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# Is there evidence for the use of an herbal "Taryaqe Vabaii" for conditions similar to COVID-19?

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## Abstract

**Introduction:** Vaccination is currently the best option to protect people against COVID-19. On the other hand, some concerns, such as efficacy against new types of viruses, have made it reasonable to consider some additional options available, such as using the capacity of herbal medicines to strengthen the immune system. The present study aimed to investigate the scientific evidence on the possibility of using a herbal compound (anthrax), emphasized in Iranian medical sources, to help control and prevent COVID-19.

**Materials and Methods:** This article is a library retrospective study that is purposeful and with certain criteria by searching the authoritative books of Iranian medicine, including Al-Hawi and Al-Qanun, and some sources of common medications such as reference books of medicinal plants and internal scientific databases and internationally including SID, PubMed, and Google scholar with related keywords, without a time limit.

**Results:** So far, no clinical study has shown the effectiveness of the herbal compound of anthrax (including yellow aloe, saffron, and myrrh) in the paired pains of COVID-19, but there is ample scientific evidence that its components are useful in similar medical conditions. It has been reported to have immune-boosting, antioxidant, anti-inflammatory, and antimicrobial effects.

**Conclusion:** Conducting clinical trials can make the use of cholera opioids more reassuring to help control conditions such as the COVID-19 pandemic, especially in people at higher risk.

**Keywords:** COVID-19, Iranian medicine, Taryaqe Vabaii

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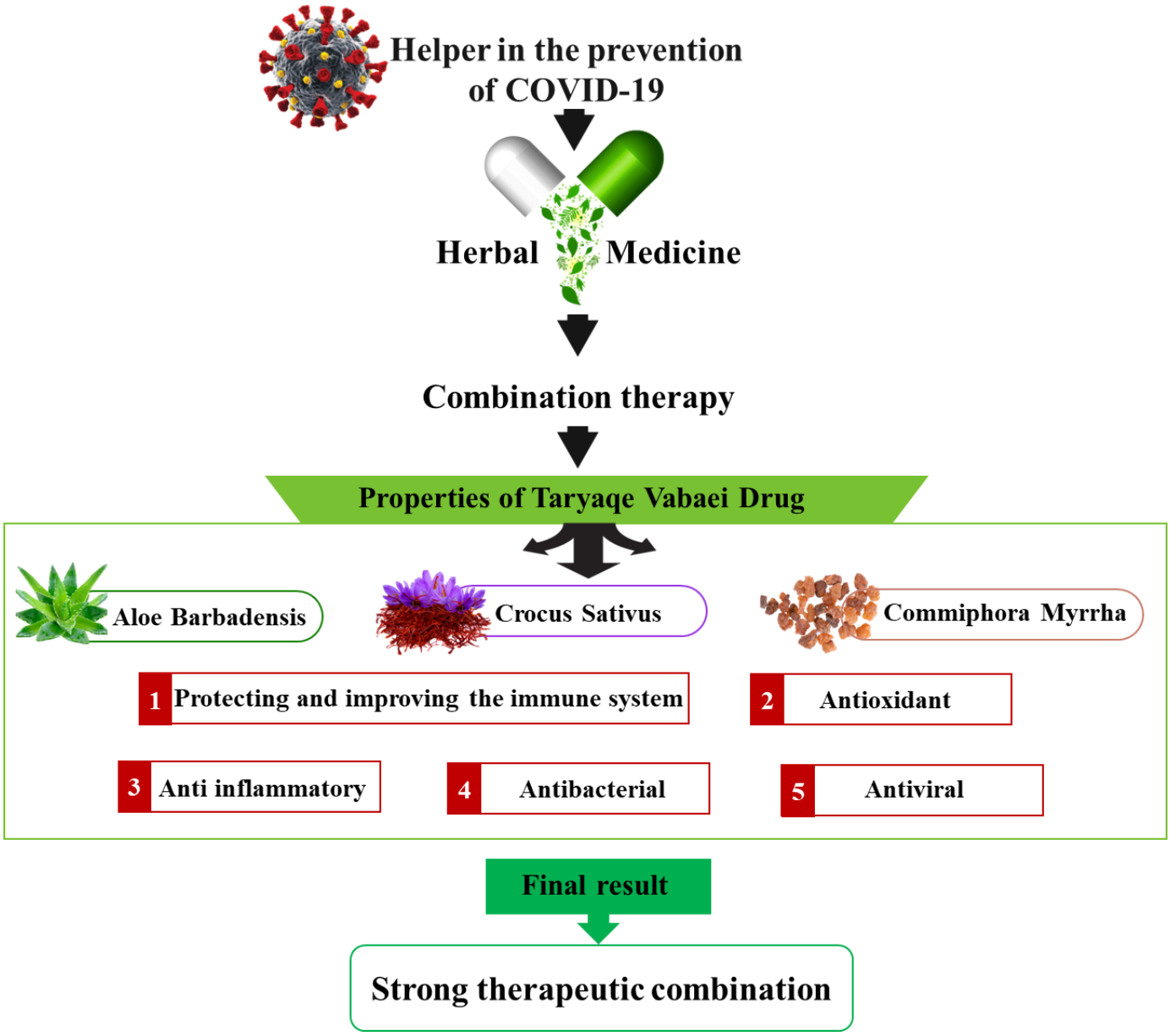
## Graphical abstract



