J Herbmed Pharmacol. 2026; 15(2): 189-206.

http://www.herbmedpharmacol.com doi: 10.34172/jhp.2026.53683

Journal of Herbmed Pharmacology

Saponins from the genus *Astragalus*: Chemical diversity, biological activities, pharmacological effects, and therapeutic potential

Zeinab Delazar[1], **Masoud Sadeghi Dinani**[1*]

[1]Department of Pharmacognosy, Faculty of Pharmacy and Pharmaceutical Sciences, Isfahan University of Medical Sciences, Iran

ARTICLE INFO

Article Type:
Review

Article History:
Received: 2 Dec. 2025
Revised: 19 Feb. 2026
Accepted: 26 Feb. 2026
epublished: 1 Apr. 2026

Keywords:
Triterpenoid saponins
Cycloartane-type triterpenes
Immunomodulation
Inflammation mediators
Signal transduction

ABSTRACT

Saponins derived from various *Astragalus* species have been recognized for many years as biologically active compounds and are associated with a variety of biological and pharmaceutical activities. Among these, cycloartane- and oleanane-type saponins have been reported to exert immunomodulatory, anti-inflammatory, antioxidant, and cytoprotective effects. Preclinical studies demonstrate that these compounds modulate key cell-signaling pathways and exhibit significant antiproliferative activity in vitro and in vivo, inhibiting cancer cell growth and tumor progression. Beyond oncology, *Astragalus* saponins have shown protective effects in experimental models of inflammatory disorders, hepatic and metabolic dysfunction, cardiovascular disease, and neurodegenerative conditions, suggesting broad pharmacological relevance. Despite the growing body of literature, current evidence remains fragmented and predominantly focused on a limited number of compounds, highlighting the need for a comprehensive synthesis of available data. This narrative review aims to provide an integrated overview of the chemical diversity of *Astragalus* saponins, critically summarize their reported biological and pharmacological activities, and identify current limitations and research priorities. Despite progress, several barriers to clinical translation remain. These include a lack of published comparative and clinical data, as most available studies have focused primarily on astragaloside IV. Additionally, there is limited pharmacokinetic and bioavailability data, no detailed human studies, and no long-term safety data. Based on these identified gaps, future studies should focus on the following areas: extracting high-quality saponins using a standardized extraction procedure; conducting comprehensive evaluations of other saponins; optimizing saponin delivery formats; and conducting well-designed clinical trials to assess the safety and efficacy of *Astragalus* saponins in therapeutic applications.

Implication for health policy/practice/research/medical education:
This narrative review summarizes current preclinical evidence on the chemical diversity and biological activities of saponins from the genus *Astragalus* and highlights critical gaps in comparative and clinical research. The findings may support future hypothesis-driven experimental studies, inform mechanistic investigations, and guide translational research priorities. In addition, this review may serve as an educational resource in pharmacology, phytochemistry, and natural product sciences by providing an integrated chemical and biological perspective on *Astragalus* saponins.

Please cite this paper as: Delazar Z, Sadeghi Dinani M. Saponins from the genus *Astragalus*: Chemical diversity, biological activities, pharmacological effects, and therapeutic potential. J Herbmed Pharmacol. 2026;15(2):189-206. doi: 10.34172/jhp.2026.53683.

Introduction

The genus *Astragalus* L. belongs to the family Fabaceae (Leguminosae) and represents one of the most speciose groups among angiosperms. Depending on the taxonomic criteria applied, the genus encompasses roughly 2,000–3,100 recognized species distributed across nearly 250 infrageneric sections. Species diversity reaches its maximum in temperate to semi-arid zones of the Northern Hemisphere, with a principal evolutionary radiation centered in the Irano-Turanian phytogeographical domain. This extensive distribution corresponds with marked ecological variability, which has driven the emergence of diverse growth forms, spanning annual and perennial herbs through to dwarf shrubs and shrubs (1,2).

***Corresponding author**: Masoud Sadeghi Dinani,
Email: m_sadeghi@pharm.mui.ac.ir

Botanically, there is considerable morphological variation within the genus *Astragalus*, particularly in its leaves, flowers, fruits, and seeds. This morphological diversity has greatly complicated the taxonomic classification of *Astragalus*, and ongoing research aims to elucidate phylogenetic relationships and better understand associated evolutionary patterns. (3).

The Irano-Turanian region, including Iran and adjacent countries, represents a major biogeographical hotspot for species diversity and endemism within the genus *Astragalus*, harboring more than 1,000 species. Additional centers of diversity occur in Anatolia (Turkey), Central Asia, and Central China. In contrast, in the New World, Neo-*Astragalus* constitutes a distinct evolutionary lineage that represents a secondary center of diversification (4-6). Iran and Turkey exhibit particularly high species richness and endemism within the genus *Astragalus*, mainly as a result of complex evolutionary histories involving orogenic events, historical climatic fluctuations, and long-term adaptation to diverse edaphic conditions. These interacting geological and environmental factors have promoted extensive species diversification and regional endemism, as supported by recent floristic and endemism studies. The genus *Astragalus* represents an important source of structurally diverse triterpenoid saponins, primarily including cycloartane-type and oleanane-type scaffolds. Cycloartane-type saponins have been reported predominantly in species occurring in the Russian flora, whereas oleanane-type saponins are more frequently described in species native to the Balkan region, including Bulgaria, as well as in several other Eurasian regions (1,7).

Although numerous studies have explored *Astragalus* species and their saponins, the resulting evidence remains fragmented and largely concentrated on a small subset of compounds, most notably astragaloside IV. Comparative data on other cycloartane- and oleanane-type saponins are scarce, and most available findings are derived from heterogeneous preclinical models with variable phytochemical and taxonomic characterization. Therefore, this narrative review aims to provide an integrated overview of the chemical diversity of *Astragalus* saponins, critically summarize their reported biological and pharmacological activities based on preclinical evidence, and identify recurring patterns, key knowledge gaps, and priorities for future research.

Methods

This review provides an integrative overview of existing research addressing the structural variety, bioactivity profiles, and therapeutic potential of saponins derived from *Astragalus* species. Information was gathered through focused exploration of the scientific literature indexed in PubMed, Scopus, Web of Science, and Google Scholar, encompassing studies published up to December 2025. Search queries combined taxonomic and phytochemical keywords—such as "*Astragalus*," "triterpenoid saponins," "cycloartane saponins," and "oleanane saponins"—along with pharmacological descriptors including "anti-inflammatory," "immunomodulatory," "antioxidant," "anticancer," "cardiovascular," "neuroprotective," "hepatoprotective," and "metabolic effects." Included were original research articles and reviews published in English reporting phytochemical characterization and/or preclinical biological or pharmacological activities of *Astragalus*-derived saponins. Priority was given to studies with isolated compounds or well-characterized extracts providing precise structural and experimental data. Excluded were studies lacking adequate methodological or chemical characterization, unclear taxonomic identification, or relevance to the scope of this review.

Saponins listed in Table 1 (n = 86) were selected based on repeated reporting, confirmed structural elucidation, and relevance to pharmacological mechanisms discussed herein. This work represents a narrative rather than a systematic review, aiming to qualitatively synthesize current knowledge, identify emerging patterns, and highlight gaps for future investigation.

Classification of saponins reported in the genus *Astragalus*

Saponins in *Astragalus* species are predominantly triterpenoid, exhibiting pronounced structural diversity arising from variations in aglycone scaffolds and glycosylation patterns. Investigations focused on the chemical and biochemical features of *Astragalus membranaceus* and related taxa have established a classification framework according to the structural core of each saponin type. Among them, cycloartane derivatives (Figure 1), constructed on the cycloartenol backbone, represent the dominant category detected within the genus. Modifications of the core glycoside structure give rise to compounds such as astragalosides and agroastragalosides, which have been identified in both subterranean and above-ground organs of *Astragalus* plants. These molecules are associated with a broad spectrum of biological activities, including immunomodulatory, antioxidant, and anti-inflammatory effects (8,9).

Although cycloartane-type saponins predominate among *Astragalus* species, recent phytochemical evidence suggests that certain species also contain oleanane-type triterpenoid saponins (Figure 2). They differ considerably in their structures, particularly in glycosidic linkages and hydroxylation patterns. Their biological and pharmacological activities have attracted increasing research attention, with particular emphasis on detailed structure–activity relationships (8,10).

Based on recent studies, we know that these triterpenoid saponins are glycosylated compounds with a specific sugar composition that elicit different cellular responses when they interact with the cell membrane and modulate specific intracellular signalling pathways. Therefore,

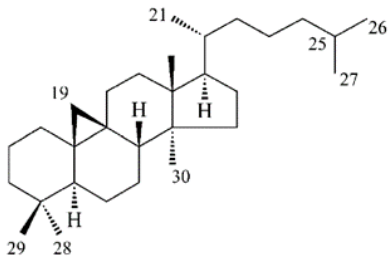


Figure 1. Cycloartane saponin (11).

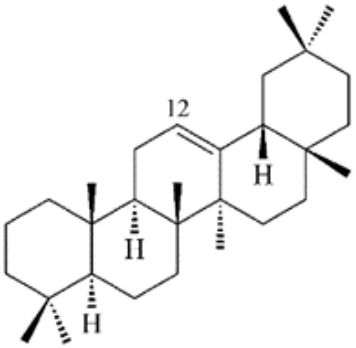


Figure 2. Δ^{12} Oleanane saponin (11).

"Oleanane-type saponin" and "Cycloartane-type saponin" serve as guideposts for predicting pharmacological effects and directing future research on these compounds (8). Table 1 summarizes structurally characterized cycloartane- and oleanane-type triterpenoid saponins reported from different *Astragalus* species.

Biological and pharmacological effects of Astragalus saponins

Immunomodulatory effects

In vitro and animal studies have demonstrated that saponins isolated from various *Astragalus* species can influence components of both innate and adaptive immune systems. Experimental studies demonstrate that these compounds affect the activity of several immune cell types, including macrophages, natural killer cells, and T- and B-lymphocyte populations. These effects reflect modulation of immune responses under specific pathological or experimentally induced conditions. Reported immunomodulatory activities include alterations in cytokine production, modulation of immune-mediated inflammatory responses, and enhancement of selected immune functions across diverse preclinical experimental settings. Together, available preclinical evidence indicates that *Astragalus*-derived saponins exert immunomodulatory pharmacological effects; however, their precise contribution to immune homeostasis and their clinical relevance remain unclear (29-36).

