

Prevention of COVID 19 by aromatic and medicinal plants: A systematic review

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Abstract

A coronavirus (covid-19) epidemic which started in Wuhan (China) spread fastly on several continents, turning into a pandemic then into a health crisis, disrupting the global balance. This viral infectious disease caused by the coronavirus SARS-CoV-2 strain, induces as most frequent symptoms: respiratory discomfort and acute respiratory distress syndrome leading to death. In the absence of medicines or vaccines against this virus, aromatic and medicinal plants constitute an alternative to relieve the severe respiratory infections associated with the COVID 19 pandemic. Hence, this study aims to enumerate and describe some efficient aromatic and medicinal plants that can be used against this virus. Required studies on acute and chronic respiratory infections and effective medicinal and aromatic plants were searched in the most famous scientific databases; by using specific, well-targeted keywords. The search was limited to publications in English and French. Covid 19 is mainly due to acute and chronic respiratory infections by the new coronavirus strain; which could be alleviated by using the alternative of medicinal and aromatic plants in the absence of treatment and vaccine to prevent this pandemic. This study enabled to identify the effectiveness of some plants such as Quinquina, Eucalyptus, Thyme, Artemisia ... etc. Moreover, several components of these plants have shown wonderful results in the fight against this virus. According to published research, it can be said that medicinal and aromatic plants can be effective in reducing and preventing the risk of contamination as well as in treating some Covid 19 symptoms.

Keywords: Covid 19, Aromatic medicinal plants, respiratory infections, symptoms treatment.

INTRODUCTION

At the beginning of the year 2020, Coronavirus (covid-19) epidemic that appeared in Wuhan (Central China) [1], spread in a frightening and turbulent way to several continents, and turned into a pandemic then into a health crisis that is currently upsetting world balance according to WHO [2]. This pneumonia, whose symptoms are mainly reminiscent of acute respiratory infections, but in severe forms causing a heavy death toll to this day [3], has spread with terrifying transmission power to most world countries, from Sub-Saharan Africa to Oceania, passing through America and the fertile crescent.

With detection of the first transmissions outside China, in Japan and Germany, WHO declared an international emergency state, without considering necessary to limit travel and trade with China, which cut itself off from the world after the death toll reached 170 by the end of January. Unfortunately, this had negative repercussions on pandemic, which spread more and more rapidly throughout world afterwards [4].

One month later, the death toll rose greatly, especially in: China (2838 deaths and 79 394 cases) and also Outside of China with 6009 confirmed cases (1318 new and 86 deaths) in 53 countries [5].

This situation, aggravated by a global equipment and protection measures shortages, has led to compulsory border closures and containment measures in several countries, while declaring an international health emergency state.

However, despite all these measures, the pandemic has continued to escalate with an increase in numbers of confirmed cases to **15 581 009** and of deaths to **635 173** [6].

In April, when Wuhan, considered for two months the pandemic cradle, gradually came out of isolation and ended its confinement, Europe has been declared the pandemic epicentre and has become the main global focus. Currently in the Americas region 8,292,311 cases were confirmed with 329,699 death, in European Region 3,192,041 confirmed cases and 209,930 deaths, South-East Asia Region: 1,678,994 confirmed cases and 38,993 deaths, Eastern Mediterranean Region: 1,456,365 confirmed cases and 37,050 deaths, Western Pacific Region: 280,595 confirmed cases and 8,148 deaths, African Region: 679,962 confirmed cases and 11,340 deaths [6].

This is mainly due to the lack of medicines or vaccines against this virus. Aromatic and medicinal plants remain an alternative to contain and prevent this pandemic in their own way.

Medicinal and aromatic plants, especially those frequently used in traditional medicine, play a very important role, as they contain bioactive compounds which could be used to develop new formal medicines to relieve patients with symptoms of COVID 19 with no or minimal adverse effects.

The purpose of this study is to describe the different aromatic and medicinal plants used to relieve the severe respiratory infections associated with the COVID 19 pandemic.