## Introduction

COVID-19 disease caused by the new coronavirus 2019 The latest coronavirus infectious disease has been discovered, which has led to an epidemic worldwide. The clinical course of COVID-19 varies from mild disease with nonspecific signs and symptoms of acute respiratory illness to severe respiratory pneumonia and septic shock (1).

The early symptoms of the SARS-CoV-2 virus are very similar to other viral infections of the respiratory tract (eg, influenza) and include lung disease, fever, muscle aches, and fatigue (2, 3). According to the World Health Organization, its mortality rate is 3.4% (4). To date, no definitive vaccine or successful antiviral drug has been clinically approved and available. Therefore, prevention and control of infection and observance of hygienic principles by the general public a priority (3, 5).

On the other hand, the development of existing vaccines against SARS-CoV-2 is good news, but there are concerns about safety, allergic reactions, free access, cost-effectiveness and safety on a large scale, unfair distribution, and efficacy against new varieties. And there is a possibility of a lethal mutation of the virus in the body in the future. What is more, according to recent laboratory and epidemiological studies, there is a growing list of mutations in the virus that increase its potential to transmit or help escape the immune response (6). These barriers have made it reasonable and necessary to consider some additional options available, such as using the capacity of traditional herbal medicines, especially natural immune-boosting products. The World Health Organization also supports cooperation with research institutes to select traditional medicine products that can be prescribed for the control and treatment of COVID-19 due to their clinical efficacy and safety (6, 7).

Therefore, because an effective treatment method for this emerging disease has not yet been discovered (2), there is a significant need for preventive policies and the use of traditional medicine experiences (2), especially in people at risk of death. And they are more inclined to it; There are people with diabetes and obesity (8, 9). For this purpose, the present study aimed to investigate the scientific evidence on the possibility of using a herbal composition based on yellow aloe and emphasized the sources of traditional Iranian medicine which in some scientific articles is referred to as " Taryaqe Vabaii " (10) for Help is written to control this situation.

## Materials and Methods

This article is a review and library review that is purposeful and with certain criteria by searching the authoritative books of Iranian medicine, including; Al-Hawi Fi Al-Tib, Al-Qanun Fi Al-Tib, Elixir Azam, Akbari Medicine, and some sources of common medications such as reference book of medicinal plants and domestic and international scientific databases including SID PubMed, Google scholar, with the keywords of Iranian medicine, plague, diseases Plague, herbal compounds and pandemics of COVID-19, performed without time limit; Information related to the research is often extracted from relevant books and articles, and the content of the study is analyzed based on a specific pattern, and finally, by re-reading the contents.

It should be noted that data analysis has been done in the form of content analysis (Content Analysis). That is, the categories of notes are put together and a theme is extracted from each note, and the collection of these themes or themes that belonged to the notes of a category are put together to form a new note; Then, by summarizing these topics, the outlines were identified. To increase the validity of the study, expert professors were consulted and direct results were obtained from the data obtained from the study samples without opinion analysis. Observance of the principle of fidelity in the expression of the contents by mentioning the source for all the contents, including ethical points, has been considered.

## Results

In the textual studies of Iranian traditional medicine sources, a term called "plague weather" or "fever or plague diseases" has been mentioned, which is largely due to the conditions created in corona-like epidemics (such as influenza and its new strains such as COVID-19) is compatible. Because the term (plague air) means the spread of pollution and infection through the air and is generally used to describe the conditions in which the

air of a geographical area is out of its moderation (temperament) for some reason; In such a way that in its nature and quality, a state of species corruption and infectiousness appears and its consequence manifests itself in the form of a high incidence of diseases with unpleasant and unpleasant complications at the same time among the population of that region. In these texts, the occurrence of such diseases and the pervasive unpleasant complications that result from a single cause such as bad weather is also referred to as "diseases" or "uninvited and migratory diseases" (11).

