

Astragalus, an Ancient Medicinal Root in Traditional Chinese Medicine, a Gift from Silk Road

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Abstract

Astragalus is a medicinal herb which has been used in traditional Chinese medicine for many years. Specifically, the root of the plant is made into many different forms of supplements, including liquid extracts, capsules, powders and teas. Its root contain many active plant compounds, which are believed to be responsible for its potential benefits. Saponins, polysaccharides, amino acids, flavonoids, organic acid, glycosides, alkaloid, and trace elements. In Traditional Chinese Medicine, Astragalus considers to used in the treatment of diabetes, mellitus, nephritis, leukemia, uterine cancer, besides its tonic agent and diuretic effects. Astragalus polysaccharide, the active component extracted from Astragali Radix which is the root of Astragalus membranaceus Bunge. Some uses of Astragalus are in kidney and urinary problems, digestion, liver problems, female reproductive system problems, muscular, skin problems, cardiovascular and blood, immune and lymphatic system, nervous system, respiratory system, and for some specific disease. It helps protect the body against various types of stress such as physical and emotional stress. Astragalus root including anti-aging properties, and also helping to prevent bone loss. It contains Astragalosides (antioxidants), which support the integrity of the respiratory tract. In addition, the polysaccharides found in Astragalus are known for their immune supporting properties. Astragalus herb also supports deep immune function by promoting normal levels of specific immune cells and aids in their function. Astragalus appears especially effective when immune function is stressed by environmental or endogenous challenges. In TCM, huang qi is never administered as a mono drug, but forms part of mixtures depending on the indications. Astragali Radix, the root of Astragalus membranaceus Bunge, has been reported to exert hepatoprotective effects, anti-oxidative effects, antiviral activity, anti-oxidative effects, anti-hypertensive effects, and immunostimulant properties; it has also been reported to strengthen superficial resistance, drainage action and new tissue growth. Although, TCM in China is partly integrating with western medicine science, researchers should learn more from TCM and carry out more studies.

Keywords: *Astragalus; Traditional Chinese Medicine; Silk Road; Pharmaceutical Science; Foodstuffs.*

Introduction

Astragalus in Traditional Chinese Medicine and other parts of the world

Chinese herbs have been used as traditional medicine immune booster for human being for thousands of years in China (Yin *et al.*, 2009; Ogbajiet *al.*, 2013; Ogbajiet *al.*, 2018; Shahrajabian *et al.*, 2018; Shahrajabian *et al.*, 2012a; Soleymani and Shahrajabian, 2012a; Soleymani and Shahrajabian, 2012b; Soleymaniet *al.*, 2016; Shahrajabian *et al.*, 2019b; Shahrajabian *et al.*, 2019c). More than 3 million tons of herb medicines were produced in China, and their medicinal parts were consumed in TCM clinic (Soleymani and Shahrajabian, 2012c; Zhang *et al.*, 2016; Ogbajiet *al.*, 2018; Soleymani and Shahrajabian, 2018). In traditional Chinese medicine, some herbals have been used for anti-aging since ancient times (Liu *et al.*, 2017). Astragalus membranaceus as one of the most important Qi tonifying adaptogenic herbs in traditional Chinese medicine, has a long history of medicinal use (Yang *et al.*, 2010; Zhong *et al.*, 2012; Liu *et al.*, 2017). In traditional Chinese medicine, which laid a lot of emphasis on Qi (vital energy) and Yin-Yang balance (negative and