Anti-inflammatory effects and modulation of signaling pathways

Evidence from in vitro and animal studies indicates that saponins isolated from *Astragalus* species exhibit anti-inflammatory activities at both cellular and molecular levels. In experimental models, these compounds attenuate inflammatory responses by reducing the production of pro-inflammatory mediators and modulating inflammation-related signaling pathways. Preclinical studies identify regulation of intracellular signaling pathways involved in inflammatory processes as a key mechanistic basis for the anti-inflammatory effects of *Astragalus* saponins. Nevertheless, the relative contribution of specific pathways, along with their translational relevance and clinical significance, remains to be fully established (32,36-43).

Antioxidant and cytoprotective effects

Evidence from in vitro and animal studies suggests that saponins isolated from *Astragalus* species exhibit antioxidant and cytoprotective activities under experimentally induced oxidative stress. In preclinical models, these compounds reduce reactive oxygen species production and enhance cellular antioxidant defense mechanisms. In experimental systems, *Astragalus*-derived saponins have also been associated with preservation of cellular integrity, attenuation of membrane damage, and improved cell viability under oxidative stress. Collectively, these findings indicate that *Astragalus* saponins exhibit cytoprotective pharmacological activities in preclinical settings; however, their relevance to physiological protection in humans remains to be established (33,42,44-49).

Antitumor and antiproliferative effects

Experimental evidence derived from cell-based assays and animal cancer models suggests that saponins obtained from various *Astragalus* species exert measurable antiproliferative and tumor-related biological effects. In preclinical settings, these compounds suppress cancer cell expansion and interfere with intracellular signaling networks that regulate cell survival and proliferative capacity. Mechanistic studies indicate that these effects arise from alterations in cell-cycle dynamics and activation of programmed cell death pathways under experimental conditions. Despite these promising preclinical observations, the clinical efficacy, safety profile, and therapeutic relevance of *Astragalus*-derived saponins in oncology remain insufficiently defined (50-56).

Inflammatory and immune-related diseases

Preclinical evidence indicates that saponins isolated from various *Astragalus* species exhibit anti-inflammatory and immunomodulatory effects in experimental models of inflammatory conditions and immune-related disorders. In in vivo experimental settings, these compounds

Table 1. Cycloartane- and oleanane-type triterpenoid saponins reported from *Astragalus* species

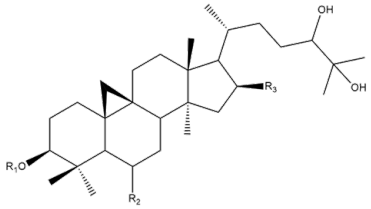
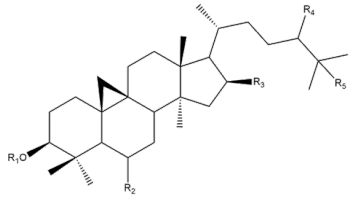
No.	Saponin (as reported)	Structure type	Key structural features	*Astragalus* species	Plant part	Reference
						
1	Laceioside (16β-Acetyloxy-3-O-B-D-Glucopyranosyloxy-Cycloartan-11α,24ξ, 25-Triol)	Cycloartane	R_1=Glc, R_2=H, R_3=OAc	*Astragalus tephrosioides* Boiss. var. lacei (Ali) Kirchoff	Aerial parts	(12)
2	6-O-β-D-Xylopyranosyl-3β,6α,16β,24(S),25-Pentahydroxycycloartane	Cycloartane	R_1=H, R_2=O-Xyl, R_3=OH	*Astragalus karjaginii* BORISS	Root and stem	(13)
3	Cyclocanthoside E	Cycloartane	R_1=Xyl, R_2=O-Glc, R_3=OH	*Astragalus karjaginii* BORISS	Root and stem	(13)
4	3-O-[A-L-Rhamnopyranosyl-(1 → 2)-A-L-Arabinopyranosyl-(1 → 2)-B-D-Xylopyranosyl]-6-O-B-D-Glucopyranosyl-3β,6α,16β,24(S),25-Pentahydroxycycloartane	Cycloartane	R_1=Rha-Ara-Xyl, R_2=O-Glc, R_3=OH	*Astragalus karjaginii* BORISS	Root and stem	(13)
5	Cyclocanthoside D	Cycloartane	R_1=Xyl, R_2=OH, R_3=O-Glc	*Astragalus karjaginii* BORISS	Root and stem	(13)
6	Huangqiyenin B	Cycloartane	R_1=Glc, R_2==O, R_3=OH	*Astragalus membranaceus* (Fisch.) Bge. var. mongholicus (Bge.) Hsiao	Stem	(14)
7	Aleksandroside I	Cycloartane	R_1=Glc, R_2=OH, R_3=OH	*Astragalus membranaceus* (Fisch.) Bge. var. mongholicus (Bge.) Hsiao	Stem	(14)
8	Caspicuside I (3-O-A-L-Rhamnopyranosyl-16-O-B-D-Xylopyranosyl-3β,6α,16β,(24S),25-Pentahydroxycycloartane)	Cycloartane	R_1=Rha, R_2=OH, R_3=Xyl	*Astragalus caspicus* Bieb.	Root	(15)
9	3-O-B-D-Xylopyranosyl,16- O-B-D-Glucopyranosyl-3β,6α,16β,24(S),25-Pentahydroxy-Cycloartane	Cycloartane	R_1=Xyl, R_2=OH, R_3=Glc	*Astragalus amblolepis*	Root	(16)
						
10	3-O-[A-L-Rhamnopyranosyl-(1 → 2)-B-D-Xylopyranosyl]-6-O-B-D-Glucopyranosyl-24-O-A-(4'-O-Acetoxy)-L-Arabinopyranosyl-16-Oacetoxy-3β,6α,16β,24(S),25-Pentahydroxycycloartane	Cycloartane	R_1=Rha-Xyl, R_2=O-Glc, R_3=OAc, R_4=(4'-O-acetoxy) ara, R_5=OH	*Astragalus wiedemannianus* Fischer	Aerial part	(17)
11	3-O-[A-L-Rhamnopyranosyl-(1→2)-B-D-Xylopyranosyl]-6-O-B-D-Glucopyranosyl-24-O-A-L-Arabinopyranosyl-16-O-Acetoxy-3β,6α,16β,24(S),25-Pentahydroxycycloartane	Cycloartane	R_1= Rha-Xyl, R_2=O-Glc, R_3=OAc, R_4=Ara, R_5=OH	*Astragalus wiedemannianus* Fischer	Aerial part	(17)

Table 1. Continued

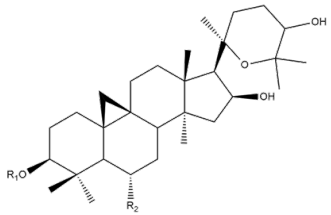
No.	Saponin (as reported)	Structure type	Key structural features	*Astragalus* species	Plant part	Reference
12	3-O-B-D-Xylopyranosyl25-O-B-D-Glucopyranosyl-3β,6α,16β,24(S),25-Pentahydroxy-Cycloartane	Cycloartane	R_1=Xyl, R_2=OH, R_3=OH, R_4=OH, R_5=O-Glc	*Astragalus amblolepis*	Root	(16)
13	3-O-[B-D-Glucuronopyranosyl- (1 → 2)-B-D-Xylopyranosyl]-25-O-B-D-Glucopyranosyl-3β,6α,16β, 24(S),25-Pentahydroxy-Cycloartane	Cycloartane	R_1=Glc-Xyl, R_2=OH, R_3=OH, R_4=OH, R_5=O-Glc	*Astragalus amblolepis*	Root	(16)
14	6-O-A-L-Rhamnopyranosyl-16,24-Di-O-B-D-Glucopyranosyl-3β,6α,16β,24(S),25-Pentahydroxy-Cycloartane	Cycloartane	R_1=OH, R_2=O-Rha, R_3=O-Glc, R_4=O-Glc, R_5=OH	*Astragalus amblolepis*	Root	(16)
15	6-O-A-L-Rhamnopyranosyl-16,25-Dio-A-D-Glucopyranosyl-3β,6α,16β,24(S),25-Pentahydroxy-Cycloartane	Cycloartane	R_1=OH, R_2=O-Rha, R_3=O-Glc, R_4=OH, R_5=O-Glc	*Astragalus amblolepis*	Root	(16)
						
16	Cycloascauloside B	Cycloartane	R_1=Rha-Glc, R_2=OH	*Astragalus karjaginii* BORISS	Root and stem	(13)
17	Cyclocephaloside I	Cycloartane	R_1=Xyl, R_2=O-Glc	*Astragalus karjaginii* BORISS	Root and stem	(13)
18	3-O-[A-L-Rhamnopyranosyl-(1 →2)-A-L-Arabinopyranosyl-(1 →2)-B-D-Xylopyranosyl]-6-O-B-D-Glucopyranosyl-3β,6α,16β,24α-Tetrahydroxy-20(R), 25-Epoxycycloartane	Cycloartane	R_1=Rha(1→2)Ara(1→2)Xyl, R_2=O-Glc	*Astragalus karjaginii* BORISS	Root and stem	(13)
19	3-O-[A-L-Arabinopyranosyl-(1 →2)-B-D-Xylopyranosyl]-6-O-B-D-Glucopyranosyl-3β,6α,16β,24α-Tetrahydroxy-20(R),25-Epoxycycloartane	Cycloartane	R_1= Ara(1→2)Xyl, R_2=O-Glc	*Astragalus karjaginii* BORISS	Root and stem	(13)
20	6-O-B-D-Glucopyranosyl-3β,6α,16β,24α-Tetrahydroxy-20(R),25-Epoxycycloartane	Cycloartane	R_1=OH, R_2=O-Glc	*Astragalus karjaginii* BORISS	Root and stem	(13)
21	3-*O*-[B-D-Glucuronopyranosyl-(1→2)-B-Dxylopyranosyl]-3β,16β,24α-Trihydroxy-20(*R*),25-Epoxycycloartane	Cycloartane	R_1=GlcA(1→2)Xyl, R_2=OH	*Astragalus pennatulus*	Whole plant	(19)
22	Cyclodissectoside	Cycloartane	R_1=Xyl, R_2=Xyl	*Astragalus pennatulus*	Whole plant	(19)
23	Hareftoside C	Cycloartane	R_1=Xyl, R_2=OH	*Astragalus pennatulus*	Whole plant	(19)
24	6-O-B-D-Glucopyranosyl-3β,6α,16β,24α-Tetrahydroxy-20(R),25-Epoxycycloartane	Cycloartane	R_1=OH, R_2=O-Glc	*Astragalus pennatulus*	Whole plant	(19)
25	Cyclosephaloside I	Cycloartane	R_1=Xyl, R_2=Glc	*Astragalus pennatulus*	Whole plant	(19)

