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Efficiency of Herbal Medicines in Containment of COVID-19: A Narrative Review

Shadi Sarahroodi

Department of Pharmacology and Toxicology, Faculty of Pharmacy and Pharmaceutical Sciences, Tehran Medical Sciences, Islamic Azad University, Tehran, Iran

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Abstract

Background: SARS-CoV-2 is the causative agent of the novel coronavirus disease (COVID-19). This virus is responsible for the pandemic which has resulted in the current global health crisis. Remdesivir is now used as an FDA-approved medication in addition to some emergency use authorization (EUA) agents such as Actemra (Tocilizumab), Sotrovimab, and REGEN-COV (Casirivimab and Imdevimab) to contain the COVID-19 infection. However, they are not 100% effective in all cases, and there are several hundreds of daily deaths worldwide. Furthermore, since nearly one year as of the beginning of global vaccination, various vaccines have been evaluated not completely efficient in containing new variants of SARS-CoV-2, although they have significantly reduced mortality. Herbal medicines with evidence-based beneficial effects can have positive roles in immunity enhancement, prevention of infection, and antiviral effects. This review presents the updates of some herbal medicines that may have potential effects on the containment of the COVID-19, especially those with antitussive, antipyretic, anti-viral, anti-inflammatory, and antioxidant effects.

Methods: In this narrative review, a thorough literature review was conducted on the entries of Google Scholar, PubMed, Web of Science (Clarivate Analytics), Scopus and, and Science Direct published since 2019. This study includes the recently published papers, randomized clinical trials (RCTs), and World Health Organization updates about the COVID-19. The inclusion criteria were the papers that described the effects of the most efficient types of herbal medicines on the containment of the COVID-19.

Results: Analyzing nearly more than 40 medicinal plants, we found seven herbals (Myrtus communis, Zingiber officinale, Allium Sativum, Nigella Sativa, Glycyrrhiza glabra, and Thymus Vulgaris) that might have some positive effects on deferent stages of the COVID-19.

Conclusion: Since some herbal medicines might help alleviate or relieve the symptoms of the COVID-19 or have other therapeutic effects, randomized controlled trials should be conducted to confirm these effects.

Keywords: Covid-19, herbal medicine, SARS-CoV-2, traditional medicine, antivirals, phytochemicals, coronavirus

1. Introduction

In December 2019, a novel coronavirus infection has been reported in Wuhan, China (1, 2). The numbers of new active cases and deaths are on the rise of worldwide. Since nearly two years as of the beginning of the pandemic, it is still a severe public health emergency in the world (3). The World Health Organization (WHO) declared it a public health emergency of international concern (PHEIC) on January 30, 2020. It was then declared a pandemic just a few days later on March 11, 2020 (4, 5). SARS-CoV-2 is a member of the genus beta coronavirus (6), the sequence of which is similar to the MERS-CoV and SARS-CoV (7). The S protein is the most important structural protein binding to a receptor; in the meantime, it is the main antigenic structure in this virus (8).

Not only do we now face a lack of precise antiviral treatment for this disease, but we also lack the sufficient supplies of developed vaccines to vaccinate all the population (9). Moreover, we are now facing the emergence of new

Corresponding author:
Dr. Shadi Sarahroodi. Tel: +98.9123095228, E-mail: sarahroodi@yahoo.com
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variants of SARS-CoV-2 such as B.1.1.7 and B.1.351, which raised concerns about the reduced vaccine efficacy as well as the increased virus transmissibility (10). Since the COVID-19 is a viral infectious disease, some antiviral drugs and other chemical medicines have been analyzed in clinical trials. However, the only established treatments are now considered supportive therapies as well as remdesivir proving to be efficient in mitigating the COVID-19 symptoms and reducing the hospitalization course, although they have had no effects in the mortality rate (11, 12). Moreover, a recent RCT indicated that the use of dexamethasone resulted in a lower 28-day mortality rate among the patients receiving either invasive mechanical ventilation or oxygen alone but not among those receiving no respiratory support (13). At the same time, different antibodies and vaccines are now under trial around the globe; however, there is no certainty about their effectiveness and safety unless they are tested on a large human population (14, 15). Evidently, the viral evolution of the COVID-19 will continue and lead to novel variants that might escape immune responses (16). For example, the recently introduced SARS-CoV-2 known as the Lambda variant (the C.37 lineage), which is currently spreading in South American countries, is proficient in escaping from the antiviral immunity elicited by vaccination (17). As a result, there are growing concerns about the safety of the vaccinated population around the globe. Therefore, it is necessary to use the available potentials, the efficiency of which has been experienced with no significant harm to the containment of the COVID-19. A possible option is the use of traditional and herbal medicines, which had been used for thousands of years, if the clinical trials prove their efficiency and safety in the treatment of the COVID-19 (18). In many regions of the world, especially in the rural parts of developing countries, herbal medicines are the only form of traditional medication (19) that had been used for decades by many people as self-medication or recommendations (20, 21). According to the WHO, nearly 70-95% of the world's population use herbals as a kind of medicine (19). The advantages of traditional medications are their efficacy and safety experienced for centuries. However, their efficacy and safety for SARS-CoV-2 must be confirmed by clinical trials (22). Traditional Chinese medicine (TCM) has proved effective in the prevention and treatment of influenza (23-25). TCM has also been widely used in the prevention and treatment of SARS-COV-2 in China and some other countries such as Italy (26), especially in mild cases (27-29). There are some herbal medications in the Persian traditional medicine as well as Ayurveda and other traditional medicines with significant antiviral and antibacterial activities (30, 31) which might be effective in the COVID-19 symptoms such as fever, cough, muscle pain, vomiting, diarrhea, and chest pain (32). Therefore, they can be considered potential solutions against the COVID-19 (26, 33, 34). The aim of this study was to review and summarize the proposed herbal medications for the treatment of the COVID-19 patients.

