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Review in traditional herbs to prevent Corona virus

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Abstract

Throughout history, many different cultures have recognized the potential use of herbs for prevention and treatment of different diseases. Recent studies support the effects of these herbs and its extracts in a wide range of applications. These studies raised the possibility of revival of them therapeutic values in different diseases. In this article we have reviewed the antiviral activities of *Allium sativu, Glycyrrhiza glabra, Salvia officinalis and Echinacea purpurea* based on several studies. Such studies show the anti-viral activity of the Common Sage extract 144/5 against viruses HSV and VSV and other extracts activity that inhibits the intercellular multiplication of the viruses when use a high concentration. And also, for The *Echinacea* species have a long history of medicinal use particularly infections, mainly is focused on its immunomodulatory effects, anti-inflammatory, antioxidant effects and anti-viral effects, particularly in the prevention and treatment of upper respiratory tract infections. Different studies have shown that licorice possess a wide range of antiviral activity attributed to its triterpenoids especially (GL) and (GA) that make licorice effective against HCV, HIV, CVB3, DHV, EV71, CVA16, HSV and H5N1 by weakening virus activity, such as inhibiting virus gene expression and replication However, further investigation are necessary to establish the safety profiles of different preparations. Safety issues include the possibility of allergic reaction, dose dependent adverse effects and overdose.

Introduction

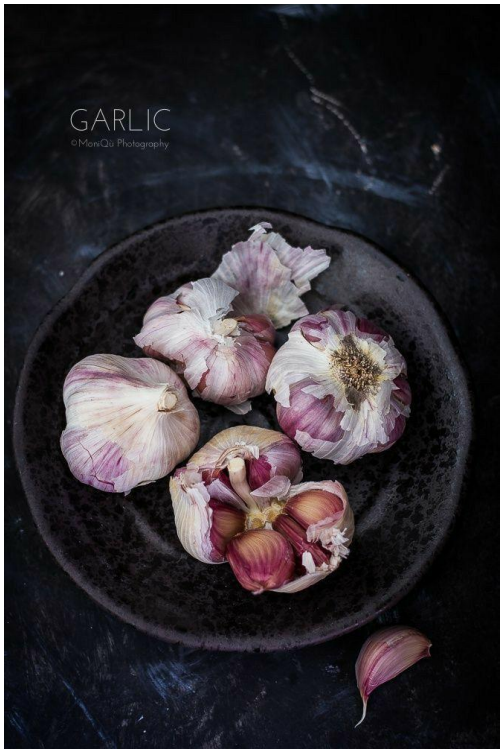
Coronaviruses are enveloped single-stranded RNA positive sense viruses with an average size between 60 nm and 140 nm in diameter with a crown-like shape under electron microscopy [1]. The novel coronavirus (nCoV-2019), coronavirus disease 2019 [2] or Severe Acute Respiratory Syndrome Corona Virus 2 (SARS-CoV-2) is being first reported from Wuhan of Hubei Province of China before being detected in other countries [3]. The first case was reported in December 2019, then, five patients were hospitalized with acute respiratory signs that one of these patients died [4]. On 30 January 2020, the World Health Organization [5] declared a public health emergency of international concern for COVID-19 [6]. Although the WHO said: "There is no specific medicine recommended to prevent or treat the novel coronavirus till now. The WHO, European Medicines Agency [7], US Food and Drug Administration (FDA) and the Chinese government and drug manufacturers are coordinating with researchers and industrials to accelerate the development of new drugs for COVID-19 [8].

Viruses are responsible for a number of human pathogeneses including cancer. Several hard-to-cure diseases and complex syndromes including Alzheimer's disease, type 1 diabetes, and hepatocellular carcinoma have been associated with viral infections.[9] Moreover, due to increased global travel and rapid urbanization, epidemic outbreaks caused by emerging and re-emerging viruses represent a critical threat to public health, particularly when preventive vaccines and antiviral therapies are unavailable. Examples include the recent emergence of

dengue virus, influenza virus, measles virus, severe acute respiratory syndrome (SARS) virus, and West Nile virus outbreaks.[10] To date, however, many viruses remain without effective immunization and only few antiviral drugs are licensed for clinical practice. The situation is further exacerbated by the potential development of drug-resistant mutants, especially when using viral enzyme-specific inhibitors, which significantly hampers drug efficacy.[11] Hence, there is an urgent need to discover novel antivirals that are highly efficacious and cost-effective for the management and control of viral infections when vaccines and standard therapies are lacking.

