Dietary therapy and herbal medicine for COVID-19 prevention: A review and perspective

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A B S T R A C T
A novel coronavirus disease (COVID-19), transmitted from humans to humans, has rapidly become the pandemic responsible for the current global health crisis. COVID-19 is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which is said to be of zoonotic origin. This review describes the etiology and signs and symptoms as well as the current allopathic therapy for COVID-19. Additionally, findings of previous studies on the immunomodulatory effects and antiviral activities of particular foods and herbs on influenza virus and coronaviruses have been collated, with the aim of promoting the use of dietary therapy and herbal medicine as COVID-19 preventive therapies, while specific drugs and vaccines are yet to be discovered or are still under development. The volume of existing reports is irrefutable evidence that foods and herbs possess a potential antiviral ability against SARS-CoV-2 and can prevent COVID-19. Foods and herbs could be used as dietary or complementary therapy to prevent infection and strengthen immunity, as antiviral agents for masks, as disinfectants to curb aerosol transmission, or as sanitizing agents to disinfect surfaces. However, these hypotheses need to be experimentally verified for SARS-CoV-2 and COVID-19 patients.

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1. Introduction
At the end of December 2019, the coronavirus outbreak caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) occurred in Wuhan, Hubei, China,1 leading to the rapid spread of 2019 novel coronavirus (COVID-19) into a pandemic responsible for the current global health crisis.2,3 In May 2020, there have been approximately 5 million confirmed cases of COVID-19 and more than 30 thousand deaths worldwide, as reported by the WHO.4 In this review, we aim to report historical records on the antiviral activity of a particular diet and herbal medicine on influenza virus, SARS-CoV-1, and SARS-CoV-2. This will promote the use of dietary therapy and herbal medicine as complementary COVID-19 prevention therapies, given the current absence of an effective drug and/or vaccine against COVID-19/SARS-CoV-2. Several doctors and researchers have already attempted to use herbal medicines on clinical trials against SARS-CoV-2.5 The longstanding use of dietary therapy and herbal medicine to prevent and treat diseases cannot be overemphasized, as several herbs exhibit antiviral activity.6 Using dietary therapy and herbal medicine to prevent SARS-CoV-2 infections could be a complementary COVID-19 therapy, while drugs remain under development.

2. Methods
In this review and perspective, the authors searched and collected data related to COVID-19, herbal medicine, and dietary therapy. Google Scholar, PubMed, SciFinder, and ScienceDirect were the main search engines used. The search terms used included: coronavirus; etiology; signs; symptoms; allopathic therapy against COVID-19; immunomodulatory and antiviral activities of herbs...
against influenza, SARS-CoV-1, and SARS-CoV-2. The chosen articles were reviewed and interpreted by the authors. The perspective is an opinion of the authors regarding the use of foods and herbs as a prevention and complementary therapy against COVID-19.

3. Results and discussion

3.1. Etiology, signs, and symptoms of COVID-19

Early discoveries of COVID-19 pneumonia patients were suspected to be associated with the Huanan seafood market in Wuhan, where wild-animal trading occurred.7 SARS-CoV-2 is postulated to have originated from a bat, because its full-length genomes are similar to the bat-derived SARS-CoV genome: 88% identical (Fig. 1). Phylogenetic analyses indicate that SARS-CoV-2 belongs to the subgenus Sarbecovirus of the genus Betacoronavirus. More so, homology modeling studies reveal that the receptor-binding domain structure of SARS-CoV-1 is similar to that of SARS-CoV-2.4 SARS-CoV-2 might amplify in the intermediate mammalian host, probably pangolin, since the whole-genome of pangolin-CoV is 91.02% identical to SARS-CoV-2.9 In a previous study, molecular and phylogenetic data showed that SARS-CoV-2 did not emerge directly from the pangolin-CoV.10 However, the origin of the transmission from pangolin-to-human is still in debate. Trading pangolin in wet markets could be a reason for the origin of the transmission.8,9

![Fig. 1. SARS-CoV-2 etiology, transmission cycle, and structure. SARS-CoV-2 reportedly originates from bats, zoonotically transmitted to the intermediate mammalian host pangolin,8,9 however, its origin is still under debating. SARS-CoV-2 belongs to the subgenus Sarbecovirus of the genus Betacoronavirus. Its genome mutates to form 3 types: A, B, and C.12 It is an airborne disease transmitted from human-to-human. COVID-19 is currently a pandemic and global health crisis.7]
markets should therefore be strictly prohibited to reduce the risk of future zoonotic transmission. SARS-CoV-2 genomes have now mutated into 3 types; A, B, and C. Type A is closest to the ancestral bat-derived coronavirus. Great proportions of types A and C have been observed in Europeans and Americans, while type B is mainly found in East Asia.

