Chinese Herbs: A Clinical Review of Astragalus, Ligusticum, and Schizandrae

by Steven Sinclair, N.D. L.Ac.

Abstract

Although Astragalus, Ligusticum and Schizandrae have a long history of medicinal use within the traditional Chinese system, only recently has the West begun to understand their pharmacological possibilities and clinical applications. Astragalus has demonstrated a wide range of immunopotentiating effects and has proven efficacious as an adjunct cancer therapy. Ligusticum, and its active components, have been investigated for enhancement of the immune system, treatment of ischemic disorders, and as an anti-inflammatory. Clinically, the hepato-protective and antioxidant actions of Schizandrae have proven beneficial in the treatment of chronic viral hepatitis.
Altern Med Rev 1998;3(5):338-344.

Introduction

Chinese medicinal herbs are increasingly the subjects of pharmacological research. As researchers identify and isolate the bioactive components, our understanding of their physiological, therapeutic, and clinical actions increases. Traditionally, these herbs have a history of safe and effective treatment of many diseases, and while classically prescribed in multi-herb combinations, analysis of single constituents allows us to better understand their individual pharmocological actions.

Astragalus membranaceus

Astragalus membranaceus is one of the important " Qi tonifying" or adaptogenic herbs from the Chinese materia medica. It has been prescribed for centuries for general debility, chronic illnesses, and to increase the overall vitality of the system. Currently, much of the pharmacological research is focused on its immune stimulating polysaccharides and other active ingredients from the plant, useful in treating immune deficiency conditions.

Traditional Indications: In the Chinese medical system, Astragalus affects both the spleen and the lung meridians. It is indicated for spleen deficiency symptoms such as diarrhea, fatigue, spontaneous sweating, and lack of appetite.[1] Astragalus tonifies the lungs and is used in cases of frequent colds and shortness of breath.[1] Other traditional indications include wasting disorders, night sweats,[2] chronic ulcerations and sores,[1] numbness and paralysis of the limbs, and edema.[1] Astragalus is classically prescribed in combination with other Chinese medicinal herbs depending on the desired therapeutic effect and the exact diagnosis.

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Chemical Constituents: Astragalus contains the plant pigments: formononetin, astraisoflavan, astrapterocarpan, 2'-3'-dihydroxy-7,4'-dimethooxyisoflavone, and isoliquiritigenin.[2] Other major constituents include D-ß-asparagine, calycosin, cycloastragenol, astragalosides I-VII, choline, betaine, kumatakenin, sucrose, glucuronic acid, ß-sitosterol 1, and soyasaponin I. Astragalan, a polysaccharide fraction with a molecular weight between 20,000 and 25,000, has been extracted and researched in China for its ability to enhance the *in vitro* secretion of tumor necrosis factor.[3] See Figure 1.

Astragalus membranaceus

Immunotherapy: The use of recombinant interleukin-2 (rIL-2) in immunotherapy is limited by the toxicity associated with higher doses. Astragalus was given with 100 u/ml of rIL-2 versus 1,000 u/ml of rIL-2 alone in an *in vitro* study on murine renal carcinoma cells. The Astragalus-rIL-2 group had a tumor cell lysis rate of 88 percent versus 86 percent in the group with 1000 u/ml rIL-2 alone. This suggests a 10-fold potentiation in the *in vitro* antitumor activity of rIL-2 generated lymphokine-activated killer (LAK) cells.[4] These results were confirmed in another study where Astragalus was shown to potentiate the LAK cell inducing activity of rIL-2 against a Hs294T melanoma cell line. Fifty u/ml of rIL-2 with Astragalus extract F3 was more effective than 500 u/ml rIL-2 alone (64% vs. 60%).[5]

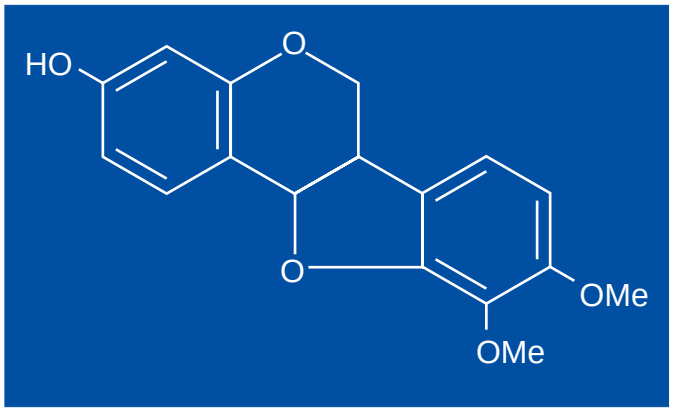
A mixture of Astragalus and two other herbs was fed to mice at 9g/kg or 20g/kg for seven days. Thymus and splenic weight increased when compared to those in the control group. Serum IgG levels were raised 41-47 percent and the conversion percentage of lymphocytes was also elevated. The Astragalus herbal mixture increased resistance to the immunosuppressive effects of cyclophosphamide[6] while stimulating macrophages to produce interleukin-6 and tumor necrosis factor.[7]