Methods

A systematic and advanced search, using key words on this thematic, was carried out in the following Databases: Google Scholar, Science Direct, Pub Med, Scopus, Web of science, Springer in addition to a standard search using the search engines. The key concepts used in this study

included "herbal medicines", "covid 19", "severe and acute respiratory infection", "pneumonia" and "aromatic and medicinal plants". The search was limited to English and French papers, all reports found during the search were independently studied and evaluated for competence and inclusion by two different authors. After meeting the inclusion criteria, we went on to assess the effect of medicinal and aromatic plants on respiratory problems and severe respiratory infections; and due to irrelevance or lack of access to originals, some articles were excluded.

Current status of knowlegde

Coronavirus is a large class of viruses that cause diseases ranging from colds, coughs, hyperthermia to more serious illnesses, even lethal, such as severe acute respiratory syndrome (SARS-CoV). A new coronavirus corresponds to a new strain that has not previously been found in humans [7].

The consequences of probable outbreaks of this epidemic could be serious for some people who are fragile and immunologically sensitive towards this virus. Therefore, identification of advantages of some medicinal and aromatic plants which have antiviral and antibacterial properties, is very important for the management and prevention of this pandemic. In this section we will present the top 10 medicinal and aromatic plants known for their antiviral activities and able to reduce and/or prevent the coronavirus contamination risk as well as to treat some Covid 19 symptoms, especially respiratory troubles (Table 1).

Quinquina (*Cinchona*)

Cinchona (Quinquina) plants are shrubs or trees of the Rubiaceae family, native to South America, particularly Peru and Ecuador. So, it grows at high altitudes. It has opposite lanceolate leaves; pink to red inflorescences,

sometimes white, depending on species, slightly hairy flowers corolla lobes and small capsule fruits.

Since its discovery, in Loja region of Peru, in the 17th century, *Cinchona* bark has become an effective treatment against fever, especially intermittent fever (malaria) [8]. Alkaloids are the main components of *Cinchona* and include: quinidinone, piquinidine, piquinine, quinidine, cinchonine; cinchonidine, quinine, hydro-quinidine, hydroquinine [9, 10]. Among the drugs contained in cinchona hydroxochloroquine shows a marvellous effectiveness in the COVID 19 treatment according to the university hospital institute of Marseille team chaired by Professor Didier Raoult [11, 12].

Eucalyptus

Eucalyptus belongs to the Myrtaceae family which includes 140 genera and about 3800 species distributed in tropical and subtropical regions of the world [13]. Eucalyptus is a tree species native to Australia and represents more than 90% of its natural forests. It is also found in Tasmania (island of Oceania in southeast of the Australian continent) and in the Indonesian archipelago. This genus is large as there are more than 600 species. Eucalyptus has a very powerful action on the human body; thanks to its recognized antiviral, antibacterial and anti-fungal activities enabling to fight all viruses, bacteria and fungi [14]. Its essential oil has broncho-dilating property; and is also a bronchopulmonary congestion agent which can improve the functional respiratory tract thanks to some activities: mycolytic, expectorant, drying respiratory mucous membranes and improving mucociliary clearance [15]. Eucalyptol (1,8 cineole), main compound from Eucalyptus essential oil, can be used as a potential inhibitor of the COVID-19 infection pathway and may represent potential treatment options [16, 17].

