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Wissem Aidi Wannas
Laboratory of Aromatic and
Medicinal Plants, Biotechnologic
Center Borj-Cedria Technopark,
Hammam-Lif, Tunisia

Moufida Saidani Tounsi
Laboratory of Aromatic and
Medicinal Plants, Biotechnologic
Center Borj-Cedria Technopark,
Hammam-Lif, Tunisia

Corresponding Author:
Wissem Aidi Wannas
Laboratory of Aromatic and
Medicinal Plants, Biotechnologic
Center Borj-Cedria Technopark,
Hammam-Lif, Tunisia

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Can medicinal plants contribute to the cure of Tunisian COVID-19 patients?

Wissem Aidi Wannas and Moufida Saidani Tounsi

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Abstract

The recourse to the medicinal plants in treating flu is frequent in Tunisia. In fact, Tunisian patients have been attracted by using medicinal plants as an informal way to treat COVID-19 illness. A questionnaire concerning the use of medicinal plants has been proposed to seven COVID-19 patients. Results showed that 16 medicinal plants, namely *Allium cepa*, *Allium sativum*, *Camelia sinensis*, *Capsicum annum*, *Cinnamomum zeylanicum*, *Citrus limon*, *Citrus sinensis*, *Eucalyptus globulus*, *Mentha spicata*, *Nigella sativa*, *Rosmarinus officinalis*, *Syzygium aromaticum*, *Thymus capitatus*, *Trigonella foenum-graecum*, *Verbena officinalis* and *Zingiber officinale*, have been used by COVID-19 patients for their antiviral activities due to the presence of various complex chemical substances as organosulfur compounds, phenols, flavonoids, saponins, triterpenoids, sterols, vitamins, monoterpenes, phenylpropanoids and alkaloids. Other medications (Zithromax and paracetamol) and other natural substances (honey, zinc, vitamin C and vitamin D) were simultaneously used with medicinal plants to treat COVID-19 illness establishing for these patients an important solution to solve the problems related to COVID-19.

Keywords: Coronavirus, COVID-19, disease, medicinal plants, Tunisian patients

Introduction

Since December 2019, the novel coronavirus disease (COVID-19) has marked to be a major pandemic menace firstly in China and then over the world ^[1]. Acute respiratory tract inflammation caused by COVID-19 is an infectious disease, often fatal, that is characterized by the rapid and unexpected spread. COVID-19 enters the body by binding to its receptor, angiotensin converting enzyme-2 or ACE-2. ACE-2 has been found to be abundantly present in humans in the epithelia of the lung and small intestine, and these organs might provide possible routes of entry for the SARS-CoV-2 virus ^[2]. The main symptoms of COVID-19 are coughs, shortness of breath, and diarrhea. About 20% of patients progress to pneumonia and respiratory failure ^[3]. Until now, World is in great depression and it is experiencing the second wave of COVID-19 which has affected majority of the countries with 44,966,876 confirmed cases and about 1,181,721 confirmed deaths as of 29th October 2020. In Tunisia, COVID-19 statistics are 54,278 infections and 1,153 deaths ^[4]. The actual number of infected is probably much higher due to asymptomatic cases that may contribute to the development of the pandemic and it is not known how long this situation will continue ^[5]. Restrictions, such as the use of personal protective equipment (masks, gloves, antibacterial gels), self-isolation or quarantine, and even border closing to reduce the number of cases have been introduced in several countries ^[6]. Although that there is no specific medicine recommended to prevent or treat the novel coronavirus till now ^[6], many patients turn to herbalists to combat the coronavirus. According to the World Health Organization ^[7], about 80% of the world's population depends on medicinal plants or herbs to fulfill their medicinal needs. The objective of this study was to determine if medicinal plants had really contributed to the cure of Tunisian COVID-19 patients.

