· Reviews ·

Review of *Astragali Radix*

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Abstract: *Astragali Radix* (AR), known as *Huangqi* in China, is one of the most popular herbal medicines learnt worldwide to reinforce Qi (the vital energy). AR is traditionally prepared from the dried roots of *Astragalus membranaceus* or *A. membranaceus* var. *mongholicus*. It has been reported to have cardiotonic, hepatoprotective, hypotensive, immunostimulant, anti-aging, anti-oxidative, antidiabetic, and anti-inflammatory activities. The bioactive compounds were found to be flavonoids, saponins, polysaccharides, amino acids, and some trace elements. The present paper reviews the studies on AR including history, phytochemistry studies, pharmacological functions, and clinical application in recent years.

Key words: *Astragali Radix*; *Astragalus membranaceus*; *Astragalus membranaceus* var. *mongholicus*; clinical application; pharmacological effects

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Introduction

Astragali Radix (AR) is a common traditional Chinese herbal medicine known as *Huangqi* in China. It has been widely used as an immunostimulant, cardiotonic, hepatoprotective, antidiabetic, antitumor, and antiviral drug (Li *et al*, 2003; Shon, Kim, and Nam, 2002; Toda and Shirataki, 1999; Liu *et al*, 2010; Li *et al*, 2010). According to the latest edition of the *Chinese Pharmacopoeia* 2010, AR is the dried roots of *Astragalus membranaceus* (Fisch.) Bunge var. *mongholicus* (Bunge) Hsiao or *A. membranaceus* (Fisch.) Bunge (Fabaceae). It has been reported that the constituents most often associated with the activity of AR are flavonoids, saponins, polysaccharides, amino acids, and various trace elements (Liu *et al*, 2006; Song *et al*, 2004). The main pharmacological activities of AR include cardiotonic, hepatoprotective, hypotensive, immunostimulant, anti-aging, anti-oxidative, antidiabetic, and anti-inflammatory activities (Li, Li, and Fang, 2006; Wu *et al*, 2005; 2006; Zhang *et al*, 2005).

AR is mostly obtained from cultivated plants, as wild ones are increasingly scarce (Qian *et al*, 2009). *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* (Liu *et al*, 2009a). There are many commercial specifications of AR in the herb market in China. The herb suppliers usually divide the herb into the first-, second-, and third-class specifications by the diameter of the AR roots. Crude drug of the first-class specification has the thickest diameter. Meanwhile, there are also many different specifications of crude drugs sold in the market, such as different cultivation places, age of cultivation at harvest, and the season of collection.

This review summarized the history, traditional uses, phytochemical studies, pharmacological studies, safety, and clinical application of AR based on the literatures in recent years.

History and traditional uses

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AR was first recorded as a superior herbal medicine in *The Divine Husbandman's Classic of Materia Medica* (*Shennong Bencao Jing*), which is one of the most ancient herbal medicine literatures. It has been used over 2000 years to benefit the deficiency of Qi (the vital energy). By the theory of traditional Chinese medicines (TCM), AR is sweet and slightly warm, and enters lung and spleen meridian. It is used to reinforce Qi, consolidate the exterior, induce urination, express toxins outward, and make new tissues grow. AR is traditionally important for the treatment of fatigue, diarrhea, and lack of appetite. It is also believed to treat abnormal uterine bleeding, spontaneous sweating due to weakened superficial resistance, edema due to deficiency of Qi, abscesses, anemia, and wasting-thirst caused by internal heat and diabetes. According to TCM theory, AR combined with other crude drugs is used as many classical formulae in clinical applications for many millennia including *Danggui Buxue* Decoction (AR and *Angelicae Sinensis Radix*), *Buyang Huanwu* Decotion (AR, *Angelicae Sinensis Radix*, *Paeoniae Rubra Radix*, *Ligustici Chuanxiong Rhizoma*, *Carthami Flos*, *Persicae Semen*, and *Lumbricus*), *Yupingfeng* Powder (AR, *Saposhnikoviae Radix*, and *Atractylodis Macrocephaiae Rhizoma*), *Huangqi Guizhi* Decoction (AR, *Paeoniae Alba Radix*, *Cinnamomi Ramulus*, *Zingiberis Recens Rhizoma*, and *Jujubae Fructus*), *Huangqi Jianzhong* Decoction (AR, *Cinnamomi Ramulus*, *Paeoniae Alba Radix*, *Zingiberis Recens Rhizoma*, *Jujubae Fructus*, and *Glycyrrhizae Radix* et *Rhizoma*), and so on.

Phytochemical studies

Phytochemical studies have demonstrated that AR possessed various components, including flavonoids, saponins, polysaccharides, amino acids (Liu *et al*, 2010; Ma *et al*, 2002), and various trace elements (Katsura and Yamagishi, 1984). The *Chinese Pharmacopoeia* 2010 specifies that the content of astragaloside IV should be not less than 0.040%, while calycosin-7-*O*-β-*D*-glucoside not less than 0.020%, respectively as determined by HPLC, in order to control the quality of AR.

Flavonoids

About 30 flavonoids were isolated and identified from the roots of *A. membranaceus* and *A. membranaceus* var. *mongholicus*, which belonged to four structural groups as flavones (A), isoflavones (B), isoflavanones (C), and pterocarpans (D) (Fig. 1).

Five flavones, namely kaempferol (**1**), quercetin (**2**), isorhamnetin (**3**), rhamnocitrin (**4**), and kumatakenin (**5**) were isolated from the roots of the plant (Qi, 1987). Two flavone glycosides, rhamnocitrin-3-glucoside (**6**) and quercetin-3-glucoside (**7**) were isolated from the aerial part of the plant (Ma *et al*, 1991). The structures of these flavones were shown in Fig. 1A.

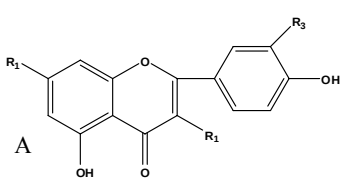
The structures of isoflavones were shown in Fig. 1B. Formononetin (**8**), calycosin (**9**) (Qi, 1987), 3'-methoxy-5'-hydroxy-isoflavone-7-*O*-β-*D*-glucoside (**15**) (Cao *et al*, 1999), (3*R*)-2',3'-dihydroxy-4',7-dimethoxy-isoflavone (**16**), and ononin (**17**) (Ma *et al*, 2003) were isolated from AR. Song *et al* (1997a; 1997c) reported that four isoflavones, 3',8-dihydroxy-4',7-dimethoxy-isoflavone (**10**), odoratin-7-*O*-β-*D*-glucopyranoside (**11**), 3',7-dihydroxy-4',8-dimethoxyisoflavone (**12**), and calycosin-7-*O*-β-*D*-glucopyranoside (**13**), were identified from AR. Calycosin-7-*O*-β-*D*-glucoside-6"-*O*-malonate (**14**) was separated and identified from AR for the first time (Xiao, Han, and Shi, 2009).