Table 1. Continued

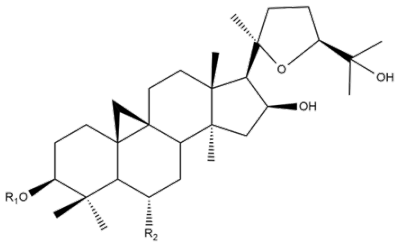
No.	Saponin (as reported)	Structure type	Key structural features	*Astragalus* species	Plant part	Reference
						
26	Astragaloside IV	Cycloartane	R_1=Xyl, R_2=O-Glc	*Astragalus karjaginii* BORISS	Root and stem	(13)
27	Astrachrysoside A (3-O-[A-L-Rhamnopyranosyl-(1→2)]-B-D-Xylopyranosyl]-Cycloastragenol)	Cycloartane	R_1=Rha(1→2)Xyl, R_2=OH	*Astragalus karjaginii* BORISS	Root and stem	(13)
28	3-*O*-[B-Dglucuronopyranosyl-(1→2)-B-D-Xylopyranosyl]-3β,16β,25-Trihydroxy-20(*R*),24(*S*)-Epoxycycloartane	Cycloartane	R_1=Glc(1→2)Xyl, R_2=H	*Astragalus pennatulus*	Whole plant	(19)
29	Astrolanosaponin A_1	Cycloartane	R_1=Glc, R_2=O-Glc	*Astragalus membranaceus* (Fisch.) Bge. var. mongholicus (Bge.) Hsiao	Stem	(14)
30	Astrolanosaponin D	Cycloartane	R_1=Glc, R_2=OH	*Astragalus membranaceus* (Fisch.) Bge. var. mongholicus (Bge.) Hsiao	Stem	(14)
31	Cycloastragenol-3-Oβ-D-Glucopyranoside	Cycloartane	R_1=Glc, R_2=OH	*Astragalus membranaceus* (Fisch.) Bge. var. mongholicus (Bge.) Hsiao	Stem	(14)
32	Astraverrucin II	Cycloartane	R_1=GlcA, R_2=OH	*Astragalus membranaceus* (Fisch.) Bge. var. mongholicus (Bge.) Hsiao	Stem	(14)
33	Astrasieversianin I(Cycloastragenol-3-*O*- (2' ,3' , 4' - T R I -*O*-Acety L) - B -D-Xylopyranosy L -6-*O*- B -Dxylopyranoside)	Cycloartane	R_1=(2' ,3' , 4' - t r i -*O*-acety l)Xyl, R_2=Xyl	*Astragalus tmoleus* Boiss var. *tmoleus*	Root	(20)
34	Astrasieversianin II(Cycloastragenol-3-O-(2',3'-Di-O-Acetyl)-B-D-Xylopyranosyl-6-O-B-D-Xylopyranoside)	Cycloartane	R_1=(2',3'-di-*O*-acetyl)Xyl, R_2=Xyl	*Astragalus tmoleus* Boiss var. *tmoleus*	Root	(20)
35	Cyclocephaloside II(Cycloastragenol-3-*O*-(4'-*O*-Acetyl)-B-D-Xylopyranosyl-6-*O*-B-Dglucopyranoside)	Cycloartane	R_1=(4'-*O*-acetyl)Xyl, R_2=O-Glc	*Astragalus tmoleus* Boiss var. *tmoleus*	Root	(20)
36	Acetylastragaloside I(Cycloastragenol-3-*O*- (2' ,3' , 4' - T R I -*O*-Acety L) - B -D-Xylopyranosy L -6-*O*- B -Dglucopyranoside)	Cycloartane	R_1=(2' ,3' , 4' - t r i -O-acety l)Xyl, R_2=O-Glc	*Astragalus tmoleus* Boiss var. *tmoleus*	Root	(20)
37	Cycloastragenol	Cycloartane	R_1=OH, R_2=OH	*Astragalus wiedemannianus Fischer*	Aerial part	(17)
38	Astragaloside IV	Cycloartane	R_1=Xyl, R_2=Glc	*Astragalus wiedemannianus Fischer*	Aerial part	(17)
39	Brachyoside B	Cycloartane	R_1=OH, R_2=O-Glc	*Astragalus wiedemannianus Fischer*	Aerial part	(17)
40	Astragaloside II	Cycloartane	R_1=(2'-O-acetyl)Xyl, R_2=O-Glc	*Astragalus wiedemannianus Fischer*	Aerial part	(17)

Table 1. Continued

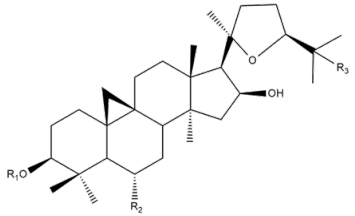
No.	Saponin (as reported)	Structure type	Key structural features	*Astragalus* species	Plant part	Reference
41	Astrachrysoside A	Cycloartane	R_1=Rha(1→2)Xyl, R_2=OH	*Astragalus wiedemannianus Fischer*	Aerial part	(17)
42	Astrasieversianin X	Cycloartane	R_1=Xyl, R_2=Xyl	*Astragalus wiedemannianus Fischer*	Aerial part	(17)
43	Caspicuside II(20(R), 24(S)-Epoxy-3-O-[B-D-Xylopyranosyl-(1→3)-B-D-Glucopyranosyl]-6-O-B-D-Xylopyranosyl-3β,6α,16β,25-Tetrahydroxycycloartane)	Cycloartane	R_1=Xyl(1→3)Glc, R_2=Xyl	*Astragalus caspicus* Bieb.	Root	(15)
44	Astragaloside I	Cycloartane	R_1=(2',3'-di-O-acetyl)Xyl, R_2=O-Glc	*Astragalus membranaceus*	Root	(21)
45	Astragaloside II	Cycloartane	R_1=(2'-O-acetyl)Xyl, R_2=O-Glc	*Astragalus membranaceus*	Root	(21)
46	Astragaloside III	Cycloartane	R_1=Glc(1→2)Xyl, R_2=OH	*Astragalus membranaceus*	Root	(21)
47	3-O-A-L-Arabinopyranosyl-(1→2)- B-D-Xylopyranosyl-6-O-[B-D-Glucopyranosyl]-20(R),24(S)-Epoxy-3β,6α,16β,25-Tetrahydroxy-Cycloartane, (Trojanoside H)	Cycloartane	R_1=Ara(1→2)Xyl, R_2=O-Glc	*Astragalus sempervirens*	Root	(22)
48	Huangqiyesaponin F	Cycloartane	R_1=(2'-O-Ac)Glc, R_2=H	*Astragalus membranaceus*	Leaves	(18)
49	Huangqiyesaponin G	Cycloartane	R_1=(6'-O-Ac)Glc, R_2=H	*Astragalus membranaceus*	Leaves	(18)
50	Huangqiyesaponin H	Cycloartane	R_1=Xyl, R_2= H	*Astragalus membranaceus*	Leaves	(18)
51	Huangqiyesaponin I	Cycloartane	R_1=Glc, R_2=H	*Astragalus membranaceus*	Leaves	(18)
52	Huangqiyesaponin J	Cycloartane	R_1=(2',6'-O-Ac)Glc, R_2=H	*Astragalus membranaceus*	Leaves	(18)
53	Huangqiyesaponin K	Cycloartane	R_1=(3',6'-O-Ac)Glc, R_2=H	*Astragalus membranaceus*	Leaves	(18)
						
54	3,25-Di-*O*-B-D-Glucopyranosyl-6-*O*-B-D-Xylopyranosyl-3β,6α,16β,25-Tetrahydroxy-20(*R*),24(*S*)-Epoxycycloartane	Cycloartane	R_1=Glc, R_2=O-Xyl, R_3=O-Glc	*Astragalus pennatulus*	Whole plant	(19)
55	Astrolanosaponin A_2	Cycloartane	R_1=GlcA, R_2=OH, R_3=O-Glc	*Astragalus membranaceus* (Fisch.) Bge. var. *mongholicus* (Bge.) Hsiao	Stem	(14)
56	Astrolanosaponin B	Cycloartane	R_1=Glc, R_2= =O, R_3=O-Glc	*Astragalus membranaceus* (Fisch.) Bge. var. *mongholicus* (Bge.) Hsiao	Stem	(14)
57	Cycloaraloside E	Cycloartane	R_1=Glc, R_2=OH, R_3=O-Glc	*Astragalus membranaceus* (Fisch.) Bge. var. *mongholicus* (Bge.) Hsiao	Stem	(14)
58	3-O-[A-L-Rhamnopyranosyl-(1 → 2)-B-D-Glucopyranosyl]-25-O-Bd-Glucopyranosyl-20(R),24(S)-Epoxy-3β,6α,16β,25-Tetrahydroxycycloartane	Cycloartane	R_1=Rha(1→2)Glc, R_2=OH, R_3=O-Glc	*Astragalus wiedemannianus* Fischer	Aerial part	(17)

Table 1. Continued

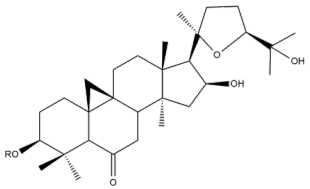
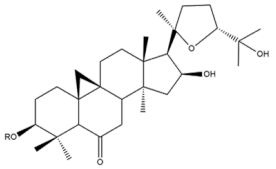
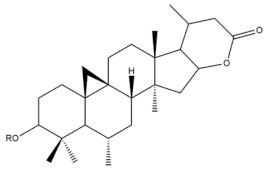
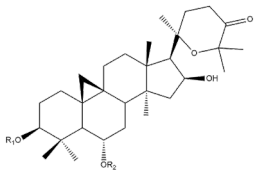
No.	Saponin (as reported)	Structure type	Key structural features	*Astragalus* species	Plant part	Reference
						
59	Huangqiyenin A	Cycloartane	R=Glc	*Astragalus membranaceus* (Fisch.) Bge. var. *mongholicus* (Bge.) Hsiao	Stem	(14)
60	Huangqiyesaponin A	Cycloartane	R= (3′-O-Ac)Glc	*Astragalus membranaceus*	Leaves	(18)
61	Huangqiyesaponin B	Cycloartane	R= (6′-O-Ac)Glc	*Astragalus membranaceus*	Leaves	(18)
62	Huangqiyesaponin C	Cycloartane	R= (2′-O-Ac)Glc	*Astragalus membranaceus*	Leaves	(18)
63	Huangqiyesaponin D	Cycloartane	R= (4′,6′-O-Ac)Glc	*Astragalus membranaceus*	Leaves	(18)
						
