ASTRAGALUS

Astragalus membranaceus (Fisch.) Bunge

Family

The Fabaceae or Leguminosae family and Papilionoideae subfamily, commonly known as the legume, pea or bean family. The liquorice genus is also in this family.

Parts Used

Root

Description

The Australian Therapeutic Goods Administration current approved herbal name is *Astragalus membranaceus* (Fisch.) Bunge which is a synonym for the accepted name *Astragalus propinquus* Schischkin.[1] Astragalus is both the common name of *Astragalus membranaceus* as well as the name of the very large genus to which the herb belongs. The non-medicinal astragalus plants are often called 'milkvetches'. These milkvetches include an incredible span of ornamental, edible and poisonous plants with some 3000 species throughout the world. The primary medicinal species *Astragalus membranaceus* is also known as membranous milk-vetch root and Huang Qi in Chinese, which means yellow leader. This name refers to both the coloured interior of the root and the plant's position of prestige among Chinese medicine practitioners. It is defined in the Pharmacopoeia of the People's Republic of China as Radix Astragali. It is a perennial flowering plant with a hairy stem that grows to between 60 and 150 centimetres tall. Its leaves are made up of 12 to 18 pairs of leaflets and it has small flowers that grow in elongated spikes. It is native specifically to north eastern China, Mongolia, Korea and Siberia.[2,3]

Traditional Use

Astragalus was first recorded in the Traditional Chinese Medicine (TCM) classic Shen Nong's Materia Medica about two thousand years ago. This text is the foundation of TCM and within it herbs were arranged by type of material (herb, tree, etc), and then graded into categories of potency: upper, middle and lower. Astragalus was listed in the highest class. It was believed to stimulate immune function and have antioxidant effects and other benefits in the treatment of viral infections and cardiovascular disease. It has been prescribed for centuries for general weakness, chronic illnesses, to increase overall vitality and as a tonic to build stamina. Astragalus is among the most popular and important Qi (energy) tonifying adaptogenic herbs in China which means it vitalises the non-specific immune defences and wards off infections. Ancient Chinese texts record the use of astragalus for tonifying the spleen, blood and Qi. It is considered to be a sweet tonic herb that is slightly warming. In TCM as well as being classified as a herb that tonifies the Qi it is indicated for symptoms of spleen Qi deficiency such as diarrhoea, fatigue and lack of appetite. It also raises the yang Qi of the spleen and stomach thus addressing prolapses of organs such as the uterus, stomach or anus. In this capacity it can also address uterine bleeding. Astragalus tonifies the lung Qi and is used in cases of frequent colds, spontaneous sweating and shortness of breath. Other traditional indications include wasting disorders, night sweats, chronic ulcerations and sores, numbness and paralysis of the limbs, and oedema (from deficiency). Astragalus is typically prescribed as a dried root as an additive to meal preparations, powdered or in a decoction however Western herbalists have started tincturing the root as well. Classically it is prescribed in combination with other Chinese medicinal herbs depending on the desired therapeutic effect and the specific TCM diagnosis. Although originally from China astragalus has quickly integrated itself into Western herbalism and is now one of the primary immune tonic herbs in the Western pharmacopoeia. It has demonstrated a wide range of potential therapeutic applications in immunodeficiency syndromes, as an adjunct cancer therapy and for its adaptogenic effect on the heart and kidneys. It has similar Qi strengthening properties to *Panax ginseng* but is less heating and stimulating. It is often said that those younger in years will benefit most from astragalus while those more seasoned with years may find ginseng more beneficial.[4,5]

Constituents

Saponins such as cycloastragenol and astragalosides, polysaccharides (astroglucans A-C), flavonoids, amino acids, trace elements. Zinc, iron, copper, magnesium, manganese, calcium, potassium, sodium, cobalt, rubidium, molybdenum, chromium, vanadium, tin and silver have also been found in the root of astragalus. Phytosterols, a volatile oil, and amino acids, including gamma-aminobutyric acid (GABA) and L-canavanine, have been isolated from the root. Organic compounds identified in the roots include choline, betaine, gluconic acid and beta-sitosterols, as well as aromatic compounds, essential oil, linoleic acid, α-aminobutyric acid, bitter compounds and asparagine.[6]