These sources, while explaining how this condition occurs and how to diagnose it, as well as detail its general symptoms such as fever, respiratory symptoms, lung involvement, and sometimes other organs along with climate and environmental changes (11-13), for prevention and control These conditions, as well as strengthening the body's basic and defensive forces, include recommendations and instructions; 1) Modifying the air of the residential environment, with measures such as daily cleaning of the residential environment, disinfection of home surfaces with cold and dry nature materials such as vinegar and its combination products such as vinegar and halite (Kundel gum or Ferula Foetida), creating proper ventilation with measures Such as frequent smoking (Fumigation) of aromatic plants or their gums in residential environments such as; Pomegranate peel, turmeric, frankincense, halite, camphor and aromatherapy with aromatic agents such as frequent watering at home. 2) Improving nutrition; With measures such as avoiding overeating, reducing the volume and amount of food consumed, using fast-digesting and soft or light foods, tending to consume food to sour taste with cold and dry factors such as vinegar, juice, lemon, orange juice, Tamarhandi, pomegranate and plum juice and the use of beverages such as peppermint and jalab (heated mixture of rose and sugar), use of foods with antioxidant properties (antioxidants) such as onions and garlic. 3) Avoid strenuous work and physical activity Heavy, which leads to weakness of physical strength. 4) Avoid oversleeping. 5) Cleansing impurities and excess body fluids (body fluids) depending on the situation with methods such as diarrhea, urine, feces, and the use of laxatives. And 6) finally, strengthening the heart and brain and avoiding any unnecessary fears and worries; Today, scientific evidence shows the effects of modulating and strengthening the body's defense system if these recommendations are used correctly (2, 11).

But in addition to these preventive recommendations, including herbal combinations, which are emphasized by the elders of this medical school such as Razi and Ibn Sina, their use has been mentioned as a way to get rid of such conditions; the Use of a herbal composition based on yellow aloe; Aloe is yellow, myrrh and saffron. "Razi" (925-854 AD) was one of the most important medieval medical figures in favor of experimental medicine, in his encyclopedia called "Al-Hawi fi al-Tib" (14) - quoted by Rufus (Greek physician) in this regard He says: I have not seen anyone use this medicine in cholera unless they survived. And that medicine is a combination based on two units of yellow aloe and one unit of mecca and saffron, which should be powdered and a small amount of it should be consumed every day (13). Ibn Sina (1037-980 AD) also mentions this as one of the most important thinkers and scientists of all later periods in his book "Law in Medicine" (14); Among the beneficial compounds that help get rid of and safe from plague or infectious epidemics; Use a combination of aloe vera (two units), myrrh and saffron (one unit each) at a rate of about one dirham (3.5 grams) per day. (12).

Ibn Rushd (1826-1198 AD) also considered the use of this compound in the book "Alcohols in Medicine" useful for the conditions of the plague and its consumption, especially at the beginning of this type of infectious epidemic, makes a person safe. Knows the effects of cholera (15, 16).

According to the scholars of Iranian medicine such as Ibn Sina, a patience has a warm and dry nature and has general properties such as; Absorption power, drying of excess body fluids, is useful in poor quality wounds, and slow healing. He introduces the consumption of about 5 grams of it with hot water twice a day, but with benefits, as an effective laxative and evaluates its effect on cleansing the stomach and digestion (18). Razi, quoting previous physicians such as Disqorides, Galen, Ibn Masouyeh, Hanin Ibn Ishaq, etc., in addition to the mentioned cases, considered yellow patience useful in various inflammations and ailments and considered it as the protector and protector of the body and one of

the best Medications for stomach upsets (19). Hakim Gilani also considers the consumption of food, sprinkling on the stand, and eating (smoke) of yellow aloe in great conditions to have great properties (20).

Ibn Sina Murr has a warm and dry nature and has general properties such as; Openness in evaluating the win-win analysis of all types of winds and at the same time the property of receiving, linting, preventing the infectivity of materials, and eliminating the infection of wounds and also preparing the materials (surplus and waste) for expulsion from the body. Smoke introduces it as an air modifier and highly drying agent and introduces myrrh as one of the prominent combination drugs due to its many benefits. He found it useful for respiratory ailments such as chronic whooping cough and shortness of breath, as well as a loose stomach and bloating (18). Razi mentions the same properties in his encyclopedia, quoting former physicians (19).