64	Huangqiyesaponin L	Cycloartane	R=Xyl	*Astragalus membranaceus*	Leaves	(18)
65	Huangqiyesaponin M	Cycloartane	R=(2′-O-Ac)Glc	*Astragalus membranaceus*	Leaves	(18)
66	Huangqiyesaponin N	Cycloartane	R=(6′-O-Ac)Glc	*Astragalus membranaceus*	Leaves	(18)
						
67	17(R),20(R)-3β,6α,16β-Trihydroxycycloartanyl-23-Carboxylic Acid 16-Lactone 3-O-B-D-Glucopyranoside	Cycloartane	R=Glc	*Astragalus glycyphyllos* L.	Aerial parts	(23)
						
68	3-*O*-B-D-Xylopyranosyl-6-*O*-B-D-Glucopyranosyl-3β,6α,16β-Trihydroxy-24-Oxo-20(*R*),25-Epoxycycloartane	Cycloartane	R_1=Xyl, R_2=Glc	*Astragalus pennatulus*	Whole plant	(19)

Table 1. Continued

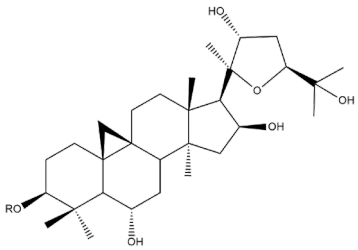
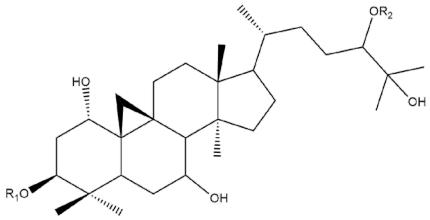
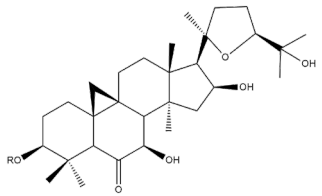
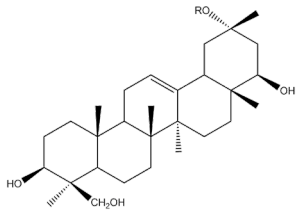
No.	Saponin (as reported)	Structure type	Key structural features	*Astragalus* species	Plant part	Reference
						
69	Astrolanosaponin E	Cycloartane	R=Glc	*Astragalus membranaceus* (Fisch.) Bge. var. *mongholicus* (Bge.) Hsiao	Stem	(14)
						
70	Cyclomacroside D	Cycloartane	R_1=Rha, R_2=Xyl	*Astragalus armatus*	Pod	(24)
						
71	Huangqiyesaponin E	Cycloartane	R=Glc	*Astragalus membranaceus*	Leaves	(18)
						
72	29-O-A-L-Rhamnopyranosyl-Abrisapogenol B	Oleanane	R=Rha	*Astragalus pennatulus*	Whole plant	(19)

Table 1. Continued

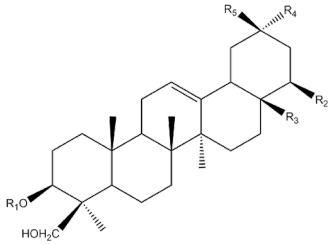
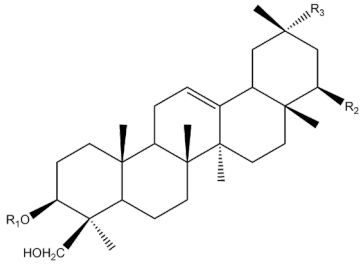
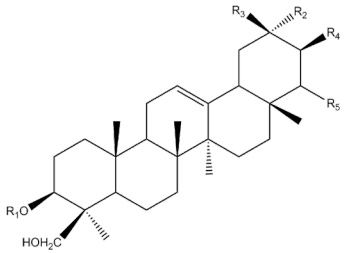
No.	Saponin (as reported)	Structure type	Key structural features	*Astragalus* species	Plant part	Reference
						
73	Hareftoside E(3-O-[B-D-Xylopyranosyl-(1→2)-O-B-D-Glucopyranosyl-(1→2)-O-B-D-Glucuronopyranosyl]-Soyasapogenol B)	Oleanane	R_1=Xyl-Glc-GlcA, R_2=OH, R_3=CH_3, R_4=CH_3, R_5=CH_3	*Astragalus hareftae*	Whole plant	(25)
74	29-O-A-L-Rhamnopyranosyl-Abrisapogenol B	Oleanane	R_1=H, R_2=OH,R_3=CH_3, R_4=CH_3, R_5=CH_3	*Astragalus pennatulus*	Whole plant	(19)
						
75	3-O-[A-L-Rhamnopyranosyl-(1→2)-B-D-Xylopyranosyl-(1 → 2)-B-D-Glucuronopyranosyl]-29-O-B-Dglucopyranosyl-3β,22β,24-Trihydroxyolean-12-En-29-Oic acid.	Oleanane	R_1=Rha-Xyl-GlcA, R_2=OH,R_3=COO-Glc	*Astragalus tauricolus*	Whole plant	(26)
76	3-O-[A-L-Rhamnopyranosyl-(1→2)-B-Dglucopyranosyl-(1→2)-B-D-Glucuronopyranosyl]-29-O-B-D-Glucopyranosyl-3β,22β,24,-Trihydroxyolean-12-En-29-Oic acid.	Oleanane	R_1=Rha-Glc-GlcA, R_2=OH, R_3=COO-Glc	*Astragalus tauricolus*	Whole plant	(26)
77	3-O-[A-L-Rhamnopyranosyl-(1→2)-B-D-Glucopyranosyl-(1 →2)-B-D-Glucuronopyranosyl]-29-O-B-D-Glucopyranosyl-3β,22β,24,29-Tetrahydroxyolean-12-Ene.	Oleanane	R_1=Rha-Glc-GlcA, R_2=OH, R_3=CH_2O-Glc	*Astragalus tauricolus*	Whole plant	(26)
78	3-O-[A-L-Rhamnopyranosyl-(1 → 2)-B-D-Xylopyranosyl-(1 → 2)-B-D-Glucuronopyranosyl]-22-O-A-L-Rhamnopyranosyl-3β,22β,24-Trihydroxyolean-12-Ene.	Oleanane	R_1=Rha-Xyl-GlcA,R_2=O-Rha, R_3=CH_3	*Astragalus tauricolus*	Whole plant	(26)

Table 1. Continued

No.	Saponin (as reported)	Structure type	Key structural features	*Astragalus* species	Plant part	Reference
79	3-O-[A-L-Rhamnopyranosyl-(1→2)-B-D-Glucopyranosyl-(1→2)-B-D-Glucuronopyranosyl]-3β,24-Dihydroxyolean-12-Ene-22-Oxo-29-Oic acid	Oleanane	R_1=Rha-Glc-GlcA, R_2= =O, R_3=COOH	*Astragalus tauricolus*	Whole plant	(26)
80	3-O-[B-D-Glucopyranosyl-(1 → 2)-B-D-Glucuronopyranosyl]-29-O-B-Dglucopyranosyl-3β,22β,24,-Trihydroxyolean-12-En-29-Oic acid	Oleanane	R_1=Glc-GlcA, R_2=OH, R_3=COO-Glc	*Astragalus tauricolus*	Whole plant	(26)
81	3-O-[B-D-Xylopyranosyl-(1→2)-B-D-Glucuronopyranosyl]-29-O-B-D-Glucopyranosyl-3β,22β,24,-Trihydroxyolean-12-En-29-Oic Acid	Oleanane	R_1=Xyl-GlcA- R_2=OH, R_3=COO-Glc	*Astragalus tauricolus*	Whole plant	(26)
82	3-O-[A-L-Rhamnopyranosyl-(1 →2)-B-D-Glucuronopyranosyl]-22-O-B-Dapiofuranosyl-Soyasapogenol B	Oleanane	R_1=Rha-GlcA, R_2=O-Api,R_3=CH_3	*Astragalus caprinus*	Root	(27)
						
83	3-O-[A-L-Rhamnopyranosyl-(1→2)-B-D-Xylopyranosyl-(1→2)-B-D-Glucuronopyranosyl]-3β,21β,22α,24,29-Pentahydroxyolean-12-Ene	Oleanane	R_1=Rha-Xyl-GlcA, R_2=CH_2OH, R_3=CH_3, R_4=OH, R_5= α-OH	*Astragalus angustifolius*	Whole plant	(28)
84	3-O-[A-L-Rhamnopyranosyl-(1→2)-B-D-Xylopyranosyl-(1→2)-B-D-Glucuronopyranosyl]-3β,22β,24-Trihydroxyolean-12-En-29-Oic Acid	Oleanane	R_1=Rha-Xyl-GlcA, R_2=CH_3, R_3=COOH, R_4=H, R_5= β-OH	*Astragalus angustifolius*	Whole plant	(28)
85	3-O-[A-L-Rhamnopyranosyl-(1→2)-B-D-Xylopyranosyl-(1 →2)-B-D-Glucuronopyranosyl]-22-O-A-L-Arabinopyranosyl-3β,22β,24-Trihydroxyolean-12-Ene	Oleanane	R_1=Rha-Xyl-GlcA, R_2=CH_3, R_3=CH_3, R_4=H, R_5=β-O-β-Glc	*Astragalus angustifolius*	Whole plant	(28)
86	29-O-B-D-Glucopyranosyl-3β,22β,24,29-Tetrahydroxy-Olean-12-Ene	Oleanane	R_1=H, R_2=CH_2O-β-Glc,R_3=CH_3, R_4=H, R_5= β-OH	*Astragalus angustifolius*	Whole plant	(28)

attenuate inflammatory responses and modulate immune system activity. For instance, in animal models, Astragalus saponins reduce inflammatory cell infiltration and preserve tissue integrity in affected organs. Collectively, these observations are consistent with the immunomodulatory and anti-inflammatory mechanisms described above in the Biological Effects section; however, their translational relevance to human inflammatory and immune-mediated diseases remains to be established (32,33,36,41,45,57-66).