Five isoflavanones, 2'-hydroxy-3',4'-dimethoxy-isoflavan-7-*O*-β-*D*-glucopyranoside (**18**) (Cao *et al*, 1999), 2'-hydroxy-3',4',7-trimethoxyisoflavan (**19**) (Subarnas, Oshima, and Hikino, 1991), 2',7-dihydroxy-3',4'-dimethoxyisoflavan-7-*O*-β-*D*-glucoside (**22**) (Ma *et al*, 2004), 8,2'-dihydroxy-4',7-dimethoxyisoflavan (**20**), and 2',3',7-trihydroxy-4'-methoxyisoflavan (**21**) (Song *et al*, 1997b) were isolated from AR and listed in Fig. 1C.

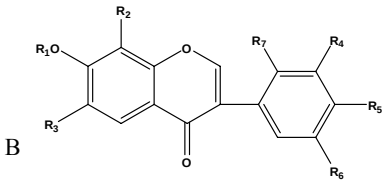
Three pterocarpans listed in Fig. 1D were isolated from AR and reported as 3,9,10-trimethoxypterocarpan (**23**) (Subarnas, Oshima, and Hikino, 1991), (6a*R*,11a*R*)-10-hydroxy-3,9-dimethoxypterocarpan (**24**) (Song *et al*, 1997c), and 9,10-dimethoxypterocarpan-7-*O*-β-*D*-glucopyranoside (**25**) (Ma *et al*, 2004).

Saponins

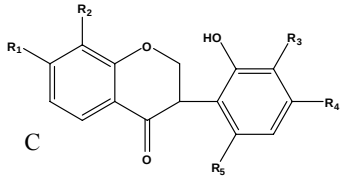
In recent years, about 40 saponins were isolated and identified from the roots of *A. membranaceus* and *A. membranaceus* var. *mongholicus*. Many saponins belonged to cycloartane tetracyclic triterpenoids including the structures of three rings without furan ring (A) and the structures of three rings with furan ring (B), while a few saponins belonged to oleanane pentacyclic triterpenoids (C) (Fig. 2).



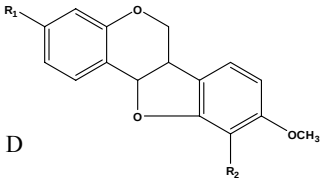
1 R_1=OH; R_2=OH; R_3=H
2 R_1=OH; R_2=OH; R_3=OH
3 R_1=OH; R_2=OH; R_3=OCH_3
4 R_1=OH; R_2=OCH_3; R_3=H
5 R_1=OCH_3; R_2=OCH_3; R_3=H
6 R_1=Glc; R_2=OCH_3; R_3=H
7 R_1=Glc; R_2=OH; R_3=OH



8 R_1=H; R_2=H; R_3=H; R_4=H; R_5=OCH_3; R_6=H; R_7=H
9 R_1=OCH_3; R_2=H; R_3=H; R_4=OH; R_5=OCH_3; R_6=H; R_7=H
10 R_1=OCH_3; R_2=OH; R_3=H; R_4=OH; R_5=OCH_3; R_6=H; R_7=H
11 R_1=Glc; R_2=H; R_3=OCH_3; R_4=OH; R_5=OCH_3; R_6=H; R_7=H
12 R_1=H; R_2=OCH_3; R_3=H; R_4=OH; R_5=OCH_3; R_6=H; R_7=H
13 R_1=Glc; R_2=H; R_3=H; R_4=OH; R_5=OCH_3; R_6=H; R_7=H
14 R_1=Glc-6''-*O*-malonate; R_2= H; R_3=H; R_4=OH; R_5=OCH_3; R_6=H; R_7=H
15 R_1=Glc; R_2=H; R_3=H; R_4=OCH_3; R_5= H; R_6=OH; R_7=H
16 R_1=OCH_3; R_2=H; R_3=H; R_4=OH; R_5=OCH_3; R_6=H; R_7=OH
17 R_1=Glc; R_2=H; R_3=H; R_4=H; R_5=OCH_3; R_6=H; R_7=H



18 R_1=Glc; R_2=H; R_3= OCH_3; R_4=H; R_5=H
19 R_1=OCH_3; R_2=H; R_3=OCH_3; R_4=H; R_5=H
20 R_1=OCH_3; R_2=OH; R_3=H; R_4=OCH_3; R_5=H
21 R_1=OH; R_2=H; R_3=OH; R_4=OCH_3; R_5=H
22 R_1=OH; R_2=H; R_3=OCH_3; R_4=OCH_3; R_5=H



23 R_1=OCH_3; R_2=OCH_3
24 R_1=OCH_3; R_2=OH
25 R_1=O-Glc; R_2=OCH_3

Fig. 1 Structures of flavones (A), isoflavones (B), isoflavanones (C), and pterocarpans (D) from AR

Agroastragaloside I (**1**), agroastragaloside II (**2**), huangqiyegenin II (**3**), huangqiyenin B (**4**), mongholicoside I (**5**), mongholicoside II (**6**), cycloastragenol (**10**), huangqiyenin A (**24**), and huangqiyegenin I (**26**) were isolated from AR (Kitagawa *et al*, 1983b). It was reported that astragaloside I (**11**), astragaloside II (**12**), isoastragaloside I (**17**), isoastragaloside II (**18**), acetylastragaloside I (**22**), and astragaloside IV (**27**) were identified (Kitagawa, Wang, and Yoshikawa, 1983). Astragaloside III (**13**), astragaloside V (**14**), and astragaloside VI (**15**) were isolated from AR (Kitagawa *et al*, 1983a).

It was reported that isoastragaloside IV (**19**), agroastragaloside III (**20**), agroastragaloside IV (**21**), huangqiyenin D (**23**), and astramembrannin II (**26**) were isolated from AR (Qi, 1987). Astragaloside VII (**16**), astragaloside VIII (**31**), and soyasaponin I (**32**) were also identified (Kitagawa, Wang, and Yoshikawa, 1983).

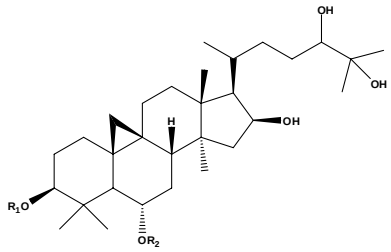
Huangqiyiesaponin C (**28**) was isolated and identified from the aerial part of *A. membranaceus* (Ma *et al*, 1993), while mongholicoside A (**7**) and mongholicoside B (**8**) were two new saponins isolated from the aerial part of *A. membranaceus* var. *mongholicus* (Yu *et al*, 2007a).

Astramembranoside A (**29**) and astramembranoside B (**9**) were two new cycloartane saponins isolated from the roots of *A. membranaceus* (Kim *et al*, 2008). Malonylastragaloside (**30**) was isolated and identified as a novel astragaloside malonate form AR (Chu *et al*, 2010).

