کارگاه‌های آموزشی مرکز اطلاعات علمی

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- اصول تنظیم قراردادها
- آموزش مهارت های کاربردی در تدوین و چاپ مقاله
Candidate herbal medicines with antiviral activity against covid 19

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Abstract
Coronavirus disease (COVID-19), is an extremely infectious disease. Since 2019, a terrible pandemic of this disease has swept the globe, and it hasn't stopped, with regular mutations transforming into aggressive and contagious versions. As the world struggles with coronavirus infection, patients are being treated with a variety of antiviral medications and symptomatic therapies, and clinical trials are in progress. In these circumstances, it is more important to consider all of the treatment options for COVID-19, including herbal medicine. People reckon that the COVID-19 patient would be relieved from symptoms and cured by using herbal immunomodulators. In many countries, herbal medication has already been used to manage corona such as China, Africa, Iran. On account of not having adequate preclinical and clinical studies regarding the effect of herbal medication on coronavirus, some herbal medicine plants could be effective to treat patients based on the previous experiments. Some herbal medicines, such as Curcuma longa, Garlic, Cinchona, Echinacea, Ginger, and Curcuma xanthorrhiza are discussed in this article as effective treatments for COVID-19 due to their antiviral effects. Although their effectiveness is still controversial and further research is needed, we also review some impacts of herbal and draw conclusions at the end of the session.

Keywords: COVID-19, Herbal, Curcuma, Garlic, Cinchona, Echinacea, Ginger, Xanthoriza
1. Introduction

Coronavirus disease (COVID-19) is caused by a coronavirus that causes infection among people all around the world, ranging from a flu-like syndrome to severe health-related problems. [1] COVID-19 was diagnosed first in December 2019, and the World Health Organization (WHO) it a pandemic in March 2020. [2] There have been more than 178,700 confirmed patients in at least 140 countries as of March 2020. The number of cases was documented in mainland China, with Italy, Iran, Spain, and South Korea following closely behind. [3] As of February 15, 2022, there have been 408,910,752 documented cases of COVID-19 and 5,802,226 deaths have been announced worldwide (Figure 1). [4]

COVID-19 has common symptoms such as fever, fatigue, shortness of breath, and cough. In Serious cases, pneumonia and organ failure may occur and lead to even death. [5] After exposure to transmissible sources including droplets, direct contact, aerosol, droplets fomites, animal-human, and fecal-oral transmission, SARS-CoV-2 has an incubation period of 2–14 days. The initial stage of the infection might be asymptomatic or characterized by lower and upper respiratory tract infection (RTI) symptoms, such as typical symptoms, and closely correlated with smell and taste disorders or with gastrointestinal problems. 7 to 10 days after the beginning of symptoms, some patients may experience a rapid clinical deterioration, marked by respiratory symptoms which may be linked with thromboembolic complications. Finally, a subsequent step in the acute development of SARS-CoV-2 has been recognized as acute respiratory disease. [6]

There are no available specific medicines as an effective treatment of COVID-19 Currently. During this COVID-19 pandemic, different treatment approaches have been asserted, including herbal and traditional medicine, which has been used as an antiviral medication against some viruses such as H1N1 influenza. [7] Consumption of herbal containing active chemicals with antibacterial, immunostimulatory, antiviral, and anti-inflammatory effects, such as curcumin, echinacea, and quinine, is a new trend in society. These herbal substances are thought to have the ability to modify immune responses, and hence to have therapeutic effects in treating and preventing COVID-19. [8, 9] This article explains that herbal medication may have antiviral effects to treat the COVID-19 as a non-viral medication.
2. Candidate herbal medicines

Herbal medicines are often used by many individuals in the community in this circumstance, when preventative and therapeutic agents have not been established and approved for administration to patients. As explained previously, we conducted a review of multiple publications from various journals. At least six herbals have been identified as having the potential to prevent or the treatment of COVID-19 patients due to having antiviral and other beneficial effects.