Hepatic and metabolic diseases

Preclinical evidence suggests that saponins isolated from *Astragalus* species exhibit hepatoprotective and metabolism-related biological effects in experimental models of liver and metabolic disorders. In animal studies, these compounds attenuate the progression of liver fibrosis and modulate biochemical markers of hepatic function under experimentally induced pathological conditions. Experimental findings further indicate that treatment with *Astragalus* saponins is associated with preservation of tissue architecture and reduction in the severity of histopathological alterations in the liver and metabolically affected tissues. Collectively, these effects are consistent with the anti-inflammatory and antioxidant pharmacological activities described above in the Biological Effects section; however, their translational relevance to human hepatic and metabolic diseases remains to be established (33,46,48,67-70).

Neurological and neurodegenerative diseases

Available preclinical studies indicate that saponins derived from *Astragalus* species exert neuroprotective effects in experimental models of neurological and neurodegenerative disorders. Evidence from animal models demonstrates that these compounds can reduce the extent of neuronal damage and support neuronal viability under pathophysiological conditions. At both cellular and molecular scales, such effects are commonly attributed to mechanisms discussed earlier in this review, including the mitigation of oxidative stress, modulation of inflammatory signaling, and maintenance of cellular structural integrity. Nevertheless, the extent to which future research can translate these experimental observations into effective therapeutic strategies for human neurological and neurodegenerative diseases remains uncertain (71-77).

Cardiovascular diseases

Preclinical evidence suggests that saponins isolated from *Astragalus* species exhibit cardioprotective biological effects in experimental models of cardiovascular disorders. In animal-based investigations, experimental evidence indicates that these compounds attenuate the severity of ischemia/reperfusion injury and modulate parameters associated with cardiac function under pathophysiological conditions. Additional experimental findings indicate that *Astragalus* saponin treatment is associated with reduced endothelial dysfunction and preservation of cardiovascular tissue integrity. Collectively, these observations are consistent with the anti-inflammatory, antioxidant, and cytoprotective mechanisms discussed above in the Biological Effects section; however, their translational relevance to human cardiovascular diseases remains to be fully established (78-83).

Cancers

A substantial body of preclinical research supports the antitumor and antiproliferative potential of saponins isolated from *Astragalus* species in diverse experimental cancer systems. Experimental evidence from cell-based assays and animal cancer models indicates that saponins isolated from various *Astragalus* species exert measurable antiproliferative and antitumor biological effects. In preclinical settings, these compounds suppress cancer cell expansion and interfere with intracellular signaling networks that regulate cell survival and proliferative capacity. Data from both in vitro and in vivo studies further demonstrate that *Astragalus* saponins modulate tumor-associated biological processes by altering signaling pathways involved in cell-cycle control and apoptotic regulation, resulting in reduced cancer cell proliferation. Moreover, experimental studies suggest that *Astragalus*-derived saponins enhance the sensitivity of malignant cells to conventional anticancer agents under controlled laboratory conditions. Collectively, these findings align with the broader regulatory effects of *Astragalus* saponins on cellular survival and death signaling pathways discussed in the Biological Effects section; however, their translational relevance and prospective clinical application remain insufficiently characterized (50,56,84-86). Moreover, experimental studies suggest that *Astragalus*-derived saponins may increase the sensitivity of malignant cells to conventional anticancer agents under controlled laboratory conditions. Taken together, these findings align with the broader regulatory influence of *Astragalus* saponins on cellular survival and death signaling networks discussed in the Biological Effects section. Experimental evidence from cell-based assays and animal cancer models indicates that saponins isolated from *Astragalus* species exert measurable antiproliferative and antitumor pharmacological activities in preclinical settings. These compounds suppress cancer cell proliferation by interfering with tumor-associated biological processes and by modulating intracellular signaling pathways involved in cell-cycle regulation and apoptotic control. In addition, experimental studies suggest that *Astragalus*-derived saponins increase the sensitivity of malignant cells to conventional anticancer agents under controlled laboratory conditions. Collectively, these findings are consistent with the broader regulatory effects of *Astragalus* saponins on cellular survival and death signaling networks discussed in the Biological Effects section. Nevertheless, current evidence does not yet clarify

their translational significance or prospective application in clinical oncology (50,56,84–86). (50,56,84-86).

Pharmacokinetics and bioavailability of Astragalus saponins

Although *Astragalus* saponins have potential therapeutic applications, their clinical use remains limited, primarily due to poor oral bioavailability. Astragaloside IV exhibits very low intestinal permeability, as demonstrated by in situ intestinal perfusion studies. It also transports experiments using Caco-2 cell monolayers, resulting in low plasma concentrations following oral administration. Pharmacokinetic studies in rats have reported an absolute oral bioavailability of approximately 2.2%, indicating limited systemic absorption after oral use (87).

Other studies have corroborated these findings and suggest that low oral bioavailability may also result from multiple variables, including (i) high molecular weight; (ii) poor intracellular penetration; and (iii) low solubility in biological fluids. In addition, preliminary evidence indicates that gut microbes may metabolize astragaloside IV into more absorbable metabolites, such as cycloastragenol, which appear in the systemic circulation following intramuscular injection. Unfortunately, much of the information regarding this metabolic conversion process and its potential significance in humans has yet to be collected or published (88).

Studies in animals suggest that astragaloside IV, upon intravenous injection, is distributed to various organs, particularly in the liver, kidneys, lungs, and heart. However, due to astragaloside IV's limited ability to cross the blood-brain barrier, its distribution to the brain is restricted, potentially preventing it from reaching therapeutic levels in some target tissues (89).

On the other hand, pharmacokinetic analysis in mice and dogs has revealed that astragaloside IV has a relatively short half-life and linear systemic clearance, with no apparent dose-dependent differences between low and high doses. This indicates that the dose predicts the pharmacokinetics and pharmacodynamics of astragaloside IV, allowing for reliable anticipation of its distribution and elimination profiles. Astragaloside IV is eliminated primarily via urine and feces. About 83% of the compound binds to plasma proteins, which may affect its distribution to other tissues and the duration of its pharmacologic activity in those tissues (90).

Safety and toxicity of Astragalus saponins

Preclinical studies suggest that most *Astragalus* saponins are relatively safe, including astragaloside IV and cycloastragenol. In studies evaluating their safety profiles at possible therapeutic doses, there was little to no evidence of acute toxic effects on major organs, and both compounds exhibit high tolerability across a wide dose range (including higher doses), with no evidence of systemic toxicity (91).

Few human studies have shown that astragalosides can be administered IV for multiple days without causing significant side effects or significantly altering liver or kidney function. However, very little data is available regarding long-term safety in humans (91).

Some studies have also indicated that certain considerations when using astragalosides in specific situations, like pregnancy, administering doses of astragaloside IV, can affect fetal development/survival. Therefore, these findings necessitate caution regarding use during pregnancy. Further, the safety of *Astragalus* saponins requires investigation in other special situations, such as while nursing or caring for a baby, over a prolonged period (91).

Interactions with other drugs

Besides pharmacokinetic and safety considerations, several studies indicate that astragalosides may interact with drug-metabolizing enzymes, such as CYP1A2, and inhibit their activity. Consequently, *Astragalus* saponins may interact with concomitant drug therapies. Therefore, preclinical safety and interaction data necessitate careful evaluation of the clinical use of astragaloside IV to minimize the risk of adverse outcomes (92).

The pharmacokinetic profiles of astragalosides indicate low oral bioavailability and limited organ distribution in animal models. They also demonstrate a clear understanding of their metabolism and elimination. The preclinical safety data appear favourable; however, there are still many unknowns regarding the long-term safety and potential drug interactions in humans, which warrant further investigation of these compounds' human pharmacokinetics and safety.

Research gaps and limitations, and suggestions

While there is a large amount of information on the biological and pharmacological effects of saponins from plants of the genus *Astragalus*, a thorough review reveals limitations and gaps in knowledge that may affect the interpretation of existing data and their introduction into clinical use. One significant gap is that astragaloside IV receives more attention than all other saponins found in many different *Astragalus* spp. At the same time, there is a large degree of variability in structure, particularly among cycloartane- and oleanane-type saponins. Therefore, pharmacological studies of most *Astragalus* saponins have been conducted on only a small subset, limiting the ability to extrapolate results to the entire class. Additionally, the evidence base for the present research primarily comprises in vitro laboratory experiments and animal studies, with a limited number of human clinical studies. Without properly controlled clinical trials, the ability to accurately assess the efficacy, safety, and appropriate dosage of this therapeutic modality in clinical practice will remain limited, leaving the majority of its therapeutic implications at the preclinical stage. Another notable limitation of

the current research is the lack of standardization in the extraction, purification, and identification of the saponins as separate compounds. Additionally, in some reports on these saponins, key information on the plant source material, species identification, and the chemical characterization of the saponins investigated has not been adequately documented.

Like most natural compounds, there are limitations to the pharmacokinetics, bioavailability, and metabolism of saponins in the body. Very low oral bioavailability, extensive intestinal metabolism, and an incomplete understanding of organ-specific distribution collectively hinder accurate evaluation of the therapeutic potential of these saponins. Likewise, little information is available on the potential long-term toxicity and safety, as well as on any possible drug-drug interactions, for these compounds.

Furthermore, most studies to date on the therapeutic effects of saponins have focused on their pharmacological actions via a single mechanistic pathway. However, few integrated analyses have addressed interactions among multiple molecular mechanisms and signalling pathways. This reductionism has limited our understanding of how saponins from the genus *Astragalus* work in the treatment of complex, multifactorial diseases. Therefore, while existing preclinical evidence underscores the potential of *Astragalus* saponins as effective therapeutic agents, rigorous methodological standardization, comparative investigations, and systematic pharmacokinetic profiling remain indispensable to validating their clinical relevance and translational applicability.

Despite the aforementioned limitation, a growing body of literature supports the potential clinical use of saponins, particularly astragaloside IV and other cycloartane-type saponins extracted from various *Astragalus* species. As demonstrated in preclinical models, these saponins exhibit a wide range of biological and pharmacological activities. In addition, the comprehensive literature reviews and multicentre studies have provided detailed information on the anti-inflammatory, antioxidant, immunomodulatory, anticancer, and protective activities of these compounds in preclinical models. However, most available evidence is based primarily on in vitro and animal studies, and clinical validation in humans remains very limited (93).

One of the primary strategies for advancing the therapeutic development of *Astragalus* saponins involves their incorporation into advanced pharmaceutical delivery platforms, including targeted delivery systems and nanocarriers. Such approaches offer a rational means of enhancing bioavailability, improving physicochemical stability, and enabling tissue-specific delivery. Notably, nano-formulated delivery systems of astragaloside IV have demonstrated enhanced absorption and controlled release in target tissues, underscoring the potential of nanotechnology-based formulations to optimize the pharmacokinetic and therapeutic profiles of *Astragalus* saponins (91).

