

Chapter 9

Astragalus membranaceus 黄芪 (Huangqi, Milkvetch Root)

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9.1 Botanical Identity

Huangqi has been used in Traditional Chinese Medicine for over 2000 years. The genus Milkvetch, belonging to the Pea Family, is a very large group of more than 2000 species distributed worldwide. Huangqi is traditionally prepared from the dried roots of the Chinese species *Astragalus membranaceus* (Fisch.) Bge. and the related *A. membranaceus* (Fisch.) Bge. var. *mongholicus* (Bge.) Hsiao, and it has been recorded in the Chinese Pharmacopoeia 2010 [1].

A. membranaceus and *A. membranaceus* var. *mongholicus* are similar plants botanically. They are perennial plants, approximately 50–80 cm tall with erect stems. They have hairy stems with leaves made up of 13–37 pairs of leaflets. Inflorescence with 10–20 flowers is raceme, with 2–5 mm long linear and lanceolate bracts. The fruit has a typical pea-pod shape and it is membranous. They are in flower from June to August, and the seeds ripen from July to September. In China, it is distributed in regions of the north, northeast, and northwest. As wild ones are increasingly scarce, Huangqi is mostly obtained from cultivated plants. *A. membranaceus* is cultivated in the northeastern part of Heilongjiang province and the southwestern part of Sichuan province of China. *A. membranaceus* var. *mongholicus* is cultivated mainly in the northern part of Shanxi, Inner Mongolia, Hebei, and Gansu provinces. In recent years, most of the herb sold commercially is *A. membranaceus* var. *mongholicus* [1–3].

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Fig. 9.1 Flowering *Astragalus membranaceus* (Fisch.) Bge. (a) and processed slices (b) of Huangqi

Huangqi is harvested from four-year-old plant roots in spring and autumn. Fresh roots are white, yellow, or cream-colored with many small fibrous shoots. After removing the aerial part, fibrous roots, soil and other impurities, the root will be dried either as a whole or after being cut into slices. Other processing methods include stir-fried with honey, alcoholic, salt, rice, bran, etc. [1, 4] (Fig. 9.1).

9.2 Chemical Constituents

The main constituents of Huangqi include flavonoids, saponins, and polysaccharides [3–6].

9.2.1 Flavonoids

About 30 flavonoids were isolated and identified from Huangqi, which belong to four structural groups as flavones, isoflavones, isoflavanones, and pterocarpan. The main bioactive flavonoids include calycosin, calycosin-7-O- β -D-glucoside, formononetin, ononin, (3R)-8,2'-dihydroxy-7,4'-dimethoxyisoflavan, 9,10-dimethoxypterocarpan-3-O- β -D-glucoside, 3-hydroxy-9,10-dimethoxypterocarpan, quercetin, and kaempferol. These are shown in Fig. 9.2.

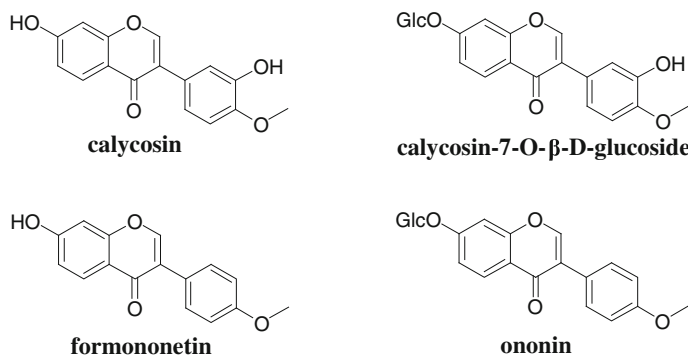


Fig. 9.2 Structures of main flavonoids in *A. membranaceus*

Calycosin has potential in the prevention and treatment of vascular disease, and has antihypertensive and neuroprotective effects. Formononetin can protect osteoblasts from hypoxia and enhance the osteogenic differentiation of osteoblasts, and also has positive effects on osteoblasts. Formononetin also has antihypertensive, antiperoxidase, phytoestrogenic and hemorrheology improving effects. Calycosin-7-O-β-D-glucopyranoside exerted significant antiviral activities against CVB3 both in vitro and in vivo, and it is one of active ingredients in *A. membranaceus* for the treatment of viral myocarditis. Calycosin-7-O-β-D-glucopyranoside can also modulate endothelial cell dysfunction by ameliorating AGEs-induced cell apoptosis and inflammation [7, 8].