Finally, Ibn Sina saffron has a warm and dry nature and has general properties such as; Astringent, which knows the winning analysis and preparation of materials (excess and waste) for excretion from the body. It is also described as invigorating, administering, and strengthening the heart, respiratory system, stomach, liver, and spleen (21). In addition to the above, Razi is also considered a food digester, appetite suppressant, sexual stimulant, respiratory facilitator, and an excellent booster for the respiratory system (22).

It is noteworthy that according to the sources of Iranian medicine, the use of the above-mentioned combination is not allowed in any situation and its use is recommended, especially in cold weather conditions or in people with a predominance of cold temperament. Therefore, in hot weather or hot weather, its consumption should be done with caution. And in such cases, it is better to use a minimum amount, ie half a derm or half a pound (about two grams) or its occasional consumption, and of course with rose or a potion with honey or sugar to reduce its possible side effects (20, 23).

The compositions and main effects of the Taryaqe Vabaii in Iranian traditional medicine and modern medicine studies are briefly mentioned in table 1 and 2.

**Table 1.** The nature and therapeutic effects of the components of "Taryaqe Vabaii" in Iranian traditional medicine.

| Elements | Nature | Properties |
|---|---|---|
| **Aloe barbadensis** | Warm and dry | Astringent, desiccant of excess body fluids, useful in poor-quality and slow-healing wounds, all kinds of abscesses and swellings, and conditions of infectious epidemics transmitted through the air, laxative. |
| **Crocus sativus** | Warm and dry | Astringent, digestive and preparing substances for elimination from the body, invigorating, regulating, strengthening the heart, respiratory system, stomach, liver and spleen, digesting food, reducing appetite, sexual stimulant, facilitating breathing and an excellent tonic for the system breathing |
| **Commiphora myrrha** | Warm and dry | Opener and opener of ducts and vessels, dispels all kinds of wind, astringent, lint remover, prevents infection of materials and removes infection of wounds, prepares materials for elimination from the body, improves air and is extremely drying, useful in respiratory ailments such as Chronic wet cough and shortness of breath, as well as loose and weak stomach and flatulence |

**Table 2.** Components and major medical effects of " Taryaqe Vabaii " in modern medicine studies.

| Elements | Compounds | Properties |
|---|---|---|
| **Aloe barbadensis** | Anthracene derivatives, glycosyls such as aloin, hydroxyanthraquinones such as alo-amudin, alkyl chromones including allorsin, flavonoids, saponins, cinnamic acid, essential oil | Anti-influenza, antibacterial, immune-enhancing and wound-healing functions, anti-inflammatory and pain-relieving, antioxidant and increasing T lymphocytes, anti-cancer effects, laxative or laxative effect |
| **Crocus sativus** | Apocarotenoid glycosides, especially crocin, picrocrocin, volatile oil, containing safranal and | Anti-virus, antioxidant, bronchodilator, anti-inflammatory, anti-depressant, modulating and |

| | | |
|---|---|---|
| | picrocrocin decomposition products, carotenoids and fixed oil and starch | strengthening the function of the immune system, heart and blood vessel tonic, anti-cough, pain-reliever, reducing fat and blood sugar, anti-coagulant, inhibition of cell proliferation and sedative |
| **Commiphora myrrha** | Volatile oil, which mainly includes sesquiterpenes, triterpenes and mucilages | Antimicrobial, astringent, anti-flatulent, expectorant, anti-secretion, antiseptic and wound healing, anti-hyperglycemia, antioxidant, liver protector, pain reliever and anti-inflammatory, anti-tumor and anti-coagulant. |

## Discussion

COVID-19 is the latest coronavirus infectious disease to be discovered, leading to epidemics worldwide. The clinical course of COVID-19 varies from mild disease with nonspecific signs and symptoms of acute respiratory illness to severe respiratory pneumonia and septic shock. It can be transmitted by air (mainly) and so on. The pathogenesis and clinical features of COVID-19 are similar to the clinical manifestations of epidemic fever (1). In the sources of traditional Iranian medicine, it is referred to as the "disease of cholera" (11).