Various preparations have been studied in pharmacological models including the astragalus polysaccharides, individual or complex saponin isolates, crude aqueous or ethanol extracts, and a commercial preparation known as astragalus injection. The relevance of the injection research in oral use is low. Since polysaccharides are very large molecules with relatively low oral availability the relevance of any *in vitro* outcomes is questionable, especially to the oral use of an astragalus decoction. This also applies to the *in vivo* models where the polysaccharides were administered by injection. Saponins do have reasonable bioavailability but they are generally changed by gut flora before systemic absorption so the relevance of saponin *in vitro* research is uncertain. Kerry Bone, in his book Principles and Practice of Phytotherapy, says: "of course the relevance of any pharmacological research to human use needs to be interpreted with caution, especially in the case of medicinal plants (given their chemical complexity)." In this monograph emphasis will be placed on whole ethanolic astragalus research and other research may be mentioned briefly or omitted entirely.[7]

Actions

Immunomodulator, antioxidant, hepatoprotective, diuretic, cardioprotective, adaptogen, antibacterial, antiviral.

Pharmacological Activity

Immune Modulation, Antioxidant, Anticarcinogenic and Antiviral Activity

Astragalus is frequently used alongside chemotherapy to alleviate the side effects of the chemotherapy treatments. It has also been shown to inhibit the growth of tumours and bolster the immune system. Few details are available of clinical studies looking at the potential for astragalus to alter patient survival outcomes as most information has been published in non-English journals. Although this monograph is not focusing on intravenously administered astragalus this one study is worth mentioning because it suggests that intravenously administered astragalus may have potential benefit as adjunctive therapy when given with chemotherapy. Astragalus injection supplemented with chemotherapy could inhibit the development of tumour, decrease the toxic adverse effect of chemotherapy, elevate immune function and improve the quality of life in patients. One hundred and twenty tumour patients were randomly divided into the treated group and the control group. Both groups were treated with chemotherapy but to the treated group astragalus injection was given additionally by intravenous dripping, 20mL in 250mL of normal saline once per day for 21 days as one course and four courses were given successively. Compared with the control group the treated group showed a lower progressive incidence, lesser decrease of peripheral white blood cell and platelet count.[8]

A 2013 review found astragalus granules may reduce the incidence of upper respiratory tract infection in children with nephrotic syndrome (a collection of symptoms due to kidney damage) compared with prednisone treatment alone. The dose of astragalus was 2.25g (equivalent to 15g crude astragalus) twice a day, at least for three to six months.[9]

In an open, randomised clinical trial 115 patients with leukopenia (a decreased number of white blood cells which can leave a person vulnerable to infections) received a high dose of a concentrated astragalus preparation (equivalent to 30g of astragalus daily) or a low dose (equivalent to 10g astragalus daily) over a period of eight weeks. In both groups there was a significant increase in average white blood cell counts after treatment. On the basis of these findings it was suggested that astragalus is an effective treatment for leukopenia and increasing the dosage could enhance its effectiveness.[10]

Astragalus has been shown *in vitro* to increase resistance to the immunosuppressive effects of chemotherapy drugs while stimulating macrophages to produce interleukin-6 and tumour necrosis factor. The results suggest that astragalus has immunomodulating activity and this activity could be used clinically for the modulation of immune responses.[11]