9.2.2 Triterpenoid Saponins

In recent years, about 40 saponins were isolated and identified from the roots of *A. membranaceus* and *A. membranaceus* var. *mongholicus*. Many saponins are cycl-oartane tetracyclic triterpenoids, including the structures of three rings without furan ring and the structures of three rings with a furan ring, while a few saponins are oleanane pentacyclic triterpenoids. The main bioactive saponins include astragaloside I, astragaloside II, astragaloside IV, isoastragaloside I, isoastragaloside II, acetylastragaloside I, astramembrannin II, and soyasaponin I. Some of these are shown in Fig. 9.3.

Astragaloside IV is a main active constituent of Huangqi. It is widely used for the treatment of cardiovascular disease, such as coronary heart disease, heart failure, hypertension. Astragaloside IV was reported to provide immune regulation, organ protection, hypoglycemic effects, apoptosis regulation, anti-inflammatory, and anti-viral effects [9].

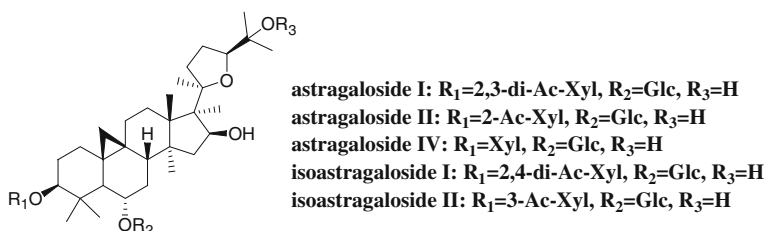


Fig. 9.3 Structures of main saponins in *A. membranaceus*

9.2.3 Polysaccharides

Several polysaccharides have been isolated from Huangqi, which play important roles in the pharmacological effects of this medicinal herb. Astragalus polysaccharides (APS), an extract of Huangqi, is one of the main effective components. APS-I and APS-II are well known to be the major structural components of APS. APS-I (molecular weight = 1,699,100 Da) consists of arabinose and glucose in a molar ratio of 1:3.45, while APS-II (molecular weight = 1,197,600 Da) consists of rhamnose, arabinose and glucose in a molar ratio of 1:6.25:17.86. In China, APS has been extensively used to treat viral infections, acute myocarditis, glomerulonephritis, diabetes, tumors, and many other illnesses, with no toxic record in clinic. APS have been widely studied, especially with respect to their immunopotentiating properties, their ability to counteract the side effects of chemotherapeutic drugs, and their anticancer properties. APS has been reported to increase insulin sensitization and to ameliorate diabetes in animal models. APS has anti-inflammatory, antioxidant, antihypertensive, and anti-aging effects. APS is also a potential natural cholesterol lowering agent, working through mechanisms distinct from statins [3, 10–12].

9.2.4 Quantitative Determination

The quality of Huangqi was predicated on the analysis and determination of several compounds like isoflavones or saponins. For example, the Chinese Pharmacopoeia 2010 specifies that the content of astragaloside IV should not be less than 0.04 %, while calycosin-7-O- β -D-glucoside not less than 0.02 %, respectively as determined by HPLC, in order to control the quality of Huangqi. The typical HPLC chromatogram of crude Huangqi is shown in Fig. 9.4 [13].

