

Pharmacology and Ethnomedicine of the Genus *Astragalus*

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Abstract. The genus *Astragalus*, consisting of about 3000 species, is a valuable source of herbal drugs. The review article comprises scientific data concerning morphological, distribution and phytochemical characters of the genus. Polysaccharides, saponins, and flavonoids are considered main active principles. *Astragalus spp.* have long been used as medicinal plants in folk medicine as cardiovascular, antihypertensive, diuretic, choleric, as well as antimicrobial and antiviral agents. The plants of the genus exhibit a broad spectrum of pharmacological effects, among which major include diuretic, anti-inflammatory, bactericidal, hypotensive, and sedative ones. The review focuses on uses of about 30 *Astragalus* species in official medicine and ethnomedicine and their pharmacological action.

1. INTRODUCTION

Astragalus L. (*Fabaceae*), as the largest genus of vascular plants, contains an estimated number of 3000 species [28], and nearly 133 in Europe [25]. Plants of the genus *Astragalus* are of great importance for current medicinal practice.

1.1. Morphological characters

Astragalus plants are annual or perennial stemmed herbs or small shrubs (up to 150-200 cm), growing from underground roots. The leaves are alternate, imparipennate or paripennate, sometimes terminating in a spine. Flowers are leguminous, in racemic or axillary clusters, sessile or pedicellate. The fruit is a legume pod, usually dehiscent, with kidney shaped seeds [25].

1.2. Distribution

This genus is widely distributed throughout the temperate and arid regions of the world, and is principally located in Asia (1500 species), North America (500 species) and South America (150 species), and Europe (120 species), but also on mountains in Africa. However, the center of origin and biodiversity of *Astragalus* plants is Eurasia, specially the mountainous parts of South-Western and South-Central Asia [39].

1.3. Phytochemistry

The *Astragalus* plant species produce exudates when they are tapped or otherwise stressed, perhaps as a protective mechanism. The hydrophylic exudates, termed gums, are composed principally of water soluble polysaccharides, frequently with a small covalently bound protein residue. About 130 saponins have been described in *Astragalus spp.* Triterpenoid sapogenin and saponins isolated from the genus *Astragalus* belong mainly to the cycloartane skeleton. By comparison with the large variety of flavone and flavonol glycosides (these latter are the most abundant in *Astragalus spp.*), the number of isoflavonoid glycosides is small. Kaempferol and quercetin occur more widely among flavonols, while astragalol, and rutin, are the most representative glycosides [25].

2. OFFICIAL SPECIES OF THE GENUS ASTRAGALUS: APPLICATION AND PHARMACOLOGY

2.1. Sources of Tragacanth

The European Pharmacopoeia defines Tragacanth (*Tragacantha*) as the air-hardened, gummy exudate, flowing naturally or obtained by incision from the trunk and branches of *Astragalus gummifer* Labill. and certain other species of *Astragalus* from western Asia [8]. Gum tragacanth is used as an emulsifier, stabilizer and thickening agent in pharmaceuticals and foodstuffs [25].

2.2. *Astragalus mongholicus* root

The European Pharmacopoeia [8] also comprises the monograph for *Astragalus mongholicus* root (*Astragali mongholicici radix*), the whole, dried root of *A. mongholicus* var. *mongholicus* (syn. *A. membranaceus* Bunge var. *mongholicus* (Bunge) P.K.Hsiao) and *A. mongholicus* var. *dahuricus* (DC.) Podlech (syn. *A. membranaceus* Bunge), freed from rootlets and rootstock, collected from spring to autumn, containing minimum 0.040 per cent of astragaloside IV (dried drug).

Application, described in pharmacopoeias and in traditional systems of medicine for *Astragalus* root, is as adjunctive therapy in the treatment of colds and influenza. The herb is used to enhance the immune system and to increase stamina and endurance; also in the treatment of chronic diarrhoea, oedema, abnormal uterine bleeding, and diabetes mellitus, and as a cardiogenic agent. Uses described in folk medicine comprise treatment of nephritis, chronic bronchitis, postpartum urine retention, leprosy, and the sequelae of cerebrovascular accidents [40].

Both *in vitro* and *in vivo* investigations have confirmed that *Astragalus membranaceus* enhances the immune system. Using the local xenogenic graft-versus-host reaction (assessed in cyclophosphamide-treated rats) as a model assay for T-cell function, mononuclear cells, derived from cancer patients, which were preincubated with a polysaccharide fraction from *A. membranaceus* had significant immunopotentiating activity, and they fully corrected *in vitro* T-cell function deficiency found in cancer patients. The immune enhancing polysaccharide molecules have relative molecular masses of approximately 25 000 [4].