Viral myocarditis patients, when given an oral Astragalus extract, showed enhanced T3, T4 and T4/T8 cell ratios[8] suggesting improved immune response. In mice infected with coxsackie B-3 virus, Astragalus inhibited viral replication in the myocardial tissue while improving abnormal myocardial electric activity.[9,10]

Twenty-eight patients with systemic lupus erythematosus had significantly decreased natural killer cell activity when compared to normal controls. Preincubation of their peripheral blood mononuclear cells with Astragalus stimulated natural killer cell cytotoxicity in SLE patients and in healthy controls.[11]

Astragalus has also demonstrated *in vitro* antibacterial activity against *Shigella*

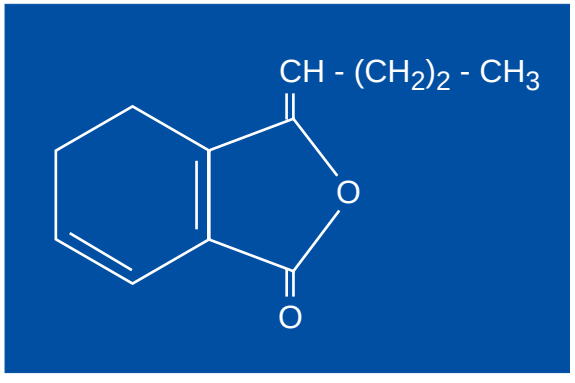
Figure 1. Chemical structure of Astrapterocarpan.



dysenteriae, Streptococcus hemolyticus, Diplococcus pneumonia, and *Staphylococcus aureus.* [2]

Adjunct Cancer Therapy: One hundred and sixteen Chinese herbal formulas were screened and evaluated for their ability to ameliorate the toxic side-effects of anticancer agents. A formula including Astragalus and Ligusticum, Shi-Quan-Da-Bu-Tang, was selected as the most effective in stimulating hemopoietic factors and interleukin production. It was also shown to potentiate the activity of chemotherapeutic agents, inhibit recurrences, prolong survival time, and reduce the adverse toxicities of antineoplastic agents.[12]

Figure 2. Chemical structure of Ligustilide.



Two randomized groups of mice received renal cell carcinoma implants. One group was treated intraperitoneally with 500 mg of Astragalus and *Ligusticum lucidum* daily for ten days. The other group received saline as a control. The cure rate in the Astragalus/Ligusticum group was 57 percent when the tumor load was 2 x 10^5 and 100 percent when the tumor load was 1 x 10^5.[13]

In another study, 10 out of 12 small-cell lung cancer patients, including 4 with extensive disease, gained between 3 and 17 years of survival time when Chinese herbs such as Astragalus were included with chemotherapy and radiation.[14]

Cardiovascular Studies: Astragaloside IV was isolated and injected into 19 patients with congestive heart failure daily for two weeks. After two weeks symptoms of chest distress and dyspnea were alleviated in 15 of the 19 patients. Heart rate slowed from 88.21 +/- 17.19 to 64.55 +/- 13.06 beats/min ($P<0.05$).[15]

Ninety-two patients with ischemic heart disease were treated with Astragalus. Not only did they get significant relief from angina, but also the effective rate of EKG improvement was 82.6 percent.[16] In another study on angina pectoris, 20 patients were given Astragalus for two weeks and evaluated by echocardiogram. Cardiac output increased from 5.09 +/- 0.21 to 5.95 +/- 0.18 L/min ($P<0.01$). Adenosine triphosphatase activity was not inhibited with Astragalus, unlike that of digitalis.[17]

The saponins contained in Astragalus were found to have a positive effect on the function of the heart through the inhibition of the formation of lipid peroxides in the myocardium as well as by decreasing blood coagulation.[18]

Nephritis: Astragalus proved effective against experimentally induced glomerulonephritis in rats, especially in treating proteinuria.[2] Rats given high doses of Astragalus

had less proteinuria and milder pathological tissue changes than the control group.[1]