Material and Methods

To obtain information on medicinal plants that are used for treating COVID-19, patients were communicated through an informal network and they were informally interrogated using messenger, instagram and facebook. The questionnaire was composed of different questions which were divided into four distinct parts: (I) Gender and age of patient, Date of diagnosis

(II) symptoms of COVID-19 disease (III) nature of medications, medicinal plants and home remedies taken to treat COVID-19, mode of preparation and administration. (IV) the outcome of the treatment of COVID-19 patients. This work took place from March 2020 to October 2020.

Results

Patient 1

MK was a male of 32 years. The patient contracted COVID-19 in France holidays on March 2020. He quickly had a test done and removed himself for self isolation at home in Ariana city, Tunisia. Negative COVID-19 test obtained after 20 days. Symptoms: Fever, cough, difficulty breathing, fatigue, muscle aches, severe headache, loss of taste and smell, sore throat, congestion nose.

Home remedies: Infusion of rosemary (*Rosmarinus officinalis*), thyme (*Thymus capitatus*), Eucalyptus (*Eucalyptus globulus*) leaves, honey, sweet orange (*Citrus sinensis*) juice and tea.

Medication: The patient did not take medications because he had type II diabetes with insulin injection and he was immuno-sensible.

Patient 2

AT was a female of 27 year ago. The patient contracted COVID-19 in Sousse, Tunisia on April 2020, and following positive test self -isolated at home in Sousse until total recovery (16 days). Symptoms: Shortness of breath, fatigue, headache, diarrhea, cough, sneeze and body aches Home remedies: inhalation of boiling water vapor contained the flower buds of clove (*Syzygium aromaticum*).

Medication: Paracetamol (1000 mg twice per day), vitamin C (1000 mg/day) and vitamin D (10 000/day).

Patient 3

AS was a female of 23 year ago. The patient contracted COVID-19 in Tunis city, Tunisia on April 2020, and following positive test self -isolated at home in Tunis. Amelioration of patient after 10 days.

Symptoms: Loss of taste and smell and sore throat.

Home remedies: Infusion of ginger (*Zingiber officinale*) rhizomes, honey, natural vitamin C from juice of sweet orange (*Citrus sinensis*) fruits. Medication The patient did not take medication

Patient 4

SL was a female of 25 year ago. The patient contracted COVID-19 in Monastir city, Tunisia on September 2020, and following positive test self-isolated at home in Monastir during two weeks. Symptoms: The first week slight fever, cough, fatigue, Muscle aches, headache, loss of taste and smell. Then the second week vomiting and diarrhea.

Home remedies: Infusion of spearmint (*Mentha spicata*) leaves, clove (*Syzygium aromaticum*) flower buds and lemon (*Citrus limon*) fruit. Medication: paracetamol (1000 mg twice per day), vitamin C (1000 mg/day) and vitamin D (10 000 mg/day).

Patient 5

WIO was a female of 33 year ago. The patient contracted COVID-19 in Kasserine, Tunisia on September 2020, and following positive test self-isolated at home in Monastir until total recovery. Symptoms: Fever, chills, fatigue, loss of taste and smell, difficulty breathing, body aches, headache, and diarrhea.

Infusion of black seeds (*Nigella sativa*) seeds with honey, decoction of fenugreek (*Trigonella foenum-graecum*) seeds and soup made with onion (*Allium cepa*), garlic (*Allium sativum*) and hot pepper (*Capsicum annuum*). Medication: She take only paracetamol (1000 mg twice per day) because she was breastfeeding.

Patient 6

SM was a female of 27 years. The patient contracted COVID-19 in Tunisia, and following positive test self-isolated at home in Tunisia, illness during 2 weeks.

Symptoms: Headache, loss of smell and taste, fever.