positive equilibrium), Astragalus is considered as benefiting Qi and helping to pass water (Li *et al.*, 2011). It has been used as therapy for Wei Zheng, a term for skeletal muscle fatigue and wasting (Zhou and Mei, 2014). The dried root of *A. membranaceus*, first documented in Shennong Bencao Jing (Shennong's Classic of MateriaMedica, 200-300 AD), is one of the most popular health promoting herbal medicines commonly used in China for more than 2000 years. In modern Chinese medicine, it is used in Fu zheng therapy as an immune stimulant (Ionkova *et al.*, 1997). Also known as Huang Qi (Chinese), Milk-Vetch (English), Hwanggi (Korean), and Ogi (Japanese) (Chou *et al.*, 2007; Li *et al.*, 2019). It is sold in dietary supplements in tea or capsule form in the USA, and in the tea, beverages, soup, and trail mix (gorp) in Asia (Song *et al.*, 2008; Zhang *et al.*, 2011). Chinese milk vetch (*Astragalussinicus L.*) is also a traditional leguminous green manure which plays an important role in maintaining paddy soil fertility and in the popularizing of the double-rice farming system in southern China; it is ploughed into soil at full blooming stage and serves as an alternative to chemical nitrogen fertilizer in the region (Zhu *et al.*, 2012). *Astragalus membranaceus* was originally described in the Shennong's Classic of Meteriamedica, the earliest complete Pharmacopoeia of China written from Warring States Period to Han Dynasty (Heiet *et al.*, 2005; Auyeunget *et al.*, 2016). It is valued for its ability to strengthen the primary energy of the body which we know as the immune system, as well as the metabolic, respiratory and eliminative functions (Liu *et al.*, 2017). This fact is being increasingly substantiated by pharmacological studies showing that it can increase telomerase activity, and has antioxidant, anti-inflammatory, immunoregulatory, anticancer, antitumor, antioxidant, hypolipidemic, antihyperglycemic, hepatoprotective, expectorant, immunomodulatory activity, and diuretic effects (Anon, 2003; Ma *et al.*, 2011; Zhao *et al.*, 2011). *Astragalus membranaceus* (Fisch.) Bunge. has been widely used as an anti-osteoporosis herb in traditional Chinese medicine for many years (Du *et al.*, 2004; Wong *et al.*, 2007; Xi *et al.*, 2008; Jiao *et al.*, 2014; Li *et al.*, 2016). In Traditional Chinese Medicine, *Astragalus membranaceus* is a major component in a prescription to treat chronic phlegmatic disorders and general gastrointestinal disturbances including stomach ulcer, chronic diarrhea and intestinal inflammation (Kim *et al.*, 2008; Yang *et al.*, 2014). Other researchers have reported the values of *Astragalus* roots in traditional Chinese medicine with the function of strengthening exterior and promoting health for thousands of years (Ma *et al.*, 2017; Zhao *et al.*, 2011). Traditional Chinese herbs are generally applied in the form of multi-herb formulas in medical treatments and as dietary supplements (Takagi and Ishii, 1967; Li *et al.*, 2011). Lu *et al.* (2013) reported that *Radix Astragali* is the root of *Astragalus membranaceus* Bunge, and as a famous traditional Chinese medicine (TCM), it has been used to improve muscle wasting-related disorders for a long history. They have also introduced *Astragalus polysaccharide* (APS) as an important bioactive and a therapeutic agent in the management of muscle wasting. *Astragalus trojanus* Stev. is an endemic plant mostly found in eastern and central Anatolia (1300-3500 m), central Aegean region and slopes of Toros mountain (1300-2300 m) in Turkey (Nartop *et al.*, 2015). This genus is widely distributed throughout the temperate and arid regions of the world, and is principally located in Asia (1500 species), North American (500 species) and South American (150 species), and Europe (120 species), but also on mountains in Africa. However, the centre of origin and biodiversity of *Astragalus* plants is Eurasia, especially the mountainous parts of South-Western and South-Central Asia (Lysiuk and Darmohray, 2016). Iran alone, being the richest centre of *Astragalus* habitation, shelters more than 850 species, 527 of which are endemic in the flora of Iran (Ranjbar and Karamian, 2002; Aslanipour *et al.*, 2017; Ghasemian-Yadegari *et al.*, 2017). Aslanipour *et al.* (2017) stated that the crude drugs prepared from *Astragalus* roots are used for treating some illnesses such as leukemia, respiratory infections and diabetes in Iranian folk medicine. In South Eastern Turkey (Anatolia district), the aqueous extract of the roots of different *Astragalus* spp. are traditionally used against leukemia and for its wound-healing properties (Yesilada *et al.*, 2005; Nalbantos *et al.*, 2012; Napolitano *et al.*, 2013). In the district of Anatolia, located in South Eastern Turkey, an aqueous extract of the roots of *Astragalus* is traditionally used against leukemia and for its wound

