IC₅₀ values ranged from 98.4 to 332.1 micromolar. The quinoline alkaloid gamma-fagarine exhibited the strongest antiplasmodial activity.

Maria *et al.*, 2012, confirm the popular use of *Aspidosperma species* to treat malaria in Brazil and other Central and South American countries. The great chemical diversity of alkaloids from *Aspidosperma species* (Pereira *et al.* 2007), the low number of those that were assayed for antiplasmodial activity and the traditional use of several *Aspidosperma species* to treat malaria/fever turn this investigation of great interest.

***Nigella Sativa L.* and COVID-19**

***Nigella Sativa L.* for Immunity and Cure from Every Illness**

It is a perennial plant native to Mediterranean countries, it is cultivated in a greatest scale in Egypt and Syria and so on in many African countries, there is an ancient uses in old Egypt and other countries about the uses of its seeds in folkloric remedy, the seed constituents, and its remedy for many diseases will clarify.

Chemical Composition of *Nigella Sativa L.*

Dinagaran, *et al.*, 2017 [1], cited that *Nigella sativa* seed contains fixed oil that ranges between 28 to 36% and chiefly composed of unsaturated fatty acids that are arachidonic, eicosadienoic, linoleic and linolenic and saturated fatty acids that includes palmitic, stearic and myristic. (Hajhashemi, *et al.* 2004) [2], added that the seed oil contains compounds such as cholesterol, campesterol, stigmasterol, β -sitosterol, α -spinasterol, (+)-citronellol, (+)-limonene, p-cymene, citronellyl acetate, carvone, nigellone, arachidic, linolenic, linoleic, myristic, oleic, palmitic, palmitoleic and stearic acids (Rastogi, and Mehrotra, 1993) [3] and (Nickavar, *et al.*, 2003) [4] published that seed oil contains fixed oils like linoleic acid (55.6%), oleic acid (23.4%) and palmitic acid (12.5%) and volatile oils like trans-anethole (38.3%), p-cymene (14.8%), limonene (4.3%), and carvone (4.0%).

Aftab, *et al.*, 2013 [5], published that many active compounds have been isolated, identified and reported so far in different varieties of black seeds. The most important active compounds are thymoquinone (30%-48%), thymohydroquinone, dithymoquinone, p-cymene (7%-15%), carvacrol (6%-12%), 4-terpineol (2%-7%), t-anethol (1%-4%), sesquiterpene longifolene (1%-8%) α -pinene and thymol *etc.* (Atta, 1995) [6] found that Black seeds also contain some other compounds in trace amounts and contain two different types of alkaloids; i.e. isoquinoline alkaloids e.g. nigellicimine and nigellicimine-N-oxide, and pyrazole alkaloids or indazole ring bearing alkaloids which include nigellidine and nigellicine. Moreover, *N. sativa* seeds also contain alpha-hederin, a water soluble pentacyclic triterpene and saponin, a potential anticancer agent.

Nickavar, *et al.*, (2003) [4], noticed some other compounds e.g. carvone, limonene, citronellol were also found in trace amounts. Most of the pharmacological properties of *N. sativa* are mainly attributed to quinine constituents, of which TQ is the most abundant. On storage, TQ yields dithymoquinone and higher oligocondensation products. They added that seeds of *N. sativa* contain protein (26.7%), fat (28.5%), carbohydrates (24.9%), crude fibre (8.4%) and total ash (4.8%), the seeds are also containing good amount of various vitamins and minerals like Cu, P, Zn and Fe *etc.* The seeds contain carotene which is converted by the liver to vitamin A. Root and shoot are reported to contain vanillic acid. (Cheikh, *et al.*, 2008) [7] reported that the seeds contain a fatty oil rich in unsaturated fatty acids, mainly linoleic acid (50-60%), oleic acid (20%), eicosadienoic acid (3%) and dihomolinoleic acid (10%). Saturated fatty acids (palmitic, stearic acid) amount to about 30% or less. α -sitosterol is a major sterol, which accounts for 44% and 54% of the total sterols in Tunisian and Iranian varieties of black seed oils respectively, followed by stigmaterol (6.57-20.92% of total sterols).