Home remedies: Infusion of vervain (*verbena officinalis*) leaves, ginger (*Zingiber officinale*) rhizomes roots, spearmint (*Mentha spicata*) leaves, cinnamon (*Cinnamomum zeylanicum*) bark, clove (*Syzygium aromaticum*) flower buds, lemon (*Citrus limon*) fruit with honey and soup made with onion (*Allium cepa*) and garlic (*Allium sativum*) and hot pepper (*Capsicum annuum*). Medication: The patient took zitromax (500 mg twice per day for five days), paracetamol (1000 mg twice per day), Zinc (50 mg/day), Vitamin C (1000 mg/day) and Vitamin D (10 000 mg/day).

Patient 7

HH was a male of 57 years age. He also hailed from Tunisia. he started feeling sick on the end of September 2020 and COVID-19 tested and confirmed on October, 2020. The patient was confined for 16 days.

Symptoms: slight headache and congestion, loss of taste and smell. Disappear of symptom after 7 days.

Home remedies: Infusion of vervain (*verbena officinalis*) leaves. Other medications: Vitamin C (1000 mg/day), Zinc (50 mg/day), Zitromax (500 mg twice per day for five days).

Discussion

Until now, there is no known cure for the new coronavirus, but several traditional remedies mainly based on medicinal plants were taken by Tunisian COVID-19 patients. In this study, 16 medicinal plants have been used by COVID-19 patients for their antiviral activities owing to the presence of various complex chemical substances as organosulfur compounds, phenols, flavonoids, saponins, triterpenoids, sterols, vitamins, monoterpenes, phenylpropanoids and alkaloids (Table 1). In fact, patient 1 took an infusion of rosemary (*Rosmarinus officinalis*), thyme (*Thymus capitatus*) and eucalyptus (*Eucalyptus globulus*) leaves with honey, juice of sweet orange (*Citrus sinensis*) and tea (*Camellia sinensis*), as a home remedy against his COVID-19 illness.

Rosemary is known as a common herb and household plant broadly used all around the world for different medicinal purposes, being a component of various established anti-inflammatory plant drug preparations, and having a long tradition of use for treating headaches, colds and colic, as well as other diseases [8]. Rosemary extract had potent anti-inflammatory and antioxidant activities [9]. Rosemary extract and its constituents, especially carnosic acid, exhibited a potent antiviral activity against respiratory syncytial virus [10]. Additionally, Venu and Austin [11] reported that carnosic acid could help to combat against Covid 19.

Thyme is endemic to Algeria and Tunisia and also the most widespread North African species. In Tunisia, Thyme is widely used in folk medicine as stomachic, diaphoretic, antispasmodic specifically for whooping cough, stimulant for the blood circulation, and aphrodisiac [12]. Thyme leaves had a potent antioxidant activity [13]. The essential oil of thyme was

characterized by its richness in carvacrol (37.30%) and thymol (26%) as bioactive compounds [14]. In silico study findings revealed that among the evaluated EOs, carvacrol, and thymol showed better potential to inhibit S1 subunit of COVID-19 S proteins [15].

Eucalyptus is a flowering tree native to south-eastern Australia and Tasmania [16], but also widely cultivated in the Mediterranean region [17]. Eucalyptus leaves have been used as traditional remedies for treatment of various diseases as pulmonary tuberculosis, common cold, sinus congestion, influenza, respiratory diseases, influenza, fungal infections and diabetes [18]. Eucalyptus plants have drawn the attention of researchers worldwide due to its fast-growing ability and as a source of wood and essential oil used for various purposes. The essential oil extracted from the its leaves, bark, buds and fruits; has been experimentally reported to be possess antiseptic, antiviral, anticancer, antidiabetic, antioxidant, anti-inflammatory, antibacterial and antinociceptive activities [19]. Having established the antiviral activity of eucalyptus oil and eucalyptol against respiratory viruses, multiple researchers have attempted to explore the antiviral efficacy of eucalyptus oil and its active ingredients, especially 1,8-cineole (eucalyptol), against COVID-19 using *in vitro* assays and molecular docking techniques [20].