healing properties (Bediret *et al.*, 2001). *Astragalus corniculatus* Bieb. (Fabaceae) is distributed in Southeastern Romania, South Ukraine and Moldova (Tutin *et al.*, 1972). *Astragalus Tragacantha* L. (Fabaceae) is a western Mediterranean perennial cushion-like plant species well-adapted to drought that grows even in the trace metal and metalloids polluted soils (Salducci *et al.*, 2019). It has been reported that *Astragalus* is an adaptogen and is usually used in combination with other herbs, such as, ginseng, Echinacea, and glossy privet. *Astragalus* is primarily used in American medicine to potentiate the function of the immune system and in cardiovascular disease. In traditional Chinese medicine, it is used for influenza and the common cold (McKenna *et al.*, 2002). Nishiyama *et al.* (1995) reported that in traditional oriental medicine, it is conventional to combine different herbs in order to achieve a variety of treatment purposes simultaneously, or to enhance a single effect without causing severe side effects. Erect milkvetch (*Astragalus adsurgens* Pall.), also as a palatable forage, are also widely used in returning farmland to grassland, it has an important role in restoring the degraded ecosystems and could be an effective and applicable to improve soil nutrients and prevent further soil degradation and erosion, because it grows rapidly, and was characterized by barren-tolerance, wide adaptability and strong resistance (Wang and Wang, 2013).

Bioactive phytochemicals, medicinal uses and potential health benefits of *Astragalus* in traditional and modern medicine industry

Constituents of the dried roots of *Astragalus spp. Radix Astragali* provide significant protection against heart, brain, kidney, intestine, liver and lung injury in various models of oxidative stress-related disease (Hong *et al.*, 1992; Shahzad *et al.*, 2016). Zhang *et al.* (2007) stated that *Astragalus* is an important traditional Chinese medicine (TCM), and now widely used as an immune modulator, especially to support immune health for various chronic degenerative diseases. Recently, *Astragalus radix* was proved efficacious to be an adjunctive therapy medicine for cancers (Wang *et al.*, 2003). In the Bulgarian traditional medicine, *Astragalus glycyphyllos* is used as an antihypertensive, diuretic and anti-inflammatory remedy (Nikolov, 2006). Major classes of compounds of *Astragalus* species are polysaccharides, saponins and isoflavonoids, alkaloid, choline, betaine, folic acid, organic acid, various amino acids, mucic acid, gum, cellulose and fourteen trace elements, including selenium, zinc, and iron, which are essential micronutrients for man and animals (Bedir *et al.*, 2000; Block and Mead, 2003; Yin *et al.*, 2006; Lu *et al.*, 2016). *Astragalus* genera are the richest source of cycloartanes, the unique triterpenoids with a characteristic 9,19-cyclopropane (Nartop *et al.*, 2015). According to the systematic review by Chinese scientists on the chemical constituents of the plants (genus *Astragalus* L.) more than 140 cycloartane-type triterpene glycosides, 60 flavonoids and 18 different polysaccharides have been identified so far (Li *et al.*, 2014). Under high soil moisture and wet conditions, *Astragalus* is susceptible to root rot caused by fungi, which is the main constraint to cultivation. Land must be well drained for *Astragalus*. Loose soil and raised beds can be used to control soil moisture (Shannon *et al.*, 2014). The chemical structures and chain conformations of polysaccharides play a vital role in their biological activities; however, polysaccharides belong to a structurally diverse class of macromolecules (Jin *et al.*, 2014). Cycloastragenol (CA) is the main aglycon of many cycloartane-type glycosides which only found in *Astragalus* genus, extends T cell proliferation by increasing telomerase activity which helps delay the onset of cellular aging (Valenzuela *et al.*, 2009). *Astragalus* root also contains a series of cycloartane triterpene glycosides, including astragalosides I-VIII, acetylastragaloside, isoastragaloside I and III, astramembrannin II, cycloastragenol, cyclosieversigenin, soyasaponin I, soyasapogenol B, and lupeol (Ko and Chik, 2009). Among these, *Astragalus membranaceus* has a high content of astragaloside IV, which is commonly used as a qualitative marker. The most important compounds of *Astragalus* are presented in Table 1.