Traditional Uses of *Nigella Sativa* (Folk Remedies)

Ebrahim, *et al.*, in 2019 [8], arranged that *Nigella sativa* has been widely used as a spice and flavoring agent in variety of food preparations such as in bread, yogurt, pickles, sauces, and salads. (Javed, *et al.*, 2010) [9] added that Black seed or black cumin (English), *Habbatul Barakah* (Arabic), *Tikur azmud* (Amharic), has long been used in traditional remedy in the Arabian countries, Far East Asia, Europe, and Africa. Meanwhile (Ahmad, *et al.* 2013) [10], cited that *Nigella sativa* has also been described as the miraculous plant and considered by earliest herbal specialists as the herb from heaven Avicenna, a well-known physician of 10th century famous for his book of Canon of Medicine, has recommended use of *Nigella* seeds for enhancement of body's energy and also support during recovery from fatigue and dispiritedness. *Nigella sativa* is also mentioned for its curative property in the Holy Bible and is also labelled as *Melanthion* by Hippocrates and Dioscorides according to (Tariq, 2008) [11]. The medicinal use of black cumin seeds in various traditional herbal systems is known for a wide range of ailments which include different airway disorders, for pain such as chronic headache and back pain, diabetes, paralysis, infection, inflammation, hypertension, and digestive tract related problems administered in different kind of preparations. It has also been used topically where it is applied directly to the blisters, nasal abscesses, orchitis, eczema, and swollen joints.

Krishnapura, 2018 [12], arranged that the black cumin seeds have traditionally been used in the Southeast Asian and Middle East countries for the treatment of diseases such as asthma, bronchitis, rheumatism, and other inflammatory diseases. *Nigella sativa* has extensively been used because of its therapeutic potential and possesses a wide spectrum of activities, namely, diuretic, antihypertensive, antidiabetic, anticancer, immunomodulatory, antimicrobial, anthelmintic, analgesic and anti-inflammatory, spasmolytic, bronchodilator, gastroprotective, hepatoprotective, and renal protective properties. While (Goreja, 2003) [13] noticed that traditionally, seeds of *N. sativa* are widely used for asthma, diabetes, hypertension, fever, inflammation, bronchitis, dizziness, rheumatism, skin disorders, and gastrointestinal disturbances. It is also used as a liver tonic, digestive, antidiarrhoeal, emmenagogue, and to control parasitic infections and boost immune system.

Forouzanafar, *et al.*, 2014 [14], found that *N. sativa* seeds have been used traditionally in Middle Eastern folk medicine as a treatment for various diseases for more than 2000 years ago. The seeds were used as pungent appetizer, aromatic, thermogenic, diuretic, expectorant, purgative, stimulant, sudoriferous, sedative

and carminative. (Sayed, 1980) [15] added that Black cumin seeds have a history of use in traditional Arabic herbal medicine to treat many diseases 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.

Aftab, *et al.*, (2013) [5], added that *N. sativa* has been traditionally used for the treatment of a variety of disorders, diseases and conditions pertaining to respiratory system, digestive tract, kidney and liver function, cardio vascular system and immune system support, as well as for general well-being. (Sharma and Yelne, 2005) [16] in Avicenna, refers to black seeds in the Canon of Medicine, as seeds stimulate the body's energy and helps recovery from fatigue and dispiritedness. (Yarnell and Abascal, 2011) [17] referred that Black seeds and their oil have a long history of folklore usage in Indian and Arabian civilization as food and medicine. The seeds have been traditionally used in Southeast Asian and the Middle East countries for the treatment of several diseases and ailments including asthma, bronchitis, rheumatism and related inflammatory diseases. (Warrier, *et al.*, 2004) [18] illustrated that there many uses have earned *Nigella* the Arabic approbation Habbatul barakah, meaning the seed of blessing, a tincture prepared from the seeds was useful in indigestion, loss of appetite, diarrhoea, dropsy, amenorrhoea and dysmenorrhoea and in the treatment of worms and skin eruptions. Externally the oil is used as an antiseptic and local anesthetic. Roasted black seeds are given internally to stop the vomiting.

***Ecballium Elaterium* (EE) and Virus**

Ecballium elaterium (EE) is one of the cucurbitaceous family. It is known as a squirting cucumber, it is abundant in North Africa and South- West Europe and the Mediterranean countries (Greige-Gerges *et al.*, 2007) [19]. (Saker *et al.*, 2012) [20], cited that (Ee) grows in Egypt in north Sinai and El-Dabaa. In Jordan, (Salhab, 2013) [21], showed that it is founded in many places, including the waysides and cultured areas. (Raikhlin-Eisenkraft and Bentur, 2000) [22] added that the fruits of the plant contain black seeds and juice. It has been known as a natural remedy for the treatment of several diseases. It has been used as a traditional medicine to treat rhino sinusitis according to (Uslu *et al.*, 2006) [23]. EE also has antimicrobial and anticancer activities [24].