In addition to formulation development, systematic investigation of the pharmacological properties of other saponins that have received limited systematic investigation in *Astragalus* and related species remains a critical research priority. Chemical and pharmacological reviews suggest that, beyond astragaloside IV, the genus *Astragalus* harbors a diverse array of bioactive saponins whose pharmacological properties remain insufficiently characterized, representing a substantial yet underexplored reservoir for future therapeutic discovery (94).

In oncology, the combination of conventional chemotherapies with *Astragalus* saponins is a promising area for future research. Co-administration of astragaloside IV with standard chemotherapeutic agents may improve drug response and diminish tumor resistance to these agents, and warrants further evaluation in preclinical and clinical settings (56,95).

The standardization of plant sources, extraction process, and evaluation techniques remains a significant obstacle in the development of *Astragalus* saponins as therapeutic agents. Variations in species selection, growing conditions, extraction methods, and compound purity create considerable variability in the resulting data, suggesting that standardized and reproducible methods are necessary (93).

At the preclinical level, available data support the significant therapeutic potential of *Astragalus* saponins. Future research will include developing advanced formulation strategies, systematically evaluating underrepresented saponins, conducting high-quality clinical trials, and developing standardized methods for extracting and characterizing the saponins. Continued research investment in these areas could advance *Astragalus* saponins from basic research to clinical applications.

Discussion

The genus *Astragalus* reaches its highest species diversity in the Iran–Turan phytogeographical region and serves as a primary centre of diversification for the genus. Phylogenetic studies have distinguished Old World lineages from the New World clade, commonly referred to as Neo-*Astragalus*. Current phytochemical and pharmacological research predominantly targets Old World *Astragalus* species, particularly those distributed in Asia and the Middle East, which exhibit a high prevalence of cycloartane-type triterpenoid saponins. In contrast, the Neo-*Astragalus* lineage remains comparatively underexplored and appears to possess a more heterogeneous and less clearly defined secondary metabolite profile. Consequently, comprehensive comparative evaluations of chemical diversity between Old World and Neo-*Astragalus* lineages remain limited.

Although *Astragalus* species produce a chemically diverse spectrum of cycloartane- and oleanane-type saponins, most mechanistic, pharmacokinetic, and safety

data are concentrated on astragaloside IV, which is therefore widely used as a reference compound in preclinical investigations. Evidence suggests that several structurally related saponins exhibit comparable biological activities. However, their molecular mechanisms, structure-activity relationships, and translational relevance remain insufficiently characterized, highlighting the need for broader comparative studies across *Astragalus* saponins. Preclinical investigations suggest that saponins derived from *Astragalus* species play a regulatory role in immune and inflammatory processes through their influence on intracellular signaling cascades, most notably NF-κB and NLRP3. Modulation of these pathways correlates with diminished production of pro-inflammatory mediators and functional adjustments in immune cell responses (36). In parallel, antioxidant and cytoprotective properties have been linked to activation of the Nrf2 signaling axis, leading to enhanced expression of endogenous antioxidant systems such as superoxide dismutase and glutathione (35).

Beyond immunological effects, *Astragalus* saponins have shown broad antiproliferative activity in experimental disease models. In cancer-related settings, these compounds have been reported to interfere with cell-cycle progression, promote apoptotic signaling, suppress tumor cell migration and invasion, and enhance cellular responsiveness to conventional chemotherapeutic agents under laboratory conditions (84,86). Preclinical cardiovascular and hepatic models demonstrate protective actions of *Astragalus* saponins, including attenuation of ischemia–reperfusion injury, fibrotic remodeling, and post-injury endothelial or myocardial dysfunction (67,79). Moreover, in models of neurological and neurodegenerative disorders, neuroprotective effects have been attributed to reductions in neuronal apoptosis, oxidative burden, and neuroinflammatory responses, contributing to the preservation of neuronal function (73,77).

Despite the substantial body of preclinical evidence, essential limitations remain, including the scarcity of controlled clinical trials in humans, limited pharmacokinetic and bioavailability data, a pronounced research bias toward astragaloside IV, and the absence of long-term safety evaluations. Addressing these gaps will require well-designed clinical studies, improved formulation strategies, and expanded investigation of less-studied *Astragalus* saponins to define their clinical relevance and translational applicability (93).

Conclusion

Saponins derived from *Astragalus* species represent a structurally diverse group of bioactive natural compounds with a wide range of preclinical pharmacological activities. Available evidence indicates that these saponins exert immunomodulatory, anti-inflammatory, antioxidant, antitumor, cardioprotective, hepatoprotective, and neuroprotective effects through multiple molecular mechanisms. However, current knowledge derives largely from preclinical models and disproportionately emphasizes a limited number of compounds, particularly astragaloside IV. Future studies integrating comparative phytochemistry, pharmacokinetics, and well-designed clinical investigations are essential to better define the therapeutic potential and translational relevance of *Astragalus* saponins.

Authors' contribution

Conceptualization: Masoud Sadeghi Dinani, Zeinab Delazar.
Data curation: Zeinab Delazar.
Funding acquisition: Masoud Sadeghi Dinani.
Investigation: Zeinab Delazar.
Methodology: Zeinab Delazar.
Project administration: Zeinab Delazar.
Resources: Zeinab Delazar.
Software: Zeinab Delazar.
Supervision: Masoud Sadeghi Dinani.
Validation: Zeinab Delazar, Masoud Sadeghi Dinani.
Visualization: Zeinab Delazar.
Writing–original draft: Zeinab Delazar.
Writing–review & editing: Masoud Sadeghi Dinani.

Conflict of interests

The authors declare no conflict of interest.

Ethical considerations

All ethical issues, including plagiarism, research misconduct, data fabrication, falsification, and duplicate or redundant publication, were carefully considered and fully avoided by the authors.

References

1. Li X, Qu L, Dong Y, Han L, Liu E, Fang S, et al. A review of recent research progress on the *Astragalus* genus. Molecules. 2014;19(11):18850–80. doi:10.3390/molecules191118850
2. Atasagun B, Aksoy A, Martin E. Morphological, anatomical, palynological, karyological and ecological remarks of *Astragalus argaeus* (Fabaceae) endemic to Turkey. Phytotaxa. 2018;379(1):118–30.
3. Zarre S, Azani N. Perspectives in taxonomy and phylogeny of the genus *Astragalus* (Fabaceae): a review. Prog Biol Sci. 2013;3(1):1–6.
4. Maassoumi A, Khajoei Nasab F. Richness and endemism centers of mega genus *Astragalus* (Fabaceae) in Iran. Collect Bot. 2023 Apr 5;42:e001.
5. Buono D, Kadereit G, Liston A, Zarre S, Morales-Briones DF. Building a robust backbone for *Astragalus* using a clade-specific target enrichment bait set. Am J Bot. 2025; 112(8):e70084. doi:10.1002/ajb2.70084
6. Ateş MA, Karaman S, Aytaç Z, Kaya Z. Molecular insights into the diversification and biogeographic history of six *Astragalus* L. sections in the Turkish flora. Plants. 2025;14:2226.
7. Stambolov I, Shkondrov A, Kunert O, Bucar F, Kondeva-