Table 1: *Astragalus membranaceus* compounds.

Compound	Effect
Flavonoids	Plant metabolites with antioxidant effects; give plants yellow color
Isoflavones	Polyphenolic compounds that are classified as phytoestrogens; formononetin is one of the prominent ones
Lectin	Carbohydrate-binding proteins
Polysaccharides	Carbohydrates whose molecules contain linked monosaccharides; starch, inulin, cellulose
Saponins	Amorphous glycosides of terpenes and steroids that can form emulsions and can foam (soap-like); Astragaloside IV is one the most-studied saponins in Huang Qi

On the basis of traditional Chinese medicine view of cancer, causes are endogenous causes and exogenous causes. Endogenous causes are the seven emotional states (anger, grief, fear, worry, over joy, shock and melancholy) can be seen as the way that stress, worry, over work, and emotional grief can suppress the immune system and allow predispositions for cancer growth to take hold. So, while it can seem simplistic to attribute cancer to normal emotions such as sadness, worry, fear, etc., the TCM view is that when these emotions are excessive, prolonged or unresolved, they can cause disease. The concept of Jing in TCM can be likened to the role of genetics in cancer, which is an important factor indeed. Exogenous causes consists of six exogenous causes for all illness, including cancer, are climatic factors of wind, cold, dampness, dryness, summerheat and fire. And, other miscellaneous causes are environmental causes, dietary causes, and drugs. The TCM concepts of yin/yang balance, the need for calmness of mind, absence of strife, the practice of health promotion through movement, all support modern ideas on the role of psychological, neurological and immunological health in cancer prevention. Liu *et al.* (2011) reported that in many parts of the world, especially in China and Germany, the combined use of herbal treatment and conventional cancer treatment is far more widespread than in America. They have also mentioned that 66.44% of cancer patients in China combined the use of herbal medicine with Western treatment. A prospective, controlled study conducted in Israel (Yaal-Hahoshenet *al.*, 2011) found significant improvement in anemia and neutropenia in breast cancer patients who were given an herbal mixture containing Huang Qi and other Chinese herbs. Rios and Waterman (1997) reported that cycloastragenol (CAG) is a secondary metabolite isolated from Radix Astragali, present in all known Astragalus spp., CAG (9,19-cycloanostane-3,6,16,25-tetrol,20,24-epoxy-(3 β , 6 α ,16 β ,20R,24S)); is both a triterpeneaglycone and the most common genuine aglycone in the bioactive triterpenoidsaponins called astragalosides. Astragalus polysaccharides (APS) are one of the main efficacious principles of Radix Astragali (*Astragalus membranaceus*), which is reported to have anti-oxidant, anti-diabetic, anti-hypertensive, and immunomodulatory activities (Wu and Chen, 2004; Wu *et al.*, 2005). It has been noted that the crude polysaccharide extract of *A. membranaceus* was mainly composed of carbohydrates with small amount of proteins (Cho and Leung, 2007). It has been demonstrated that the main components of the ethylacetate extract of Astragalus were isoflavonoids such as calycosin-7-O- β -D-glycoside, formononetin-7-O- β -D-glycoside and (6R, 10R)-9,10-dimethoxypterocarpan-3-O- β -D-glycoside, and these glycosides and other their aglycones were proved to exhibit strong antioxidant activity (Zhang *et al.*, 2007). Li *et al.* (2010) also mentioned that the dried root of Astragalus contains 2',4'-dihydroxy-5,6-dimethoxyisoflavone, kumatakenin, choline, betaine, polysaccharides, saponins, glucuronic acid, sucrose, amino acids, traces of folic acid and astraisoflavanin. So many other scientists also