2. Material and Methods

In this narrative review, a thorough literature survey was conducted on the entries in Google Scholar, PubMed, Scopus, Web of Science (Clarivate Analytics), and ScienceDirect published from 2019 until June 2021. The search keywords and phrases included coronavirus, COVID-19, SARS-CoV-2, herbal medicine, traditional medicine, antiviral effects of herbs, and immunomodulatory effects of herbs. The inclusion criteria were the recently published papers, the randomized clinical trials (RCTs) from peer-reviewed journals regarding the effects of the most effective types of herbal medicines on the containment of the COVID-19, and the WHO updates on the COVID-19. The selected papers were reviewed and interpreted by the author with regard to the use of herbal medicines, a complementary therapy against the COVID-19.

3. Discussion

3.1. Myrtus Communis L.

Known as Mourd in Persian, Truly Myrtle (Myrtus communis L.) is a small flowering shrub from the Myrtaceae family with a height of 1–3 m. This plant grows in Mediterranean regions and the Middle East, especially in the arid areas of Iran. Many products of traditional medicine are prepared from the extract or essential oil of this plant (35, 36). In Persian medicine, it was believed that Myrtle possessed wound healing, hemostatic, and astringent effects (37). According to Persian medicine manuscripts, the combination of sugar and aqueous extract of M. communis fruit as a syrup is an ancient remedy for pneumonia accompanied by coughs and diarrhea (38). The other mentioned activities of this plant include heart tonic, lung tonic, antitussive, and antidiarrheal activity (39). Recent studies proposed the antiviral activity of Myrtle (40) in the replication of Herpes simplex virus-1 (41) as well as its anti-microbial effects (42). Moreover, some other studies reported the antioxidant (43), anti-inflammatory (44), antipyretic (45), and antitussive (46) properties of this plant. Myrtucommulone (with several Stereoisomeric Compositions) is the main component responsible for anti-inflammatory and antimicrobial activity of Myrtus communis (47, 48). Since Myrtus C. is an antivitral agent, it might be a good treatment option in the early stage of COVID-19, for it has anti-inflammatory effects. Therefore, it might be useful in reducing the cytokine storm (39, 49).

3.2. Zingiber Officinale

Ginger (Zingiber Officinale Roscoe) belongs to the Zingiberaceae family and the Zingiber Genus. It has been consumed as spice and herbal medicine for centuries. The plant root has been used for treatment or attenuation of different common diseases such as cold, headache, nausea and vomiting (50). Moreover, this plant has several biological activities such as antioxidant, anti-inflammatory, antimicrobial and respiratory protective activities (51). Many recent studies analyzed the antiviral effects of Ginger on different various viral infections such as hepatitis C (52), influenza A (H1N1) (53), herpes simplex virus type-2 (HSV-2) (54), herpes simplex virus type-1 (HSV-1) (55), SARS-Cov, and SARS-Cov-2 (56). According to the results of a recent study, the phytochemical compounds in citrus medica and zingiber officinale were efficient in diminishing viral load and shedding of SARS-CoV-2 in the nasal passages.

Another recent study indicated that fresh ginger, not the dried one, might dose-dependently inhibit human respiratory syncytial virus-induced plaque formation in HEp-2 and A549 cell lines (57). Moreover, fresh ginger can dose-dependently inhibit viral attachment and internalisation (58). High-concentration fresh ginger can also stimulate mucosal cells to secrete interferon-β that would possibly counteract viral infections (59). It is hypothesized that ginger and cedrat compounds inhibit the SARS-Cov-2 spike glycoprotein as well as the ACE-2 enzyme of a host, both of which are crucial factors for the SARS-CoV-2 to enter the cells (59). In a recent docking study, Rathinavel et al. reported that phytocompound 6-gingerol from zingiber officinale demonstrated anti-viral efficiency against the COVID-19 by showing the highest interaction and binding affinity with several targets of SARS-CoV-2 including spike protein, viral RNA binding protein (60).

3.3. Citrus Medica L.

Citrus medica L. is a small plant with short thorns, rectangular large leaves, and elliptical fruits (61). According to the recent findings, the alcoholic extract of citrus medica might have antibacterial components (61), whereas its flavored essential oils (located in its peel's pigmented layer) are used as antibiotics (62). Some other recent studies reported that hesperidin and vitamin C, i.e., two major components of citrus fruits, might be efficient in preventing cell infection by SARS-CoV-2 and could modulate the systemic immuno-pathological phases of COVID-19 (63).