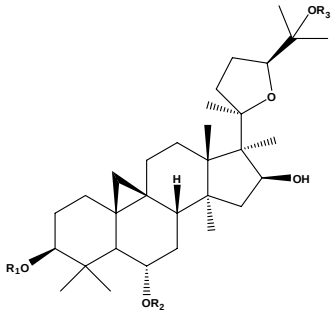
Polysaccharides

Polysaccharides play an important role in pharmacological effects in AR. In these years there are a lot of researches which focused on polysaccharides in AR.

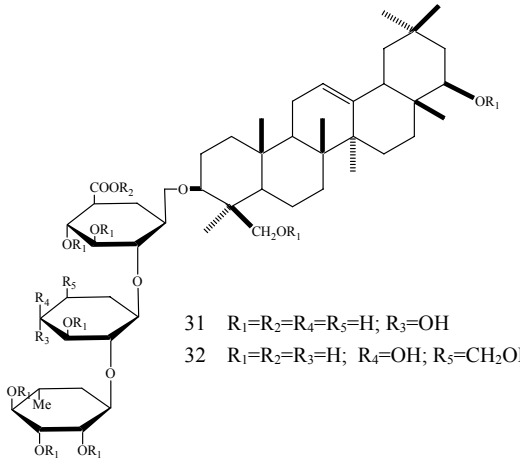
Two glacans AG-1, AG-2 and two heterosaccharides AH-1, AH-2 were isolated and purified from water extract of AR (Huang *et al*, 1982). AG-1 was identified as α-(1,4) and α-(1,6) glucan (5:2). AG-2 was elucidated as α-(1,4) glucan. AH-1 was an acidic polysaccharide and composed of hexouronic acid, glucose, rhamnose, and arabinose as a ratio of 1:0.04:0.02:0.01. AH-2 was composed of glucose and arabinose as a ratio of 1:0.15.



1 R_1=2,3-di-Ac-Xyl; R_2=Glc
2 R_1=2-Ac-Xyl-(1→6)-Glc; R_2=H
3 R_1=H; others: C_6=O
4 R_1=Glc; others: C_6=O
5 R_1=H; others: $\Delta^{24(25)}$, $C_{1,26}$-OH , $C_{6,24,25}$ without -OH
6 R_1=H; others: $\Delta^{24(25)}$, $C_{1,12,26}$-OH , $C_{6,24,25}$ without -OH
7 R_1=Glc; R_2=H
8 R_1=Glc; others: C_6=O
9 R_1=Xyl-Glc; R_2=H



10 R_1=H; R_2=R_3=H
11 R_1=2,3-di-Ac-Xyl; R_2=Glc; R_3=H
12 R_1=2-Ac-Xyl; R_2=Glc; R_3=H
13 R_1=Glc-(1→2)-Xyl; R_2=R_3=H
14 R_1=Glc-(1→2)-Xyl; R_2=H; R_3=Glc
15 R_1=Glc-(1→2)-Xyl; R_2=Glc; R_3=H
16 R_1=Xyl; R_2= R_3=Glc
17 R_1=2,4-di-Ac-Xyl; R_2=Glc; R_3=H
18 R_1=3-Ac-Xyl; R_2=Glc; R_3=H
19 R_1=Xyl; R_2=H; R_3=Glc
20 R_1=2,3-di-Ac-Xyl; R_2=Glc; R_3=Glc
21 R_1=2-Ac-Xyl; R_2=H; R_3=Glc
22 R_1=2,3,4-tri-Ac-Xyl; R_2=Glc; R_3=H
23 R_1=Glc; R_2=Ac; R_3=H
24 R_1=Glc; R_2= H; others: C_6 without -OH
25 R_1=R_3=H
26 R_1=Xyl; R_2=R_3=H
27 R_1=Xyl; R_2=Glc; R_3=H
28 R_1=Glc; R_2=R_3=H
29 R_1=H; R_2=R_3=Glc
30 R_1=2,3-di-Ac-4-malonyl-Xyl; R_2=Glc; R_3=H



31 R_1=R_2=R_4=R_5=H; R_3=OH
32 R_1=R_2=R_3=H; R_4=OH; R_5=CH_2OH

Fig. 2 Structures of saponins from AR

Three polysaccharides, named Astragalan I, II, and III, had been isolated by water extraction from AR (Fang *et al*, 1982). Astragalan I was a heterosaccharide composed of *D*-glucose, *D*-galactose, and *L*-arabinose in the molar ratio of 1.75:1.63:1. Its average molecular weight was 36 300. Astragalan I and II were elucidated as α-(1,4) glucans.

APS I and APS II were obtained from AR by using water extraction-alcohol precipitation (Zou, Gu, and Chen, 1987). The ratio of APS I and APS II was 0.31:0.69. The content of glucose in APS I was lower than which in APS II. APS I had a high content of xylose while galactose and arabinose could not be detected in APS I.

A water-soluble glucan was isolated from the alkaline aqueous extract of AR (Fang and Wagner, 1988). Its molecular weight was estimated to be 50 000. The structure of this glucan was α-(1→4)-linked α-*D*-glucan with glucosyl side chains attached to 6-*O* of the glucosyl residues of the main chain.

An acidic polysaccharide, designated as AMon-S, was isolated from AR (Shimizu *et al*, 1991). Its molecular weight was estimated to be 76 000. AMon-S was composed of *L*-arabinose, *D*-galactose, *D*-galacturonic acid, and *D*-glucuronic acid in the molar ratio of 18:18:1:1, in addition to small amounts of *O*-acetyl groups and peptide moiety. A part of the hexuronic acid residues existed as the methyl esters. It was shown significant reticuloendothelial system-potentiating activity in the carbon clearance test.

A glycan, designated as AMem-P, has been isolated from the hot water extract of the roots of *A. membranaceus* by treatment with cetyltrimethyl-ammonium bromide followed by column chromatography

on Toyopearl HW60F and Con A-Sepharose columns (Tomoda *et al*, 1992). AMem-P possessed mainly α-1,2-linked-rhamno-α-1,4-linked-galacturonan structure. Terminal and α-1,5-linked-arabinofuranose, terminal, β-1,3-, β-1,4-, and β-1,6-linked and 3,6-branched-*D*-galactose, and 2,4-branched-*L*-rhamnose residues were also identified as the component sugar units. The glycan was shown remarkable reticuloendothelial system-potentiating activity in the carbon clearance test.

Astragalan were extracted by water and by ion exchange resin 732 (H^+) from AR and purified preliminarily (Liu *et al*, 1994). The crude astragalan was purified by ultra-filtration Sephadex G-150 and dialysis. White powder astragalan was obtained with a molecular weight of 37 500. It was proved that astragalan was linked by α-glycoside bond. Quantitative analysis showed the molecular ratio of glucose, galactose, and arabinose was 1:0.95:0.70.