Sweet orange fruits represent the largest *Citrus* cultivar group grown around the world, accounting for about 70% of the total annual production of *Citrus* species [21]. Orange juice made from sweet orange fruits, also taken by patient 3, is the most popular juice beverage around the world as an excellent source of vitamin C, a powerful natural antioxidant that builds the body immune system [22]. The essential oils in orange juice contain many constituents, including monoterpenes and sesquiterpenes with limonene, as a major constituent [23], having a potent anti-inflammatory role in different diseases [24]. Narirutin or Naringenin 7-Orutinoside is an important flavonoid present abundantly in orange juice [25]. It is absorbed well and shows good bioavailability [26]. It is also shown to possess anti-inflammatory [27], antioxidant [28], anti-allergic and anti-asthmatic effects [29]. Recently, Bellavite and Donzelli [30] reported that sweet orange juice is well known for its vitamin C and hesperidin (flavonoid) content, which seem to be active antiviral candidates against COVID-19.

Tea is consumed as green, black or oolong one [31]. Tea is the most widely consumed beverage in the world after water. Several clinical studies have suggested that the regular consumption of green tea decreases influenza infection rates and some cold symptoms, and that gargling with tea catechin may protect against the development of influenza infection [32-41]. Sixty-five biomolecules of tea plant were evaluated by molecular docking for their binding affinities to the main protease (Mpro) of COVID-19, which is considered a prime target for development of anti-viral drugs. Among them, oolonghomobisflavan-A (flavanol gallate dimer ester), theasinensin-D, and theaflavin-3-O-gallate (flavonoids) demonstrated good binding to Mpro of COVID-19 [42].

Patient 2 inhaled water vapor in which water clove (*Syzygium aromaticum*) flower buds were boiled. Meanwhile vapor from water in which the various spices were boiled was inhaled, it is possible that what was inhaled were the essential oils from these spices, these oils being volatile and would be vaporized in boiling water. Essential oils (and their components) may play an important role in the inhibition of COVID-19 [43]. Additionally, sniffing of clove aroma reduces lethargy, restlessness, and headaches. Application of one drop of clove oil can soothe headache. Producing the oil from clove buds

mainly contains eugenol (70-92%) having potent anti-inflammatory, anti-fungal, antibacterial, carminative and antiemetic capacities. Clove's flavonoids (eugenin, kaempferol, rhamnetin, and eugenitin) also contribute to the strong antioxidant activity of clove essential oil. Clove essential oil is also studied for its analgesic, antiseptic, antistress, immune system booster, antitumor, and antiviral effects [44, 45]. Clove flower buds are widely used in traditional medicine to treat cholera, digestive disorder, cough, teeth troubles, headaches, earaches, nausea, hypertension, respiratory problems and great air freshener [44].

As cloves could be used in whole, ground or oil form, patient 4 and 6 took it intactly in infusion with other medicinal plants, namely spearmint (*Mentha spicata*) leaves, vervain (*verbena officinalis*) leaves, ginger (*Zingiber officinale*) rhizomes, cinnamon (*Cinnamomum zeylanicum*) bark and lemon (*Citrus limon*). It is interesting to mention that patient 3 took only an infusion of ginger.

Mint is an aromatic herbaceous plant growing throughout all regions in the world. In term of medical uses, spearmint is considered as an herbal medicine in folkloric remedies for treating obesity, dementia, hypertension, abdominal pain, digestive disorders, memory enhancer, nerve sedative, muscle spasm, flatulence, headache, sore throat, fever, menstrual pain, asthma, cough, cold and depression [46, 47]. Spearmint have been studied for its antioxidant, anti-inflammatory, sedative [48], analgesic [49] and antinociceptive [50] effects on account of the presence of phenolic acids, flavonoids, essential oil and ascorbic acid [51]. Different studies have reported the biological activities of spearmint essential oil and its main abundant compounds as carvone, pulegone, limonene and menthol [49, 52-54]. Asif *et al.* [15] give an evidence about the potential role of menthol and pulegone in the treatment of COVID-19. Menthol is the major compound of *Mentha peppermint* and it is known to promote free breathing and also relax the muscles of the respiratory tract [55].