Alternative medicine is used for the treatment of several diseases worldwide. Numerous publications, about the complications of different plant usage for different treatment goals are present in literature. *Ecballium elaterium* belongs to Cucurbitaceae family, takes place in alternative medicine because of cytotoxic, analgesic and purgative effects of the bioactive materials included [21,25]. The plant's juice is used as diluted nose drip for the treatment of rhinosinusitis in the community, uvula edema is a life-threatening condition that occurs as a result of several reasons such as trauma, infection and allergic reactions [26].

Stephen *et al.*, 2017 [27], published that derivatives or components of *Ecballium elaterium* belongs family Cucurbitacea have been used as a natural medicine in Mediterranean and African countries for centuries. The described actions of this herb include antihepatotoxicity, the prevention of hepatitis induced liver cirrhosis and the treatment of jaundice in rats or humans, the effective management of sinusitis or nasal obstruction and reversal of tissue edema in mice. The crude juice of *Ecballium elaterium* (Ee) has been used most often in herbal medicinal practice, but it is often toxic. Reports of variable toxicity exist with crude

concentrates of Ee, has included antifertility effects in female mice, cytotoxicity, and occasional deaths from poisoning. In contrast, water-distilled fractions of Ee juice given at approximate homeopathic dilutions 1x (LD times) are considered safe with retention of efficacy for several designated uses (vide infra). *Ecballium elaterium* has been widely used as a treatment for Hepatitis C (viral infection (HCV) in Egypt.

This use of Ee in treating liver disease is deeply rooted in Egyptian folklore medicine, the interest in Ee has been reactivated largely as a consequence of the emerging epidemic of Hepatitis C virus infection (HCV) in Middle Eastern countries, especially Egypt. Hepatitis C virus infection produces an indolent disease or diathesis that accounts for a large proportion of all patients with chronic liver disease. Hepatitis C is anticipated to cause major global increases in morbidity and mortality in the future.

Current treatments for HCV possess major disadvantages and limitations. While PEGylated interferon alpha combined with ribavirin are preferred treatments for HCV, these interventions are expensive, difficult to tolerate and limited in safety and effectiveness. Interferon/ribavirin treatments have unpredictable outcomes¹³ in patients with HCV.

Hepatitis C virus infection is a recalcitrant disorder that afflicts tens of millions of individuals worldwide. The emergence of HCV in third world countries cannot be impacted readily by expensive, high-technology approaches, such as those that utilize interferon and antiviral drugs (ribavirin). These treatments require skilled administration and extensive monitoring. In addition, these management strategies are not portable and they are often prohibitively expensive. Any alternative, low cost intervention for HCV, with even partial effects on the clinical course of HCV, would represent a major breakthrough in therapeutics. This article describes the ethnobotanical discovery of derivatives of Ee as a potentially-viable, natural treatment for HCV and other disorders.

Herbal remedies supports natural healing phenomenon through blocking the progression of the degenerative pathological processes. We concluded that *Ecballium elaterium* fruit juice ameliorates the detrimental effects of hepatotoxicity induced by Cyclophosphamide through its anti-inflammatory and antioxidant effects.

Plant-derived antimicrobial agents have played an essential role in the treatment of bacterial and viral diseases. Plant-derived antimicrobial agents may not serve directly as drugs, but they provide leads for the development of potential antiviral drugs. In addition, further studies need to be performed to evaluate its mechanism of action and structure activity relationship *in vivo* and in clinical trials.

Ginger and Respiratory

Ginger (*Zingiber officinale* Roscoe), which belongs to the Zingiberaceae family and the Zingiber genus, has been commonly consumed as a spice and an herbal medicine for a long time [28].

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, anti-nausea, and antiemetic activities.