Three polysaccharides named AE, AEF-1, and AEF-2 were extracted from AR. They were composed of 64.3% ─ 103.4% saccharides (Kajimura *et al*, 1997). AEF-1 was shown the effect of promoting the antibody *in vitro*, while AEF-2 would inhibit the antibody *in vitro*.

A homogeneous polysaccharide A2Nb was obtained from AR and showed the ability of promoting the proliferation of the splenocytes of mice (Wang *et al*, 2001b). It had a molecular weight of 36 000, and was composed of *D*-glucose with a major linkage form α-*D*-(1→4)-glucose. Side chains were found at 6-*O* positions once in every 25 glucose residues.

The composition of monosaccharides of the polysaccharides both in roots of *A. membranaceus* (APS) and hair roots of *A. membranaceus* (HAPS) were determined by acidic hydrolysis, acetylation, and GC chromatography (Shan *et al*, 2002). The result showed that the content of HAPS was 1.85% and the content of APS was 2.61%. HAPS was composed of rhamnose, arabinose, xylose, mannose, galactose, and glucose. The molar ratio was 1:2.26:0.21:0.74:2.49:19.47. APS had the same composition of monosaccharides as HAPS, and the molar ratio of APS was 1:4.34:3.92: 1.95:11.41:20.52.

Two polysaccharides, ASP-I and ASP-II obtained from AR were analyzed by HPLC-RID. The result showed that ASP-I was composed of arabinose and glucose and ASP-II was composed of rhamnose, arabinose, and glucose. Their ratios were 1:3.45 and 1:6.25:17.86, respectively (Xu *et al*, 2008a).

A heteropolysaccharide was extracted from AR and identified with a molecular weight of 11 000 (Li *et al*, 2009). This heteropolysaccharide consisted of Rha, Glc, Gal, and Ara with the molecular ratio of 1.19:72.01:5.85:20.95. The main configuration was α-pyran ring with the principal chain linked by Glc 1→6 glucosidic bond. It was unstable to strong light, heat, and humidity.

Pharmacological studies

It was reported that the main pharmacological activities of AR included cardioprotective, immuno-modulation, anti-oxidative, anti-aging, antitumor, anti-virus, anti-inflammatory, antidiabetic, neuron protective, hepatoprotective, diuretic, and hematopoiesis activities. The summary of the pharmacology studies of AR was shown in Table 1.

Cardioprotection

Recent studies have shown that astragalosides had a protective effect on myocardial injury in rats (Guan, Li, and Yang, 2010). Astragalosides had the effects on reducing intracellular calcium concentration ($[Ca^{2+}]_i$) and sarcoplasmic reticulum calcium load, enhancing free radical removal, and decreasing lipid peroxidation in isoproterenol-treated cardiomyocytes, which might account for their protective effect on myocardial injury (Meng *et al*, 2005).

Comparing with the myocarditis mice treated with perindopril [0.44 mg/(kg·d)], an angiotensin-converting enzyme (ACE) inhibitor, AR feeding [2.2 mg/(kg·d)] achieved a similar effect on survival rate, sarcoplasmic reticulum calcium ATPase (SERCA2), and ET system. These results indicated that AR had the protective effects on the function of SERCA2 activity and endothelin system at acute and chronic periods of myocarditis mice induced by Coxsackie B_3 (CVB_3) infection and the beneficial effects for treating viral myocarditis might be partly mediated by preserving the functions of SERCA2 activity and ET system (Chen *et al*, 2006).

Studies on cardiac hemodynamics, heart coefficient, and marker enzymes in serum showed that AR prevented isoproterenol-induced myocardial damage. The anti-oxidative property and partial prevention of

Table 1 Summary of active constituents in AR and their related pharmacological bioactivities

Active constituents	Pharmacological activities
astragalosides; aqueous-extracted AR; astragaloside IV; lyophilized AR powder	cardioprotection
aqueous-extracted AR; ethanol-extracted AR; APS	immunomodulation
total flavonoids of AR; total saponins of AR; aqueous-extracted AR; HDTIC-1, and HDTIC-2	anti-oxidant
aqueous-extracted AR; APS	anti-aging
aqueous-extracted AR; astragaloside IV	antitumor
astragalosides; APS; astragaloside IV	antivirus
aqueous-extracted AR; calycosin-7-*O*-β-*D*-glucopyranoside	anti-inflammatory
APS; aqueous-extracted AR; astragaloside II and isoastragaloside I	antidiabetic effect
aqueous-extracted AR	neuron protection
total flavonoids of AR; total saponins of AR; aqueous-extracted AR;	hepatoprotective
aqueous-extracted AR	diuretic
APS	hematopoiesis

changes in protein and gene expression of cardiac sarcoplasmic reticulum Ca^{2+} regulatory proteins which might be mediated through the cAMP pathway could help to explain the beneficial effects of AR on myocardial injury *in vivo* (Xu *et al*, 2008b).

In an experimental model of autoimmune myocarditis, AR treatment significantly attenuated autoimmune myocarditis-induced myocardial inflammation and fibrosis and alleviated autoimmune myocarditis-triggered overt lymphocyte proliferation. This treatment also significantly attenuated elevated levels of the Th1 cytokines (IFN-γ and IL-2), and increased the Th2 cytokines (IL-4 and IL-10) in autoimmune myocarditis. In conclusion, the data revealed that AR effectively protected animals against cardiac functional and morphological aberrations in experimental autoimmune myocarditis (Zhao *et al*, 2008b).

A study showed that astragaloside IV (ASI) extracted from AR had the effect on congestive heart failure (CHF) induced by ligation of the left coronary artery in rats. ASI [1.0 mg/(kg·d)] attenuated the decrease of left ventricular systolic pressure (LVSP). ASI treatment inhibited compensatory hypertrophy of myocardial cells and lowered the number of apoptotic myocytes (Zhao *et al*, 2009).

The lyophilized AR powder injection was iv administered to dogs, and the hemodynamic parameters and myocardial consumption of oxygen of the dogs were measured. The results showed that the drugs significantly decreased heart rate, diastolic blood pressure, and mean arterial pressure of dogs with myocardial ischemia in 5 — 30 min after drug administration ($P < 0.05$). The lyophilized AR powder injection could significantly benefit all the indexes and strengthen the heart function of the dogs with myocardial ischemia (Jiang *et al*, 2010).

Immunomodulation

The effect of *A. membranaceus* on lymphocytes was studied *in vitro* using murine spleen cells. It markedly stimulated murine spleen cells to proliferate. AR enhanced the production of immunoglobulin and the induction of allo-antigen specific cytotoxic T lymphocytes. AR also stimulated macrophages to produce interleukin-6 and tumor necrosis factor. These results suggested that AR had immunomodulating activity *in vitro* and this activity could be used clinically for the modulation of immune responses (Yoshida *et al*, 1997).

