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REVIEW PAPER

Traditional Chinese herb, *Astragalus*: possible for treatment and prevention of COVID-19?

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Summary

Astragalus is a traditional herb which has been used in China for a long time. It regulates blood circulation (vital energy), invigorates body fluid circulation, protects the flow of blood to fight against the attack of pathogens, and strengthens “blood deficiencies” according to Bencao Congxin. *Astragalus* was approved by the Food and Drug Administration in 2009 as a dietary supplement for upper respiratory infections, allergic rhinitis (hay fever), asthma, chronic fatigue syndrome, and chronic kidney disease. Thirty journals published in the past ten years were reviewed by using library search engines such as SCI/SCIE, PubMed, and Scopus. In this mini-review, we focus on the anti-inflammatory of *Astragalus* features, discuss the background of *Astragalus* and its function in various diseases from water-extracted *Astragalus membranaceus*, *Astragalus* saponins, and *Astragalus* polysaccharides. Based on the traditional Chinese medicine theory, *Astragalus* is a potential candidate to treat and prevent COVID-19.

Key words: *Astragalus*, traditional Chinese herb, treatment, prevention, COVID-19

Słowa kluczowe: *Astragalus*, traganek, tradycyjna chińska roślina lecznicza, leczenie, zapobieganie, COVID-19

INTRODUCTION

Severe acute respiratory syndrome caused by coronavirus 2 (SARS-CoV-2) was identified in December 2019 and named as coronavirus disease 2019 (COVID-19) by the World Health Organization (WHO). On the 11th of March, a global pandemic has been announced [1]. The human-to-human transmission rate of COVID-19 by droplets or direct contact is extremely high [2]. There were more than 24,190,116 cases of infection up to the 27th of August, 2020 [3]. Limited information concerning severe acute respiratory syndrome coronavirus 2 including its genomics, structural biology, virology, pathology, epidemiology, and the specific immune response, vaccine development becomes a huge challenge for scientists [4]. Thus, there is no vaccine for COVID-19 as of today [mid-2020, Editorial note]. Traditional Chinese medicine is one of the possible ways that may replace vaccines. Many traditional Chinese herbal decoctions such as *Qingfei paidu* decoction and *Gan cao gan jiang* decoction, *She gan ma huang* decoction and *Qingfei Touxie Fuzheng* decoction are implied for the treatment of COVID-19 without side effects [5]. Recently, investigations on a single traditional Chinese herb, *Astragalus* (*Huang Qi*) for the treatment and prevention of COVID-19 got started (fig. 1).

of flowering plants with over 1,750 species. *Huang Qi* was classified as a high-class herb 2000 years ago based on the *Shen Nong Ben Cao Jing*. *Huang* is the “yellow” interior of the root and “*Qi*” is the superior tonic roots termed as “leader” [6]. According to *Bencao Congxin* [7], *Astragalus* acts as traditional Chinese medicine regulating blood (vital energy), invigorating the body fluids, preparing the flow of blood to fight against the attack of external evils (pathogens), and strengthens body defences, which regulates the blood exhaustion and mainly uses to treat syndromes of various “blood deficiencies” in spleen, stomach, and lungs. It also has been promoted as a dietary supplement for upper respiratory infections, allergic rhinitis (hay fever), asthma, chronic fatigue syndrome, and chronic kidney disease that was approved by Food and Drug Administration in 2009 [8].

Water extract of *Astragalus membranaceus* root

The water extract of *A. membranaceus* root was found to have an antiviral activity for the treatment and prevention of common cold [9]. It enhanced the immune system and production of immunoglobulin to restore the loss of T-cells during viral upper respiratory infections [10]. There was