Herbal medicines and purified natural products provide a rich resource for novel antiviral drug development. Identification of the antiviral mechanisms from these natural agents has shed light on where they interact with the viral life cycle, such as viral entry, replication, assembly, and release, as well as on the targeting of virus–host-specific interactions. In this brief report, we summarize the antiviral activities from several natural products and herbal medicines against some notable viral pathogens including Newcastle Disease Virus (NDV), Sheep red blood cells (SRBC), Vesicular stomatitis virus (VSV), Herpes simplex virus type 2 (HSV - 2).

Garlic



Scientific Name: *Allium sativum*
Common Name: Garlic
The active part of the plant: fresh bulbs

Garlic has been and for a long time a plant the used in different areas in the world especially Asia for food, spiritual ceremony and medicine. As traditional use, garlic has been described by folks for improve health, treat cardiac problems, common cold, and immune system and even for cancer.

And for that many uses, and the fast spread of the new covid-19 virus, many has suggested the use of garlic for cure or prevention of the virus. As for cure no studies prove that it can in any way cure the virus. Garlic remedies including raw garlic, commercial powders, oil and extracts have been used for millennia, and are popularly thought to be effective against the common cold. 0Garlic contains allicin (S-allyl-L-cysteine sulfoxide), a Sulphur-containing phytonutrient, likely to be the source of its antibacterial and anti-viral properties.

The wide variety of effects that has been reported of garlic preparations and extracts with beneficial and useful properties may be due to their numerous compounds (organosulfur and others) contained in different concentrations, which is being a challenge to separate and identify compounds with potential beneficial properties on the human immune and cardiovascular systems.[12]

Modulation of Cytokine Secretion

Hanieh *et al* [13] proved that dietary Allium sativum and Allium cepa at low doses in white Leghorn chickens, following immunization with Newcastle Disease Virus (NDV), Sheep red blood cells (SRBC), and Brucella abortus (BA), enhanced anti-NDV, anti-SRBC, and anti-BA antibody production. The authors concluded that enhanced T cell proliferation with dietary garlic might has directly/indirectly enhanced B-cell proliferation and differentiation.

Phagocytosis Promotion and Macrophage Activation allicin treatment stimulated the expansion of CD4+ T cells and macrophages 34. Allicin enhances host pro-inflammatory immune responses and protects against acute murine malaria infection [14]. The antimicrobial activity of allicin was demonstrated by modulation of the cytokines activating macrophages that controlled the parasitic infection.

Immunostimulatory Activities of Garlic

Fructooligosaccharides (FOS) are fructans that are naturally present in garlic. Chandrashekar et al. isolated fructans present in AGE: high molecular weight (>3.5 kDa; HF) and low molecular weight (<3 kDa; LF), which were assessed in an immunostimulatory mouse model. Both HF and LF displayed mitogenic activity and activation of macrophages including phagocytosis. These activities were comparable with those of known polysaccharide immunomodulators, such as zymosan and mannan.[15]

Licorice

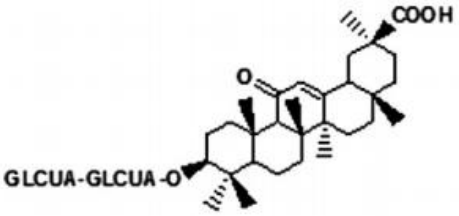
Scientific Name: *Glycyrrhiza glabra* L

Common Name: Licorice

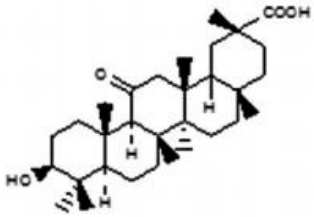
The active part of the plant: roots and rhizomes

Numerous studies have revealed many pharmacological activities of licorice, such as antiviral[15,16], anti-inflammatory[17,18], antitumor[19,20], antimicrobial[21,22] and many other activities[23,24]. Among the pharmacological activities of licorice mentioned above, the antiviral and antimicrobial activities have been most commonly reported.