revealed that *Astragalus membranaceus* has a notable functional role in various pharmacopoeias as a herbal immunomodulator and an anti-diabetic drug (Wei *et al.*, 2011; Agyeman *et al.*, 2013). Its roots have been used in many state-approved Chinese Herbal formulas for the treatment of diabetes (Jai *et al.*, 2003; Wei *et al.*, 2011). Some experiments have showed that *Astragalus* exhibits immunomodulating and immunorestorative effects both in vitro and in vivo (Guo *et al.*, 2005), and have shown preliminary promise against the experimental coccidial infection when used in conjunction with vaccine (Cho and Leung, 2007). Song *et al.* (2017) reported that *Astragalus* extract mixture HT042 is a combination of three standardized herbal extracts from *Astragalus membranaceus* root, *Elutherococcus senticosus* stem, and *Phlomis umbrosa* root, and it has been developed to promote height growth in children with short stature. Sun *et al.* (2012) revealed that *Astragalus membranaceus* is a popular traditional Chinese medicine, commonly used in Chinese herb prescription to treat liver disease, and the extract prepared from the roots of *Astragalus membranaceus* and *Paeonia lactiflora* demonstrated better hepatoprotective activity than the herbs used individually. Ko and Chik (2009) demonstrated that root extract of *Astragalus membranaceus* administered orally and locally can protect rats against hapten-induced colitis through attenuation of TNF- α and IL-1 β and up-regulating of IL-10. Shen *et al.* (2008) indicated that *Astragalus Membranaceus* has a potential role in treating allergic asthma. Zhang *et al.* (2009) *Astragalus membranaceus* and its effective components are effective in reducing fasting blood glucose and albuminuria levels, in reversing the glomerular hyperfiltration state, and in ameliorating the pathological changes of early diabetic nephropathy in rat models. Ko and Chik (2009) demonstrates that both oral and locally administered *Astragalus membranaceus* possess protective effects against experimental colitis through differential modulation of colonic cytokines. Yang *et al.* (2013) found that *Astragalus membranaceus* polysaccharide (AMP) has antitumor activity in vivo at least partly via improving immune responses of host organism, and seems to be safe and effective for the use of anti-tumor therapy. Lv *et al.* (2017) suggest that *Astragalus polysaccharide* (APS) which is a bioactive extract of *Astragalus membranaceus* may represent a natural therapeutic approach for treating inflammatory bowel disease, such as ulcerative colitis. Yan *et al.* (2010) found that administration of *Astragalus mongholicus* polysaccharides could significantly increase serum and liver antioxidant enzyme activities in mice and decrease peroxidative lipid levels. Jalsra *et al.* (2010) found that doses of *Astragalus mongholicus* extract which did not interfere with locomotor activity and situational anxiety appear to be useful in the treatment of convulsive disorders. Kim *et al.* (2016) highlighted the ability of *Astragalus membranaceus* to increase CREM and ACT expression to facilitate sperm development and semen quality. Tian *et al.* (2016) reported that *Astragalus* may be beneficial as an adjuvant therapy in the treatment of type 2 diabetes. Adesso *et al.* (2018) indicated that *Astragalus membranaceus* root extract significantly reduced the inflammatory response and the pro-oxidant status in IEC-6 cells. Zhou *et al.* (2018) demonstrated that the extract from *Astragalus membranaceus* with water extraction-ethanol supernatant method inhibit cell growth and induce apoptosis in cultured breast cancer cells. This effect AM extract to suppress breast cancer cells growth was associated with its ability to inhibit PI3K/Akt/mTOR activity. Maresca *et al.* (2017) concluded that the 50% hydroalcoholic extract of *Astragalus radix* is a valuable candidate for the adjuvant treatment of articular disease. Liu *et al.* (2017) concluded that the appropriate dose of *Astragalus* depends on several factors, such as the user's age, health status, and several other conditions. They have also found that natural products are not always necessarily safe, and dosages can be important. Sheng *et al.* (2005) found that one of the most important biological role of saponins is modulating the cellular oxidant antioxidant balance. Ten proven benefits of *Astragalus* root is shown in Table 2. Modern pharmacological actions of *Radix Astragali* is shown in Table 3.

Table 2: 10 proven benefits of Astragalus root.

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- 1- Acts as an Anti-inflammatory
 - 2- Boost the immune system
 - 3- Slows or prevents the growth of tumors
 - 4- Protects the cardiovascular system
 - 5- Regulates and prevents diabetes and illnesses related to diabetes
 - 6- Contains anti-oxidative and anti-aging capabilities
 - 7- Aids in wound healing and minimizes scarring
 - 8- Alleviates symptoms of chemotherapy
 - 9- Treats colds and flu
 - 10- Provides supplemental therapy for chronic asthma
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Table 3: Modern pharmacological actions of *Radix Astragali*.