2.1. Curcumin longa

Curcumin (Figure 2) is extracted from roots of rhizome. People are known it as Curcuma longa (C. longa). This plant is used in science and medicine. Turmeric is a member of the ginger family. In Asian, C. longa is used as a medicine against several diseases (such as inflammatory bowel disease (IBD), diabetes mellitus, psoriasis, asthma, neurodegenerative disease, obesity, cardiovascular disease, and allergy), due to having anti-cancer, anti-inflammation, and antioxidant effects. [10, 11]

Curcumin has antiviral properties against a wide range of viruses such as influenza, HIV, HSV-2, hepatitis virus, adenovirus, Zika virus, and HPV. [12, 13] Other studies revealed that curcumin has had immunostimulatory impacts (by increasing tumor necrosis factor (TNF-α) and IL-6) as well as anti-inflammatory effects (by decreasing TNF-α, phosphatidylinositol-3 kinase (PI3K), nuclear factor-kappa B (NF-κB), and IL-6). [14-16]

In many hospitalized patients in India, nutritional supplementation of curcumin with zinc and vitamin C has shown promising benefits in strengthening natural immunity and preventive defense against infections. It's also reported that curcumin's pharmacological formulation in a nanoemulsion system resulted in increasing bioavailability and solubility as well as a stronger antihypertensive impact. [17] Some studies have reported that curcumin has a long-term (more than 3 months) antihypertensive effect. [18] Increasing the level of angiotensin-converting enzyme (ACE) is one reason for hypertension and ACE inhibitor is one mechanism to control high blood pressure. According to the studies, COVID-19
patients have hypertension as usual comorbidity and Curcumin works as an ACE inhibitor. So, Curcumin may be efficient in controlling hypertension in COVID-19 patients. [19-21].

![Curcumin longa](image)
![Garlic](image)
![Cinchona](image)

2.2. Garlic
Garlic (Allium sativum) (Figure 3) contains phytochemicals like sulfur which have positive effects such as immunosuppressor, anticancer, cardioprotective, anti-inflammatory, and anti-inflammatory. [22] Garlic has been used as a food and flavoring herb for thousands of years, as well as a traditional treatment for a variety of ailments, such as viral disorders. [23, 24] The antiviral effects of garlic against HIV, Influenza B, a gammaretrovirus, herpes simplex virus, and coxsackievirus species were revealed. [25] Khubber et al. claimed that adding garlic and its products into a daily diet can be effective as adjuvant therapy and may improve the toxicity and side effects of the main medication. Furthermore, garlic can decrease the rate of infection due to SARS-CoV-2. SO, it has a beneficial role in the incidence decline of COVID-19 in various communities. [26] Another study reported that garlic is beneficial for respiratory diseases such as bronchitis infection due to coronavirus and influenza and improves the immune system. [27]

2.3. Cinchona
Cinchona trees were discovered to heal fever first. Then people found that the bark of these trees (Figure 4) might be beneficial as a cure for malaria which is called quinine. The anti-malaria effect of quinine is the same as chloroquine. [28, 29] Some studies revealed that chloroquine could use as an antiviral for SARS-CoV infection. Therefore, quinine (chloroquine analog) might show positive effects on COVID-19 patients. [30, 31]
Baroni et al reported that quinine had an antiviral effect by several process such as inhibiting NF-kB, running the protein heat shock response, and blocking virus replication. [32] Quinine has an antiviral activity that suppresses both the immune system and antiviral activity. If quinine increases IFN-α cytokine levels, it acts as an immune stimulant. In contrast, if quinine reduces TNF-α levels by inhibiting release, it is known as an immunosuppressant. Although both of these activities can have positive effects on patients with Covid-19, some studies recommended not to use of quinine routinely. [33]
2.4. Echinacea

Echinacea (Figure 6) species especially Echinacea purpurea (E. purpurea), one of the most popular clinically studied herbal medicines in part of North America and Europe and for this reason reveals promising impacts as a treatment for viral infections.[34] Earlier research revealed that Echinacea might decline the severity and duration of respiratory infections. [35] Although some studies announced that it had significant antiviral effect, other impacts on immune system and inflammation are still controversial. Sharma et al. reported that echinacea extract could be used as an herbal antiviral treatment for the enveloped virus such as influenza and herpes simplex virus and less impact on naked virus including adenoviruses and rhinoviruses. According to this report, E. purpurea can be used as an effective treatment against coronavirus as a membrane virus. [36] Some production containing echinacea assert that they act as an immunostimulatory and not as an immunosuppressor. Burger et al. reported that echinacea may increase the release of several cytokines from macrophages such as IL-1, IL-10 and TNF-α. [37] Macrophages can phagocytose SARS-CoV-2 and release TNF-α with other cytokines. [38]

