

**The Longwood Herbal Task Force**  
(<http://www.mcp.edu/herbal/default.htm>) and  
**The Center for Holistic Pediatric Education and Research**  
***Astragalus (Astragalus membranaceous)***  
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**Principal Proposed Use: Immunomodulator to prevent upper respiratory tract infections (URTIs)**

**Other Proposed Uses: Adjunctive therapy for cancer, HIV, asthma and allergic disorders; cardiotonic and liver tonic. The gummy sap is used as demulcent, antidiarrheal and denture adhesive.**

### ***Overview***

The major clinical use for astragalus root is as an immunomodulator to prevent viral illnesses; it is also used as an adjunctive therapy for cancer, HIV and atopic diseases. Traditionally it is used in conjunction with other herbs rather than as a single agent. The root is also used as a cardiotonic and liver tonic. Preliminary in vitro and animal studies lend support to its use as a cardiotonic and immunomodulator, but the only human data are from case series and methodologically weak trials. Data on its use as an adjunctive therapy for cancer have also been methodologically weak. There are no controlled trials evaluating its use as a sole therapeutic agent for any serious disorder. The gummy sap from astragalus is used as a demulcent, denture adhesive and antidiarrheal agent. There are no data on its use during pregnancy, lactation and childhood.

### ***Historical and Popular Uses***

Astragalus root is a staple of Traditional Chinese Medicine (TCM), where it is also known as *Huang Qi*. It is considered a sweet, warming herb with particular effects on the lung, spleen and heart meridians. Traditionally it is used in the treatment of fatigue, decreased appetite,

general debility (particularly in the elderly), susceptibility to viral infections, non-healing wounds, fever, sweating, uterine prolapse, uterine bleeding, edema (nephritis), numbness, muscle pain, diabetes mellitus, and uterine, ovarian or colon cancer<sup>1</sup>. Astragalus is a component of numerous TCM tonics and is often combined with ginseng, angelica, licorice and other herbs.

The gummy sap from astragalus (tragacanth) has been used since ancient times as a thickener and emulsifier. It continues to be used today as a thickening agent for ice cream<sup>2</sup>. Some herbalists have used it to treat diarrhea, and others have recommended it as a laxative.

Western herbalists began using the roots of *A. membranaceus* in the 1800's as a tonic and diuretic. Modern herbalists have adopted astragalus primarily as an immunostimulant to prevent the common cold, prevent asthma and allergy symptoms, and aid in the recovery from viral infections and asthma. It has been proposed as an herbal remedy for everything from AIDS, chronic fatigue syndrome, hepatitis, and myasthenia gravis to cancer<sup>3,4</sup>. In the early 1980's, the popularity of astragalus soared on the heels of publicity in *USA Today* and other popular newspapers and magazines with headlines such as "Chinese herbs may battle cancer", "Secret herbs help in war against cancer" and "Chinese derive cancer treatments from ancient herbal tonics"<sup>5,6,7</sup>. In 1996, it was the 27<sup>th</sup> most commonly purchased herbal remedy in natural food stores in the US; by 1997, it had moved up to number eight.

## ***Botany***

*Medicinal species:* There are over 1750 species in this genus. The main species used medicinally is *Astragalus membranaceus*, but *A. trigonus* and *A. gummifera* are also sometimes used. Two American species, *A. mollissimus* and *A. lentiginosus*, are known as loco weed because of their CNS effects on livestock: depression, lethargy, tremor and even death<sup>1,8</sup>.

*Common names:* Goat's horn, green dragon, gum dragon, gummi tragacanthae, hog gum, *Huang Qi*, membranous milk vetch, Syrian tragacanth, tragacanth<sup>2</sup>

*Botanical Family:* Leguminosae (pea)

*Plant description:* Astragalus is a thorny shrub growing up to three feet tall. The branches have 8 – 12 pairs of leaflets. The sap is gummy and is used in commercial food preparation as an emulsifier and thickening agent; it has been used medicinally as a demulcent, denture adhesive and anti-diarrhea remedy. The roots are the primary parts used medicinally; they

are cylindrical, not usually branched, 30 –90 cm long, and covered with a tough, yellowish-brown skin with a sweet white inner pulp. The roots are harvested when the plants are four to five years old. Harvesting at different times may affect concentrations of active ingredients<sup>9</sup>.