The use of recombinant interleukin-2 (rIL-2) in immunotherapy is limited by the toxicity associated with higher doses. Astragalus and 100 Units(U)/mL of rIL-2 were compared with 1,000U/mL of rIL-2 alone in an *in vitro* study. The astragalus/rIL-2 group had a tumour cell lysis (rupture) rate of 88 percent, versus 86 percent in the group with 1,000U/mL rIL-2 alone. This suggests a 10-fold potentiation of the *in vitro* antitumour activity of rIL-2-generated lymphokine-activated killer (LAK) cells. The study outcome indicated that astragalus is an effective immune modulator capable of potentiating *in vitro* the antitumour activity of rIL-2-generated LAK cells. The authors also suggest that by reducing the dosage required in treating cancer patients the severe side effects of rIL-2 therapy (e.g. acute renal failure, capillary leakage syndrome, myocardial infarction and fluid retention) might be reduced.[12]

Astragalus reduced the free radicals, had antioxidant activity and effectively controlled blood glucose in a study on 84 pregnant women with gestational diabetes. The women were divided into insulin and insulin plus astragalus groups after regular dietary control and insulin treatment to maintain stable blood glucose level. The patients with both insulin and astragalus treatments showed significantly increased serum superoxide dismutase activity and decreased malondialdehyde level, renal function and blood lipids in comparison with those with exclusive insulin treatment.[13]

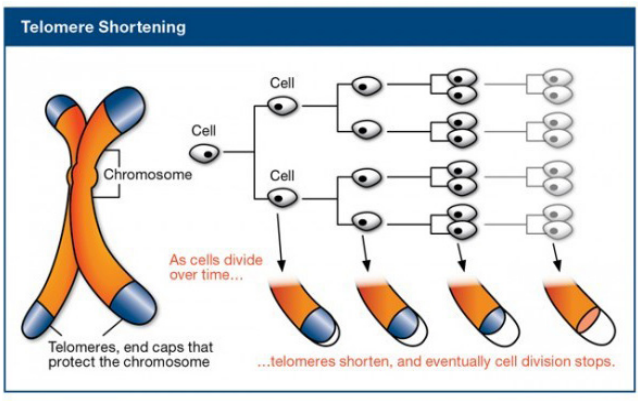
An *in vivo* study showed a combination of a water extract of astragalus with *Ligustrum lucidum* (500mcg each intraperitoneally) significantly inhibited the growth of renal cell carcinoma in mice. The herbal extract combination restored depressed oxidative burst activity of splenic macrophages from

tumour-bearing mice and improved the generation of lymphokine-activated killer cells of splenocytes when exposed to interleukin-2.[14]

Astragalus has been shown to have inhibitory effects on oxidative stress induced by metal. The results of an *in vitro* study showed the free radical scavenging effects were similar to, and stronger than, those of mannitol (an allopathic drug) and superoxide dismutase (an enzyme), respectively, demonstrating inhibitory effects on oxidative stress induced by copper.[15]

Astragalus has also been shown to possess *in vitro* antibacterial activity against *Shigella dysenteriae, Streptococcus hemolyticus, Diplococcus pneumonia and Staphylococcus aureus.*[16]

A telomere is a structure found at the end of a chromosome and is a region of repetitive DNA. Its job is to prevent deterioration of the chromosome. Telomeres become shorter every time a cell divides which is one of the main biological principles of ageing. The enzyme 'telomerase' can lengthen telomeres, slow degeneration and thus promote longevity. The link between cellular ageing and 'telomere length' is well established and backed with solid research. The triterpenoid saponin Astragaloside IV has been isolated and repeatedly shown to activate the telomerase enzyme. In addition to its tonic qualities astragalus has gained popularity in both complementary and orthodox approaches due its remarkable anti-ageing and rejuvenating qualities. Astragalus has also shown that it can slow telomere shortening, giving a further clue as to how it promotes longevity.[17]



Picture credit: http://www.wholehealthinsider.com/newsletter/2012/a-genetic-solution-to-slowing-aging-and-preventing-disease/