Vervain was also taken by patient 7 as an infusion to treat COVID-19 illness. Vervain is a medicinal plant species knowing by its sedative, antispasmodic and diaphoretic properties. Vervain is frequently used in the treatment of acute and chronic rhinosinusitis and respiratory viral infections such as common cold. This plant is widely studied for its anti-inflammatory, analgesic [56], anti-depressant, antioxidant and antifungal [57], anti-arthritis [58], renal impairment [59], neuroprotective effect [60], common cold [61], liver diseases [62], cancer [63], nephrosis [64], and prostritis [65]. The main constituents are verbascoside [66], irydoic glycosides and phenolic acids (ferulic and caffeic acids) [67]. Verbascoside possesses several biological capacities as cytoprotective, anti-inflammatory and antiviral activities [68]. Furthermore, Molecular docking analysis advocated verbascoside as a potential druggable anti-COVID-19 [69].

Ginger is native to Southeastern Asia which has long been valued for its aromatic, culinary, and medicinal properties [70]. Powdered dry ginger is typically used as a flavoring for recipes such as gingerbread, cookies, crackers and cakes, ginger ale, coffee, milk, juices, tea and beer. Dry and fresh ginger is used as a spice for making vegetable curry, salad, pulse, soup, meat, tofu and noodle preparations. In herbal therapy, ginger is used in the treatment of diabetes [71], migraine headache [72], nausea and vomiting [70]. Ginger is also taken to promote digestion [73] and salivation [74]. Ginger is an important medicinal plant including 1-3% of volatile oils, which attributes to its unique flavor and fragrance as well as zingerone and gingerols [75]. Ginger and its bioactive

compounds also contribute to their antimicrobial [76], antioxidant [77], antiviral [78], anticancer [79], bronchodilator [80], anti-inflammatory [81] activities. Interestingly, in silico studies suggest that 6-gingerol from ginger could be a promising drug for treating COVID-19 [82]. Ginger is also known to contain the flavonoid quercetin, which has shown in silico potential to bind with the active catalytic site of the main protease (3CLpro) of COVID-19 as reported in molecular docking [83]. Cinnamon is a small and evergreen tree, most well-known for its bark, which offers the world with the normally recognized spice, cinnamon. Numerous pharmacological investigations have confirmed that the ability of this plant is to exhibit hepatoprotective, cardio-protective, antibacterial, antioxidant, antifungal, antidiabetic, anticancer, anti-inflammatory, and neuroprotective activities supporting the traditional uses [84]. Cinnamon bark that is found to decrease INF- γ and IL-4, Cinnamon consists of various resinous compounds, including numerous essential oils, cinnamaldehyde, cinnamic acid and cinnamate. The spicy taste and fragrance of the cinnamon is mainly due to the compound cinnamaldehyde which could be protective against COVID-19 as mentioned by Asif *et al.* [15]. Eugenol, the major component of cinnamon essential oil (45-90%), possessed the most potent anti-influenza activity in both liquid and vapour phases [85]. Docking scores revealed that this compound has binding affinity toward COVID-19 spike protein [43]. Li *et al.* [86] reported that the greatest concentrations of polyphenols found in cinnamon extract is rutin (90.06%). Rutin exhibited a good characteristic of binding with COVID-19 Mpro and TLRs, indicating it as a novel therapeutic option via virus-based and host-based anti-CoV strategies [87].