*Where it's grown:* *A. membranaceus* is indigenous to the Middle East and eastern Asia; it is widely grown in Mongolia, China, Japan and Korea.

## **Biochemistry**

### **Astragalus: Potentially Active Chemical Constituents**

- Polysaccharides and triterpenoid saponins from the root: astragalans, astraglacans, astragalosides I – IV and trigonosides I-III
- Flavonoids from the root: afromormosin, calycosin, odoratin
- Others: indolizidine alkaloids, aliphatic nitro compounds, selenium, and biogenic amines such as  $\gamma$ -aminobutyric acid, GABA (0.024%)
- Tragacanthin or tragacanth gum from the sap

The root's medicinal properties have been attributed to its polysaccharides, the *cycloartane glycosides* in particular<sup>10</sup>. These glycosides include astragalosides I – IV and trigonosides I- III<sup>11, 12</sup>. The concentrations of these constituents vary depending on growing conditions<sup>13, 14, 15</sup>.

The root's *isoflavones* have been attributed with astragalus' antiviral effects<sup>16</sup>. Antioxidant compounds isolated from astragalus root include afromosin, calycosin and odoratin<sup>17</sup>.

Potentially toxic compounds include alkaloids, aliphatic nitro compounds and selenium.

The small amount of  $\gamma$ -aminobutyric acid is thought to account for astragalus' hypotensive activity<sup>18</sup>.

The sap contains a mixture of several substances, mostly complex sugars, which form a thick gum or gel when exposed to water. *Tragacanth gum* is used as a thickening agent in

cooking, and has been used traditionally as a demulcent to soothe sore throats and quiet coughs, as an adhesive for dentures and, like pectin, to make diarrheal stools less runny<sup>2</sup>.

### ***Experimental Studies***

#### **Astragalus: Potential Clinical Benefits**

1. Cardiovascular: Coronary artery disease; congestive heart failure
2. Pulmonary: Upper respiratory tract infection (URTI) prophylaxis: – see Antimicrobial
3. Renal and electrolyte balance: Acute renal failure
4. Gastrointestinal/hepatic: Hepatoprotective; antidiarrheal; laxative
5. Neuropsychiatric: none
6. Endocrine: Antidiabetic
7. Hematologic: Anticoagulant
8. Rheumatologic: none
9. Reproductive: none
10. Immune modulation: Immunostimulant; asthma and allergies
11. Antimicrobial: URTI prophylaxis; treatment of HIV and other viral infections
12. Antineoplastic: Antineoplastic; attenuation of side effects of chemotherapy
13. Antioxidant: Antioxidant
14. Skin and mucus membranes: none
15. Other/miscellaneous: Denture adhesive

1. **Cardiovascular:** Coronary artery disease; congestive heart failure; see also Hematologic
  - a. Coronary artery disease. In China, an herbal mixture containing astragalus (*Sanhuang* mixture) is used to treat coronary artery disease<sup>19</sup>.
    - i. *In vitro data*: In cultured human endothelial cells, astragaloside IV increased the fibrinolytic potential by decreasing plasminogen activation, thereby facilitating intravascular lysis of fibrin clots<sup>20</sup>. In isolated rabbit aortas, 3-nitropropionic acid from astragalus exerted vasodilating effects and hypotensive properties<sup>21</sup>.