A. membranaceus extract (AME) had effect on enhancing human immuno-function and antitumor activity. It could be applied in clinical practice for immuno-modulation and tumor treatment. AME could promote the proliferation of human peripheral blood mononuclear cells (PBMC), elevate the tumor cell-killing activity of T-lymphocyte (CTL), strengthen the tumor cell phagocytosis and cytokines (TNF-α and IL-6) production of PBAM, and promote the IgG production of peripheral blood B cells (PBBC) (Wang, Shan, and Li, 2002).

Aqueous-extracted AR (ARE) enhanced mitogenic activity in methotrexate (MTX)-treated mouse spleen cells

in the dose-response manner in spleen cell proliferation assay. ARE significantly reduced the suppression of cell proliferation by MTX in mouse spleen cells. Further investigation showed the immunomodulatory effects of ARE might be, in part, associated with the expressions of IL-1α and IL-12p40 mRNA as well as the mitogenic effect on spleen cells (Lee *et al*, 2003).

AR ethanol extract administration significantly increased IL-4 production in both the serum and supernatant of splenocyte culture, while IFN-γ secretion was diminished upon *in vivo* activation with anti-CD_3 antibody. The studies demonstrated that AR selectively altered Th1/Th2 cytokine secretion patterns (Kang *et al*, 2004).

Polysaccharopeptide (PSP) combined with APS as a new complex prescription (PSP + APS) could restore the immunological effects against adriamycin (AMD)-induced immunosuppression, such as the subset of leukomonocyte, the expression of IL-2/IL-2R in the spleen, and the thymus index. The immunomodulatory effects of this new formula (PSP + APS) were better than PSP alone and also could resist immuno-suppression induced by AMD (Li *et al*, 2008).

Water extract of AR used as a supplementation in drinking water could induce an immune stimulation response in immunosuppressed chickens. But in clinically healthy chickens hemagglutination inhibition (HI) antibody titers against Newcastle disease virus (NDV) and H5 avian influenza virus (H5-AIV) after vaccination were not influenced by supplementation with AR extract in drinking water (Liu, Sun, and Cui, 2009).

Treated with AR injection, the number of dead rats with obstructive jaundice (OJ) decreased. And the TNF-α level on days 7 and 21, the pathological severity score for spleen on days 7 and 14 and for lymph nodes on days 21 and 28, the product staining intensity and positive rate of Bax protein in spleen and thymus on days 14 and 28, and the apoptotic indexes in spleen and thymus on days 14 and 21 were significantly lower. These experiments suggested that AR had protective effects on immune organs of OJ rats by relieving the pathological changes in immune organs, reducing TNF-α level, and inhibiting Bax expression and apoptosis in spleen and thymus (Zhang *et al*, 2009).

Anti-oxidative activity

The anti-oxidative activities of components extracted from AR were tested by using reactive oxygen species (ROS) initiated lipid peroxidation of purified human erythrocyte membrane. The results showed that the total flavonoids of AR and total saponins of AR could significantly inhibit the membrane lipid peroxidation generated by O_2^-, H_2O_2, and UV rays, while the total polysaccharides of AR could possess weaker protective activity (Wang *et al*, 1996; Zhang *et al*, 2010).

Isoflavones in the roots of *A. membranaceus*, afrormosin, calycosin, formononetin, and odoratin were reported to have anti-oxidative effect on lipid peroxidation by ROS. Calycosin inhibited lecithin peroxidation which was induced by hydroxy radical-generation by interaction of haemoglobin and H_2O_2. Calycosin and formononetin inhibited lecithin peroxidation which was induced by superoxide anion generation by xanthine-xanthine oxidase (Toda and Shirataki, 1998).

Anti-oxidative effects of AR were also investigated on oxidative stress such as lipid peroxidation (LPO) and protein oxidative modification by copper. The results showed that these effects were similar to those of mannitol and superoxide dismutase as a free radical scavenger, and AR had inhibitory effects on oxidative stress induced by copper (Toda and Shirataki, 1999).

Investigation led to isolation of the two isomers from AR, HDTIC-1, and HDTIC-2, which could delay replicative senescence of human fetal lung diploid fibroblast (2BS cells), and indicated that the senescence-delaying effect of HDTIC appeared to be due to its many biological properties including its potentials of proliferation improvement, inhibitory effect of the advanced glycosylation end product (AGE) formation, and its anti-oxidative activity. The differences of optimum concentrations of HDTIC-1 (0.1 mmol/L) and HDTIC-2 (1.0 mmol/L) for delaying senescence also indicated that the structure of HDTIC might be very sensitive to its activity (Wang *et al*, 2003). Further study indicated that expression of p16 by 2BS cells was strongly inhibited by HDTIC compounds, which could contribute to their delayed replicative senescence by the way of p16 (INK4a)/Rb/MAPK. The anti-oxidative activities of HDTIC-1 and HDTIC-2

might be indirectly related to their inhibition of p16 expression (Wang *et al*, 2008).

Anti-aging effect

The changes in density of M-cholinergic receptors in different areas of senile rats and the regulatory action of AR were observed by autoradiography. The gray scale displayed in brain sections was clear and mainly distributed in the cortex, hippocampus, and striate body, while that due to nonspecific combination was negligible. The gray scale in the cortex, hippocampus, and striate body of the experimental group was markedly lower than that in the young control rats; But it was obviously higher than those in the senile control rats. The data indicated that AR might up-regulate the decreased density of M-cholinergic receptors in the brain of senile rats (Shi *et al*, 2001).

Ig administration of APS in *D*-galactose-induced aging mice increased thymus and spleen indexes, the activites of superoxide dismutase, glutathione peroxidase (GSH-Px), and nitric oxide synthase in the kidneys. APS also decreased MDA levels in serum and the liver, and lipofuscin level in the brain (Ge, Xu, and Yang, 2004).

Antitumor effect

The extract of AR prevented the cytotoxic activity of lymphocytes against YAC-1 cells from the depression by a carcinogen, *N*-butyl-*N*'-butanolnitro-soamine (BBN). It also protected the production of interleukin-2 and γ-interferon of lymphocytes from the depression by BBN. The results showed that the extract of AR exerted an anticarcinogenic effect in carcinogen-treated mice through activation of cytotoxic activity and the production of cytokines (Kurashige, Akuzawa, and Endo, 1999).

The inhibition rates of AR on the different cancer cell lines were detected by trypan blue exclusion, MTS method, and tritium thymidine incorporation assay. Apoptosis was detected by DNA ladder method. The results indicated AR specifically inhibited gastric cancer cells growth *in vitro* and the mechanism was mainly cytostatic but not cytotoxic or inducing apoptosis (Lin *et al*, 2003).

The water extract of AR inhibited the proliferation of human hepatocarcinoma cells, SMMC-7721, and their mitochondria metabolic activity *in vitro*. Studies also showed this water extract decreased the weight of S_{180} tumor in tumor-bearing mice, and increased the T/B-lymphocyte ratio and the activity of peritoneal macrophages (Xiao *et al*, 2004).