In these sources, various herbal medicines have been described for these conditions by the great scholars of Iranian medicine, especially "Razi and Ibn Sina" under the title of epidemics. As these two prominent scientists of traditional Iranian medicine in the period of Islamic civilization (3-4th century AH) (14), while describing the conditions of airborne epidemics under the title of "plague air" (11) - in the book Al-Hawi Fi Al-Tib (13) and Al-Qanun Fi Al-Tib (12) and the "plague diseases" created by it, have also pointed out how and how to protect people in these conditions (24) and while providing health advice, some of the effective herbal compounds in prevention And people suffering from this type of infectious epidemics (25, 26), including, daily use of a plant combination based on yellow aloe, consisting of yellow aloe (Aloe barbedensis) (2 units), Mecca Myrrha (1 unit) ) And saffron (Crocus sativus) (1 unit) at a rate of about 3.5 grams - also emphasize as an "opium or antidote" (1). New scientific evidence also suggests the usefulness and possibility of using this combination in such circumstances. for example;

A 2013 clinical trial by Nigar Z and Itrat M at the National Institute of Unani Medicine Hospital, Bangalore, on a plant compound called Tiryaq wabai to investigate its immune-stimulating effects in the elderly. This plant composition consisted of three ingredients: saffron, saffron, and myrrh. The results of this study showed that this herbal compound at a dose of 500 mg three times a week for 45 days has immunosuppressive effects. Significant increase in total lymphocyte count (TLC) (P-Value <0.001), lymphocyte percentage (P-Value <0.001), absolute lymphocyte count (ALC) (P-Value <0.001) and count (P-Value <0.001) It resulted in CD4 without any side effects (10).

In the study of other sources of modern medicine, it has been shown that each of these plants contains effective compounds and substances and has scientific documents that confirm the properties mentioned in the sources of traditional Iranian medicine. For example; Aloe barbedensis shrub with the scientific name (Aloe barbedensis Mill. Or Aloe Vera L.) of the Liliaceous family, whose medicinal part consists of dried leaf sap (27). This plant (aloe vera), also known as the "miracle plant" or "miracle plant", is a medicinal plant that has been used in various cultures for more than 3,000 years (28). And is one of the most studied and used medicinal plants in the world, whose medicinal and phytochemical properties are well documented (29, 30). In general, this plant has compounds such as anthracene derivatives, glycosyls such as alloys, hydroxy anthraquinones such as allo-amodine, alkyl chromones including allorzines, flavonoids, saponins, cinnamic acid, ether oil, etc. It has antimicrobial and antiviral properties (plum-amodine inhibits the growth of H. pylori and is effective against 4 methicillin-resistant strains of Staphylococcus aureus. It also inactivates coated viruses on types 1 and 2). Herpes simplex virus as well as varicella zoster virus, pseudo rabies, and influenza virus have a direct antiviral effect, anti-inflammatory and analgesic effect (by its

salicylates and by inactivating bradykinin, inhibiting the production of histamine and reducing synthesis) Prostaglandin), wound healing (by increasing the amount of granular tissue collagen), anti-cancer effects (by amoudine present in the plant) and laxative or laxative effect (mainly through anthraquinones by stimulating the colon mucosa and increasing its movements) have been mentioned (27).

Since the advent of COVID-19, there has been informed about the use of this plant alone or in combination with other herbal remedies against COVID-19. In one of these studies, to accurately determine the best drugs from a set of 10 aloe vera metabolites, molecular docking, and adsorption, distribution, metabolism, excretion, and toxicity (ADMET) properties were performed. The reactivity of the major protease COVID-19 (Mpro) (responsible for the replication of coronaviruses) with 10 isolated aloe vera compounds showed that; The most stable complex is ferralolide or ligand 6 (−7.9 kcal / mol) followed by aloe vera or ligand 1 (7.7.7 kcal / mol) and alveresin or ligand 8 (7.7.7 kcal / mol). Lipinski confirms ligand 6 as the best drug candidate based on ADME analysis. In other words; Virtual screening results of 10 aloe vera-derived metabolites based on binding scores, hydrogen bonding interactions, and Lipinski's five-dimensional law show that the three molecular substances are ferrolide (ligand 6), aloe vera (ligand 1), and aloe vera (ligand protease 3); An enzyme that plays a key role in regulating post-translational proteins, particularly the cleavage of viral polyproteins into functional protein units. In the meantime, ligand 6 or ferralide is known as the best drug candidate. Because in addition to full obedience to Lipinski's law five, it shows the highest connection energy. (5)

It should be noted that among the several proteins that play a key role in COVID-19 viral infection and are currently considered for potential therapeutic purposes; "Corona core protein" or (3CLpro / Mpro) is known as one of the most important drug targets studied in the research and development of anticoagulants-19, especially in terms of the number of patents and the number of potential drug candidates ( 31). The protein is a proteolytic enzyme that is essential for the cleavage of viral polyproteins into several active protein units. Its choice as a drug target is justified by the fact that its active site is fully preserved and is not affected by mutations (32).