SARS-CoV-2 is a human-to-human aerosol transmission, making the fear of contracting COVID-19 a major panic-trigger amongst numerous individuals. Based on data collected from 99 COVID-19 patients admitted in Jinyintan Hospital, Wuhan, the typical signs and symptoms include fever (83%), cough (82%), and shortness of breath (31%), which are often accompanied by muscle ache (10%), confusion (9%), headache (8%), and sore throat (5%) (Fig. 2). Approximately 75% of these patients also presented with bilateral pneumonia (75%), 17% of them had acute respiratory distress syndrome, and 11% died over a short time span, owing to multi-organ failure. Another study observed that the time from illness onset to dyspnea is approximately 8 days. In this study, 63% of patients had lymphopenia, and all the patients presented with pneumonia. Other reliable indicators include the loss of taste and smell.

3.2. Allopathic therapy against COVID-19

During the SARS-CoV-2 spread in Wuhan, allopathic therapy was used for COVID-19 treatment in the Wuhan Jinyintan Hospital (based on 99 patients), including antiviral treatment (76%), antibiotic treatment (71%), oxygen therapy (75%), and intravenous immunoglobulin therapy (27%), although no COVID-19 drug has been approved by the US Food and Drug Administration. There is also no effective pharmacologic treatment against COVID-19. Determining the drug target requires an understanding of the viral lifecycle. SARS-CoV-2 is a single-stranded RNA-enveloped virus. SARS-CoV-2 and SARS-CoV-1 share similar host-entry mechanisms. It targets the cells by using the viral structural spike (S) protein bind with angiotensin-converting enzymes 2 (ACE2) receptor forming endosomes which enter the cells. TMPRSS2 is a host type 2 transmembrane serine protease helping virus enter through S protein. After the virus enters the cell, it synthesizes viral polyprotein, and RNA subsequently assembles and releases the new virus particles. Inhibiting viral cell entry and replication and modulating the immune system could be a potential target for drug therapy. Current clinical tries on COVID-19 pharmacological treatments include hydroxychloroquine and remdesivir. Hydroxychloroquine, which reduces the viral load in COVID-19 patients, appears to be more effective when used in combination with azithromycin. Remdesivir proved its potential against COVID-19 by displaying clinical improvement. While many clinical trials aimed at discovering a potential effective COVID-19 drug are ongoing, using herbal medicines with well-known antiviral activity might be a complementary SARS-CoV-2 preventive therapy.

3.3. Immunomodulatory effect of foods and herbs and their antiviral activities against influenza, SARS-CoV-1, and SARS-CoV-2

Coronavirus can be treated using nutrition; for instance, treating influenza with very large amounts of vitamin C has been practiced for decades. The common cold, SARS-CoV-1, and SARS-CoV-2 fall under the same coronavirus family; hence, are regarded as the same viral type. Therefore, vitamin C may be effective against...
COVID-19; clinical studies are required. An evidence showed that vitamin D decreased the risk of COVID-19 outbreak in winter, which is a time when 25-hydroxyvitamin D (25(OH)D) level is low. Thus, vitamin D intake may reduce the risk of influenza and COVID-19 infections and related deaths. Many foods and herbs are known to display antiviral and immunomodulatory activities. Many foods and herbs have been reported to exhibit immunomodulatory properties. Their activities are based on selectively stimulating cytokines, activating lymphocytes, increasing natural killer cell counts, and enhancing macrophage actions. Rice bran, wheat bran, Lawsonia alba (hina), Echinacea purpurea (eastern purple coneflower), Plumbago zeylanica (Ceylon leadwort), and Cissampelos pareira Linn (velvetleaf) also exhibit immunomodulatory properties by stimulating phagocytosis. Eucalyptus essential oil is reported to improve the innate cell-mediated immune response that can be used as an immunoregulatory agent against infectious diseases. Collectively, using these immunomodulatory foods and herbs could enhance the immune system and protect the body against COVID-19. However, these observations must be verified through scientific or clinical studies.