In a double-blind clinical trial 235 patients with chronic cervicitis associated with human papillomavirus type 16, Herpes simplex virus type 2 and cytomegalovirus infections were divided into four groups receiving the following substances applied locally by gauze: recombinant interferon-1 interferon (5mcg); recombinant interferon-1 interferon (10mcg); both interferon (5mcg) and astragalus extract (0.5mL of a 1:1 extract) or astragalus alone (0.5mL of a 1:1 extract). Application of the substances was made twice weekly for three weeks. The astragalus-plus-interferon group demonstrated results similar to the high-dose interferon group, with approximately 60 percent of patients showing striking improvement or complete resolution of the cervicitis. In the group of patients receiving astragalus alone only eight percent had marked improvement and none were completely cured. The authors conclude the astragalus acted synergistically with the interferon therapy.[18]

Patients with systemic lupus erythematosus have significantly decreased natural killer cell activity when compared to normal controls. Pre-incubation of peripheral blood mononuclear cells with astragalus stimulated natural killer cell cytotoxicity dose dependently in both systemic lupus erythematosus patients and healthy controls.[19]

In viral myocarditis patients given an oral astragalus extract enhanced T3, T4 and T4/T8 cell ratios were demonstrated suggesting improved immune response.[20]

In an *in vitro* study astragalus demonstrated significant protective effects in cultured rat heart cells against coxsackie B-2 virus when given in the early period of infection. According to the authors the results suggest astragalus should be valuable in preventing and treating acute myocarditis caused by coxsackie-B virus.[21]

Cardiovascular Activity

Astragalus (either as an injection or granules) showed significant positive effects in viral myocarditis in symptom improvement, normalisation of electrocardiogram results, creatine phosphokinase levels and cardiac function. Several earlier trials from the 1990s had shown that astragalus might have potential for treating viral myocarditis, or alleviating symptoms and signs, and

decreasing cardiac enzymes and few trials reported adverse effects. The possible modes of action include enhancing natural killer cell activity, inducing production of alpha- and gamma-interferon, improving cardiac microcirculation, and anti-free radical and lipid peroxidation. Referring to the intervention of astragalus granules one trial showed significant difference between astragalus granules plus supportive therapy.[22]

Astragalus has an established history of use in China to assist recovery after stroke. A trial with a sample size of 68 subjects has demonstrated that when stroke patients are administered astragalus (3g of freeze dried astragalus three times/day for 14 days) within 24 hours of the stroke their functional independent outcome measures, such as dressing, eating and bladder control, were significantly improved when compared to controls at four and 12 weeks after the event. The researchers speculate that this may be due to the anti-inflammatory and antioxidant actions of astragalus, therefore reducing oedema.[23]

Astragalus was shown to strengthen left ventricular function and had an antioxidant effect in 43 patients suffering from acute myocardial infarction. After administration of astragalus the ratio of pre-ejection period/left ventricular ejection time was decreased, the superoxide dismutase activity of red blood cells was increased and the lipid peroxidation content of plasma was reduced. Additionally there was a significant difference between the astragalus group and the control group in the aforementioned parameters. The authors suggest the antioxidant effect of astragalus is one of the mechanisms of its cardiotonic action.[24]

In 92 patients with ischemic heart disease treated with astragalus significant relief from angina was achieved, and the effective rate of electrocardiogram improvement was 82.6 percent.[25]

In another study of 20 patients with angina pectoris given astragalus for two weeks cardiac output was significantly increased and, unlike digitalis, adenosine triphosphatase activity was not inhibited.[26]

Astragalus can alleviate the calcium overload-induced myocardial damage and improve both systolic and diastolic functions of heart in patients with chronic heart failure. Oral medication of astragalus granule was given to 45 patients at the dose of 2.25g twice a day for two weeks alongside standard treatment for correcting heart failure, including digoxin, diuretics, etc.[27]

A 2017 *in vitro* study demonstrated that astragalus and its saponin constituents are able to improve vascular dysfunction and remodelling in hyperhomocysteinemia (elevated plasma levels of homocysteine play an important factor in cardiovascular disease), which may be attributed to its potent effects against oxidation.[28]