Lemon (*Citrus \times limon*) is a hybrid of the plant genus *Citrus*, as well as the common name of the popular edible fruit of this small tree. Lemon is an important medicinal plant originated in tropical and subtropical Southeast Asia. Very rich in vitamin C, so it has potassium and calcium antiscorbutic characteristics. It is very much desirable to reinforce body defenses and prevent numerous illnesses, as acne, rheumatism, arthrosis, gout, cholesterol, arteriosclerosis, uric acid, eczema, inflammation, infections, fever, fatigue, colds and flu [88]. The most important lemon flavone is hesperetin, which is found in the fruit in a glycosylated form as hesperidin [30]. hesperidin is a potential therapeutic agent for liver I/R lesions [89], cardiovascular and cancer diseases [90]. Hesperidin successfully reversed the signs and symptoms, inflammatory markers and lipid peroxidation [91]. Hesperidin and vitamin C appear to be effective candidates to counteract the cell infection by SARS-CoV-2, and to modulate the systemic immunopathological phases of the disease [30]. Additionally, lemon essential oils and their major compounds, citronellol, geraniol, limonene, linalool and neryl acetate, could downregulate ACE2, a COVID-19 spike receptor-binding domain in epithelial cells, thereby blocking virus entry into host cells, and eventually preventing viral infection [92]. Patient 5 took an infusion of black seeds (*Nigella sativa*) seeds with honey and a decoction of fenugreek (*Trigonella foenum-graecum*) seeds to treat COVID-19 disease.

Black seed from an annual flowering plant has been reported for its range of medicinal applications for different health disorders including jaundice, conjunctivitis, rheumatism, diabetes, anorexia, gastrointestinal problems, intrinsic haemorrhage, asthma, cough, bronchitis, fever, bronchitis and influenza [93]. Regarding its implication as antiviral properties, at least 8 in silico studies have shown that some compounds of black seeds, including nigelledine (alkaloid), α -hederin

(sponin), hederagenin (triterpenoid), and thymoquinone (monoterpene), had high to moderate affinity with COVID-19 enzymes and proteins. These compounds may potentially inhibit COVID-19 replication and attachment to host cell receptors [94].

Fenugreek is a leguminous herb cultivated in India and North African countries [95]. Fenugreek seeds and leaves are used for food and traditional medicine all over the world. In food preparation, fenugreek seeds and leaves included in stews in Iran, cheese flavoring in Switzerland, syrup and bitter rum in Germany, mixed seed powder for baking flat bread in Egypt, curries, dyes, roasted seeds as coffee substitute in Africa, whereas young seedlings are consumed as vegetables [96]. In traditional medicine, fenugreek is used to prepare infusions, water and alcohol extracts, tinctures, meads, tonics with antidepressant and psychotonic properties, and muscle growth supplements. Fenugreek is used in the treatment of seborrhea, acne and dermatitis. Fenugreek seed preparations are used in the treatment of gastrointestinal disorders. Aqueous solutions and macerated fenugreek oils exert protective effects on the mucosa in ulcer disease [97] and prevent colon cancer [98]. In Iran, fenugreek leaves are used in the treatment of eye diseases [99] and gynecological disorders [100]. Its biological actions include antibacterial [96], antidiabetic [101], antiulcerogenic [97], hypocholesterolaemic [102], antinociceptive [103] antioxidative [104], antihypertensive [105], hepatoprotective [106], chemoprotective [107] and immunostimulatory [108] effects. Fenugreek is a source of saponins, flavonoids, choline, carotene and essential oils [95, 109]. The docking results revealed that fenugreek phytochemicals, as apigenin, kaempferol, luteolin, naringenin, quercetin, quercitrin, rutin and vitexin (flavonoids), fenugreekine (steroidal saponin peptide ester), gentianine (pyranopyridine), stigmasterol (sterol), yamogenin (saponin) and yuccagenin (steroidal saponin), showed an efficient inhibition of 3CLpro, the main protease of COVID-19 [110].

Patients 5 and 6 also took a soup made with onion (*Allium cepa*), garlic (*Allium sativum*) and hot pepper (*Capsicum annum*) as a home remedy to combat COVID-19 illness.