- ii. *Animal data*: Alcoholic and aqueous extracts of astragalus roots (subsequently identified as  $\gamma$ -aminobutyric acid, GABA) had mild hypotensive effects in anesthetized rats<sup>18</sup>.
  - iii. *Human data*: Several Chinese case series support the use of astragalus-containing herbal remedies in the treatment of coronary artery disease. In case series from China of adults suffering from angina (N=20) and acute myocardial infarctions (N=43), treatment with an astragalus-containing herbal tonic was associated with improved left ventricular function<sup>22,23</sup>. In 92 patients with acute ischemic chest pain, treatment with an astragalus extract (dose unspecified) significantly improved chest pain and ECG abnormalities<sup>24</sup>. Among adults with acute myocardial infarction, treatment with an astragalus-containing herbal mixture was associated with a reduced risk of hypotension, congestive heart failure and death<sup>25,26</sup>. There are no randomized controlled trials evaluating astragalus alone in the treatment of acute or chronic coronary artery disease.
- b. Congestive heart failure
- i. *In vitro data*: none
  - ii. *Animal data*: In rats with experimentally induced chronic heart failure, treatment with astragalus (1 gram daily) improved left ventricular systolic function and improved renal response to atrial natriuretic peptide<sup>27</sup>.
  - iii. *Human data*: In a series of 19 Chinese patient with congestive heart failure who were treated for two weeks with astragaloside IV, 15 had symptomatic improvement (reduced dyspnea, decreased chest pain, increased exercise tolerance) and improved left ventricular systolic function on cardiac imaging studies<sup>28</sup>. There are no controlled trials evaluating the effectiveness of astragalus as a treatment for congestive heart failure.
2. **Pulmonary**: Upper respiratory tract infection (URTI) prophylaxis: see Antimicrobial
3. **Renal and electrolyte balance**: Acute renal failure
- i. *In vitro data*: none

- ii. *Animal data*: In rabbits with glycerol-induced acute renal failure, treatment with astragalus preserved renal function and morphology<sup>29</sup>. In guinea pigs exposed to gentamicin, an astragalus-containing herbal mixture protected against renal toxicity<sup>30</sup>.
  - iii. *Human data*: There are no controlled trials evaluating the effectiveness of astragalus in treating acute renal failure in adults or children.
4. **Gastrointestinal/hepatic**: Hepatoprotective. Traditional uses as antidiarrheal or laxative have not been evaluated in scientific studies.
- i. *In vitro data*: none
  - ii. *Animal data*: In several Chinese studies, mice were given potent hepatotoxins; the animals that were treated with astragalus root extracts had less hepatic damage and better liver function than the control animals that received the toxin alone<sup>31,32,33</sup>. In a rat model of nephrotic syndrome, treatment with astragalus was associated with improved hepatic synthesis of albumin<sup>34</sup>.
  - iii. *Human data*: In a preliminary report of a randomized controlled trial in 40 adults with chronic hepatitis C, those randomized to an astragalus-containing herbal mixture for six months had significant improvements in liver enzymes; side effects included diarrhea and severe palpitations<sup>4</sup>.
5. **Neuropsychiatric**: none
6. **Endocrine**: Antidiabetic. Part of traditional herbal blend used in China<sup>35</sup>.
- i. *In vitro data*: none
  - ii. *Animal data*: In diabetic rats, astragalus treatment was associated with lowered serum glucose levels<sup>36</sup>.
  - iii. *Human data*: None. There are no controlled trials evaluating the effect of astragalus in treating diabetes or on its effect as a co-therapy with insulin or oral hypoglycemic agents.
7. **Hematologic**: Anticoagulant
- i. *In vitro data*: In cultured human endothelial cells, astragaloside IV increased the fibrinolytic potential through effects on plasminogen activation, thereby facilitating intravascular fibrin clot lysis<sup>20</sup>. In another study, an herbal mixture containing astragalus (*Sanhuang* mixture; *Xinmai* brand of capsules) inhibited platelet aggregation in adults;

unfortunately, the precise dose of astragalus and other components, and the patient characteristics and diagnoses were not described in Western medical terms<sup>37</sup>.

ii. *Animal data*: none

iii. *Human data*: none. There are no controlled trials evaluating the effects of astragalus in terms of its anticoagulant effects, nor any studies evaluating its potential interaction with anticoagulant medications.

8. **Rheumatologic**: none

9. **Reproductive**: none

10. **Immune modulation**: Immunostimulant; allergies and asthma

a. Immunostimulant. Traditionally, the extract of purified astragalus root is used in multi-herb mixtures such as *Fu-Zheng* mixture, as an immunostimulant to prevent and treat a wide variety of illnesses ranging from the common cold to cancer.

i. *In vitro*: In murine spleen cells, astragalus markedly stimulated normal cells to proliferate; it also enhanced activation of macrophages (production of cytokines, TNF and IL-6) and B cells (production of polyclonal IgG), but had no impact on natural killer (NK) cell activity<sup>38</sup>.