![Figure 5: Ginger](image1)
![Figure 6: Echinacea](image2)
![Figure 7: Curcuma xanthorrhiza](image3)

2.5. Ginger

Ginger (Figure 5) has numerous therapeutic usages, such as anticancer, antioxidative, antimicrobial, anti-inflammatory, anti-fungal, hepatoprotective, hypo-cholesterolemic, immunomodulatory, antimigraine, antidiabetic, anti-nausea, cardioprotective, anti-obesity, neuroprotective, anti-emetic, and respiratory protective effects. [39] Fresh ginger has antiviral effects against viruses such as rhinovirus and human respiratory syncytial virus (HRSV). And also, it is more beneficial to treat airway infection due to viruses. Before inoculation of HRSV (1-2 hours), the extract of ginger can inhibit the virus attaching to cells of epidermoid carcinoma or lung carcinoma. Stimulating the release of interferon α and β from the epithelial cell is another effect of ginger to inhibit spreading viruses to the lower-respiratory tract.[40] After dehydration or cooking ginger, shogaol is produced. Shogaol has anticancer, antiemetic, antioxidant, neuroprotective, and anti-inflammatory impacts. Paradol is synthesized from shogaol and exhibits anti-inflammatory, anticancer, neuroprotective, and cardioprotective effects.[41, 42] Zingerone which is produced from drying and heating or roasting the ginger, has enormous benefits, including antispasmodic, antidiabetic, anxiolytic, anticancer, antimicrobial, protection from radiation, anti-hyperlipidemia, anti-inflammatory, anti-oxidant, antimicrobial, antiemetic, and antidiarrheic effects.[43]
According to different studies, the cover 19 patient who consumed ginger with or without main treatment, had fewer symptoms especially coughing, muscular pain, and breath shortness (In Bangladesh, Tunis, and Iran studies). [44-46]

Moreover, the rate of hospitalization for getting treatment for COVID 19 was lower among the patients consuming ginger (In Saudi Arabia and Iran studies). [47-48] In Africa, ginger mixes with other herbal plants to use as a treatment for COVID-19. [49]

2.6. Curcuma xanthorrhiza
Xanthorrhizol (XNT) (Figure 7) or Curcuma xanthorrhiza Roxb (C. xanthorrhiza) is used in Asian countries as an herbal plant. [50] C. xanthorrhiza (Curcuma Zedoaria) has some beneficial impacts such as an antioxidant, antihypertensive, anti-inflammatory, anticancer, antimicrobial, antiplatelet, nephroprotective, antihyperglycemic, and useful for systemic diseases like systemic lupus erythematosus (SLE). [51-54]

The study regarding xanthorrhizol revealed that this compound decline inflammatory genes in the liver, muscle, and adipose tissue in diabetes mellitus patients. And also, it can inhibit the production of inflammatory cytokine and the expression of tumor necrosis factor (TNF-α) and interleukin (IL-1β). [55] Singgih Wahono et al. reported that xanthorrhiza is able to decline the level of IL-6 as well as raise serum transforming growth factor (TGF-β) in patients diagnosed with SLE. [56]

Another study claim that Xanthorrhizol can be used as an immunosuppressant for COVID-19. Owing to inhibiting proinflammatory cytokines. However, it needs further investigations before recommending xanthorrhizol for prevention and treatment in COVID-19 patients. [57]

3. Conclusion

This review suggests that these selected herbal medicines may have the ability to regulate the synthesis and secretion of cytokines, interfere with the virus's growth in host cells, and have antiviral effects, according to the preceding explanation. Herbal medication might be effective in the battle against COVID-19. Furthermore, patients should be advised that using supplements with one of these chemicals to prevent COVID-19 or treat the illness without particular advice or under the direct supervision of a doctor or a specialist is still not suggested. A recommendation for the clinician is that patients should be prescribed these herbal remedies carefully, even if they do not have any illnesses owing to the debate regarding this information. Moreover, further research is needed on the antiviral effects of herbal medicines against COVID-19.

Available information

This information in this article comes from previously published research and datasets that have been referenced.
References


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