Table 1: List of major best plants for the COVID 19 prevention

Plant « English Name »	Family	The main components	References
Quinquina (<i>Cinchona</i>)	Rubiaceae	quinidinone; épiquini. dine; épiquinine; quinidine; cinchonine; cinchonidine; quinine; hydroquinidine;	BAUER and al, 1980; KACPRZAK and al ,2013 [9,10]
Eucalyptus	Myrtaceae	α -Pinene ; β -Pinene ; α -Thujene ; β -Phellandrene, p-Cymene ; 1,8 cineole	BACHIR and al, 2012 ; sabo and al ; 2019[13,14]
Garlic	Amaryllidaceae	Alliin; Allicin ; E-Ajoene; Z-Ajoene; 2-Vinyl-4H-1,3-dithiin; Diallyl sulfide (DAS); Diallyl disulfide (DADS) ; Diallyl trisulfide (DATS) Allyl methyl sulfide (AMS)	EL-SABER BATIHA, Gaber, and al, 2020
Thyme	Lamiaceae	camphor, camphene, α -pinene, 1,8-cineole, borneol, β -pinene	IMELOUANE, B., et al, 2009 [23]
Cinnamon (<i>Cinnamomum sp.</i>)	Lauraceae	Tannins, Flavonoids, Anthocyanes, Free quinones, Coumarins, Terpenes, Sterol substances and Alkaloids	MERGHACHE, D and al, 2012 [29]
Ginger	Zingiberaceae	phenolic, saponin, tannin and flavonoids	OKIKI PIUS, A and al, 2015 [34]
Dianthus	Caryophyllaceae	monoterpene hydrocarbons	ALI ESMAIL Al-Snafi, 2017 [39]
Mentha	Lamiaceae	monoterpenes and terpenoids	CHAGAS and al, 2020 [45]
Laurel	Lauraceae	1,8-cineole, terpinyl acetate, sabinene, α - pinene, β -pinene, terpinin-4-ol and 4 -terpineol	ÖZCAN and al, 2005 [49]
Artemisia	Asteraceae	eucalyptol, chrysanthenone, α -thujone, verbenone, cischrysanthenyl acetate, myrtenyl acetate and heptadienal	BEZZA, L and al 2010 [57]

Garlic

Garlic is an herbaceous plant, of the Liliaceae family, that can reach a height of up to 70 cm, like onions, shallots or leeks. The bulbs form a perennial part and stems, which are long and thin, are produced during flowering period which occurs at the end of summer in Europe, while it covers all year round in Asian countries. It has a typical pungent smell. The main garlic part used is the bulb, which consists of a bundle of pods surrounded by a very thin sheath. There are different varieties which can be identified by their color (white, pink or purple) [18]. Garlic is believed to have several biological properties, including anticarcinogenic, antioxidant, antidiabetic, renoprotective, anti-atherosclerotic, antibacterial, antifungal, antiprotozoal and antihypertensive activities. Garlic is also well known to have immune-modulatory and anti-inflammatory activities. In Europe and India, colds, cough and asthma are treated with garlic-based medicines, and respiratory tract infections are treated with garlic in Africa [19]. Allicin is a garlic extract which plays a very important role in antimicrobial and antifungal activity, by blocking the oxidation of thiol which inhibits microbial respiratory activity probably by inhibiting succinate dehydrogenase. Moreover, the adhesion of *Candida* is also greatly reduced in the presence of garlic extracts [20]. Hence, garlic is a healthy food that may have some antimicrobial properties [21], especially to inhibit the bacterial infection concomitant to the COVID-19 infection.

Thyme

It is a perennial herbaceous plant genus of the Lamiaceae family, 10-30 cm high. The grey-green leaves are opposite, oblong-lanceolate to linear, 5-10 mm long and 0.8-2.5 mm wide and dotted. The flowers are light purple, double-lipped, 5 mm long with a hairy glandular calyx. Besides this genus we also find *Origan* genus which is from the same Lamiaceae family [22].

The main constituents of thyme essential oil are camphor, camphene, α -pinene, 1,8-cineole, borneol, β -pinene [23]. Thyme is used in many kitchen dishes and as an alternative system of medicine since ancient times as a remedy for cough, toothache, bronchitis, inflammation, skin infections and also for its diuretic properties [24]. In the pandemic COVID-19 the thyme is advised to use frequently as a spice and in some foods as a preventive measure to decrease the viral load of coronavirus [25, 26].

Cinnamon (*Cinnamomum sp.*)

It is a tree species of the Lauraceae family, comprising 52 genera and 2,550 species distributed in tropical and warm regions, particularly in Southeast Asia and America [27]. Cinnamon has mainly antioxidant, antibacterial and anti-inflammatory effects. It is mainly used to stimulate the immune system [28]. According to a study carried out on the evaluation of the antifungal activity of essential oils extracted from Chinese cinnamon the main chemical components of the latter are: Tannins, Flavonoids, Anthocyanins, Free quinones, Coumarins, Terpenes, Sterol substances and Alkaloids [29]. Furthermore, the essential oil of cinnamon has shown an incredible effectiveness

against bacterial strains causing respiratory infections [30]. In addition, a recent study has shown the effectiveness of cinnamon with other ingredients (Gene-Eden-VIR) to exert a variety of antiviral effects on beta coronaviruses and SARS-CoV, by inhibiting of cell entry and infection, inhibiting of replication and inhibiting the viral proteases, to improve the antiviral immune response and reduce the formation of virulent quasi-species [31].