Hepatoprotective Activity

Astragalus has been scientifically shown to decrease the replication of the hepatitis B virus. The effectiveness of two months' treatment with Astragali compound (AC), containing Radix Astragali and adjuvant components, was studied for the treatment of chronic viral hepatitis in 116 patients; 92 patients were given other drugs in regular clinical use for viral hepatitis (controls). The clinical efficacy of AC was significantly better in AC-treated patients than in controls. The results indicate that AC may promote recovery from viral hepatitis and inhibit HBV replication.[29]

Oral administration of an astragalus ethanol extract alleviated drug induced liver injury *in vivo*.[30]

Respiratory Activity

A recent study researched the clinical efficacy of astragalus in preventing the recurrence and regulatory effects on Th1/Th2 cytokines in 90 asthmatic children during the remission stage. Astragalus played a role in preventing the recurrence of asthma. The combination of astragalus and hormones showed better effects.[31]

Hypoglycaemic, Kidney and Diuretic Activity

The anti-diabetic potential of astragalus has been progressively studied in the recent past. Its crude extracts have been reported in several ethnopharmacological studies as potential prospect for further anti-diabetic studies.[32]

Treatment with astragalus can maintain stable levels of estimated glomerular filtration rate and delay the initiation of dialysis in patients with progressive chronic kidney disease (CKD) stage 4. A clinical study conducted in Japan treated patients with progressive chronic kidney disease with astragalus

for more than three months. Thirty-five patients completed the study. Participants were treated with 5g/day of dried astragalus root powder mixed in water and they continued to take their conventional treatments.[33]

A meta-analysis of *in vivo* studies on rats found that astragalus significantly lowers fasting blood glucose levels. The review followed the results of experimental studies that suggest astragalus has an inhibitory effect on the oxidative stress that characterizes early diabetic nephropathy, a leading cause of end-stage renal disease.[34]

Digestive Activity

Astragalus strengthens the movement and muscle tone of the small intestine (especially the jejunum) in animal tests which may account for its clinical application in a variety of common digestive symptoms.[35]

Fertility Activity

Astragalus can enhance the motility of human spermatozoa *in vitro*.[36] In an earlier *in vitro* study an aqueous extract of astragalus showed a significant stimulatory effect in sperm motility in semen at 10mg/ml.[37]

Indications

- Immune system dysfunction (for treatment and prophylaxis of viral infections such as frequent colds and influenza, bronchitis, *Herpes simplex* and HIV, Lyme disease (but not late stage), adjunctive cancer treatment, allergic rhinitis)
- General prevention of infection and autoimmune diseases such as Hashimoto's disease, increasing vitality, stamina and endurance (e.g. athletes), fatigue, anaemia, weak limbs.
- Enhancing cardiac function, angina, hypertension, oedema
- Hepatitis
- Asthma
- Prolapsed organs
- Chronic diarrhoea
- Abnormal uterine bleeding
- Diabetes mellitus

Energetics

Sweet, warming and moist.

Use in Pregnancy

Safety is unknown although no evidence of foetal damage has been reported in animal studies. There were no reported safety concerns in a trial of pregnant women with gestational diabetes.[38]

Contraindications

As per TCM astragalus is avoided when there are heat signs or yin deficiency signs. It is often said that astragalus is contraindicated in acute infection however if someone is sick, and also exhibits symptoms of weakness, astragalus might be used to strengthen the person's reserves to boost them towards wellness. Astragalus is a herb that slowly builds the system so it does not give immediate results.[39] For some people astragalus is contraindicated in certain kinds of late-stage Lyme disease because it can exacerbate autoimmune responses in that particular disease.[40]

Drug Interactions

Avoid with those on immunosuppressive drugs and transplanted organs.

Administration and Dosage

Liquid Extract:	1:1
Alcohol:	25%
Weekly Dosage:[41]	20 to 40mL

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