In human mononuclear cells, astragalus extracts enhanced secretion of tumor necrosis factor (TNF) -alpha and TNF-beta<sup>39</sup>. In a similar study, astragalus extracts significantly increased the spontaneous incorporation of thymidine and PHA-induced lymphocyte proliferation<sup>40</sup>.

In the mononuclear cells of immunocompromised cancer patients, astragalus extracts restored local graft versus host immune response to normal levels and enhanced PHA-induced lymphocyte proliferation in a dose dependent fashion<sup>40, 41</sup>. Astragalus extracts induced LAK cell activity even in the relatively resistant peripheral lymphocytes of oncology and HIV patients<sup>42</sup>.

ii. *Animal data*: Immunosuppressed mice treated with astragalus extracts had restoration of immunologic function, heightened response to T-dependent antigens, and enhanced lymphokine-activated killer (LAK) cell and macrophage activity<sup>43,44,45,46,47,48</sup>. The immunostimulant effects in mice depended somewhat on the route of administration. In orally treated mice, the predominant cells affected

were macrophages, whereas mice who received astragalus via intraperitoneal injection had greater effects on neutrophil function<sup>9</sup>.

iii. *Human data*: In 115 adults with leukopenia (cause not specified), eight weeks of treatment with high dose astragalus (5 or 15 grams of astragalus twice daily) was associated with a significant dose-dependent increase in the number of white blood cells<sup>49</sup>. There are no randomized controlled trials evaluating the immunostimulant effects of astragalus either alone or in combination with other therapies.

b. Allergies and asthma. There are no in vitro, animal or human studies evaluating the effectiveness of astragalus as an anti-inflammatory treatment for allergies or asthma.

11. **Antimicrobial**: URTI prophylaxis; treatment of HIV and other viral infections. Astragalus is most commonly used in Traditional Chinese Medicine (TCM) as part of an herbal mixture to prevent upper respiratory tract infections. It has been adopted by Western herbalists as a natural remedy for HIV and other viral infections.

a. URTI prophylaxis

i. *In vitro data*: none

ii. *Animal data*: In mice exposed to the Sendai virus or NDV virus, those who were pre-treated with astragalus for four days had significantly higher pulmonary interferon levels than the mice that had not been pre-treated<sup>50</sup>.

iii. *Human data*: Numerous case series from China support the historical use of astragalus-containing herbal mixtures as prophylaxis for URTI and influenza, presumably by enhancing endogenous interferon levels<sup>51</sup>. For example, among 1137 adults with chronic bronchitis, an herbal mixture containing astragalus given daily in conjunction with interferon significantly reduced the incidence and duration of URTIs compared with placebo treatment or treatment with interferon alone; precise dosages and outcome measures were not specified<sup>50</sup>.

In a controlled trial of 28 healthy adults, the 14 assigned to daily treatment with astragalus (8 grams daily) had red blood cells with significantly higher interferon inducing activity than the untreated group<sup>50</sup>.

There are no randomized, controlled trials evaluating the effectiveness of astragalus alone as a prophylactic therapy for URTIs.

b. Treatment of HIV and other viral infections

- i. *In vitro data*: In cell cultures, astragalus had neither cytotoxic nor antiviral activity against HIV infection<sup>52,53</sup>.
- ii. *Animal data*: Mice experimentally infected with viral myocarditis had clinically improved cardiac function, reduced viral loads and reduced viral replication<sup>54,55,56</sup>. Astragalus also provided protection to mice infected with Japanese encephalitis virus, primarily through macrophage stimulation<sup>57</sup>. In mice, injections of purified polysaccharides from two related species, *Astragalus echidnaeformis* and *A. brachycentrus*, protected against infections with bunyavirus, significantly reducing mortality, viral titers and transaminases; there were no apparent effects on lymphocytes or natural killer cells, nor an induction of interferon production. Rather, treatment effectiveness appeared to depend on macrophage activation<sup>58</sup>.
- iii. *Human data*: There are no controlled trials in humans evaluating the effectiveness of astragalus or its extracts in preventing or treating viral infections.