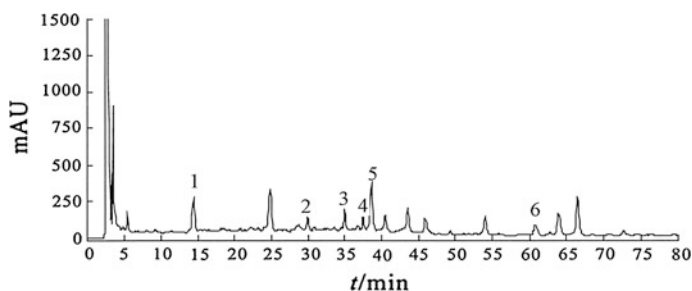


Fig. 9.4 HPLC chromatogram of *A. membranaceus*

9.3 Pharmacological Studies

It was reported that the pharmacological activities of Huangqi include cardioprotective, immunomodulation, anti-oxidative, anti-aging, anti-tumor, anti-viral, anti-inflammatory, anti-diabetic, neuron protective, hepatoprotective, diuretic, and hematopoiesis activities [3–6].

Studies show that astragalosides, aqueous extracts of Huangqi and lyophilized Huangqi powder have cardioprotective effects. Aqueous and ethanol extracts of Huangqi and APS have immunopotentiating properties. Total flavonoids, total saponins of Huangqi and aqueous extracts of Huangqi have anti-oxidant effects. Aqueous extracts of Huangqi and astragaloside IV have antitumor effects. APS, aqueous extracts of Huangqi, astragaloside II and isoastragaloside I have antidiabetic effects. Aqueous extracts of Huangqi and calycosin-7-O- β -D-glucopyranoside have anti-inflammatory effects.

9.4 TCM Applications and Dietary Usage

9.4.1 TCM Applications

In traditional Chinese medicine (TCM), Huangqi is used to “invigorate vital energy (*Qi*) and strengthen body resistance.” It has been used for symptoms of *Qi* deficiency such as diarrhea, fatigue, and lack of appetite. It also raises the *Qi* of the stomach, thus preventing prolapses of organs such as the uterus, stomach, or anus. In this capacity it can also address uterine bleeding. Huangqi 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 edema [4, 14].

Huangqi is typically prescribed as a dried root, powdered, or in a decoction. Classically, it is often combined with other herbs to strengthen the body against disease, depending on the desired therapeutic effect and the specific TCM

diagnosis. Common Huangqi preparations clinically used include the following: Huangqi Injection (Astragalus injection): a preparation of an aqueous extract of Huangqi. The major components are astragalosides, and the other pharmacological ingredients include polysaccharides, flavones and amino acids. It is mainly used for the treatment of *Qi* deficiency, cardiac insufficiency, viral myocarditis caused by obstruction of blood, and hepatitis caused by *Qi* deficiency and phlegm-wet, and used for treatment of chronic hepatitis and chronic active hepatitis caused by low cellular immune function. It also can be used for the treatment of leukopenia, thrombocytopenia purpura, chronic nephritis, nephrotic syndrome and diabetic nephropathy. Huangqi Jing: a mixture of aqueous extract of Huangqi and honey. The major components are polysaccharides and other water soluble compounds. It is used for blood enriching, *Qi* tonifying, body strengthening, and hydroschesis. It is also used for shortness of breath and palpitation, deficiency of *Qi* and blood, hypodynamia, spontaneous perspiration, and loss of appetite and energy. Huangqi granule: the total extract of Huangqi. It is used for *Qi* tonifying, body strengthening, shortness of breath and palpitation, exhaustion, spontaneous perspiration, chronic nephritis, prolapse of rectum, protracted diarrhea, and promoting granulation.

9.4.2 Dietary Usages

Huangqi is a typical traditional Chinese medicinal plant, used as food, and has been present on the Western market (in Europe and USA) as a food supplement for many years. The following preparation forms can be easily made at home [4].

9.4.2.1 Huangqi Tea

Composition: Huangqi 15–25 g, red tea 0.5–1 g.

Preparation: Sliced Huangqi is decocted in water until boiling, and then continually boiled for 5 min. The red tea is then put into the water while it is hot. Consume three times daily.

Function: *Qi* tonifying, body strengthening, inducing diuresis to alleviate edema, evacuation of pus, spontaneous perspiration, and chronic trachitis.

9.4.2.2 Huangqi Porridge

Composition: Huangqi 30 g, rice 100 g.