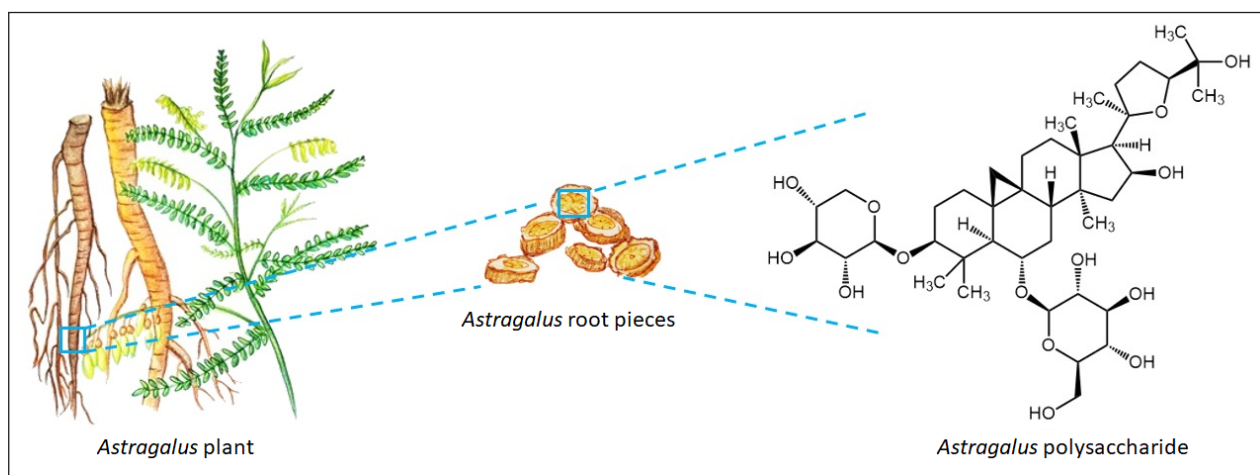


Figure 1.

Possible *Astragalus* form used for the treatment and prevention of COVID-19.

Design and diagram draw by Dr. Chuiman Lo.

ASTRAGALUS (HUANG QI)

Astragalus derived from the root of *Leguminosae* plant called *Astragalus membranaceus* (Fisch.) Bunge or *Astragalus mongholicus* (Bunge) P. K. Hsiao with Latin name *Radix Astragali*. These are the largest genera

an effect on water extract of *A. membranaceus* root in TH cell subset function in children with recurrent tonsillitis. This had an important significance in the treatment of recurrent tonsillitis and improved TH1 cell subset function because the level of interferon-gamma (IFN-gamma) increased

and decreased the level of interleukin-4 (IL-4) [11]. Moreover, the clinical trials had shown that *A. membranaceus* root could stimulate and rejuvenate depressed immune function. It significantly stimulated the number of white blood cells in healthy volunteers administered orally with 8 g of *A. membranaceus* root per day for 2 months. It also increased the IgM, IgE, and cAMP in the blood of healthy adults in 20 days [12]. In another clinical study, with the same dose and time of administration, the water extract of *A. membranaceus* root indicated an immune-supporting effect on the macrophage phase. It acted as a natural killer of inhibition of the activity in T-helper cell type 2 cytokines [13]. In most studies it was proven that *Astragalus* was an immune tonifying herb for lung, increasing the resistance against respiratory infections mediated by humoral and cell-immunity [14].

In 2011, Lin Y *et al.* showed that the extract of *Astragalus* root administered orally played an important role in preventing the recurrence of asthma in 90 children. It significantly increased the levels of peak expiratory flow rate (PEFR) and immunoreactive fibronectin-gamma (IFN-gamma) but decreased the level of interleukin-4 (IL-4) [15]. Late in 2013, Zou C *et al.* discovered that 2.25 g of *Astragalus* granules (equivalent to 15 g of crude *Astragalus* root) administered twice a day, at least for 3 to 6 months improved the immune function, enhanced the serum level of IgG, and prevented the relapse of nephrotic syndrome by reducing the incidence of upper respiratory tract infection (URTI) in children [16]. After 2016, Su G *et al.* reported that water-extracted *Astragalus* was effective in the prevention of frequent episodes of acute respiratory tract infection in children. This compensated for the problem of “blood deficiency” [17]. The extract of *Astragalus* root given orally stimulated the immune system, increased the production of white blood cells, also accelerated peripheral blood mononuclear cells and cytokine proliferation [18]. It significantly decreased soluble interleukin-2 receptor (sIL-2R) and interleukin-8 levels but increased the level of IgA, IgM, and IgG to prevent upper respiratory tract infections (URTIs) [19].

Astragalus saponins

There was another research about the exploration of clinical research on *Astragalus* in the treatment of respiratory system disease after SARS occurrence in 2003. Lu Y *et al.* discovered that *Astragalus* saponins

(in a dose of 50 mg kg⁻¹ daily) increased blood flow in the lungs, improved pulmonary circulation, and took some inflammatory substances or toxins away from the blood. This helped stabilize and reduce inflammatory exudation of cell membranes and lysosomal membranes. Moreover, *Astragalus* saponins significantly increased cardiac output, pulse volume, and cardiac index, which led to improve the hypoxia tolerance of myocardium. It had vasodilatory and diuretic effects, which was beneficial to reduce cardiac load and its cardiac function promoting pulmonary circulation. *Astragalus* saponins also inhibited the STAT3 signal transition pathway for virus replication. It regulated the immune system to make T cells, B cells, and monocytes played a synergistic effect to improve the body's non-specific or specific immune functions and enhance the ability to resist pathogens [20-21]. In 2016, Wang Y *et al.* reported that *Astragalus* saponins inhibited lipopolysaccharide-induced inflammation in mouse macrophages, also suppressed the LPS-induced iNOS and TNF- α expression in the mouse macrophage RAW264.7 by the inhibition of p38 MAPK/NF- κ B signaling [22].