12. **Antineoplastic**: Antineoplastic; attenuation of side effects of chemotherapy

- a. Antineoplastic. In China, the astragalus-containing herbal mixture, *Fu-Zheng*, is commonly used in conjunction with chemotherapy to treat cancer patients<sup>40</sup>.
  - i. *In vitro data*: Astragalus extracts restored macrophage function impaired by renal cell carcinoma and bladder cell tumors in mice<sup>59</sup>. In mice with renal cell carcinoma, there was a 10-fold potentiation of interleukin-2 (IL-2)-generated lymphokine activated killer (LAK) cell cytotoxicity, manifested as tumor lysis when the cells were incubated with astragalus extracts<sup>60</sup>. In mice, astragalus markedly potentiated the antitumor effects of interleukin-2, reducing the dose required for cytotoxic effects<sup>61</sup>.

Improvements have been noted in the white blood cell function of cancer patients and immunosuppressed mice treated with astragalus<sup>62</sup>. Astragalus enhanced the blastogenic response of lymphocytes to mitogens in mice and cancer patients<sup>40,46</sup>. Co-culture of T-cells from 10 cancer patients with astragalus restored T-cell function to normal in nine<sup>40</sup>. In 13 cancer patients, pre-incubation of mononuclear cells with an astragalus extract led to a significant increase in local

- xenogeneic graft-versus-host reaction (compared with untreated cells), indicating a significant restoration of deficient T-cell function<sup>63</sup>.
- ii. *Animal data*: Data on antineoplastic effects in animals have been conflicting. Astragalus reduced mutagenesis measured by the Ames assay using aflatoxin B1 in rat livers and calf thymus, but was less effective than two other commonly used Chinese herbs<sup>64</sup>. In other studies in mice, an astragalus-containing herbal combination remedy directly inhibited the tumor growth of transitional cell carcinoma and renal cell carcinoma while augmenting macrophage and LAK (lymphokine-activated killer) cell activities<sup>45,65</sup>. However, in rats with chemotherapy-induced myelosuppression, an astragalus-containing herbal remedy did not confer any restorative effects<sup>70</sup>.
  - iii. *Human data*: In two randomized trials of patients with stage II cervical carcinoma and breast carcinoma, those receiving standard radiotherapy plus an astragalus-containing herbal mixture (*Fu-Zheng*) had improved ten-year survival rates compared with patients receiving radiotherapy alone<sup>66,67,68</sup>. A similar survival advantage was seen in adults with stage II hepatomas or advanced non-small cell lung cancer receiving standard chemotherapy and radiation plus an astragalus-containing herbal mixture (*Fu-Zheng*) compared with patients who did not receive the herbal supplements<sup>68</sup>.

In one report of two children (nine and 15 years old) who were treated with an astragalus-containing herbal mixture in addition to standard chemotherapy and radiation, there was no apparent clinical improvement<sup>69</sup>.

There are no randomized controlled trials evaluating the effects of adjunctive therapy with astragalus alone in treating any kind of cancer in adults or children.

b. Attenuation of side effects of chemotherapy

- i. *In vitro data*: none
- ii. *Animal data*: none
- iii. *Human data*: In a case series of 176 adults with malignant tumors of the digestive tract, adjunctive therapy with an astragalus-containing herbal mixture (*Shen-Qi*) reduced weight loss, maintained white blood cell counts and maintained cellular

immune function; precise dosages and detailed outcome measures were not specified<sup>71</sup>.

In nearly 1000 Chinese adults with several different types of cancer treated with chemotherapy and/or radiation, adjunctive therapy with an astragalus-containing herbal remedy (*Fu-Zheng*) protected adrenal cortical function, reduced gastrointestinal toxicity and ameliorated bone marrow suppression<sup>66,68</sup>; precise dosages, co-therapies and objective standards for outcomes were not provided in the report.