Preparation: Huangqi is soaked in 10 times the volume of water for 30 min. The water then is boiled and keep the boiling status for another 30 min with mild heat. After removing the first decoction, the residue was added with 10 times volume of water and boiled. Repeat the decocting procedure for 3 times. Three decoctions are

mixed and residue of Huangqi is discarded. Rice is put into the decoction solution and boiled to porridge.

Function: it is good for *Qi* deficiency, weakness, elderly, recovering from illness and operation, and chemotherapy patients. It is suitable to be taken in the morning, but not for flu patients.

9.4.2.3 Huangqi-Danggui Tea

Composition: Huangqi 30 g, Danggui (root of *Angelica sinensis* (Oliv.) Diels) 6 g.

Preparation: Put Huangqi and Danggui in 10 times the volume of water, then boil for 30 min. Drink it when it becomes cold.

Function: benefitting *Qi* and blood. It is suitable for persons in illness and operation recovery periods, as well as the elderly. However, it is not good for flu patients, females on their menstrual period, and people with excess fire for *Yin* deficiency.

9.4.2.4 Huangqi Wine

Composition: Huangqi 60 g, yellow wine 500 mL.

Preparation: Ground Huangqi is put into a container, add yellow wine, seal and soak for 7 days. Drink 20–30 mL of wine each time, twice daily.

Function: deficiency of the *Qi* and stomach, eating less with poor appetite, indigestion, palpitations, shortness of breath, limb weakness, and hyperidrosis for deficiency of the body.

9.4.2.5 Huangqi-Gouqi Tea

Composition: Huangqi 5 g, Gouqizi (fruits of *Lycium barbarum* L.) 10 g.

Preparation: Put Huangqi and Gouqizi into a cup. Add 10 times the volume of boiling water and cover for about 75 min. Drink it like an ordinary tea. Add water repeatedly until the color of the tea become very light and tasteless.

Function: Nourishing the liver and kidney, diuretic and antihypertensive, suitable for the elderly with mild hypertension.

9.4.2.6 Huangqi-Honey Drink

Composition: Huangqi 30 g, Chenpi (fruit peel of *Citrus reticulata* Blanco) 10 g, honey 30 g.

Preparation: Put Huangqi and Chenpi in a water pot or other glass container, add about 300 mL of water and boil for 20 min. Then add honey into it and it is ready for consumption.

Function: It is beneficial to treat constipation.

9.4.2.7 Huangqi-Shandi Porridge

Composition: Huangqi 30 g, Shanyao (roots of *Dioscorea opposita* Thunb.) 100 g, Dihuang (roots of *Rehmannia glutinosa* Libosch.) 15 g.

Preparation: First decoct Huangqi and Dihuang, then add ground Shanyao slowly into the boiling decoction and keep stirring until it becomes porridge.

Function: high blood pressure, diabetes, deficiency of *Qi* and Yin, thirst, dry mouth, and frequent urination.

9.4.2.8 Shenqi-Dazao Porridge

Composition: Huangqi 15 g, Danshen (roots of *Salvia miltiorrhiza* Bunge) 10 g, Dazao (Dry fruit of *Ziziphus jujuba* Mill.) 30 g, rice 100 g.

Preparation: First decoct Huangqi and Dangshen, then put Dazao and rice into the decoction and cook until it becomes porridge.

Function: It is beneficial to deficiency of *Qi*, fatigue, sweating, eating less, and improving the immune system instead.

9.4.2.9 Huangqi-Chicken Soup

Composition: Huangqi 50 g, a medium sized black-bone chicken.

Preparation: Cut black-bone chicken into pieces, mix with Huangqi, stew until the meat become soft.

Function: nourishing *Qi* and lung, *Yin* and blood.

9.5 Clinical Evidences

Current applications of Huangqi are primarily for restoring and strengthening the immune response, enhancing cardiovascular function, and increasing vitality. Indications supported by clinical trials include impaired immunity, adjunctive cancer treatment, viral infections, bronchial asthma, diabetes, peptic ulcer, cancer, respiratory tract infection, and the common cold [4]. The most common preparation is Huangqi injection, which is now clinically used to treat psoriasis, coronary disease, diabetes, cancer, heart failure, nephropathy, and hepatitis B [4, 15–17].