Numerous studies, although limited to in vitro, in vivo, and in ovo studies, have reported the bioactive components of foods and herbs against the influenza virus and SAR-CoV-1. Only a few clinical studies have been carried on the effects of specific foods and herbs against the influenza virus and SAR-CoV-1, as most clinical studies have been done on food and herb combinations, or the traditional Chinese formulas. The antiviral activities reported for foods and herbs against the influenza virus are shown in Table 1. The antiviral influenza study models have mainly been Madin-Darby Canine Kidney cells (MDCK) and murine models, with the influenza strains being the influenza A virus subtype H1N1, H9N2, and H1N9. The extracts or bioactive compounds of garlic, ginger, Korean red ginseng, eucalyptus, tea tree, Tianmingjing, Machixian, fish mint, Chinese mahogany, cape jasmine, zhebeimu have been shown to exhibit antiviral activity against the influenza virus.

The mode of action for influenza A inhibition is via inhibition of proliferation or penetration into MDCK cells. Garlic and

### Table 1

<table>
<thead>
<tr>
<th>Herbs</th>
<th>Bioactive compound and extract</th>
<th>Experimental model</th>
<th>Mode of action</th>
<th>References</th>
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<tr>
<td><em>Allium sativum</em> (Garlic; 大蒜)</td>
<td>Garlic aqueous extract</td>
<td>H9N2 virus infection in MDCK cells and chicken embryo</td>
<td>Anti-avian influenza virus H9N2 activity in both chick embryos and cell models</td>
<td>Rasool et al. (2017)</td>
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<tr>
<td></td>
<td>Garlic extract</td>
<td>H1N1 virus infection in MDCK cells</td>
<td>Inhibits H1N1 penetration and proliferation in cell culture</td>
<td>Mehrbod et al. (2008)</td>
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<tr>
<td><em>Zingiber officinale</em> (Ginger; 姜; Jiāng)</td>
<td>Ginger aqueous extract</td>
<td>H9N2 virus infection in MDCK cells and chicken embryo</td>
<td>Anti-avian influenza virus H9N2 activity in both chick embryos and cell models</td>
<td>Rasool et al. (2017)</td>
</tr>
<tr>
<td><em>Panax ginseng</em> C.A. Meyer (Korean red ginseng; 红参; Hồng sâm)</td>
<td>Korean red ginseng powder capsule</td>
<td>H1N1 virus-induced respiratory tract infection in mice and MDCK cells</td>
<td>Ginseng enhances immunity by increasing the levels of influenza A virus-specific antibodies and their neutralizing activities. It modulates CD69-expressing immune cells and exhibits significant enhancement of influenza virus-specific IgA antibody in mice lungs.</td>
<td>Quan et al. (2006)</td>
</tr>
<tr>
<td><em>Eucalyptus polybractea</em> (Eucalyptus; 尤尤; You yu jia li)</td>
<td>Aerosol and vapor of eucalyptus oil</td>
<td>H11N9 virus infection in MDCK cells</td>
<td>Inhibits avian influenza virus H11N9 in aerosol and vapor form</td>
<td>Usachev et al. (2013)</td>
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<tr>
<td><em>Melaleuca alternifolia</em> (Tea tree; 茶树; Chá shù)</td>
<td>Tea tree oil</td>
<td>H11N9 virus infection in MDCK cells</td>
<td>Pre-coated tea tree oil inactivates captured H11N9 virus in fiber material</td>
<td>Pyankov et al. (2012)</td>
</tr>
<tr>
<td><em>Carpesium abrotanoides</em> L. (Tianmingjing; 天名精)</td>
<td>Water extract of <em>P. oleracea</em> L.</td>
<td>H1N9 virus infection in MDCK cells</td>
<td>Inhibits H11N1 virus activity</td>
<td>He et al. (2020)</td>
</tr>
<tr>
<td><em>Portulaca oleracea</em> L. (Machixian; 马齿苋; Mā chǐ xiàn)</td>
<td>4x,5x-dihydroxyguaia-11(13)-en-12,8s-lactone</td>
<td>H1N9 virus infection in MDCK cells</td>
<td>Inhibits H1N1 and H3N2 in the early stages of influenza A virus infection, inhibits the binding of virus to cells, and exhibits good virucidal activity.</td>
<td>Li et al. (2019)</td>
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<tr>
<td><em>Houttuynia cordata</em> (Fish mint; 鱼腥草; Yú xīng cǎo)</td>
<td>Ethanol extract</td>
<td>H1N1 virus-induced acute lung injury in mice and RAW 264.7 cell model</td>
<td>Alleviates H1N1-induced acute lung injury in mice through antiviral and anti-inflammatory effects. Inhibition of viral neuraminidase activity and toll like receptor signaling, Alleviates lung injury and intestinal dysfunction</td>
<td>Ling et al. (2020)</td>
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<tr>
<td><em>Toona sinensis</em> (Chinese mahogany; 树梅; Xiàng chén)</td>
<td>Catechin and gallic acid</td>
<td>H1N1 virus-induced acute lung injury mouse model</td>
<td>Inhibits H1N1 mRNA replication and MDCK plaque formation, neuraminidase activity, and viral glycoprotein</td>
<td>Chen et al. (2019)</td>
</tr>
<tr>
<td><em>Gardenia jasminoides</em> Ellis (Cape jasmine; 檀香; Zhi zì)</td>
<td>Geniposide</td>
<td>H1N1 virus-induced respiratory tract infection in mice and MDCK cells</td>
<td>Protects MDCK from H1N1 virus-induced cell injury and inhibits virus-induced alveolar wall changes, alveolar hemorrhage, neutrophil-infiltration, and inflammation in mice lungs</td>
<td>You et al. (2018)</td>
</tr>
<tr>
<td><em>Fritillaria thunbergii</em> (Zhebeimu; 浙贝母; Zhe bei mú)</td>
<td>Aqueous extract</td>
<td>H1N1 virus-induced respiratory tract infection in mice, virus infection in MDCK cells and in vivo studies</td>
<td>Inhibits H1N1 replication in embryoanted eggs. Protects MDCK cells from H1N1 virus-induced cell injury. Increases mice survival rate from viral infection.</td>
<td>Zhang et al. (2017)</td>
</tr>
</tbody>
</table>