In addition, each of the top three aloe vera compounds has biological activity. Korizaki et al. Reported the antioxidant, anti-cancer, and antifungal activity of ferralide (Ligand 6) (33), while Ligand 1 exhibits anti-cancer and anti-inflammatory activity (34), and Ligand 8 has an anti-inflammatory effect (35).

Aloe vera also contains antiviral secondary metabolites (anthraquinones) that, like lupinavir (an antiretroviral), can act alone or in combination with SARS-CoV-2 protease 3CLpro (36). To this end, aloe vera can be considered an herbal medicine with a high potential to fight Quid-19 to manage this disease in the world. Several experimental studies have shown that aloe vera has extraordinary virulence properties with a wide range of action (5).

In addition to its inherent antiviral properties, aloe vera also has anti-inflammatory and immunomodulatory properties. Thus, an herbal medicine based on aloe vera extract can reduce the risk of acute respiratory distress - the leading cause of death associated with COVID-19 - by reducing pro-inflammatory factors and boosting the immune system. And since combination therapies based on viral protease inhibitors are the best treatment option; Aloe vera and its major secondary metabolites can play an important role in the management of COVID-19 (5).

In addition to its secondary metabolites, which have antiviral properties, aloe vera also contains "zinc" (40.8ppm). Therefore, its use as an herbal medicine brings this trace element to the patient. Although this chemical is essential as an enzymatic cofactor, a slight increase in its intracellular concentration inhibits the proliferation of retroviruses, including SARS-CoV-1, which is important in the management of COVID-19 (36, 37). Thus, all of this scientific evidence raises growing interest in the immediate formulation of aloe vera as an essential drug for the management of COVID-19 (5).

In other studies, the properties of aloe vera such as; It is anti-influenza, antibacterial, immune-boosting and wound-healing, anti-inflammatory, antioxidant, and thymophyte T lymphocyte proliferation (38). Its dry extract, due to its anthraquinones and pre-anthraquinones, is mainly used as a cleansing agent (39). The leaf pulp and its leachate act against various microorganisms (40) and the ethanolic extract in it causes a significant and dose-dependent increase in the total number of white blood cells and macrophages

(41). In acute gastric mucosal lesions, this extract has been used to inhibit gastric acid secretion and to protect the stomach (42). Aloe vera gel has the same therapeutic effects on the mucous membranes of the gastrointestinal tract as it does on external wounds. The dry extract of aloe also stimulates the vagus nerve by creating a bitter taste and then increases the secretion of gastric juices, thus improving digestion. This bitter substance also acts as a cardiovascular tonic (43). In addition, its anti-diabetic and lipid-lowering effects have been proven in human studies (44). Therefore, it can be useful in people with underlying diseases such as diabetes and obesity who are at higher risk for these types of complications and diseases.

However, from the point of view of toxicity, the harmlessness of the extracts of this plant has been experimentally proven both in laboratory conditions and in vivo (5). However, its use is prohibited in pregnant women, lactating women, and children under two years of age, and if used for more than 2 weeks, there is a possibility of hypokalemia. Therefore, its long-term use should be avoided. Its use with anti-diabetic drugs is also associated with an increased risk of hypoglycemia, and concomitant use with digoxin can lead to hypokalemia and digoxin toxicity. To prevent these side effects, concomitant use of this plant with these drugs should be avoided (27). In one study, a decrease in serum thyroid hormone levels was also reported by patience (45), which seems to be better used with caution in hypothyroid patients.