Licorice contains more than 20 triterpenoids and nearly 300 flavonoids. Many studies have demonstrated that two triterpenoids, glycyrrhizin (GL)[25,26] and 18β-glycyrrhetinic acid (GA)[27], are responsible for the antiviral activity.



Glycyrrhizin (GL)



18*β*- Glycyrrhetinic acid (GA)

Studies that show the antiviral activity of licorice

Matsumoto *et al* study[2,5] reported that GL targeted the release step in which infectious anti-hepatitis C virus (HCV) particles were infecting cells. These findings indicated possible novel roles for GL to treat patients suffering from chronic hepatitis C.

Previous [28] studies showed that intercellular adhesion molecules played an important role in some viral infections, such as human immunodeficiency virus (HIV).

Zhang's study[29] reported that GL showed a significant improvement of coxsackievirus B3 (CVB3)–induced myocarditis by improving weight loss profile, reducing serological levels of cardiac enzymes and increasing survival rate

Soufy *et al*.[30] found that GL had excellent immunostimulant properties and induced a synergistic effect to duck hepatitis virus (DHV) vaccine by activating T lymphocyte proliferation.

Smirnov's study[31] indicated that GL could be considered a promising agent for the treatment of influenza
Wang's study[26] revealed that GL was an antiviral component in licorice against enterovirus 71 (EV71) and coxsackievirus A16 (CVA16) infection with defined mechanisms.

Above all, GL is an effective antiviral compound against HCV, HIV, CVB3, DHV, EV71, CVA16, HSV and H5N1 by weakening virus activity, such as inhibiting virus gene expression and replication, reducing adhesion force and stress

Table 1 The antiviral active components and their possible mechanisms for virus prevention.

Component	Antiviral mechanism	Viral type
GL	Affect release step while infectious HCV particles are infecting cells.	HCV
	Inhibit HCV full length viral particles and HCV core gene expression.	
	Reduce adhesion force and stress between CCEC and PMN.	HSV
	Block the degradation of nuclear factor κB inhibitor IκB.	CVB3
	Activate T lymphocyte proliferation.	DHV
	Weaken H5N1-induced production of CXCL10, IL-6 and CCL5, and suppress H5N1-induced apoptosis.	H5N1
	Reduce HMGB1 binding to DNA, and inhibit influenza virus polymerase activity.	Influenza virus
	Inactivate CVA16 directly, while the effect of anti-EV71 is associated with an event(s) during the virus cell entry.	CVA16 EV71
	Establish a resistance state to HSV1 replication.	HSV1
GA	Reduce the levels of viral proteins VP2, VP6 and NSP2 at a step or steps subsequent to virus entry.	Rotavirus
	Prevent viral attachment, internalization and stimulate IFN secretion.	HRSV

Sage

Scientific Name: *Salvia officinalis*

Common Name: garden sage

The active part of the plant: leaves

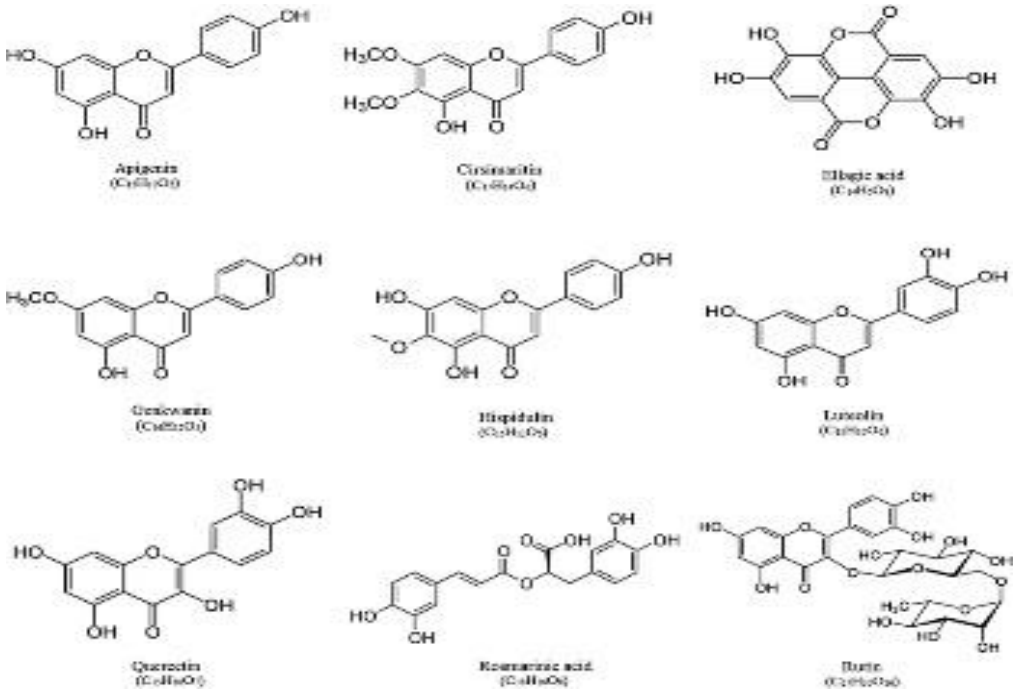
Salvia officinalis L. (Sage) is a perennial round shrub in the family of Labiatae/Lamiaceae. Salvia is the largest genus of this family and includes near 900 species. Plants of this genus grow all over the world and the specie of *S. officinalis* is native to Middle East and Mediterranean areas. Today's, it has been naturalized throughout the world particularly in Europe and North America [2].