Upon the treatment with astragaloside IV (ASI), human hepatocellular carcinoma HepG2 cells were evaluated for the colonogenic survival and anchorage-independent growth. The cellular proteins of treated and untreated cells were resolved by 2D polyacrylamide gel electrophoresis. The protein spots mostly altered by drug treatment were identified by mass spectrometry and subsequently verified by Western blotting using specific antibodies and RT-PCR technique using specific DNA primers. The results showed astragaloside IV attenuated the colonogenic survival and anchorage-independent growth of cancer cells (Qi *et al*, 2010).

Antivirus effect

The protective effects of AR by ig administration and by ip injection against Japanese encephalitis virus (JEV) infection in mice were investigated. The studies indicated that the protective effect of AR by ig administration was based on a non-specific mechanism during the early stage of infection, before shifting to antibody production, and that macrophages played an important role in this resistance to JEV infection, e.g., by inducing the production of active oxygen (Kajimura *et al*, 1996b). On the other hand, the protective effect of AR was dependent on a non-specific mechanism during the early stage of infection, before it shifted to antibody production, and that peritoneal exudate cell (PEC) played an important role (Kajimura *et al*, 1996a).

Astragalosides and APS inhibited hepatitis B virus (HBV) and the proliferation of human hepatocarcinoma HepG 2.2.15 cells. The expressions of hepatitis B surface antigen and hepatitis B e-antigen in HBV-DNA-transfected HepG 2.2.15 cells were also inhibited (Zou *et al*, 2003). Another study indicated that ASI had the inhibitory effect on HBV replication *in vitro* with IC_{50} of 13.2 mg/L. And ASI produced dose-dependent inhibition of HBsAg and HBeAg excreted by HepG 2.2.15 cells (Zhang *et al*, 2007).

In the human HBV-transfected liver cell line $HepG_2$ 2.2.15, ASI effectively suppressed secretion of HBV antigens. The inhibitory activity of ASI on secretion of HBV antigens was more potent than that of Lamivudine (3TC) without significant cytotoxicity. In duck hepatitis B virus (DHBV)-infected ducklings, ASI

caused 64.0% inhibition at 120 mg/kg, 49.6% inhibition at 40 mg/kg, and 41.7% inhibition at 10 mg/kg to serum DHBVs and also reduced serum DHBV DNA levels. The results demonstrated that ASI possessed potent anti-HBV activity (Wang *et al*, 2009a).

Anti-inflammatory effect

The effects of AR extract on interleukin (IL-6) and tumour necrosis factor (TNF-α) production, prostaglandin E2 (PGE2) biosynthesis, and leukotriene C4 (LTC4) production from lipopoly-saccharide (LPS)-stimulated human amnion cells were investigated. The data suggested that AR extract might play a role in inhibiting bacterial infection-associated preterm labor by suppressing the productions of IL-6, PGE2, and LTC4 by human amnion cells (Shon, Kim, and Nam, 2002).

Studies investigated the effect of AR extract on IL-6 and TNF-α production, PGE2 and LTC4 released from IL-1β-stimulated human amnion. The results indicated that AR had a broad anti-inflammatory effect in human amnion and might be considered a promising agent to protect preterm labor (Shon and Nam, 2003).

The protective effect of an isoflavonoid, calycosin-7-*O*-β-*D*-glucopyranoside (CG), isolated from AR was studied on the pathogenesis of osteoarthritis (OA)-like lesion in a rabbit model. The total synovial fluid volume ($P < 0.05$) was most strikingly reduced by the treatment with CG. Moreover, the CG treatment also significantly alleviated the OA-induced accumulation of prostaglandin (PG) ($P < 0.001$) and total proteins ($P < 0.001$) in the synovial fluid. The histopathologic analyses revealed that the CG treatment reduced the severity of the OA-like structural damages in the cartilage. These results indicated that the isoflavonoid CG significantly alleviated the pathologic changes in the OA-like rabbit knee joints (Choi *et al*, 2007).

It was reported that AR displayed anti-inflammation in zymosan air-pouch mice by reducing the expression of iNOS, COX-2, IL-6, IL-1β, and TNF-α, and by decreasing the production of nitric oxide (NO). In a similar manner, AR reduced the expression of IL-6, iNOS, and COX-2 in LPS-treated Raw 264.7 cells. The data revealed that AR had an anti-inflammatory effect that was mediated by the MKP-1-dependent inactivation of p38 and Erk1/2 and inhibition of NF kappaB-mediated transcription (Ryu *et al*, 2008).

Boiling water extracts of AR, soaked into a hydrophilic foam dressing, were topically applied to the wounds. The AR extracts significantly accelerated cutaneous wound healing by suppressing inflammation and stimulating basal cell growth in the wound area compared to epidermal growth factor as a positive control. Promotion of basal cell proliferation and angiogenesis by the AR extracts was remarkable in the early stages of wound healing, resulting in a significant reduction in the duration of the wound-healing process (Han, Lee, and Hahm, 2009).

Antidiabetic effect

APS was proved to have the preventive effects on type 1 diabetes in non obese diabetic (NOD) mice. The APS group has lower incidence of diabetes, higher serum C-P levels, decreased degree of the lymphocytic inflammation of pancreatic islets, stronger proliferation of CD_8 T subsets, and lower ratio of CD_4/CD_8 subgroup in splencytes than those of the normal solution group (Chen *et al*, 2001).

It was reported that APS could reduce fasting plasma glucose (FPG) and blood lipids on insulin resistance of rats with type 2 diabetes. APS could significantly decrease the blood sugar and increase the content of the blood serum HDL of 2-DM IR rats (Liu *et al*, 2007).

A crude extract of AR inhibits the formation of N^{ε}-(carboxymethyl) lysine (CML) and pentosidine during the incubation of bovine serum albumin with ribose. Astragalosides significantly inhibited the formation of both CML and pentosidine, and astragaloside V had the strongest inhibitory effect among all the isolated compounds. That suggested that AR and astragalosides might be a potentially useful strategy for the prevention of clinical diabetic complications by inhibiting AGE inhibitors (Motomura *et al*, 2009).

Astragaloside II and isoastragaloside I isolated from AR selectively were reported to increase adiponectin secretion in primary adipocytes without any obvious effect on a panel of other adipokines. Adiponectin is an adipocyte-derived insulin-sensitizing hormone with antidiabetic, anti-inflammatory, and anti-atherosclerotic properties. Chronic administration of astragaloside II and isoastragaloside I in both dietary and genetic obese mice significantly elevated serum levels of total adiponectin and selectively increased the composition of its high

molecular weight oligomeric complex. These results suggested that the two natural compounds might provide the lead as a novel class of therapeutics for obesity-related diseases (Xu *et al*, 2009).

Neuron protective effect

Studies showed that AR-treated group could protect the cultured rat neurons against anoxic damages in the anoxic circumstance. NaCN was used to develop a hypoxic model of *in vitro* cultured neurons from newborn rat cerebral cortex. In the AR-treated group, the morphological changes were mild, the effluxes of LDH and K^+ were decreased, and *A* value (cell survival number) increased as compared with that in the control group (He, Li, and Yu, 2000).