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- 1- It can promote metabolism, fight fatigue and facilitate the renewal of serum and liver proteins
 - 2- It has significant diuretic effect, which can eliminate the urine protein in experimental nephritis
 - 3- It improves anemia in animals
 - 4- It increases low blood sugar and reduces high blood sugar
 - 5- It excites breathing
 - 6- It enhances and regulates immune system, promotes the interferon system, and improves the body's resistance to disease
 - 7- It has low-grade inhibitory effects on the cell pathological change caused by influenza virus and other viruses. At the same time, it has a protective effect on influenza virus infected mice
 - 8- It has broader antibacterial effect
 - 9- It can significantly increase the number, growth and longevity of the cultured cells
 - 10- It can enhance myocardial contractility, protect the cardiovascular system, fight arrhythmia, dilate coronary artery and peripheral vessels, lower blood pressure, reduce platelet adhesion, and reduce thrombosis
 - 11- It also has anti-hyperlipidemia, anti-aging, anti-hypoxia, anti-radiation, and lipotropic effects
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Conclusion

Traditional Chinese medicinal materials have been used for thousands of years and are believed to be abundant, safe, and inexpensive. Astragalus (Huang Qi) has been a foundational herb in traditional Chinese medicine. It is also included in formulas to support Wei Qi (Chi) or the conceptual shield which serves as a primary defence mechanism against pernicious threats to the system. It is widely distributed in China, Siberia, and northern Korea. Some actions of *Astragalus membranaceus* are anti-viral, anti-bacterial, immune system enhancing, immune stimulant, anti-infective some viruses, adaptogen, cardio-tonic, diuretic, hypotensive, anti-oxidant, immunomodulator, hypoglycaemic, circulatory stimulant, vasodilator, anti-fatigue, anti-cancer and hepatoprotective. Chemical constituents are polysaccharides, triterpenoidsaponins (Astragalosides), flavonoids, choline, phytosterols, volatile oils, amino acids (Asparagine, Gamma-aminobutyric acid, Canavanine), aglycones, coumarins, astrapterocarpan, betaine, calcium, copper, isoflavonoids, rich in potassium and magnesium. *Astragalus membranaceus* classically prescribed in TCM in combination with other Chinese medicinal herbs as a dried root, powdered or as a decoction, with the combination depending on the desired therapeutic effect and the specific TCM diagnosis. Polysaccharides in *Astragalus* intensify phagocytosis in reticuloendothelial systems, stimulate pituitary-adrenal cortical activity, and restore depleted red blood cell formations in bone marrow. *Astragalus* uses are in kidneys problems, strengthens the kidneys,

incontinence and frequent urination, urinary tract infection, gastric ulcers, decreased appetite, chronic diarrhea, strengthens the spleen, poor digestion, liver problems, viral hepatitis, strengthen the liver, postpartum fever, uterine bleeding, topical adjuvant therapy for chronic viral cervicitis, vaginitis, edema, lupus, rheumatoid arthritis, myasthenia gravis, strengthens and builds bone marrow, excessive sweating, night sweats, slow healing wounds, increasing white blood cell count, leukopenia, ischemic heart disease, angina pectoris, recovery from severe loss of blood, diabetes, anemia, high blood pressure, heart palpitations, congestive heart failure, strengthens the blood, increases interferon production, impaired immunity, chronic viral infections, general debility, increases energy, HIV/AIDS, cancer, myalgic encephalomyelitis (Chronic fatigue syndrome), improves sleep quality, upper respiratory infection, common cold, chemotherapy, radiation therapy, flu, combats coxsackie B myocarditis, ameliorate side effects of drugs, appropriate herb for weak and elderly. Isoflavonoids, such as calycosin-7-O- β -D-glucoside, ononin, astraisoflavan-7-O- β -D-glucoside, calycosin and formononetin, are principle bioactive compounds found in Radix astragali-based drugs or foods. In summary, Astragalus is an ancient herb for modern medicine which can promote good health and as drugs to treat diseases.

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