The aerial parts of *S. officinalis* shrub has a long history of use in cookery and traditional medicine. Because of its flavoring and seasoning properties, this plant has been widely used in preparation of many foods. In folk medicine of Asia and Latin America, it has been used for the treatment of different kinds of disorders including seizure, ulcers, gout, rheumatism, inflammation, dizziness, tremor, paralysis, diarrhea, and hyperglycemia[33].

In traditional medicine of Europe, *S. officinalis* has been used to treat mild dyspepsia (such as heartburn and bloating), excessive sweating, age-related cognitive disorders, and inflammations in the throat and skin. German Commission E has accepted the use of *S. officinalis* for a number of medical applications included inflammation and dyspepsia.

Active constituents

The diterpenoids manool and rosmanol 9-ethyl ether. The diterpenoid 12- deoxo-carnosol is present only in wild sage, while the diterpenoids galdosol, carnosic acid 6-methyl ether, carnosic acid 6-methyl ether-γ-lactone, and triterpenoid oleanic acid are present only in cultivated sag[34]



Antiviral activity

Total yield of CO2 re-extracts obtained from dried plant material was 52.5 g (0.31%), 84.76 g (0.88%), and 110.48 g (1.175%) for the 152, 144, and 149 extracts, respectively, Then the yield extract at deferent pressure of 200, 300 and 400 bars to give (144/2, 144/3, and 144/4)

The results of investigating the intracellular antiviral activity of sage extracts showed that sage fractions 144/2 and 149/3 did not reduce the VSV (vesicular stomatitis virus) in the range of non-toxic concentrations. Although fractions of cultivated and wild sage 144/3, 144/4, and 152/2 at sub-toxic concentrations did show some reduction of VSV in cell culture, meaning that they probably inhibit to some extent virus multiplication at intracellular level, this reduction was not sufficient to pronounce fractions 144/3, 144/4, and 152/2 antiviral. According to the classification of antiviral agents.

Comparing the antiviral activity of IfN-α and fraction 144/5, we can conclude that extract 144/5 possessed antiviral activity similar to that of interferon at the intracellular level. Taken together, they obtained results indicate that the mechanism of antiviral activity of extract 144/5 involves inhibition of the early steps of the virus infective cycle without a direct veridical effect. This mechanism has been proposed for the antiviral effect of Spirulina maxima extract against HSV- 2 (herpes simplex virus type 2).[35]

When HSV-1 and HSV-2 were pretreated with the extracts for 1 h prior to host cell infection, plaque formation was significantly reduced. This result suggests that the extracts interact with structures of the virion envelope which are necessary for adsorption or entry into host cells. When host cells were pretreated with the extracts prior to virus infection, most of the

alcoholic extracts displayed a significant diminution of plaque number with highest plaque reduction for the Garden 20% ethanol extract. This extract revealed a strong reduction of viral infectivity not only for HSV-1 (68% plaque reduction) but also for HSV-2 (94% plaque reduction). These data indicate that the Garden 20% alcohol extract does not only interact with the surface of the host cells but also with the envelope of herpesviruses. [36]