9.6 Safety Evaluation and Toxicity Issue

Huangqi is used in doses of 9–15 g daily. Oral ingestion of Huangqi decoction (7.5 g/kg) cannot be determined in rats. Doses as high as 100 g/kg of the herb have been given to I.G rats with no adverse effects. The LD₅₀ of Astragalus in mice was

determined to be approximately 40 g/kg when administered by intraperitoneal injection [14].

Cases displaying adverse reactions of Huangqi were reported, including fever, allergy, nausea, abdominal distension, pruritus, skin reactions. Among various types of adverse reactions the skin reactions were very common. All the cases were recovered after immediate cessation of medication and there were no deaths or serious long term effects [18]. The causes of adverse reactions mainly related to the production of the drugs, the choice of the clinical indication, and the route of administration. The quality control of drug production should be improved. Also, the drug application should be based on the theory of TCM.

References

1. Pharmacopoeia Committee of P. R. China (2010) Pharmacopoeia of People's Republic of China. Chemical Industry Publishers, Beijing (in Chinese)
2. Editorial Committee of Flora of China of Chinese Academy of Science (1998) Flora of China, vol 42. Science Press, Beijing (in Chinese)
3. Liu et al (2011) Review of Astragali Radix. Chin Herbal Med 3(2):90–105 (in Chinese)
4. Nanjing University of Chinese Medicine (2006) Dictionary of Chinese materia medica, 2nd edn. Shanghai Science and Technology Press, Shanghai (in Chinese)
5. Chen and Huang (2008) Progress in pharmacological effects of compositions of *Astragalus membranaceus*. Chin J New Drugs 17(17):1482–1485 (in Chinese)
6. Zhang et al (2012) Chemical composition and pharmacological activities of Astragali Radix. China J Chin Mater Med 37(21):3203–3207 (in Chinese)
7. Bai et al (2013) Calycosin and formononetin from astragalus root enhance dimethylarginine dimethylaminohydrolase 2 and nitric oxide synthase expressions in Madin Darby Canine Kidney II cells. J Nat Med. 67:782–789
8. Tang et al (2011) Inhibitory effects of two major isoflavonoids in Radix Astragali on high glucose-induced mesangial cells proliferation and AGEs-induced endothelial cells apoptosis. Planta Med 77(7):729–732
9. Duan and Sun (2011) Research reviews on astragaloside IV. J Shenyang Pharm Univ 28 (5):410–416 (in Chinese)
10. Du et al (2011) Astragalus polysaccharides enhance the humoral and cellular immune responses of hepatitis B surface antigen vaccination through inhibiting the expression of transforming growth factor β and the frequency of regulatory T cells. FEMS Immunol Med Microbiol 63(2):228–235
11. Liu et al (2010) Astragalus polysaccharide improves insulin sensitivity in KKAY mice: regulation of PKB/GLUT4 signaling in skeletal muscle. J Ethnopharmacol 127(1):32–37
12. Lu et al (2013) Astragalus polysaccharide induces anti-inflammatory effects dependent on AMPK activity in palmitate-treated RAW264.7 cells. Int J Mol Med 31(6):1463–1470
13. Tian et al (2008) Fingerprint analysis of Radix Astragali by RP-HPLC. J Shenyang Pharm Univ 25(12):979–982 (in Chinese)
14. Tweet (2003) Astragalus membranaceus. Altern Med Rev 8(1):72–77
15. Wan, Feng (2009) Astragalus injection in combination with chemotherapy for malignant tumor: a clinical study. China Pharmacy 20(9):703–705 (in Chinese)
16. Song, Tao (2004) Clinical study of therapeutic effect of injection *Astragalus membranaceus* on diabetic nephropathy patients. China J Mod Med 14(7):123, 126 (in Chinese)

17. Wen et al (2011) Systemic analysis of randomized controlled trials on Radix Astragali injection for chronic heart failure. *Chin J Basic Med Tradit Chin Med* 17(12):1356–1357 (in Chinese)
18. Fu et al (2009) Analysis on case suffered from adverse reactions of Huangqi Injection. *Drug Eval Res* 32(1):54–60 (in Chinese)