Ginger

Ginger belongs to the family Zingiberaceae containing 85 kinds of aromatic herbs. The best climate for ginger growing is in Southeast Asia, its origin country, although it is cultivated in most tropical countries such as Jamaica, China, India, Nigeria and Haiti. Enjoying a humid atmosphere and a sunny exposure, it is usually found in wetland grasslands in the form of grass reaching about 2 meters in height [32]. The evergreen leaves, up to 20 cm long, are lanceolate and pointed. The inflorescence has short, tightly axillary spikes, with scale-covered stems and fragrant, white to yellowish flowers with purple bracts [33]. The most part used is the rhizome which divides in a single plane and consists of branched globular tubers. The rhizome skin is light beige and the flesh is juicy pale yellow. The smell is aromatic with a warm, pungent flavour.

Phytochemical analysis of ginger extracts indicated the presence of phenolic compounds, saponin, tannin and flavonoids [34]. Moreover, Gingerols have incredible antibacterial and analgesic properties. Ginger is used for the treatment of fever, pain, nausea, indigestion and vomiting. It has also been used to treat respiratory diseases, coughs, sore throat, and kidney infections [35]. Similarly, ginger has been shown to be effective against respiratory infections especially thanks to its methanol extracts [34]. Concerning the COVID-19 pandemic, a study carried out in this direction showed that eight compounds found in the rhizomes of *Alpinia officinarum* and *Zingiber officinalis* have been identified as potential inhibitors of SARS-CoV-2 PLpro, which means that ginger rhizome extracts can be used against SARS-CoV-2 [36].

Dianthus

Dianthus is a species of herbaceous perennial, flowering plant that belongs to the Caryophyllaceae family. It has branched underground stem, 10 to 80 cm height. *D. caryophyllus* (carnation) is one of the most important ornamental plants along with pink chrysanthemum. Several carnation cultivars have been cultivated throughout the world and many new carnations have been bred with attractive characteristics such as lower colour, flower size, modified flower shape, improved fragrance, high flower yield, disease resistance and longer vase life [37]. Commonly used in China, Japan and Korea in traditional medicine, this plant has health beneficial effects such as anti-inflammatory, anti-cancer and antioxidant properties, improving physical activity potential, beside their antiviral, antibacterial, antifungal and anti-insecticide activities [38]. Dianthus essential oil is composed mainly

of monoterpene hydrocarbons [39]. Several studies have shown the effectiveness of *Dianthus* against viral diseases such as herpes simplex virus-1 (HSV-1), hepatitis A-27 (HAV-27) and against influenza viruses A and B [40, 41]. Eventhough there is no scientific research, to our best knowledge, concerning its role against Covid 19, *dianthus* remains an effective anti-viral plant.

Mentha

Mentha is a genus of the Lamiaceae family (Labiatae), which contains about 220 genera and 3300 species [42]. This genus includes more than twenty species worldwide. This plant family contains a wide spectrum of polyphenolic compounds, which have different well-known biological properties [43]. They are commonly used in traditional and alternative medicines. They can also have anti-inflammatory, antiemetic, carminative, diaphoretic, analgesic, antispasmodic, antitussive and stimulant effects [42, 44].

Its chemical composition consists mainly on oxygenated monoterpenes and terpenoids such as menthol which have an effective antimicrobial activity [45]. In a recent study, the mint showed incredible results against *Chlamydia pneumoniae* responsible of respiratory infections, pneumopathies and bronchitis [46]. Regarding the effect of *Mentha* on covid 19, it has been showed that terpenoids found in *Mentha* can interfere with amino acids in the enzyme cavity to inhibit the Covid 19 virus protease enzyme [47].

Laurel

Laurel, from the Lauraceae family, is an evergreen shrub or small tree, of medium to large size (2 to 9 m tall), often with a twisted stem and branched. The thick, flat, leathery leaves are shiny, dark green above and pale green below; with an entire margin. Leaves vary in length from 5 to 12 cm and width from 1.5 to 5 cm. The yellowish-green petioles are 0.7 to 3 cm long. The thin, reddish-brown bark tears and breaks into ridges [48]. The main chemical components of *L. nobilis* (laurel) essential oil are 1,8-cineole, terpinyl acetate, sabinene, α -pinene, β -pinene, terpinin-4-ol and 4-terpineol [49].