(E.) purpurea

Scientific Name: *Echinacea purpurea*
Common Name: purple coneflower, red sunflower and rudbeckia.
The active part of the plant: Herb, root and flower

The Echinacea species, Echinacea angustifolia, Echinacea pallida and Echinacea purpurea have a long history of medicinal use particularly infections[37], and today Echinacea preparations are the best herbal medicine used in several countries like America, Germany, Australia, Thailand and some other European countries. Mainly Echinacea is focused on its immunomodulatory and anti-inflammatory effects[38], and antioxidant [39] effects, anti viral effects[40], particularly in the prevention and treatment of upper respiratory tract infections[41]. several groups of bioactive constituents, including alkamides and lipophilic alkamides, water-soluble phenolic compounds (mainly caffeic acid derivatives) and polysaccharides, benzalkonium chloride are considered important for its activity[42]

Active constituents

The active substances of Echinacea are polysaccharides, flavonoids, chicoric acid, alkyl amides, polyacetylenes and essential oils [42]. Polysaccharides and chicoric acid glycosides have immunostimulatory activity in Echinace [43]. lipophilic alkamides and water-soluble caffeic acid derivatives responsible for anti-oxidant activity [39]. Alkamides and caffeic acid derivatives are potent anti – inflammatory agents present in Echinacea [44]

Antiviral activity

Biological activity of the chemical Components of E. purpurea have been characterized [45], Echinacea has antiviral activity and they have found that cultured cells infected with virus and exposed to E. purpurea juice demonstrated an increased rate of presentation of viral antigen [46]. Benzalkonium chloride and phytochemicals derived from Echinacea purpurea was found to have antiviral activity against herpes virus in a human cell model [47]. Echinacea purpurea was also very effective against influenza virus [48]. The extract of E. purpurea has been found to inhibit viral replication in animal cell viral culture models [49]. Eilmes demonstrated that complex hydrophilic and lipophilic extracts of Echinacea have more viral-infection- inhibitory activity fractions [50]. Polysaccharide derived from Echinacea purpurea has been shown to stimulate macrophage activity and several functions related to cytokine production [51] and groups of phenolic compounds and alkamides, which have demonstrated antiviral and antifungal properties, respectively [52]. These activities could be related to the reports that some E. purpurea preparations were able to prevent or control upper respiratory infections (URIs) [53]. Turner and colleagues have recently described a human trial testing the efficacy of Echinacea in preventing colds induced by a cultured rhinovirus [54]

Immunostimulatory Activities

A series of studies in mice using purified polysaccharides from Echinacea plant cell cultures showed a stimulatory effect when applied to immune cells in culture or injected intraperitoneally into mice [43]. Mice with suppressed immunity due to treatment with cyclophosphamide or cyclosporin also had an increase in these immune functions when given purified polysaccharides from Echinacea [55]. These studies suggest that Echinacea stimulates immune functions in healthy or in immunosuppressed animals

Several animal and human studies have suggested that Echinacea stimulates neutrophil and macrophage phagocytic function [56].

CONCLUSION

There is currently no specific treatment available for the new virus COVID-19. Thus, identifying novel and effective treatments is imperative and would be of great benefit to the humanity. From the studies of the extract showed that different plants have a pharmacological effect, such as antiviral effect. Yet that effect cannot be achieved simply by consuming the raw or dried plants. But rather to be specifically prepared under certain condition, as in common sage the anti-viral effect, depending on the concentration and pressure along with temperature during the extraction to yield the preparation that has the anti-viral effect. Other plants such as garlic may not have the antiviral effect as a direct effect, instead it improves the immune system support it to fight the viruses and other offending agents.

Those studies show that many plant traditionally used for their medicinal value are in fact have it to a much lesser extent than it believed to be and for most of those pants farther research and studies need to be carried to discover their effect and to be used in the safest and most effective way

for COVID-19 treatment, no drug has been announced to be effective so far. Glycyrrhizin is valued for its various pharmacological effects and may be useful agent for the treatment of COVID-19. So, farther research and studies need to demonstrate the activity of Glycyrrhizin against COVID-19

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