Astragalus polysaccharides

Astragalus polysaccharide was one of the bioactive constituents of *Astragalus*. He X *et al.* proved that there was an anti-inflammatory activity of *Astragalus* polysaccharides with the concentrations of 50, 100, and 200 μ g/ml for 24 h. It suppressed NF- κ B activation and down-regulated the phosphorylation of ERK and JNK to induce the production of TNF- α and IL-1 β [23]. Shao BM *et al.* also reported that *Astragalus* polysaccharide activated mouse macrophages through triggering TLR4-mediated signaling pathways. It upregulated the expression of p-p38, p-ERK, p-JNK, induced I κ B- α degradation, and NF- κ B translocation to enhance the production of TNF- α , IL-6, and NO for anti-inflammatory purposes [24]. Lu J *et al.* showed that *Astragalus* polysaccharide in the concentrations of 100, 200, 400, and 800 μ g/ml induced IL-10 protein production and gene expression of anti-inflammatory interleukin (IL)-10, macrophage mannose receptor (MMR), dectin-1, arginase, YM-1, and YM-2. It inhibited IL-1 β protein production and expressed some pro-inflammatory genes, such as IL-1 β , iNOS, MCP-1, IL-6, and CD11c. This was effective to inhibit the pro-inflammatory responses through AMP-activated protein kinase (AMPK) activity [25]. Recently, a research team from the Southern University of

Science and Technology (SUSTech) found that a mix of *Astragalus* polysaccharides and strontium could be further developed into an anti-inflammatory drug for the COVID-19 infection or its mutation viruses [26].

Traditional Chinese medicine theory of *Astragalus* action

Based on traditional Chinese medicine theory, COVID-19 epidemic consists of external and internal factors regarding the evil of human infectious diseases and lack of the human body's righteousness. These were the principles derived from Nathan *et al.* [27]: keep healthy and do not be evil. "Eliminate" the evil by killing or inhibiting the virus, and "strengthen" the immune system by regulating human organs to achieve the antiviral effect. *Astragalus* is one of the traditional Chinese herbs able to "eliminate" evil and "strengthen" the immune system.

Possible mechanism of *Astragalus* in COVID-19

Growing evidence has shown that *Astragalus* is suitable for the prevention of COVID-19. The COVID-19 infection is caused by the SARS-CoV-2 virus, which binds to an angiotensin-converting enzyme 2 (ACE2) receptor of spike glycoprotein. The transmembrane protease serine 2 (TMPRSS2) and a disintegrin metalloproteinase domain 17 (ADAM17) interact. Infected cells and inflammatory cells are stimulated by viral antigens. It produces pro-inflammatory cytokines (PICs) and chemokines to activate immune and inflammatory responses. The macrophage-phagocytosed viruses can be transmitted to other organs through blood. A high level of angiotensin-converting enzyme 2 (ACE2) expression increases the lung vascular permeability causing pulmonary oedema, however, it could protect angiotensin-converting enzyme 2 (ACE2) or angiotensin-(1-7) or MAS axis in the lungs that alleviates lung inflammation, fibrosis, and pulmonary arterial hypertension, as well as inhibits tumor angiogenesis. However, the SARS-CoV-2 virus reduces the expression of angiotensin-converting enzyme 2 (ACE2) in the lung and cannot achieve the protect function. It is generally believed that COVID-19 first invades the human lungs and spleen, then attacks the heart [28]. In 2009, Yan P *et al.* reported that *Radix Astragali* enhanced the metabolic syndrome in the

kidney of rats through the angiotensin-converting enzyme 2 (ACE2). The expression of ACE2 mRNA decreased in the kidney of a rat which explained that *Radix Astragali* dose-dependently increased the expression of ACE2 in the rat kidney [29]. This also had been elucidated that *Astragalus* possessed pharmacological significance for the prevention and treatment of COVID-19.

CONCLUSION

All of the above information demonstrates that traditional Chinese herb, *Astragalus* might be useful in the treatment and prevention of COVID-19 as it affects the anti-inflammatory activity. However, much more work needs to be done such as clinical trials because the current state of research on *Astragalus* is only a scientific premise according to traditional Chinese medicine theory.

Ethical approval: The conducted research is not related to either human or animal use.

Conflict of interest: Authors declare no conflict of interest.

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