Garlic and onion are highly valuable for medicinal significance since ancient time period [111]. The medicinal property of *Allium* species is linked with the presence of organosulfur compounds. Both garlic and onion have a good amount of flavonols and organosulfur compounds which impart medicinal property to these plants. Garlic and onion contain flavonoids such as anthocyanins and flavanols [112]. The anthocyanins are responsible for the red/purple colour of the bulb, whereas flavanols like quercetin and its derivatives provide yellow and brown skins of many other varieties of these plants [113]. Organosulfur compounds play an important role in imparting medicinal value to garlic and onion. Garlic is rich in organosulfur compound alliin [114]. Flavonoids present in onion and garlic have a strong inhibitory effect on virus multiplication. Phytochemicals present in these plants have been observed to block the formation of protein and genetic material in the virus [115]. Garlic and onion extracts have various remarkable medical effects and powerful anti-inflammatory and antiviral properties which helps on curing various types of diseases like cardiovascular, cancer, common cold, influenza virus [116]. Both garlic and onion were observed to exhibit strong antiviral activity (Chen *et al.*, 2011) [117]. Garlic and onion are rich in antioxidant properties with free radicals which could be helpful in reducing the severity of colds, flu or COVID-19 infection. In silico study,

quercetin and epigallocatechin gallate (flavonoids) isolated from onion found to be potential inhibitors of COVID-19 main (M) protease [118, 119]. From ail, apigenin (flavonoid), allicin, diallyl trisulfide and ajoene (organosulfur compounds) and have strong interactions with the host receptor of ACE2, and exhibited M protease inhibition of COVID-19 by 70% [120]. Hot pepper originated in the South America where they used in favor of medicinal and culinary purpose. In addition to the use of capsicum fruits as a food additive, in traditional medicine, it has been used for the treatment of cough, toothache, sore throat, parasitic infections, rheumatism, wound healing [121], atonic dyspepsia, flatulence [122] and cancer [123]. Hot pepper consists of spicy compounds, responsible for hot sensation to the tongue, called

capsaicinoids including mainly capsaicin, and its derivatives [124]. Capsaicin, is the main active ingredient in capsicum fruits. It is utilized for the treatment of inflammatory disorders such as psoriasis and rheumatoid arthritis [121], diabetic neuropathy, postherpetic neuralgia, cluster headache, postmastectomy syndrome, reflex sympathetic dystrophy [122], postoperative nausea and vomiting, bladder hyperactivity [125], anorexia, haemorrhoids, liver congestion, foodborne gastrointestinal pathogens including, tonsillitis and rhinitis and fibromyalgia [121], analgesic, antiobesity, antihypertensive [121, 125], and gastroprotective agent [122]. In molecular docking study, capsaicin (alkaloid) exhibited a good binding affinity for 3-CL protease of COVID-19 [126].