Burdina M, Krasteva I. Cycloartane saponins from *Astragalus glycyphyllos* and their in vitro neuroprotective, antioxidant, and hMAO-B-inhibiting effects. Metabolites. 2023;13(7):857. doi:10.3390/metabo13070857
8. Chen K, Zhang M, Xu L, Yi Y, Wang L, Wang H, et al. Identification of oxidosqualene cyclases associated with saponin biosynthesis from *Astragalus membranaceus* reveals a conserved motif important for catalytic function. J Adv Res. 2023;43:247–57. doi:10.1016/j.jare.2022.03.014
9. Yesilada E, Bedir E, Caliş I, Takaishi Y, Ohmoto Y. Effects of triterpene saponins from *Astragalus* species on in vitro cytokine release. J Ethnopharmacol. 2005;96(1–2):71–7.
10. Nguyen MK, Nguyen VP, Yang SY, Min BS, Kim JA. Astraoleanosides E-P, oleanane-type triterpenoid saponins from the aerial parts of *Astragalus membranaceus* Bunge and their β-glucuronidase inhibitory activity. Bioorg Chem. 2024;145:107230.
11. Debnath S, Mohanta BC, Harigaya Y, Tripura S. Naturally occurring triterpenoid saponins. Chem Biodivers. 2010;7(10):2327–580.
12. Ahmad VU, Mohammad FV, Tareen RB. Laceioside, a new cycloartane saponin from *Astragalus tephrosioides* Boiss. var. lacei (Ali) Kirchoff. Nat Prod Res. 2019;33(3):393–9. doi:10.1080/14786419.2018.1455042
13. Aslanipour B, Gülcemal D, Nalbantsoy A, Yusufoglu H, Bedir E. Secondary metabolites from *Astragalus karjaginii* BORISS and the evaluation of their effects on cytokine release and hemolysis. Fitoterapia. 2017;122:26–33.
14. Wang T, Ruan J, Li X, Chao L, Shi P, Han L, et al. Bioactive cyclolanstane-type saponins from the stems of *Astragalus membranaceus* (Fisch.) Bge. var. mongholicus (Bge.) Hsiao. J Nat Med. 2016;70(2):198–206. doi:10.1007/s11418-015-0959-8
15. Fathiazad F, Khosropanah MK, Movafeghi A. Cycloartane-type glycosides from the roots of *Astragalus caspicus* Bieb. Nat Prod Res. 2010;24(11):1069–78.
16. Polat E, Caliskan-Alankus O, Perrone A, Piacente S, Bedir E. Cycloartane-type glycosides from *Astragalus amblolepis*. Phytochemistry. 2009;70(5):628–34.
17. Polat E, Bedir E, Perrone A, Piacente S, Alankus-Caliskan O. Triterpenoid saponins from *Astragalus wiedemannianus* Fischer. Phytochemistry. 2010;71(5–6):658–62. doi:10.1016/j.phytochem.2009.11.013
18. Xu W, Li X, Zhang Q, Jiang P, Zhang Y, Luo Y, et al. New triterpenoid saponins isolated from the leaves of *Astragalus membranaceus* (Fisch.) Bge. and their neuroprotective effects. Bioorg Chem. 2025;156:108149.
19. Un R, Horo I, Masullo M, Falco A, Senol SG, Piacente S, et al. Cycloartane and oleanane-type glycosides from *Astragalus pennatulus*. Fitoterapia. 2016;109:254–60.
20. Avunduk S, Mitaine-Offer A-C, Miyamoto T, Tanaka C, Lacaille-Dubois M-A. Cycloartane-Type Saponins from *Astragalus tmoleus* var. *tmoleus*. Nat Prod Commun. 2016;11(1):37–8.
21. Ionkova I, Momekov G, Proksch P. Effects of cycloartane saponins from hairy roots of *Astragalus membranaceus* Bge., on human tumor cell targets. Fitoterapia. 2010;81(5):447–51.
22. Linnek J, Mitaine-Offer A-C, Miyamoto T, Duchamp O, Mirjolet J-F, Lacaille-Dubois M-A. Cycloartane-type glycosides from two species of *Astragalus* (Fabaceae). Nat Prod Commun. 2009;4(4):477–8.
23. Shkondrov A, Krasteva I, Bucar F, Kunert O, Kondeva-Burdina M, Ionkova I. A new tetracyclic saponin from *Astragalus glycyphyllos* L. and its neuroprotective and hMAO-B inhibiting activity. Nat Prod Res. 2020;34(4):511–7. doi:10.1080/14786419.2018.1491040
24. Labed A, Ferhat M, Labed-Zouad I, Kaplaner E, Zerizer S, Voutquenne-Nazabadioko L, et al. Compounds from the pods of *Astragalus armatus* with antioxidant, anticholinesterase, antibacterial and phagocytic activities. Pharm Biol. 2016;54(12):3026–32.
25. Horo I, Bedir E, Masullo M, Piacente S, Ozgökçe F, Alankuş-Çalışkan O. Saponins from *Astragalus hareftae* (NAB.) SIRJ. Phytochemistry. 2012;84:147–53.
26. Gülcemal D, Masullo M, Napolitano A, Karayıldırım T, Bedir E. Oleanane glycosides from *Astragalus tauricolus*: Isolation and structural elucidation based on a preliminary liquid chromatography-electrospray ionization tandem mass spectrometry profiling. Phytochemistry. 2013;86:184–94. doi:10.1016/j.phytochem.2012.10.001
27. Mitaine-Offer A-C, Miyamoto T, Semmar N, Jay M, Lacaille-Dubois M-A. A new oleanane glycoside from the roots of *Astragalus caprinus*. Magn Reson Chem. 2006;44(7):713–6.
28. Gülcemal D, Masullo M, Bedir E, Festa M, Karayıldırım T, Alankus-Caliskan O, et al. Triterpene glycosides from *Astragalus angustifolius*. Planta Med. 2012;78(7):720–9.
29. Nalbantsoy A, Nesil T, Erden S, Calış I, Bedir E. Adjuvant effects of *Astragalus* saponins macrophyllosaponin B and astragaloside VII. J Ethnopharmacol. 2011;134(3):897–903. doi:10.1016/j.jep.2011.01.054
30. Yakubogullari N, Coven FO, Cebi N, Coven F, Coven N, Genc R, et al. Evaluation of adjuvant activity of Astragaloside VII and its combination with different immunostimulating agents in Newcastle Disease vaccine. Biologicals. 2021;70:28–37.
31. Nalbantsoy A, Nesil T, Yılmaz-Dilsiz O, Aksu G, Khan S, Bedir E. Evaluation of the immunomodulatory properties in mice and in vitro anti-inflammatory activity of cycloartane type saponins from *Astragalus* species. J Ethnopharmacol. 2012;139(2):574–81. doi:10.1016/j.jep.2011.11.053
32. Zhang W-J, Frei B. Astragaloside IV inhibits NF-κB activation and inflammatory gene expression in LPS-treated mice. Mediators Inflamm. 2015;2015:274314.
33. Liang Y, Chen B, Liang D, Quan X, Gu R, Meng Z, et al. Pharmacological Effects of Astragaloside IV: A Review. Molecules. 2023;28(16):6118.
34. Stępnik K, Jarząb A, Niedźwiadek R, Głowniak-Lipa A, Głowniak K, Kukula-Koch W. In Vivo Insights into the Role of Astragaloside IV in Preventing and Treating Civilization Diseases: A Comprehensive Review. Int J Mol Sci. 2025;26(9):4250. doi:10.3390/ijms26094250
35. Sun C, Jiang M, Zhang L, Yang J, Zhang G, Du B, et al. Cycloastragenol mediates activation and proliferation suppression in concanavalin A-induced mouse lymphocyte pan-activation model. Immunopharmacol Immunotoxicol. 2017;39(3):131–9.
36. Chen G, Wang W, Guan B, Zhang G, Zhang Z, Lin L, et al. Cycloastragenol reduces inflammation in CLP-induced septic mice by suppressing TLR4 signaling pathways. Phytomedicine. 2025;142:156645. doi:10.1016/j.phymed.2025.156645
37. Ying Y, Sun C-B, Zhang S-Q, Chen B-J, Yu J-Z, Liu F-Y, et al. Induction of autophagy via the TLR4/NF-κB signaling pathway by astragaloside IV contributes to the amelioration of inflammation in RAW264.7 cells. Biomed Pharmacother.

2021;137:111271.
38. Chen Z, Yao L, Liu Y, Pan Z, Peng S, Wan G, et al. Astragaloside IV regulates NF-κB-mediated cellular senescence and apoptosis of hepatic stellate cells to suppress PDGF-BB-induced activation. Exp Ther Med. 2019; 18(5):3741–50. doi:10.3892/etm.2019.8047
39. Su X, Guo H, Zhou Y, Cao A, Shen Q, Zhu B, et al. Astragaloside IV attenuates high glucose-induced NF-κB-mediated inflammation through activation of PI3K/AKT-ERK-dependent Nrf2/ARE signaling pathway in glomerular mesangial cells. Phytother Res. 2023;37(9):4133–48.
40. Yang J, Wang H-X, Zhang Y-J, Yang Y-H, Lu M-L, Zhang J, et al. Astragaloside IV attenuates inflammatory cytokines by inhibiting TLR4/ NF-κB signaling pathway in isoproterenol-induced myocardial hypertrophy. J Ethnopharmacol. 2013;150(3):1062–70.
41. Shi H, Zhou P, Gao G, Liu P-P, Wang S-S, Song R, et al. Astragaloside IV prevents acute myocardial infarction by inhibiting the TLR4/MyD88/NF-κB signaling pathway. J Food Biochem. 2021;45(7):e13757.
42. Ikram M, Jo MH, Choe K, Khan A, Ahmad S, Saeed K, et al. Cycloastragenol, a Triterpenoid Saponin, Regulates Oxidative Stress, Neurotrophic Dysfunctions, Neuroinflammation and Apoptotic Cell Death in Neurodegenerative Conditions. Cells. 2021;10(10):2719.
43. Wang G, Ma C, Chen K, Wang Z, Qiu H, Chen D, et al. Cycloastragenol Attenuates Osteoclastogenesis and Bone Loss by Targeting RANKL-Induced Nrf2/Keap1/ARE, NF-κB, Calcium, and NFATc1 Pathways. Front Pharmacol. 2021;12:810322. doi:10.3389/fphar.2021.810322
44. Yao J, Peng T, Shao C, Liu Y, Lin H, Liu Y. The Antioxidant Action of Astragali radix: Its Active Components and Molecular Basis. Molecules. 2024;29(8):1691. doi:10.3390/molecules29081691
45. Wan D, Zhu Z, Zhou J, Deng Z, Lei P, Liu Q, et al. Astragaloside IV protects LO2 cells from oxidative damage caused by radiation-induced bystander effect through Akt/Nrf2 pathway. Toxicol Res (Camb). 2023;12(4):635–47. doi:10.1093/toxres/tfad048
46. Liang X-Y, Hong F-F, Yang S-L. Astragaloside IV Alleviates Liver Inflammation, Oxidative Stress and Apoptosis to Protect Against Experimental Non-Alcoholic Fatty Liver Disease. Diabetes Metab Syndr Obes. 2021;14:1871–83.
47. Lin W, Yao H, Lai J, Zeng Y, Guo X, Lin S, et al. Cycloastragenol Confers Cerebral Protection after Subarachnoid Hemorrhage by Suppressing Oxidative Insults and Neuroinflammation via the SIRT1 Signaling Pathway. Oxid Med Cell Longev. 2022;2022:3099409. doi:10.1155/2022/3099409
48. Wang Y, Jiang F, Cheng H, Tan X, Liu Y, Wei C, et al. Astragaloside IV Protects Against Oxidative Stress in Calf Small Intestine Epithelial Cells via NFE2L2-Antioxidant Response Element Signaling. Int J Mol Sci. 2019;20(24):6131.
49. Liu Z, Zhou Z, Ai P, Zhang C, Chen J, Wang Y. Astragaloside IV attenuates ferroptosis after subarachnoid hemorrhage via Nrf2/HO-1 signaling pathway. Front Pharmacol. 2022;13:924826. doi:10.3389/fphar.2022.924826
50. Zhou L, Li M, Chai Z, Zhang J, Cao K, Deng L, et al. Anticancer effects and mechanisms of astragaloside-IV (Review). Oncol Rep. 2023 Jan;49(1):5.
51. Sheng F, Yang S, Li M, Wang J, Liu L, Zhang L. Research progress on the anti-cancer effects of *Astragalus membranaceus* saponins and their mechanisms of action. Molecules. 2024;29(14):3388. doi:10.3390/molecules29143388
52. Tin MMY, Cho C-H, Chan K, James AE, Ko JKS. *Astragalus* saponins induce growth inhibition and apoptosis in human colon cancer cells and tumor xenograft. Carcinogenesis. 2007;28(6):1347–55.
53. Wang Y, Auyeung KK, Zhang X, Ko JK. *Astragalus* saponins modulates colon cancer development by regulating calpain-mediated glucose-regulated protein expression. BMC Complement Altern Med. 2014;14:401.
54. Law P, Auyeung KK, Chan L, Ko JK. *Astragalus* saponins downregulate vascular endothelial growth factor under cobalt chloride- stimulated hypoxia in colon cancer cells. BMC Complement Altern Med. 2012;12:160.
55. Guo H, Wan B, Wang J, Zhang JIE, Yao W, Shen Z. *Astragalus* saponins inhibit cell growth, aerobic glycolysis and attenuate the inflammatory response in a DSS-induced colitis model. Int J Mol Med. 2019;43(2):1041–8.
56. Xia D, Li W, Tang C, Jiang J. Astragaloside IV, as a potential anticancer agent. Front Pharmacol. 2023;14:1065505.
57. Tian L, Zhao J-L, Kang J-Q, Guo S-B, Zhang N, Shang L, et al. Astragaloside IV Alleviates the Experimental DSS-Induced Colitis by Remodeling Macrophage Polarization Through STAT Signaling. Front Immunol. 2021;12:740565.
58. Zhong Y, Liu W, Xiong Y, Li Y, Wan Q, Zhou W, et al. Astragaloside IV alleviates ulcerative colitis by regulating the balance of Th17/Treg cells. Phytomedicine. 2022; 104:154287. doi:10.1016/j.phymed.2022.154287
59. Zhang X, Zhang F, Li Y, Fan N, Zhao K, Zhang A, et al. Blockade of PI3K/AKT signaling pathway by Astragaloside IV attenuates ulcerative colitis via improving the intestinal epithelial barrier. J Transl Med. 2024;22(1):406.
60. Wang B, Chen M-Z. Astragaloside IV possesses antiarthritic effect by preventing interleukin 1β-induced joint inflammation and cartilage damage. Arch Pharm Res. 2014;37(6):793–802. doi:10.1007/s12272-014-0336-2
61. Xu H, Wang C-Y, Zhang H-N, Lv C-Y, Wang Y-Z. Astragaloside IV suppresses inflammatory mediator production in synoviocytes and collagen-induced arthritic rats. Mol Med Rep. 2016;13(4):3289–96.
62. Auyeung KK, Han Q-B, Ko JK. *Astragalus membranaceus*: A Review of its Protection Against Inflammation and Gastrointestinal Cancers. Am J Chin Med. 2016;44(1):1–22.
63. Peng Y, Deng X, Yang S-S, Nie W, Tang Y-D. Progress in Mechanism of *Astragalus membranaceus* and Its Chemical Constituents on Multiple Sclerosis. Chin J Integr Med. 2023;29(1):89–95. doi:10.1007/s11655-022-3535-6
64. Liu R, Jiang H, Tian Y, Zhao W, Wu X. Astragaloside IV protects against polymicrobial sepsis through inhibiting inflammatory response and apoptosis of lymphocytes. J Surg Res. 2016 Jan;200(1):315–23.
65. Huang X, Zhang M-Z, Liu B, Ma S-Y, Yin X, Guo L-H. Astragaloside IV attenuates polymicrobial sepsis-induced cardiac dysfunction in rats via IKK/NF-κB pathway. Chin J Integr Med. 2021;27(11):825–31. doi:10.1007/s11655-021-2869-9
66. Xie S, Yang T, Wang Z, Li M, Ding L, Hu X, et al. Astragaloside IV attenuates sepsis-induced intestinal barrier dysfunction via suppressing RhoA/NLRP3 inflammasome signaling. Int Immunopharmacol. 2020;78:106066.
67. Wang C, Li Y, Hao M, Li W. Astragaloside IV Inhibits Triglyceride Accumulation in Insulin-Resistant HepG2 Cells via AMPK-Induced SREBP-1c Phosphorylation. Front Pharmacol. 2018;9:345. doi:10.3389/fphar.2018.00345