But in the case of saffron, the scientific evidence of modern medicine shows that; Saffron or Saffron with the scientific name of Crocus sativus from the family Iridaceae, whose medicinal part consists of stigma and cream, has compounds such as apocarotinoid glycosides, especially crocin, picrocrocin (4%), volatile oil (1.3-0.4%) containing safranal and products. It is obtained from the decomposition of picrocrocin, carotenoids, and fixed oils and starches. Safranal, picrocrocin, crocetin, and crocin are among the active ingredients of saffron and for them, properties such as stimulation of gastric juice secretion (in small amounts) and stimulation of uterine smooth muscle (in large amounts) have been stated, so its use is not recommended in pregnancy. Is (27, 46). It should be noted that the most common effective doses of saffron, which are used in clinical studies and are safe and significantly lower than toxic doses (> 5 g per day), are 30 to 50 mg per day. Be (47). Its lethal dose is between 12 and 20 grams (27).

Regarding the use of saffron during the COVID-19 epidemic, there is a lot of scientific evidence that justifies its use during this epidemic. A review of the potential role of saffron during and after COVID-19 infection, focusing on immune, respiratory, renal, and cardiovascular functions; The findings indicated that saffron due to its anti-inflammatory, antioxidant, and other medicinal properties attributed to the bioactive compounds of saffron, can help in pre-and post-infection management strategies. Also, due to its antidepressant properties, it can not only be useful in the management of these post-hospital disorders (subacute and chronic). It can also help boost the safety of ordinary people and manage depression, stress, and anxiety caused by long-term quarantine, isolation, or quarantine (6). Regarding its antidepressant properties (48), it has been reported that saffron is more effective than a placebo or approximately equivalent to therapeutic doses of fluoxetine and imipramine (49).

In addition, many in vitro and in vivo studies have confirmed saffron as an antiviral, antioxidant, bronchodilator, anti-inflammatory, and potent immune enhancer that affects humoral as well as cellular immunity (6). Even saffron petal extract (SPE) is beneficial due to the presence of flavonoids, anthocyanins, and tannins. In one study, intraperitoneal injection into mice for 14 days was associated with an increase in white blood cell count and antibody response, without any change in blood parameters (50). There is also strong scientific evidence for the antiviral effects of saffron, including anti-HSV-1 and anti-HIV-1 (6). Recently, in silicon analysis for pharmacokinetic, toxicological, and ADMET parameters (absorption, distribution, metabolism, excretion, and toxicity) of bioactive saffron molecules, it has been observed that crostine has a high drug rating against SARS-CoV-2. Crocin and crocetin have a high affinity for the main protease SARS-CoV-2 and crocetin, as a drug molecule, shows transmission through the lipid bilayer (51).

It is interesting to note; Twenty-one percent (21%) of COVID-19 management trials focused on non-vaccine approaches such as immunomodulators (18%) and dietary supplements (3%) (52). Studies related to saffron can be included. In this regard, a review study has claimed that no other spice is as attractive and

excellent as saffron (6). Because saffron is rich in B vitamins, vitamin C, carotenoids, and phytochemicals, it can boost immunity. Saffron compounds have been recorded in several herbal medicinal formulas that are used to treat cardiovascular and central nervous system diseases, as well as to strengthen the immune system and treat depression (53). Clinical trials show that saffron extract is effective in patients with diseases of the central nervous system (CNS) such as Alzheimer's and mental disorders such as depression if administered 20-200 mg per day for ten days to several weeks (6). In addition, crocetin and crocin are useful in the treatment of neurodegenerative disorders associated with memory impairment (48, 54).

A double-blind randomized placebo-controlled clinical trial was performed to determine the immunomodulatory effects of saffron and it was observed that saffron increased IgG levels and decreased IgM levels compared to baseline and placebo. In addition, it increased the percentage of monocytes compared to the placebo. Therefore, short-term daily use of 100 mg of saffron was suggested temporarily without any side effects due to its immune-modifying activities (55).

The results of a study also showed that the use of saffron petal extract at a dose of 75 mg/kg increases the antibody response without changing the hematological and histological parameters of the rat spleen (50). Another experimental study after consuming milk and milk with saffron for 6 weeks, and evaluating innate immunity by measuring the percentage and number of monocytes, neutrophils, eosinophils, basophils, platelets, and total white blood cell count, CRP concentration, and Complement concentration of C3 and C4 and humoral immunity by measuring the percentage of lymphocytes and concentrations of IgG, IgM, and IgA; Showed that 3 weeks after saffron consumption, the number of monocytes and serum IgG concentration increased significantly (P-Value <0.05) and P-Value = 0.01 (total white blood cell and platelet count also showed a significant decrease). P-Value <0.05) After 6 weeks, the number of monocytes and IgG concentration decreased significantly compared to the third week (P-Value <0.05) and P-Value <0.001) and the number of platelets increased significantly (P-Value <0.05). ) Found. These results showed that saffron consumption strengthens the innate and humoral system and has anti-inflammatory properties. Of course, these effects depend on the duration of saffron consumption (56).