The immunostimulant activity of *A. membranaceus* has been associated with the polysaccharide fractions of the root extract. A glycan AMem-P, isolated from the roots of *A. membranaceus*, was shown by use of an *in vivo* carbon clearance test to significantly potentiate reticuloendothelial system activity in mice [34].

2.3. *Astragalus complanatus* seed

Astragali complanati semen, Shayuanzi, the dried ripe seed of *A. complanatus* R.Br., collected in late fall to early winter, is listed in the Chinese Pharmacopoeia. It is used as tonic against polyuria and vertigo [25].

2.4. *Astragalus dasyanthus* herb

The plant material is considered as official in the Newly Independent States and its infusion is applied as a sedative, hypotensive and diuretic herbal drug [20]. The water infusion is used for the treatment of hypertension of 1st and 2nd stages, cardiovascular insufficiency, and chronic nephritis [26]. Preparation of *A. dasyanthus* has been approved for use in case of cardiovascular collapse and hypotonic disease. It has general anti-inflammatory and diuretic effect and can be used for treatment of kidney vascular disorders [7]. The use of *Astragalus dasyanthus* in lesions of the liver in patients with pulmonary tuberculosis was proposed [31]. *A. dasyanthus* has medicinal properties due to the presence of glycosides and flavonoids [7,13,19,27].

2.5. *Astragalus falcatus* leaf and flower

The leaves and flowers of *Astragalus falcatus*, another official herbal drug in the Newly Independent States, derived from the subjected genus, are recommended for producing the individual flavones glycoside flaronin (robinin), which is kaempferol-3-O-D-rhobinosyl-7-O-L-rhamnopyranoside, of hypoazotemic activity. Flaronin enhances the nitrogen-excretory function of

kidneys, decreases the level of residual nitrogen, urea and creatinine in blood, and increases diuresis. Since 1998, Flaronin is successfully applied to treat chronic renal insufficiency caused by pyelonephritis and other kidney diseases [12].

3. SPECIES OF THE GENUS *ASTRAGALUS*, APPLIED IN FOLK MEDICINE

Plants of the genus *Astragalus* have long been used as medicinal plants in folk medicine of numerous countries as cardiovascular, antihypertensive, diuretic, choleric, as well as antimicrobial and antiviral remedies [2, 26].

3.1. *Astragalus adsurgens* Pall.

A. adsurgens is used in Russian and Tibetan folk medicine as a diuretic remedy in oedema; in Transbaicalian regions the species is considered a wound-healing agent. The plant is also applied for labour stimulation and acceleration of separation of the placenta in gynecology [33].

3.2. *Astragalus alopecias* Pall.

The powdered herb of *A. alopecias* is applied as a wound-healing agent due to its drying properties and as a baby powder [33].

3.3. *Astragalus arenarius* L.

A. arenarius is used in Belarus for treatment of heart and gastrointestinal disorders; its aqueous alcohol extracts from above-ground portion possessed antibacterial and antifungal activity under experimental investigations [26].

3.4. *Astragalus brachyceras* Ledeb. (*A. hamosus* auct)

Roots of *A. brachyceras* are applied in the Caucasus as a diuretic and its fruits – as a coffee substitute. The fruits in mountainous parts of Turkmenistan and Iran are used as a vomiting remedy and ingredients of laxative herbal collections [26].

3.5. *Astragalus cicer* L.

The aboveground portion of *A. cicer* is used for the heart and gastrointestinal diseases in Belarus. The plant has hypotensive, diuretic, bactericidal and sedative effects, causes tachycardia, stimulates breathing, depresses the central nervous system, exhibits cholinolytic and cholesterol-lowering properties, reduces the content of lipoproteins in the blood, adrenaline and noradrenaline in the tissues [2, 26].

3.6. *Astragalus corniculatus* Bieb.

A. corniculatus is used by Bulgarian folk medicine as a diuretic for treatment of hypertension, renal disorder, nervous diseases and rheumatism, and also as a diaphoretic [11]. Preparation of hydrogel tablets based on polyethylene oxide with standardized dry extract of *A. corniculatus* was developed [5].

Investigations of the ethyl acetate extract obtained from the species *Astragalus corniculatus* _ resulted in a low acute oral toxicity and a remarkable antihypoxic activity, especially in a model of circulatory hypoxia [15].