Male Infertility: The water extracts of 18 herbs were tested for their effect on sperm motility. Astragalus was the only one that demonstrated a significant stimulatory effect. Using a solution of 10 mg/ml, sperm motility was increased to 146.6 +/- 22.6% of control.[19]

Toxicity: The LD50 of Astragalus is approximately 40g/kg when administered by intraperitoneal injection. Overall it is very safe and doses as high as 100g/kg of the raw herb have been given to rats by lavage with no adverse effects.[1]

Ligusticum wallichii

A member of the Umbelliferae family, *Ligusticum wallichii* is used in Chinese medicine for a variety of hematological disorders including ischemia and thrombosis. When combined with Astragalus, Ligusticum has demonstrated a notable immunopotentiating effect. Included in many classic Chinese formulations, it is also part of the Japanese and Korean herbal formularies.

Traditional Indications: Ligusticum's traditional actions include invigorating blood circulation, promoting the flow of Qi, dispelling wind, and alleviating pain. Classically it is prescribed for headaches, abdominal pain, arthralgias, and menstrual disorders that are due to blood stasis.[2]

Chemical Constituents: Ligusticum's active ingredients include an alkaloid, tetramethylpyrazine, ferulic acid (a phenolic compound), chrysophanol, sedanoic acid, and 1-2 percent of essential oils such as ligustilide and butylphthalide.[2] See Figure 2.

Ligusticum wallichii

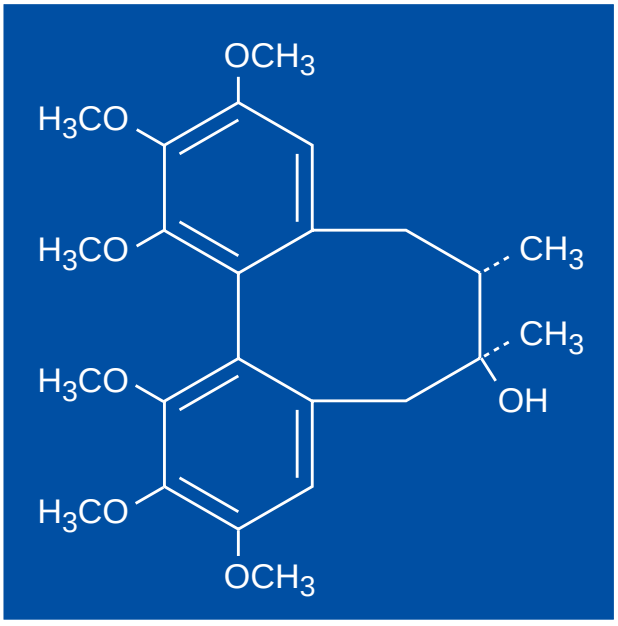
Ischemia: One hundred and fifty-eight subjects with transient ischemic attack were randomly divided into a Ligusticum group (111 cases) and an aspirin group (47 cases). The total effective rate in the Ligusticum group was 89.2 percent as compared to 61.7 percent in the aspirin group ($P<0.01$). Ligusticum increased cerebral blood flow, accelerated the velocity of blood flow, dilated the spastic artery, and decreased peripheral arterial resistance.[20]

In another study, Ligusticum was evaluated in the treatment of ischemic stroke. Injectable preparations were shown to improve brain microcirculation through inhibiting thrombus formation, decreasing platelet aggregation, and improving blood viscosity. The effect of Ligusticum was the same or better than the controls of papaverine, dextran and aspirin-persantin.[21]

Antibacterial/Antifungal Effects: Ligusticum has demonstrated *in vitro* effects against several strains of pathogenic bacteria including *Pseudomonas aeruginosa, Shigella sonnei, Salmonella typhi*, and *Vibrio cholera.*[1] The essential oil components of Ligusticum (butylphthalide) have been shown to inhibit dermatophytes *in vitro.*[2]

Anti-inflammatory Properties: When given to guinea pigs with histamine/

Figure 3. Chemical structure of Schizandrin.



acetylcholine induced bronchospasm, Ligusticum was found to decrease plasma levels of thromboxane B2, relax tracheal muscle, increase the forced expiratory volume, and inhibit the synthesis and release of thromboxane A2 with no adverse side-effects. The total effective rate was 92 percent vs. 62 percent in the control group ($P < 0.01$).[22] In a Japanese study, the active ingredients in Ligusticum, tetramethylpyrazine and ferulic acid, were found to have both significant anti-inflammatory and analgesic effects.[23]

Toxicity: Ligusticum is prescribed in traditional Chinese decoctions at dosages up to 9 grams administered over several days. Overdose symptoms may include vomiting and dizziness.[1]

Schizandrae chinensis

Schizandrae chinensis, a member of the Magnoliaceae family, has an extensive history of medical use in China. This herb's adaptogenic properties increase resistance to a wide range of physical, chemical, and emotional stresses while promoting improved overall regulation of physiological processes. Experimental evidence suggests Schizandrae has hepato-protective abilities and functions as a potent antioxidant.