3.4. Allium Sativum

Garlic (Allium sativum L., Liliaceae family) is a bulb growing to 25–70 cm with hermaphrodite flowers. Its leaves and cloves have been used as spice and food additives as well as medication in Persian, Chinese, and other traditional medicines for a long time (64). Garlic has had antibacterial (6567), antifungal (66), antiparasitic (64), and antiviral as well as anti inflammatory (67) and immunomodulatory effects (68, 69). Garlic extract is also known to be effective against the influenza B virus, parainfluenza virus type 3, and human rhinovirus type 2 (70). Furthermore, some studies proposed that allicine-containing products could prevent common cold virus infections (71). At the same time, recent molecular docking analyses reveled that alliin was the most potent one of different organosulphate compounds of garlic that might eliminate SARS-CoV-2 alone or in combination with the main therapeutic drugs (72). Hypothetically, SARS-CoV-2 viral infection reduction might be due to flavonoid (e.g., quercetin) and organosulfur (e.g., allicin) compounds of allium sativum and their inhibitory effects on MPro (main protease) of the virus (73).

3.5. Nigella Sativa

Nigella sativa (black cumin), also known as black seed (ranunculaceae family), is a globally used medicinal plant and well-known food (74). The seeds of nigella sativa are believed to have several pharmacological properties such as antiviral, antimicrobial, immunostimulatory, anti-inflammatory, antitussive, and bronchodilatory effects (75, 76). The most effective bioactive compounds of N. sativa on SARS-CoV-2 include thymoquinone (TQ), nigellidine, and α-hederin (77). Recently, silico-based modeling studies demonstrated that the docked complex between thymoquinone (TQ) and the E protein of SARS-CoV-2 presented immersive interactions indicating the potential inhibitory effects of N.Sativa natural chemical compounds (78). According to another in cillico study, nigelledine (an alkaloid component) docked with 6LU7 (SARS-CoV-2 protease) active sites and showed an energy complex score better than those of favipiravir and hydroxychloroquine (79). Moreover, alpha-Hederin (a saponin component of N. Sativa), which docked with 2GTB (SARS coronavirus peptidase) active sites showed an energy score better than those of favipiravir, hydroxychloroquine, and chlorquine (79, 80).

3.6. Glycyrrhiza Glabra L.

Glycyrrhiza glabra L., known as liquorice or licorice (Fabaceae family), is a perennial plant used as weeds and the native of Southeastern Europe and Southwestern Asia (81, 82). Dating back to thousands of years ago, licorice has been used as a medicinal plant with anti-inflammatory, antioxidant, anti-mutagenic properties as well as thrombin, expectorant effects, and reduction of cortisol and aldosterone (83). There is also some evidence of liquorice antibacterial and antiviral effects (84-86). Recent studies indicated that glycyrrhizin, i.e., a triterpene glycoside (saponin) known as a glycyrrhizinic acid, is famous for its antiviral activity against several RNA and DNA viruses (87). According to some other studies, the amphiphilic characteristics of glycyrrhizin have the potential to alter the viral lipid-bilayer membrane (88). Other studies emphasized the blocking of ACE2 receptors in oral and nasal epithelial cells effectively (87). This might be its main mechanism of action against SARS-CoV-2.

3.7. Thymus Vulgaris

Thymus vulgaris, known as thyme (Lamiaceae family), is a perennial plant growing in sunny climates as well as coarse rough soils. It is native to Asia, Europe, America, and Africa and has been used as a perfume and food seasoning since ancient times (89). According to several studies of this well-known medicinal plant, thyme has several pharmacological activities such as anti-viral, antibacterial, anti-inflammatory, anti-oxidant, antidiabetic, anticancer, anti-spasmodic, antiseptic, and anti-cough activities and performance enhancement in the immune system (90, 91). Thymol and carvacrol are thyme's main components (92). According to the results of a recent RCT by Sardari et al., thymus vulgaris essential oil managed to significantly reduce fever, muscle pain, headache, anorexia, dizziness, cough, dyspnea, weakness, fatigue, and chest wall pain in the COVID-19 patients. These effects might be due to its antiviral effects on SARS-CoV-2 (93). Another recent study reported that thymus vulgaris essential oil might inhibit feline coronavirus (FCoV) replication and be a potential solution against SARS-CoV-2 (94).

4. Conclusions

Herbal medicines have been used to cure various infectious diseases for decades. Their safety and efficacy are mainly the reliable causes of their long-term use as food additives in societies. This review discussed some of the most useful and effective herbal medicines considered efficient in treating the COVID-19. It can be concluded that the mentioned herbals might provide effective options against mild to moderate SARS-CoV-2 cases. These herbal agents are the possible complementary solutions in addition to the officially approved medications of the COVID-19 to alleviate signs and symptoms of the disease and reduce its duration. The author suggests that further clinical studies and randomized clinical trials be conducted on these medicinal plants and their possible use as the complementary treatment of the COVID-19.

Conflict of Interest:

There is no conflict of interest to be declared.

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