Modulating the safety of bioactive compounds of saffron can help as a management strategy against SARS-CoV-2. Its immunomodulatory activity may include direct targeting of Toll-like receptors (TLRs) and may also be attributed to nuclear factor (NF-κB), activating protein 1 (AP-1), and downstream signaling pathways (57).

Saffron has been shown to increase the ratio of IFN-γ to IL-4 in human lymphocytes and thus affect the balance of Th1 and Th2 in them (58). These properties may help modulate the immune response during SARS-CoV-2 infection. A study on sensitized guinea pigs showed that the total and differential white blood cell (WBC) counts were positively affected by saffron and safranal extracts (59).

Regarding the anti-inflammatory effects of saffron, studies have shown that saffron reduces inflammation by inhibiting the activity of cyclooxygenase enzyme and the release of inflammatory cytokines and the production of nitric oxide and nitrite, endothelin-1 and the secretion of total protein, and the absorption of inflammatory cells. Prevents lungs in sensitized guinea pigs. This property helps to control excessive pneumonia in SARS-CoV-2 patients due to the release of cytokines and proinflammatory chemokines and thus can be useful in the management of SARS-CoV-2 (6).

Other scientific evidence regarding saffron also indicates that; The stigmas of this plant are used as an antitussive, expectorant, and antioxidant in Greek medicine (38). The antitussive effect of safranal and crocin in saffron stigmas and petals has been documented in an experimental study in Guinea (60). Radical inhibitory, analgesic and hypolipidemic effects (61), antihypertensive activity, anticoagulant activity, inhibition of cell proliferation, and sedation of saffron extract compounds have also been reported in animal and human studies (38, 62). Saffron and its compounds are also an effective treatment for coronary artery diseases, neurodegenerative disorders, bronchitis, asthma, diabetes, fever, and colds and a promising natural remedy in the treatment of metabolic syndrome (63, 64).

Finally, new findings show that; Myrrh or Myrrh with the scientific name Commiphora molol. Engl. ex Tschirch from the family Burseraceae, genus Commiphora, is a fragrant resin gum from the shrub

"Moran". This small tropical tree is widely distributed in East Africa, Saudi Arabia, and India and contains compounds such as volatile oil (10-2%), which mainly include terracotta sesqui, triterpenes (30-30%), and mucilages (60 to 30%) and properties such as antimicrobial, astringent, anti-flatulence, expectorant, anti-secretion, antiseptic and wound healing have been mentioned (27, 65-67).

Also, scientific studies related to "Mor Maki" have shown that; It is used to treat a variety of diseases such as obesity and fat disorders. In addition, it has anti-hyperglycemic, antioxidant, liver protective, analgesic, and anti-inflammatory activities (68). In addition, myrrh is used as an antimicrobial, antiseptic, static, antiviral, and leukocytopenia agent (46). It also has anti-tumor (38) and anticoagulant (69) activities. Traditionally, cold sores have been used to relieve nasal congestion and coughs due to modulated immune response and antimicrobial activity. Antioxidant effects are a possible mediator in protection against myocardial necrosis, inhibition of platelet aggregation, and also increase fibrinolysis by myrrh resin extract (38).

Studies on COVID-19 also show that Commiphora myrrha is one of those medicinal plants that can be used for such conditions. For example, Fatima S et al. In a review study of the herbal approach to COVID-19 management; This herbal medicine has been considered one of the medicines that are considered useful in Greek medicine for epidemic fever, which is similar to the epidemic conditions of COVID-19, along with other herbal medicines such as yellow aloe and saffron (1). Nikhat S and Fazil M also evaluated the use of smoke of this drug as useful due to the similarity of epidemic fever conditions and COVID-19 (15).

## Conclusions

By reflecting on the scientific findings of these plants and a closer look at the sources of traditional Iranian medicine, it is recommended to conduct more clinical trials on the plant composition of opium poppy, to confirm its effectiveness and safety, to use it to strengthen Make the body's defense system more reassuring in situations such as the Quwid-19 pandemic, especially in people at higher risk.

### Author contribution

**SS** and **MZ** wrote the manuscript and edited and confirmed the final version.

### Conflict of interest

No potential conflict of interest was reported by the authors.

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