Traditional Indications: Classically, Schizandrae is commonly prescribed for patterns of lung and kidney deficiency. It is considered astringent in nature and is indicated in cases of chronic cough and dyspnea, diarrhea, night sweats, wasting disorders, irritability, palpitations, dream-disturbed sleep, and insomnia.[1]

Chemical Constituents: Research into the active ingredients is primarily focused on the various lignans and essential oils contained in the dried fruits of Schizandrae. The major chemical constituents include schizandrin, deoxyschizandrin, schisanhenol, schizandrol, sesquicarene, ß-chamigrene, citral, stigmasterol, and vitamins C and E.[1,2] See Figure 3.

Hepatic Activity: Recent studies from China have found Schizandrae and its active components to be effective against viral and chemical induced hepatitis.[24] Schizandrae was shown to lower SGPT levels in patients with chronic viral hepatitis and decrease the hepatotoxicity of carbon tetrachloride in animals.[25] DDB, a synthetic analogue of Schizandrin, is used widely in China as a hepato-protective drug, and while highly effective at normalizing liver function, has very few side-effects.[26] Pharmacological studies on the bioactive lignans in Schizandrae found they increased liver protein and glycogen synthesis, inhibited carbon tetrachloride induced lipid peroxidation, and had an inducing effect on the cytochrome P-450 enzyme system.[26]

In one study, powdered Schizandrae was administered to 102 patients with hepatitis. The overall success rate was 76 percent, and in cases where SGPT levels were over 300 U/L, the success rate was 72 percent. It took an average of twenty-five days for liver enzymes to return to normal with no adverse side-effects from the treatment.[1]

Schizandrae chinensis

Antioxidant Potential: Seven of the nine lignans from Schizandrae were found to inhibit vitamin C/NADPH induced lipid peroxidation in rat liver microsomes. Of these compounds, schisanhenol and schizandrin were shown to be more effective than vitamin E at the same concentration. Schizandrins B and C were found to have strongest scavenging effect against active oxygen radicals.[27] When these compounds were given orally to mice at 15 ml/kg, there was significant reduction in ethanol induced malondialdehyde formation with increased superoxide dismutase and catalase activity.[28]

Anti-bacterial Effect: Decoctions of Schizandrae were found to possess strong *in vitro* inhibitory action on *Bacillus subtilis, Bacillus dysenteraie, Bacillus typhi,* and *Staphylococcus aureus*.[2]

Dosage and Toxicity: Therapeutic dosages are 400-450 mg powdered herb in capsules three times daily or 1-2 ml of 1:3 EtOH tincture of Schizandrae three times daily. Toxic doses when orally administered to mice were approximately 10 to 15g/kg. Overdose symptoms include restlessness, insomnia and dyspnea.[1]

Discussion

Although these herbs have a long history of medicinal use within the traditional Chinese system, it has been only recently in the West that we have begun to understand their pharmacological possibilities. Astragalus has a wide range of potential therapeutic applications in immunodeficiency syndromes, as an adjunct cancer treatment, and for its adaptogenic effect on the heart and kidneys. Ligusticum has proven efficacious in treating ischemic disorders and its active ingredients are being researched for their anti-inflammatory properties. In cases of viral hepatitis, Schizandrae has demonstrated a hepato-protective effect, the ability to lower SGPT enzymes, and has significant antioxidant capabilities.

There are several inherent difficulties in researching Chinese medicinal herbs. Classic Chinese herbal prescriptions usually include between five and ten herbs per formula and contain hundreds of potentially active ingredients. They become difficult to evaluate using the Western pharmacological model of analyzing a solitary agent for a specific effect. Much of the research conducted on complex formulas was not included, as it did not fit the single herb focus of this article. Nevertheless, it is apparent that the medicinal effects of Chinese herbs, with their low toxicity and well-established traditional use, have many potential clinical and therapeutic applications in the Western medical setting.

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