### References

1. Pyankov et al. (2012)
2. Li et al. (2019)
4. He et al. (2020)
5. Rasool et al. (2017)
6. Li et al. (2019)
7. Pyankov et al. (2012)
8. Pyankov et al. (2013)
ginger were found to inactivate avian influenza virus H9N2 activity in both MDCK cells and chick embryos. The ethanolic extract and polysaccharides of fish mint have been shown to alleviate H1N1-induced acute lung injury in mice, hence simultaneously improving the immune system. The aqueous extract of zhebeimu can inhibit H1N1 replication in embryonated eggs and increase the survival rate of virus-infected mice. Some essential oils have been shown to exhibit anti-influenza activities. These include Cinnamomum zeylanicum leaf oil (cinnamon), Glycyrrhiza uralensis (licorice), Pogostemon cablin (lemongrass) and baicalin were proved as the inhibitors of SARS-CoV-2, there in both MDCK cells and chick embryos, posing a challenges for most researchers.

3.4. Perspective for using foods and herbs against COVID-19

Current literature carries strong evidence in support of dietary therapy and herbal medicine as potential effective antivirals against SARS-CoV-2 and preventive agents against COVID-19. For future studies, the authors believe there are 4 potential approaches for the application of dietary therapy and herbal medicine against COVID-19: (1) using foods and herbs as diet or supplement to prevent infection and strengthen immunity; (2) use as an antiviral agent by coating on masks; (3) use as an air-disinfectant (essential oil) to stop aerosol transmission; and (4) use as a surface sanitizing agent to provide a disinfected environment (Fig. 3). Surgical masks are good at preventing virus spread into the air and transmission to humans. However, after mask removal, the virus remains on the mask and is probably re-aerosolized, increasing the risk of human infection. Mask coating with an antiviral compound could be advantageous, but disinfectant toxicity to humans must be considered.