No randomized controlled clinical trials have evaluated the effectiveness of astragalus as a protective remedy for patients undergoing chemotherapy or radiation.

**13. Antioxidant:** Antioxidant

- i. *In vitro data:* Antioxidant compounds isolated from an alcoholic extract of astragalus roots include the flavonoids, afromosin, calycosin and odoratin<sup>17,72</sup>. Astragalus extracts protected rat heart mitochondria against lipid peroxidation<sup>73</sup>.
- ii. *Animal data:* none
- iii. *Human data:* A Chinese case series reported that four weeks of treatment with astragalus in 43 patients with acute myocardial infarction reduced red blood cell free radicals, reduced plasma lipid peroxidation and increased superoxide dismutase levels<sup>23</sup>.

**14. Skin and mucus membranes:** none

**15. Other/miscellaneous:** Denture adhesive. The use of tragacanthin (from astragalus sap) as a dental adhesive is a traditional use that has not been formally evaluated in published animal or human trials<sup>2</sup>.

## ***Toxicity and Contraindications***

*All herbal products carry the potential for contamination with other herbal products, pesticides, herbicides, heavy metals, and pharmaceuticals. This is particularly concerning with imports from developing countries.*

*Furthermore, allergic reactions can occur to any natural product in sensitive persons.*

*Allergic reactions* to astragalus have not been reported.

*Potentially toxic compounds in astragalus:* Indolizidine alkaloids, aliphatic nitro compounds, selenium<sup>74</sup>. Pigs fed the selenium-rich species *A. bisulcatus* developed weight loss and severe neurologic toxicity, including paralysis within five days<sup>75</sup>.

*Acute toxicity:* No adverse effects have been reported with daily use of tragacanth for up to three months<sup>76</sup>.

*Chronic toxicity:* Traditional herbalists recommend that astragalus should not be used for more than three weeks without close follow-up and careful monitoring.

*Limitations during other illnesses or by patients with specific organ dysfunction:* In Traditional Chinese Medicine, astragalus is not recommended after an acute febrile illness has started; it is for prophylaxis of URTIs and influenza, not their treatment.

*Interactions with other herbs or pharmaceuticals:* Unknown. Several potential interactions are possible based on *in vitro* and animal data and the presumed mechanism of action of astragalus. Due to its antidiabetic effects, dosage adjustments of diabetic medications may be required by patients taking such medications concurrently with astragalus. Caution should be used when using astragalus with hypotensive agents due to concerns about potential additive or synergistic effects. Caution should also be used by patients taking anticoagulant medications and astragalus due to potential enhancement of anticoagulant activity. Consuming too much of the high-fiber gummy sap from tragacanth might impair gastrointestinal absorption of oral medications.

*Safety during pregnancy, lactation and/or childhood:* Unknown. No data have evaluated the safety or toxicity of astragalus during pregnancy, lactation or childhood. Studies of other astragalus species, *A. lentiginosus* and *A. mollissimus* (both known as locoweed) have

found toxic effects during animal pregnancies, leading to spontaneous abortions and abnormalities in fetal cardiac function<sup>77,78</sup>.

### ***Typical dosages***

*Provision of dosage information does not constitute a recommendation or endorsement, but rather indicates the range of doses commonly used in herbal practice.*

*Doses are given for single herb use and must be adjusted when using herbs in combinations.*

*Doses may also vary according to the type and severity of the condition treated and individual patient conditions.*

There is disagreement on the optimal form and dose of astragalus. In Traditional Chinese Medicine, astragalus is typically used as part of herbal mixtures, not as an isolated remedy.

#### *Adult doses:*

*Astragalus root:* 1-4 grams (about ½ tsp) of crushed, dried root, boiled in one quart of water until the water is reduced to one cup; one cup three times daily

*Powdered root capsules:* 250 –500 milligrams; two capsules TID<sup>1</sup>

*Tincture:* 3 – 6 ml (about ½ - 1 tsp.) TID

*Pediatric dosages:* Unknown

*Availability of standardized preparations:* None

*Dosages used in herbal combinations:* Variable

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