It was reported that AR showed marked neuron protection in immature brain cortex after hypoxia/ ischemia brain damage (HIBD), which was related with the inhibition on caspase-3 expression. Treated with AR, the neuron death rate of neonatal HIBD model rats was obviously reduced, and caspase-3 mRNA and protein expression peak values decreased by 45% (mRNA) and 40%－43% (protein) (Jia, Jiang, and Qiao, 2005).

Hepatoprotective effect

It was reported that total flavonoids of AR (TFA) had potential protective effect against the paracetamol-induced hepatic damage in mice. There was an obvious dose-dependent decrease in ALT level and the area of hepatocelluar necrosis with pre-treatment with either TFA or Vitamin C (Wang *et al*, 2001a).

Inhibitory effect of total extract of AR (TEA) on hepatocye apoptosis was investigated. The results showed that TEA had anti-apoptosis effect on hepatocyte injury *in vitro* and *in vivo*. The mechanism might be related to its anti-oxidative activity (Yang and Chen, 2001).

Study was carried out to investigate the effect of crude astragalosides fraction (CAF) on Sprague-Dawley rats liver fibrosis induced by subcutaneous injection with 50% CCl_4 and its possible mechanisms. Ig administration of CAF significantly decreased indices of liver and spleen, the serum transaminase activities, HA and PC III levels, and Hyp and MDA contents in liver tissue in rats of hepatic fibrosis. Decreased SOD and GSH-Px levels were reversed after administration of CAF. Histopathological scores showed CAF had inhibitory effect on the progression of hepatic fibrosis. In *in vitro* experiments, CAF significantly reduced TNF-α and TGF-β levels in culture supernatants of Kupffer cells (KCs). The results showed CAF significantly inhibited the progression of hepatic fibrosis induced by CCl_4, and the inhibitory effect of CAF on hepatic fibrosis might be associated with its ability to scavenge free radical and inhibit the production of TNF-α and TGF-β from activated KCs (Gui *et al*, 2006).

Toxicity

Studies demonstrated that the extract of AR was safe without any distinct toxicity and side effect, and the safety dosage ranges were 5.7 － 39.9 g/kg for Sprague-Dawley rats and 2.85 － 19.95 g/kg for Beagle's dogs, which were equal to 70 or 35 times of that of human (0.57 g/kg with average body weight of 70 kg), respectively (Yu *et al*, 2007b).

The long term toxicity of AR on rats was detected for evaluating its safety of long term medication. There were no influence of consecutively medication for three months on the general status, the routine control of blood and urine, the mass, and coefficient of major organ of the rats. There were no pathological changes on heart, liver, spleen, lung, and kidney. The results demonstrated that AR had no obvious toxicity on rats for a long term medication (Liu *et al*, 2009b).

Mutagenicity and acute toxicity of APS were studied by using MTD test, Ames test, marrow micronucleus test, sperm abnormality test, and 30 d feeding test in rats. The results showed APS had no potential mutagenicity (Wang *et al*, 2009b).

Clinical studies

Recurrent respiratory tract infection

It was reported that AR injection had the therapeutic effect on infantile recurrent respiratory tract infection. Forty-five cases as control group were treated with conventional therapy while go cases as treatment group were treated with AR injection for iv dripping on the basis of routine therapy. The total effective rates were 95.56% and 53.33% in treatment group and control group, respectively. The IgG and IgA levels in treatment group were significantly higher than those in control group ($P < 0.05$) (Dong *et al*, 1998).

Pulmonary heart disease

One hundred and forty patients of pulmonary heart disease (PHD) on severe stage were randomly divided

into two groups. Seventy-three patients in the treatment group were treated with AR injection (AI) 40 mL (equivalent to 80 g crude drug) by adding in 5% glucose solution 250 mL for iv dripping, once a day. Sixty-seven patients in the control group were treated with nitrolingual injection. The levels of left ventricular ejection fraction (LVEF), fractional shortening of left ventricular short axis (FS), the ratio of maximum blood flow between the advanced and early atrial systole (E/A), stroke volume (SV), cardiac output (CO), and the cardiac index (CI) were all improved in both groups, but better improvement was shown in the treatment group than that in the control group ($P < 0.05$). The results proved AI could be taken as one of the important auxiliary drugs for treating PHD on severe case (Meng, Ji, and Li, 2006).

The effect of AI on LPO and anti-oxidase activity in patients with chronic PHD were studied. Forty-eight chronic PHD patients were divided into two groups randomly and treated with conventional treatment (control group) and conventional treatment combined with AI (treatment group) respectively for 14 d. After AI treatment, the levels of LPO and serum superoxide dismutase (SOD) were significantly lower ($P < 0.01$), and the level of GSH-Px was significantly higher ($P < 0.01$). The results demonstrated AI could attenuate markedly lipid peroxide reaction, adjust the imbalance of anti-oxidase, and enhance body's defense capability against damage of active oxygen free radical induced by LPO in chronic PHD patients (Liu and Chen, 2006).

Asthma

AI combined with routine therapy has the therapeutic effect on acute attack of bronchial asthma. One hundred and eight patients with acute attack of bronchial asthma were randomly divided into two groups. The patients in routine treatment group were treated by conventional therapy as control group, while the patients in treatment group were treated with AI on the basis of routine treatment. After treatment, the levels of forced vital capacity (FVC), 1 s forced expiratory volume (FEV_1), and peak expiratory flow (PEF) in treatment group were significantly higher than those in control group (Zhang and Li, 2009).

Chronic bronchitis

It was reported that AI on the basis of antibiotic treatment could heighten the curative effect in acute chronic bronchitis patients. One hundred acute chronic bronchitis into control group and treatment group randomly. Both groups are antibiotic with venoclysis. The treatment group combined with AI had a significantly higher effective rate than that in the control group ($P < 0.05$) (Jin and Pan, 2005).

CHF

The clinical efficacy of AI in treating CHF was studied. Sixty-two patients of CHF were randomly divided into two groups, the treatment group treated with AI and the control group treated with routine medicine. After one therapeutic course, the total effective rate in treatment group was 90.4%, while that in the control group was 80.7%. The treatment group was significantly superior to it in the control group ($P < 0.05$) (Liu and Li, 2005).

Sixty-one patients of CHF were randomly divided into two groups. Thirty-one patients of the treatment group and 30 patients of the control group were all given routine medicine. At the same time, the treatment group was administered with AI. The results showed AI had affirmatively curative effect for treating CHF (Lin, Huang, and Zhu, 2009).