<table>
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<th>Table 2</th>
<th>Antiviral activity of foods and herbs against severe acute respiratory syndrome coronavirus 1 (SARS-CoV-1).</th>
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</thead>
<tbody>
<tr>
<td>Herbs</td>
<td>Bioactive compound and extract</td>
</tr>
<tr>
<td>Toona sinensis Roem (Chinese mahogany; 香椿; Xiāng chūn)</td>
<td>Tender leaf of Toona sinensis Roem crude extract fraction</td>
</tr>
<tr>
<td>Glycyrrhiza radix (Liquorice; 甘草; Gān cǎo)</td>
<td>Glycyrrhizic Acid Derivatives</td>
</tr>
<tr>
<td>Lycoris radiata (Red spider lily; 石蒜; Shí lùcan)</td>
<td>Lycorine</td>
</tr>
<tr>
<td>Rhizoma Cibotii (Rhizome of Scythian Lamb; 赤瓊; guò ji)</td>
<td>Rhizoma Cibotii extract</td>
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<table>
<thead>
<tr>
<th>Table 3</th>
<th>Antiviral activity of herbs against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).</th>
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</thead>
<tbody>
<tr>
<td>Herbs</td>
<td>Bioactive compound and extract</td>
</tr>
<tr>
<td>Lianhuaqingwen (连花清瘟; Lìán huā qīng wēn)</td>
<td>Forsythia suspensa (Thunb.) Vahl (Weeping forsythia; 蕾薇; Liàn qiāo)</td>
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<td></td>
<td>Ephedra sinica Stapf (Chinese ephedra; 草麻黄; Cǎo má huáng)</td>
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<td></td>
<td>Lonicera japonica Thunb. (Japanese honeysuckle; 忍冬; Rěndōng)</td>
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<td>Buddhas indigotica Fortune (Wood; 紫藤; Sōng lán)</td>
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<td></td>
<td>Mentha haplocalyx Briq. (Mint; 薄荷; Bò hé)</td>
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<tr>
<td></td>
<td>Dryopteris crassirhiza Nakai (Thick-stemmed wood fern; 粗裂鳞毛蕨; Cū jiāng líng máo jué)</td>
</tr>
<tr>
<td></td>
<td>Rhodola rosea L. (Golden root; 红景天; Hóng jǐng tiān)</td>
</tr>
<tr>
<td></td>
<td>Gypsum Fibrosum (Gypsum; 石膏; Shí gāo)</td>
</tr>
<tr>
<td></td>
<td>Pogostemon cablin (Blanco) Benth. (Patchouli; 薰衣香; Guāng hǔ xiāng)</td>
</tr>
<tr>
<td></td>
<td>Rheum palmatum L. (Chinese rhubarb; 芍叶大黄; Zhāng yè dà huáng)</td>
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<tr>
<td></td>
<td>Houttuynia cordata Thunb. (魚腥草; Yú xīng cǎo; Fish mint)</td>
</tr>
<tr>
<td></td>
<td>Glycyrrhiza uralensis Fisch. (Liquorice; 甘草; Gān cǎo)</td>
</tr>
<tr>
<td></td>
<td>Armeniaca sibirica (L.) Lam. (Siberian apricot; 山杏; Shān xìng)</td>
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Aromatherapy has been used for thousands of years in Egypt and India to treat various diseases, and the antimicrobial and antiviral activity of essential oils have been confirmed by numerous studies. However, most of these studies only investigated the effect of their liquid formula, limiting their administration to only via the oral route. Using essential oils vapors could increase their application against airborne bacteria and viruses. The anti-influenza virus activity of some essential oil vapors, such as that of *Citrus bergamia* (bergamot), *Eucalyptus globulus* (eucalyptus), *Pelargonium graveolens* (geranium), *Cinnamomum zeylanicum* leaf oil (cinnamon), and *Cymbopogon flexuosus* (lemongrass), has been reported. Their inhibitory mechanism is based on the inactivation of the principal external proteins of the influenza virus. The hemagglutinin protein of the virus appeared to be a major target of most of these oil vapors, and this may provide therapeutic benefits for people suffering from influenza or other respiratory viral infections. Aerosolized tea tree oil reportedly inhibits airborne viral particles of H1N1 subtype avian influenza virus. There are currently very few studies on the potential of the vapor form of essential oils. Air sterilization without human health damage using essential oils could be a good way to prevent COVID-19. However, the minimum essential oil concentration needed for SARS-CoV-2 inhibition should be investigated.

![Fig. 3. The prospects of dietary therapy and herbal medicine for COVID-19 prevention. Dietary therapy and herbal medicine could be used against COVID-19 in the following four ways: (1) diet or supplement for infection prevention and immunity strengthening; (2) application as antiviral agent on masks; (3) air disinfection agent to stop aerosol transmission of the virus; and (4) surface sanitizing agent to afford a disinfected environment.](image-url)
Many restaurants use cleaning detergents for surface sanitization; however, their safety and disinfection efficiency need further consideration. Natural antiviral extracts from herbs could be added to cleaning detergents to increase their anti-SARS-CoV-2 activity.

4. Conclusions

Currently, there are limited number of allopathic medicines considered effective against COVID-19. The design and development of drugs and vaccines require elucidation of the mechanism of antivirals against SARS-CoV-2 and as preventive agents against COVID-19. Thus, dietary therapy and herbal medicine could be a complementary preventive therapy for COVID-19. However, these hypotheses require experimental validation in SARS-CoV-2 infection models and COVID-19 patients.

Declaration of competing interest

None of the authors has any conflict of interest.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jtcm.2020.05.004.

References