Ginger root is used to attenuate and treat several common diseases, such as headaches, colds, nausea, and emesis. Many bioactive compounds in ginger have been identified, such as phenolic and terpene compounds. The phenolic compounds are mainly gingerols, shogaols, and paradols, which account for the various bioactivities of ginger [29]. In recent years, ginger has been found to possess biological activities, such as antioxidant [30], anti-inflammatory [31], antimicrobial [32], and anticancer [33] activities. In addition, accumulating studies have demonstrated that ginger possesses the potential to prevent and manage several diseases, such as neurodegenerative diseases [34], cardiovascular diseases [35], obesity [36], diabetes mellitus [37], chemotherapy-induced nausea and emesis [38], and respiratory disorders [39].

Protective Effects Against Respiratory Disorders

Natural herbal medicines have a long history of application in the treatment of respiratory disorders such as asthma, and ginger is one of these remedies [38]. Ginger and its bioactive compounds have exhibited bronchodilating activity and antihyperactivity in several studies [40].

Zingiber officinale Roscoe is a widely used drug and food in clinical and daily life and has been used in the prevention and treatment of the digestive, circulatory, respiratory, and central nervous system diseases and other diseases. Continuing with the theme of beneficial plants for disease control, attention focused on ginger, i.e. the rhizome of *Zingiber officinale*, which has been recognized to have broad-spectrum prophylactic and therapeutic functions [41]. Previously, studies have indicated that ginger is effective for the control of a range of bacterial, fungal and parasitic conditions [42]. Also, ginger has been reported to have anti-inflammatory and anti-oxidative activity [43] and to be effective as an immuno-modulatory agent in animals, including fish [44].

Several studies indicated that ginger (*Zingiber officinale* Roscoe) enhances thermogenesis and/or energy expenditure with which to interpret the beneficial effects of ginger on metabolic disorders. It is well known that mitochondrial activity plays an essential role in these processes. Siwei Zhang *et al.*, (2019) [45] investigate the effect of ginger extract (GE) and its major components, (6-gingerol and 6-shogaol), on mitochondrial biogenesis and the underlying molecular mechanisms. They showed that GE at dose of 2g/kg promoted oxygen consumption and intrascapular temperature in mice. The mitochondrial DNA (mtDNA) copy number in muscle and liver increased. Expression levels of oxidative phosphorylation (OXPHOS) related proteins and AMP-activated protein kinase α /proliferator-activated receptor gamma coactivator 1 α (AMPK/PGC1 α) signaling related proteins in the muscle, liver, and brown adipose tissue (BAT) increased as well. In HepG2 cells, GE at concentration of 2.5 and 5mg/mL increased mitochondrial mass and mtDNA copy number. GE promoted ATP production, the activities of mitochondrial respiratory chain complex I and IV, and expression levels of OXPHOS complex related proteins and AMPK/PGC1 α signaling related proteins. The antagonist of AMPK eliminated partly the effect of GE on mitochondrial biogenesis. 6-Gingerol increased mitochondrial mass, mtDNA copy number and ATP production, and the activities of mitochondrial respiratory chain complexes in HepG2 cells as well. However, both 6-gingerol at high concentration of 200 μ M and 6-shogaol at 10 to 200 μ M inhibited cell viability. In conclusion, GE

promoted mitochondrial biogenesis and improved mitochondrial functions via activation of AMPK-PGC1 α signaling pathway, and 6-gingerol other than 6-shogaol, may be the main active component.

In conclusion, ginger contains diverse bioactive compounds, such as gingerols, shogaols, and paradols, and possesses multiple bioactivities, such as antioxidant, anti-inflammatory, and antimicrobial properties. Additionally, ginger has the potential to be the ingredient for functional foods or nutraceuticals, and ginger could be available for the management and prevention of several diseases such as cancer, cardiovascular diseases, diabetes mellitus, obesity, neurodegenerative diseases, nausea, emesis, and respiratory disorders. In the future, more bioactive compounds in ginger could be isolated and clearly identified, and their biological activities and related mechanisms of action should be further investigated [46].

Conclusion

It is cleared from the previously that some of medicinal plants may be able to cure the virus of COVID-19, because as we referred the present article that COVID-19 caused fever, cough and problem in respiratory, and article cleared some medicinal plants cure fever (malaria plants), and cleared that *Nigella sativa L.* is cure for every illness, indicated their chemical composition and its folk effects through many investigation that cited by many investigators. The article showed the effect of *Ecballium elaterium* fruit juice against the viral disease. Later is cleared that ginger has good effect with respiratory. The article covered the cure of factors that caused COVID-19 using traditional medicinal plants.

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