Effect of purified saponins' mixture (PSM) from *Astragalus corniculatus* on toxicity models in isolated rat hepatocytes was determined [23]. The PSM showed *in vivo* hepatoprotective and antioxidant activities against carbon tetrachloride (CCl₄) and paracetamol – induced liver damage comparable to that of silymarin [38]. In conditions of nonenzyme and enzyme lipid peroxidation in isolated rat microsomes, the PSM showed statistically significant antioxidative effect, similar to the effect of silymarin. In rat brain synaptosomes PMS had statistically significant protective effect, similar to those of silymarin on 6-hydroxydopamine-induced oxidative stress. In CCl₄-induced toxicity, PSM had statistically significant cytoprotective and antioxidant activity. In model of oxidative stress – induced by *tert*-butylhydroperoxide (*t*-BuOOH), PSM had statistically significant

cytoprotective and antioxidant activity, stronger than the effect of silymarin [22]. The study [30] evaluated the effect of PSM on enzyme-induced and non-enzyme-induced lipid peroxidation, in liver microsomes from spontaneously hypertensive rats (SHRs), as compared to normotensive Wistar rats (NTRs). PSM, isolated from *Astragalus corniculatus*, shows antioxidant activity both in SHRs and NTRs and the effect in NTRs is more pronounced.

Immunorestitution and augmentation of mitogen lymphocyte response in Graffi tumor bearing hamsters by PSM from *Astragalus corniculatus* was observed [36]. Influence of its PSM on phagocytic cells in Graffi tumor bearing hamsters was studied [35]. Protective effect of *Astragalus corniculatus* saponins against myeloid Graffi tumor in hamsters was shown [18].

Phytochemical analysis of volatiles from *Astragalus corniculatus* were carried and *in vitro* cytotoxic activity investigated [17].

3.7. *Astragalus corrugatus* Bert.

Fruits of *A. corrugatus* are applied as a vomiting and laxative remedy in the Tibetan medicine [33].

3.8. *Astragalus dahuricus* DC.

A. dahuricus is known in the Russian and Tibetan medicine as the agent for treatment of oedema and acceleration of labours [33].

3.9. *Astragalus danicus* Retz.

A. danicus is used in gynecological diseases in the Altai. Its infusions have tonic and restorative properties and are used in the Middle Urals and Western Siberia for women's diseases and as a means of relieving fatigue and in cases of high blood pressure and headache on the Russian Far East [2, 26].

3.10. *Astragalus exscapus* L.

A. exscapus is used in folk medicine of France and in Odessa region of Ukraine for treatment of syphilis, rheumatism, skin disorders, joint pain, and as a diuretic and a sudoripic agents [33].

3.11. *Astragalus fruticosus* Pall. (*A. suffruticosus* DC.)

A. fruticosus is applied in the Russian folk medicine as a diuretic remedy [33].

3.11. *Astragalus glycyphylloides* DC.

A. glycyphylloides is used to stimulate labour and accelerate separation of the placenta in gynecology and as a lactogenic remedy [33]. In the Caucasus, it is used as a laxative. From its herb is obtained preparation of lactogenic properties [2, 26].

The antioxidant effect of aqueous - ethanolic extract (100 mg/kg) from *Astragalus glycyphylloides* and its protection against carbon tetrachloride-induced oxidative stress and hepatotoxicity was shown in male Wistar rats [29]. Ethanol extract from *Astragalus glycyphylloides* (10 µg/mL and 100 µg/mL) had statistically significant cytoprotective and antioxidant activity, near to those of silymarin, on carbon tetrachloride (CCl₄)-induced cytotoxicity (model of metabolic bioactivation) in isolated rat hepatocytes [14].

3.12. *Astragalus glycyphyllos* L.

A. glycyphyllos has an application as the emollient, diuretic, and refreshing agent in France. Its decoction is used in Bulgaria for gastroenteritis, flatulence, hypertension, sciatica, as a lactogenic agent, and as a component of herbal collection for varicose dermatitis [2, 26].

The leaves and seeds of *A. glycyphyllos* are used in urolithiasis, oliguria, scrofula, dermatitis, and as a laxative in the Caucasus. The plant is applied in the treatment of nervous diseases in the Volga region. A decoction of the aboveground parts is used in Belarus to treat uteroptosis, leukorrhea, stomach diseases, dysentery; and externally in cases of fungal scalp infection [2, 26].

The herb in a decoction form is used in Ukraine as a laxative, diuretic, expectorant, as well as in dermatitis, sexually transmitted diseases, rheumatism. The decoction of its above-ground portion is applied in the Carpathians as diuretic in urolithiasis and other diseases of the kidneys and urinary tract; as expectorant in acute respiratory diseases; for the treatment of rheumatism, arthralgia, diarrhea, dermatitis, syphilis; to stimulate labour and accelerate separation of the placenta in gynecology [2, 26].

10% infusion of *A. glycyphyllos* showed hypotensive and anticoagulant effects in clinical trials. The plant infusion exhibited diuretic properties; its aqueous alcohol extracts - antibacterial and anti-Trichomonas activity; the ether extract *in vitro* - anti-tumor effects; the leaf extract demonstrated yeast-static action under the experimental conditions [2, 26].