Table 1: Medicinal plants with antiviral activity against COVID-19

No.	Scientific name (family)	Common name	Bioactive compound (class)	Literatures supporting COV-19 inhibition
1	<i>Allium cepa</i> (Amaryllidaceae)	Onion	Quercetin and epigallocatechin gallate (flavonoids)	In silico study, quercetin and epigallocatechin gallate found to be potential inhibitors of COVID-19 main (M) protease [118, 119].
2	<i>Allium sativum</i> (Amaryllidaceae)	Ail	Allicin, diallyl trisulfide and ajoene (organosulfur compounds) Apigenin (flavonoid)	These compounds have strong interactions with the host receptor of ACE2, and exhibited M protease inhibition by 70% [120].
3	<i>Camellia sinensis</i> (Theaceae)	Tea	Oolonghomobisflavan-A (flavanol gallate dimer ester) Theasinensin-D and theaflavin-3-O-gallate (flavonoids).	These compounds demonstrated good binding to Mpro of COVID-19 [42].
4	<i>Capsicum annum</i> (Solonaceae)	Hot pepper	Capsaicin (alkaloid)	In molecular docking study, capsaicin exhibited a good binding affinity for 3-CL protease of COVID-19 [126].
5	<i>Cinnamomum zeylanicum</i> (Lauraceae)	Cinnamon	Cinnamaldehyde (phenylpropanoid) Eugenol (monoterpene) Rutin (flavonoid)	Good characteristic of binding with COVID-19 for cinnamaldehyde [15], eugenol [43] and rutin [87].
6	<i>Citrus limon</i> (Rutaceae)	Lemon	Citronellol, geraniol, limonene, linalool and neryl acetate (monoterpenes) Hesperidin (flavonoid) Vitamin C	Monoterpenes (citronellol, geraniol, limonene, linalool and neryl acetate) [92], hesperidin and vitamin C [30] can act in the treatment of COVID-19.
7	<i>Citrus sinensis</i> (Rutaceae)	Orange	Hesperidin (flavonoid) Vitamin C	hesperidin and Vitamin C seem to be active antiviral candidates against COVID-19 [30].
8	<i>Eucalyptus globulus</i> (Myrtaceae)	Eucalyptus	1,8-cineole (monoterpene)	1,8-cineole seems to be active antiviral candidates against COVID-19 [20].
9	<i>Mentha spicata</i> (Lamiaceae)	Spearmint	Menthol (monoterpene) Pulegone (monoterpene)	Menthol and pulegone may inhibit the action of COVID-19 [15].
10	<i>Nigella sativa</i> (Renonculaceae)	Black seeds	Hederagenin (triterpenoid) α -Hederin (saponin) Nigelledine (alkaloid) Thymoquinone (monoterpene)	These compounds may potentially inhibit COVID-19 replication and attachment to host cell receptors [94].
11	<i>Rosmarinus officinalis</i> (Lamiaceae)	Rosemary	Carnosic acid (phenolic acid)	Carnosic acid could help to combat against COVID-19 [11].
12	<i>Syzygium aromaticum</i> (Myrtaceae)	Clove	Eugenol (monoterpene)	may play an important role in the inhibition of COVID-19 [43].
13	<i>Thymus capitatus</i> (Lamiaceae)	Thyme	Carvacrol (monoterpene) Thymol (monoterpene)	In silico study, carvacrol and thymol showed better potential to inhibit S1 subunit of COVOD-19 S proteins [15].
14	<i>Trigonella foenum-graecum</i> (Fabaceae)	Fenugreek	Apigenin, kaempferol, luteolin, naringenin, rutin, quercetin, quercitrin and vitexin, (flavonoids). Fenugreekine (steroidal saponin peptide ester). Gentianine (pyranopyridine) Stigmasterol (sterol) Yamogenin (saponin) Yuccagenin (steroidal saponin)	All these compounds showed an efficient inhibition of 3CLpro, the main protease of COVID-19 [110].
15	<i>Verbena officinalis</i>	Vervain	Verbascoside (phenylpropanoid)	Molecular docking analysis advocated verbascoside as a potential druggable anti-COVID-19 [69].
16	<i>Zingiber officinale</i> (Zingiberaceae)	Ginger	6-Gingerol (phenol) Quercetin (flavonoid)	Gingerol [82] and quercetin [83] showed a potential inhibition of protease enzymes.

Conclusion

Due to unavailability of accurate drugs and vaccines, Tunisian patients have been attracted towards the importance and use of traditional medicine system to treat COVID-19 illness.

This system cannot avoid the virus infection but may alleviate symptoms and potentially improve the general healthcare of patients. Additionally, this system can only be a suitable therapy for adult patient at a stage when the disease severity is

minor. It is also interesting to mention that other medications (Zithromax and paracetamol) and other natural substances (honey, zinc, vitamin C and vitamin D) were simultaneously used with medicinal plants by some patients to treat COVID-19. These products constitute for these patients a solution to solve the problems related to COVID-19. On the other hand, as it is difficult to know the independently real role of each product in defending against this virus, further studies are needed to highlight this ambiguity.

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