The laurel leaves are used in traditional medicine against rheumatism, cough, heart disease diarrhea, and viral infections, [50]. In addition, essential oils of Laurel are known for their high antibacterial, antifungal and antiviral activities [51]. The existence of 1,8 cineole in the laurel plant can play a very important role as a potential inhibitor of the COVID-19 infection pathway and may represent potential treatment options as already seen for Eucalyptus.

Artemisia

Artemisia is a large genus of the Asteraceae family. With more than 500 species, *Artemisia* is a cosmopolitan, wind-pollinated genus, mainly distributed in the temperate zones of mid to high latitudes of the northern hemisphere; and colonizing arid and semi-arid environmental landscapes, with only a few representatives in the southern hemisphere. Central Asia is its diversification center, while the Mediterranean region and North-West America

are two secondary speciation zones [52]. *Artemisia* leaves are alternately or sparsely distributed. The most characteristic features of the genus are their small, spheroidal, ovate or cylindrical capitula or flower heads, which are composed only of flossy florets inserted on a tomentose or hairless receptacle protected by an involucre with herbaceous or partially scarce bracts, with no clothing or glands. The number of florets per capitulum varies from 4 to 7 to more than 40, and the corollas are whitish, yellow or purple and inconspicuous [53]. *Artemisia* has very important anti-microbial and antioxidant effects [54] and has also been considered as having a therapeutic potential for respiratory tract infections [55, 56]. Among the main chemical components of *Artemisia* essential oil are eucalyptol, chrysanthenone, α -thujone, verbenone, cischrysanthenyl acetate, myrtenyl acetate and heptadienal [57]. Concerning the covid 19 pandemic, a study has shown an effective effect of artemisinin and its compounds (artemisinin derivatives) for patients with this virus. To this end, a recommendation for the potential reorientation for the treatment of patients with SARS-CoV-2 after successful clinical studies, by the extraction of artemisinin from *Artemisia* is proposed in order to cope with this pandemic [58].

According to the literature and to the data interpretation, a number of plants may be useful in fighting and reducing the risk of this scourge (Table 1). Among the most commonly used herbal active ingredients in the prevention of Covid 19, we found that alkaloids, such as quinidinone, quinine, hydroquinidine, hydroquinine ...etc [9, 10] shows wonderful results, according to the Marseille university team [11, 12]. Moreover, we have identified that Eucalyptol (1,8 cineole), which is the main compound of the eucalyptus, thyme and laurel essential oils [23, 49], can be used as a potential inhibitor of the COVID-19 infection pathway and may represent potential treatment options by inhibiting respiratory activity [16,17]. We have also demonstrated that cinnamon, with other ingredients (Gene-Eden-VIR), exerts various antiviral effects on beta-coronaviruses and SARS-CoV by inhibiting cell entry and infection, inhibiting replication and by inhibiting viral proteases [31]. Then we found that *Alpinia officinarum* and *Zingiber officinalis* were identified as potential inhibitors of SARS-CoV-2 PLpro, hence ginger rhizome extracts can be used against SARS-CoV-2 [36]. Finally, we demonstrated that terpenoids found in *Mentha* species can interfere with amino acids, in the enzyme cavity, to inhibit the Covid 19 virus protease [47]. It should be noted that extracts or essential oils of these aromatic and medicinal plants are mainly useful in the prevention or elimination of the Covid 19 complications; pending clinical results and further scientific studies to combat this deadly pandemic.

CONCLUSION

Medicinal and aromatic plants are effective antiviral, antibacterial, antifungal and antioxidants, in part thanks to their compounds, such as eucalyptol, quinine and other alkaloids, menthol...etc. These compounds may be effective in decreasing and preventing the contamination

risk as well as treating some symptoms of Covid 19. Further research is needed to identify the different active components of medicinal and aromatic plants, to separate them and to study their effect and also their probable synergistic effect, to fight against this scourge.

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