68. Liu H, Wei W, Sun W, Li X. Protective effects of astragaloside IV on porcine-serum-induced hepatic fibrosis in rats and in vitro effects on hepatic stellate cells. J Ethnopharmacol. 2009;122(3):502–8.
69. Zhang L, Shi J, Shen Q, Fu Y, Qi S, Wu J, et al. *Astragalus* saponins protect against extrahepatic and intrahepatic cholestatic liver fibrosis models by activation of farnesoid X receptor. J Ethnopharmacol. 2024;318(Pt A):116833.
70. Dan L, Hao Y, Song H, Wang T, Li J, He X, et al. Efficacy and potential mechanisms of the main active ingredients of *Astragalus mongholicus* in animal models of liver fibrosis: A systematic review and meta-analysis. J Ethnopharmacol. 2024;319(Pt 1):117198. doi:10.1016/j.jep.2023.117198
71. Costa IM, Lima FOV, Fernandes LCB, Norrara B, Neta FI, Alves RD, et al. Astragaloside IV Supplementation Promotes A Neuroprotective effect in experimental models of neurological disorders: a systematic review. Curr Neuropharmacol. 2019;17(7):648–65.
72. Chan W-S, Durairajan SSK, Lu J-H, Wang Y, Xie L-X, Kum W-F, et al. Neuroprotective effects of Astragaloside IV in 6-hydroxydopamine-treated primary nigral cell culture. Neurochem Int. 2009;55(6):414–22.
73. Yang C, Mo Y, Xu E, Wen H, Wei R, Li S, et al. Astragaloside IV ameliorates motor deficits and dopaminergic neuron degeneration via inhibiting neuroinflammation and oxidative stress in a Parkinson's disease mouse model. Int Immunopharmacol. 2019;75:105651.
74. Ding Y, Jie K, Xin L, Shao B. Astragaloside IV plays a neuroprotective role by promoting PPARγ in cerebral ischemia-reperfusion rats. Behav Brain Res. 2025; 476:115267. doi:10.1016/j.bbr.2024.115267
75. Shao A, Guo S, Tu S, Ammar A, Tang J, Hong Y, et al. Astragaloside IV alleviates early brain injury following experimental subarachnoid hemorrhage in rats. Int J Med Sci. 2014;11(10):1073–81.
76. Xia M-L, Xie X-H, Ding J-H, Du R-H, Hu G. Astragaloside IV inhibits astrocyte senescence: implication in Parkinson's disease. J Neuroinflammation. 2020;17(1):105.
77. Yao M, Zhang L, Wang L. Astragaloside IV: A promising natural neuroprotective agent for neurological disorders. Biomed Pharmacother. 2023;159:114229.
78. Zhang W-D, Chen H, Zhang C, Liu R-H, Li H-L, Chen H-Z. Astragaloside IV from *Astragalus membranaceus* shows cardioprotection during myocardial ischemia in vivo and in vitro. Planta Med. 2006;72(1):4–8.
79. Zhang X, Qu H, Yang T, Liu Q, Zhou H. Astragaloside IV attenuate MI-induced myocardial fibrosis and cardiac remodeling by inhibiting ROS/caspase-1/GSDMD signaling pathway. Cell Cycle. 2022;21(21):2309–22.
80. Greeny A, Viswanatha GL, Shenoy RR, Hanumanthappa S, Chellappan DK, Sandhu JS, et al. Exploring Astragaloside IV in Ischemic Heart Disease: A Comprehensive Systematic Review and Meta-Analysis of Preclinical Cardiotoxicity Models. J Biochem Mol Toxicol. 2025;39(7):e70365.
81. Yang C, Pan Q, Ji K, Tian Z, Zhou H, Li S, et al. Review on the protective mechanism of astragaloside IV against cardiovascular diseases. Front Pharmacol. 2023;14:1187910.
82. Xiao Y, Liu T, Liu X, Zheng L, Yu D, Zhang Y, et al. Total *Astragalus* saponins attenuates CVB3-induced viral myocarditis through inhibiting expression of tumor necrosis factor α and Fas ligand. Cardiovasc Diagn Ther. 2019;9(4):337–45. doi:10.21037/cdt.2019.07.11
83. Jing H, Xie R, Bai Y, Duan Y, Sun C, Wang Y, et al. The Mechanism Actions of Astragaloside IV Prevents the Progression of Hypertensive Heart Disease Based on Network Pharmacology and Experimental Pharmacology. Front Pharmacol. 2021;12:755653.
84. Cui Z, Shang Q. Mechanistic insights into the antitumor effects of astragaloside IV and *Astragalus* polysaccharide in digestive system cancers. Front Pharmacol. 2025; 16:1691011. doi:10.3389/fphar.2025.1691011
85. Auyeung KK, Woo PK, Law PC, Ko JK. *Astragalus* saponins modulate cell invasiveness and angiogenesis in human gastric adenocarcinoma cells. J Ethnopharmacol. 2012; 141(2):635–41. doi:10.1016/j.jep.2011.08.010
86. Qu X, Gao H, Zhai J, Sun J, Tao L, Zhang Y, et al. Astragaloside IV enhances cisplatin chemosensitivity in hepatocellular carcinoma by suppressing MRP2. Eur J Pharm Sci Off J Eur Fed Pharm Sci. 2020;148:105325.
87. Gu Y, Wang G, Pan G, Fawcett JP, A J, Sun J. Transport and bioavailability studies of astragaloside IV, an active ingredient in Radix Astragali. Basic Clin Pharmacol Toxicol. 2004;95(6):295–8.
88. Ran R, Zhang C, Li R, Chen B, Zhang W, Zhao Z, et al. Evaluation and comparison of the inhibition effect of astragaloside IV and aglycone cycloastragenol on various UDP-glucuronosyltransferase (UGT) isoforms. Molecules. 2016;21:1616. doi:10.3390/molecules21121616
89. Zhu Y, Chai Y, Xiao G, Liu Y, Xie X. *Astragalus* and its formulas as a therapeutic option for fibrotic diseases: Pharmacology and mechanisms. Front Pharmacol. 2022; 3(13):1040350. doi:10.3389/fphar.2022.1040350
90. Zhang W-D, Zhang C, Liu R-H, Li H-L, Zhang J-T, Mao C, et al. Preclinical pharmacokinetics and tissue distribution of a natural cardioprotective agent astragaloside IV in rats and dogs. Life Sci. 2006;79(8):808–15.
91. Xiong B-B, Zhuo Y-M, Wang H, Zheng Q-L, Tang F, Huang Q, et al. Macrophage polarization in disease therapy: insights from astragaloside IV and cycloastragenol. Front Pharmacol. 2025;16:1598022.
92. Zhang Y-H, Zhang Y-J, Guo Y-L, Li W-J, Yu C. Astragaloside IV inhibited the activity of CYP1A2 in liver microsomes and influenced theophylline pharmacokinetics in rats. J Pharm Pharmacol. 2013;65(1):149–55.
93. Li S, Hu X, Liu F, Hu W. Bioactive components and clinical potential of *Astragalus* species. Front Pharmacol. 2025; 16:1585697. doi:10.3389/fphar.2025.1585697
94. Salehi B, Carneiro JNP, Rocha JE, Coutinho HDM, Morais Braga MFB, Sharifi-Rad J, et al. *Astragalus* species: Insights on its chemical composition toward pharmacological applications. Phytother Res. 2021;35(5):2445–76.
95. Gao X, Hao W, Wang Y, Wu X, Zhu F, Zhang Y. Molecular mechanisms of astragaloside-IV in hepatocellular carcinoma therapy: a systematic review. BMC Cancer. 2025; 25(1):1407. doi:10.1186/s12885-025-14758-w