Coronary heart disease

It was reported that AI had the clinical efficacy in treating angina pectoris of coronary heart disease. Sixty patients were randomized into two groups: the control group treated with routine western medicine and treatment group treated with AI combined with routine western medicine. After treatment, the improvement of angina pectoris and electrocardiogram were better in treatment group than that in control group ($P < 0.05$). Von willebarnd factor (VWF) and vascular count of endotheliocyte (CEC) fell obviously ($P < 0.05$, 0.01). These results indicated that AI had positive effects on angina pectoris of coronary heart disease (Wang, Chen, and Liu, 2005).

Viral myocarditis

Fifty children with viral myocarditis (VMC) were randomly divided into the control group and the AR treatment group. After treatment, clinic symptoms and objective signs were markedly improved. Cardiac enzyme (CK-mB) and troponine I (cTnI) were significantly decreased ($P < 0.01$), electrocardiogram (ECG) improved more quickly ($P < 0.05$), and LVEF increased in the treatment group ($P < 0.05$). T-lymphocyte subgroups of CD_3, CD_4, and CD_4/CD_8

increased ($P < 0.05$), CD_8 decreased ($P < 0.05$), and serum immunoglobulin G, A, and M increased obviously ($P < 0.05$). These results indicated that it was safe and effective to treat the children with VMC with routine medicine combined with AR (Wu *et al*, 2009).

It was reported that AI had the therapeutic effect on VMC, and there was no obvious side effect. One hundred patients with VMC were randomly divided into the control and the treatment groups. The total effective rate was 94% in the treatment group treated with AI, while 74% in the control group treated with energy mixture and fructose (Wang, 2009).

Diabetic nephropathy

The clinical therapeutic effect of AI on diabetic nephropathy was studied on 106 patients randomly divided into control group (traditional therapy) and treatment group (traditional therapy combined with AI). Obvious reduction in proteinuria and blood uric acid of the treatment group was observed ($P < 0.05$). No obvious change was observed in blood β_2-MG, urine β_2-MG, and cholesterol between the treatment and the control groups. It suggested that AI was an efficient treatment agent for diabetic nephropathy (Zheng *et al*, 2009).

Fifty-two patients of early diabetic nephropathy were randomly divided into two groups. Hypoglycemic agent and enalapril were given to both treatment and control groups, while AI was only given to treatment group. After treatment, urinary albumin excretion rate and urine β_2-MG in the treatment group were significantly decreased than those in the control group. The results showed that the combination of AI and Enalapril had better effects in treating early diabetic nephropathy than enalapril using alone (Zeng, Liu, and Wang, 2010).

Chronic glomerulonephritis

AI had the therapeutic efficacy on proteinuria in patients with chronic glomerulonephritis. It might relate with its efficacy of T-lymphocyte subsets and cytokine receptors. The clinical investigation showed that AI could be used safely to alleviate proteinuria and adjust cellular immunological functions in certain patients with chronic glomerulonephritis (Shi *et al*, 2002).

Nephrotic syndrome (NS)

The effect of AI on urinary protein excretion and plasma protein in children with NS was studied. Thirty hospitalized children with NS were divided randomly into two groups: the treatment group treated with AI and glucocorticoid and the control group treated with glucocorticoid only. After treatment, clinical symptoms and blood biochemical markers in treatment group were obviously better than those in control group. The urinary protein excretion decreased while plasma albumin increased significantly ($P < 0.05$). It suggested that AI was effective in treating NS in children (Deng *et al*, 2003).

Clinical researches on 86 patients of refractory nephritic syndrome showed AI combined with low molecular weight heparin could treat primary NS. The treatment was obviously effective to reduce triglycerides (TG) and urine albumin (ALB), increase plasma ALB, change kidney function, and relieve oedema quickly (Wu, Wu, and Wang, 2008).

Viral enteritis

The curative efficacy of AI combined with composite *Salviae Miltiorrhizae Radix* injection was studied in virus enteritis in children. The results showed that to add AI combined with composite *Salviae Miltiorrhizae Radix* injection could shorten the treatment course, improve curative efficacy in virus enteritis in the children, and was superior to western medicine alone (Peng, Wang, and Deng, 2003).

Peptic ulcer

Huangqi Chaihu Powder (HQCHP) is a formula of AR and *Bupleuri Radix*. It was reported that taking HQCHP for a long time could control the ulcer, recover the injured mucous epithelium, and control the recurrence of peptic ulcer (Sun, 1995).

Viral hepatitis

The effectiveness of two months treatment with Astragali compound (AC), containing AR 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. Negative seroconversions of HBV antigen e and HBV DNA were also significantly higher in AC-treated patients than in controls. Of eight duck viral hepatitis B models infected with DHBV and treated with AC, three showed negative seroconversion of DHBV DNA and serum DHBV DNA levels significantly decreased after AC administration compared with the controls; DHBV

DNA was negative in biopsied liver tissue by *in situ* hybridization and immunohistochemistry in two ducks treated with AC. Pathological changes were milder in AC-treated ducks than in controls (Tang *et al*, 2009).

Systemic lupus erythematosus (SLE)

A total of 79 SLE patients with lower leukocyte count were randomly assigned into routine treatment group (treated with routine dose of corticosteroids and immunosuppressants), and AR group (treated with routine dose of corticosteroids and immunosuppressants and AI). After treatment, the numbers of leukocytes, neutrocytes, and lymphocytes in peripheral blood increased in both groups ($P < 0.05$), and the effects were better in the AR treated group ($P < 0.05$) (Wang, Wang, and Chen, 2007). The number of immunoglobulin (IgG, IgA, and IgM) and complement (C3 and C4) increased in both groups ($P < 0.05$), and the treatment effects in the AR group were proved much better than that in the routine treatment group ($P < 0.05$). These results indicated that AI could enhance the curative effect of corticosteroids and immuno-suppressants in the treatment of SLE (Wang, Wang, and Chen, 2007).

Future perspectives

For thousands of years, TCM has been used to treat diseases and improve the health of Chinese people. Nowadays, TCM is being widely used more and more throughout the world. This article provided an overview on one of the most popular TCM for benefitting the deficiency of Qi, AR. AR is one of the oldest and most frequently used herbal medicines for oriental medicine in China, Korea, Japan, and some other Asian countries. Many researches had been reported on the chemical investigation, pharmacological studies, and clinical practice of AR. This herbal medicine has shown to have cardiotonic, hepatoprotective, hypotensive, immuno-stimulant, anti-aging, anti-oxidative, antidiabetic, and anti-inflammatory activities.

According to the reports, the quality of AR was predicated on the analysis and determination of several compounds like isoflavones or saponins. Ideally, these compounds should be responsible for the efficiency of this herbal medicine. However, AR as a herbal medicine consists of numerous compounds and its bioactivity can be considered to be the synergetic effects of several compounds. Consequently, the development of new evaluation methods is required to demonstrate the comprehensive properties and quality control of AR.

Furthermore, due to chemical instability and complexity of herbal medicine, there were limited researches reported about pharmacokinetics, pharmaco-dynamics, and metabolism of active chemical constituents in AR. There is no doubt that further research should be carried on for the mechanism of treatment under TCM theory.

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