Currently, the plant *A. glycyphyllos* is regarded acting pharmacologically as *A. dasyanthus* and a promising source of vitamin-mineral complex and antioxidant biologically active compounds [2, 20].

3.13. *Astragalus hamosus* L.

A. hamosus has been used traditionally for treatment of painful and inflammatory conditions. Also it is used for treatment of some nervous diseases in Iranian traditional medicine [1]. Its roots are used as a diuretic remedy [33]. The plant is demulcent, emollient, galactagogue and laxative. It is useful in treating irritation of the mucous membranes, nervous affections and catarrh [3].

Hydroalcoholic extract of the *Astragalus hamosus* possesses anti-nociceptive and anti-inflammatory properties which are probably mediated via inhibition of prostaglandin synthesis as well as central inhibitory mechanisms [1].

Acute anti-inflammatory activity of the methanol extract of *A. hamosus* has been reported [1, 10]. Pharmacological evaluations have shown antioxidant activity of methanolic extract of *Astragalus hamosus* [32].

The antineoplastic activity of erufosine (alkylphosphocholine derivate) and the saponin mixture, derived from *A. hamosus* were found to be active against human leukemia cells; the saponin mixture showed dramatic decrease in the expression level of the mitochondrial protein BclxL, which outlines its special influence on the cell death signal transduction [6].

Evaluation of antiproliferative effect of a flavonol glycoside and saponins of *Astragalus hamosus* showed concentration-dependent inhibition of malignant cell proliferation by saponins, while the flavonoid exerted only marginal effects [16]; some of these compounds showed biological effect modulators of lymphocyte proliferation [24,] [Verotta L.]. Volatile compounds of the plant showed significant cytotoxic activity against human acute lymphoid leukemia in concentration-dependent manner [24].

3.14. *Astragalus melilotoides* Pall.

Decoctions of *A. melilotoides* are used for treatment of scare in children and as a diuretic [33].

3.15. *Astragalus monspessulanus* L.

The roots of *A. monspessulanus* are applied in the European countries as a diuretic, sudoripic in treatment of rheumatism, gout, dermatitis, syphilis [26]. The plant is used in Southern Italy as a diuretic [9].

3.16. *Astragalus montanus* Lim.

A. montanus is used as an astringent and diuretic medicine, and for cleaning of wounds and gums [33].

3.17. *Astragalus onobrychis* L.

A. onobrychis is applied for treatment of gynecological diseases in the Altai. Flavonoids' totality of its leaf extract shows lipid-lowering and fungistatic activity under the experimental investigations [2, 26]. Immunomodulating effect of triterpenoid saponins from *Astragalus onobrychis* was shown [21].

3.18. *Astragalus penduliflorus* auct. (*A. propinquus* Schischk., *A. membranaceus* Bunge f. *propinquus* (Bunge) Kitag.)

The root powder of *A. penduliflorus* is used as a potent diuretic remedy in the Russian and Tibetan folk medicine [33].

3.19. *Astragalus ponticus* Pall.

A. ponticus is used as a diuretic for treatment of hypertension, renal disorder, nervous diseases and rheumatism, and also as a diaphoretic by Bulgarian folk medicine [11].

3.20. *Astragalus pubiflorus* DC. (*A. excapus* L. subsp. *pubiflorus* (DC.) Soo, *A. excapus* auct.)

Roots of *A. pubiflorus* are applied in rheumatism and syphilis. The totality of the plant's flavonoids under experimental conditions exhibited spasmolytic effects [26].

3.21. *Astragalus sieversianus* Pall.

Seeds of *A. sieversianus* are used internally in the Russian and Arabian folk medicine in nervous disorders, hernias in children [33].

3.22. *Astragalus uliginosus* L.

A. uliginosus is applied for treatment of oedema and to accelerate the labour activity [33].

3.23. *Astragalus vergatus* Pall.

A. vergatus is used for the syphilis treatment [33].

3.24. *Astragalus vesicarius* auct. (*A. albidus* Waldst. et Kit.)

A. vesicarius is applied by Bulgarian folk medicine as a diuretic for treatment of hypertension, renal disorder, nervous diseases and rheumatism, and as a diaphoretic [11].

4. CONCLUSION

Considering that almost all of the herbs used in modern scientific medicine were derived from traditional medicine, attention to such data often has an essential impact on the effectiveness in the search of promising herbal drugs. Studying the experience of folk medicine may be one of leading methods for the search of new official medicinal plant materials. The presented scientific data might be useful for optimization both in application of official plants of the genus *Astragalus* in current phytotherapeutical practice worldwide and also pharmaceutical development of new phytopharmaceuticals, based on the most promising herbal substances, derived from *Astragalus* spp.

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