Mechanistic insights into the roles of astragalosides and *Astragalus* polysaccharides in gynecological and breast cancers (Review)

RUIXIN LIU[1], ZHANYU LIN[2], YUELIN LI[1], YUETONG CI[1], ZHENGQI GUO[1] and ZHENGUO XU[3]

[1]Department of Acupuncture and Massage College, Shandong University of Traditional Chinese Medicine, Jinan, Shandong 250000, P.R. China; [2]Department of Traditional Chinese College, Shandong University of Traditional Chinese Medicine, Jinan, Shandong 250000, P.R. China; [3]Department of General Surgery, Affiliated Hospital of Shandong University of Traditional Chinese Medicine, Jinan, Shandong 250355, P.R. China

Received November 11, 2025; Accepted February 11, 2026

DOI: 10.3892/or.2026.9102

Abstract. *Astragalus membranaceus*, a Qi-tonifying herb widely used in traditional Chinese medicine, has emerged as a promising adjuvant for female-predominant malignancies, including breast, ovarian and cervical cancers. Its major bioactive constituents, *Astragalus* polysaccharides (APS) and astragalosides (AST), exert multitarget antitumor activities and are widely used as complementary agents in clinical oncology. Nevertheless, key mechanistic gaps persist, particularly regarding the crosstalk among the PI3K/Akt/mTOR, Wnt/β-catenin, JNK/MAPK and TGF-β/Smad pathways, as well as the subtype- and context-dependent regulation of molecular effectors governing programmed cell death, epithelial-mesenchymal transition and immune reprogramming. This uncertainty constrains biomarker discovery and the rational design of combination regimens, thereby limiting the predictability of clinical benefit. The present review systematically collates current research on the molecular mechanisms and signaling networks through which APS and AST modulate breast, ovarian and cervical cancer biology. Available data indicate that these compounds suppress tumor initiation and progression by inhibiting proliferation, inducing programmed cell death, attenuating invasion and metastasis, reshaping antitumor immunity and macrophage polarization, and potentiating chemotherapeutic efficacy while mitigating treatment-related toxicity. Overall, these insights aim to provide a mechanistic rationale for the clinical integration of *A. membranaceus* as an adjuvant therapy in gynecological and breast cancers, to bridge traditional Chinese medicine with contemporary pharmacology, and to support the development of individualized, integrative therapeutic strategies for breast, ovarian and cervical cancers.

Correspondence to: Dr Zhenguo Xu, Department of General Surgery, Affiliated Hospital of Shandong University of Traditional Chinese Medicine, 16369 Jingshi Road, Jinan, Shandong 250355, P.R. China
E-mail: 464584206@qq.com

Key words: *Astragalus membranaceus*, astragalosides, *Astragalus* polysaccharides, gynecological tumors, breast cancer

Contents

1. Introduction

Gynecological malignancies, particularly cervical and ovarian cancers, remain a major threat to women's health and contribute substantially to the global disease burden. Cervical cancer is the fourth most common cancer in women worldwide and accounts for ~6.5% of all female cancer cases (1). It is often highly invasive and frequently diagnosed at an advanced stage, resulting in considerable mortality and morbidity (2). Ovarian cancer carries an estimated lifetime risk of ~2% in women, and both incidence and mortality increase with age (3). Each year, ~239,000 new ovarian cancer cases are reported globally, with an estimated 152,000 associated deaths (4). Because ovarian cancer is typically insidious in onset and effective screening strategies remain limited, the 5-year survival rate remains <20%, underscoring the urgency for improved prevention and treatment approaches (5).

Although breast cancer is not traditionally categorized as a gynecological malignancy, it is closely linked to women's health and remains a leading cause of cancer-related mortalities among women. Its complex pathogenesis and heterogeneous clinical presentation continue to pose major challenges for effective prevention and management (6). Breast cancer is the most commonly diagnosed malignancy in women, with ~1.7 million new cases annually, and both incidence and mortality are projected to rise further over the next decade (7). Beyond disease-specific symptoms such as abnormal bleeding, pain and reproductive dysfunction (8), breast cancer, ovarian

cancer and cervical cancer can necessitate mastectomy or resection of reproductive organs, and may lead to premature menopause and infertility, with profound consequences for physical and psychological well-being. They also impose substantial psychosocial burdens, affecting family relationships and overall quality of life, and have therefore attracted increasing clinical and public attention (9).

Astragalus membranaceus, known as Huangqi, is a perennial herb in the Fabaceae family. It typically reaches a height of 50 to 100 cm and bears a thick cylindrical root that is light brown on the exterior and yellow white internally, with a firm and fibrous texture. The main and lateral roots are used medicinally, and the most commonly utilized sources are *Astragalus membranaceus* (Fisch.) Bge. *var. mongholicus* and *Astragalus membranaceus* (Fisch.) Bge. (10). *Astragalus* contains diverse chemical constituents, including saponins, polysaccharides, flavonoids, amino acids, as well as trace elements, such as zinc and iron.. Among these, saponins and polysaccharides are regarded as the principal bioactive components (11). The saponin fraction consists predominantly of triterpenoid saponins, with astragalosides (AST) I, II and IV and isoastragalosides I and II accounting for >80% of total saponins (12). *Astragalus* polysaccharides (APS) are water-soluble macromolecules extracted mainly from the stems or roots and represent one of the most important naturally derived active ingredients of *Astragalus* (13). Wild *Astragalus* species are primarily distributed across northern China, Kazakhstan, Mongolia and the Russian Far East, with the largest cultivation area located in northern China (14). Increasing evidence has identified *Astragalus* as a rich source of bioactive compounds with potent antitumor potential (15-17).

Previous reviews have largely focused on the anticancer mechanisms of individual *Astragalus* constituents in single tumor types. By contrast, evidence regarding the effect of AST and APS in gynecological and breast cancers remains scattered and has not been systematically integrated. To address this gap, the present review provided a comprehensive summary of the molecular mechanisms and signaling pathways through which AST and APS exert therapeutic effects in breast, ovarian, and cervical cancers. This study aims to establish an integrated pharmacological framework and to support the development of integrative and precision treatment strategies for women's cancers worldwide, as illustrated in Fig. 1.

2. Clinical applications and pharmacological basis of Astragalus membranaceus

Major bioactive components of Astragalus membranaceus. Astragalus membranaceus produces a broad spectrum of biologically active secondary metabolites, with triterpenoid saponins and polysaccharides representing the major classes. Triterpenoid saponins are formed through conjugation of triterpene aglycones with sugars or other substituent groups, and their biosynthesis proceeds via multiple enzyme-mediated steps that include precursor generation and carbon ring assembly. Polysaccharides derived from *Astragalus* comprise heteropolysaccharides, neutral polysaccharides, glucans and acidic polysaccharides, with β- (1→4)-glucosidic linkages as the predominant glycosidic bonds (18). Due to the amphiphilic properties of saponins, a variety of extraction approaches using aqueous or alcoholic solvents have been developed. Among these, n-butanol and methanol are considered particularly efficient for isolating triterpenoid saponins (19). Conventional preparation of APS typically relies on solvent or aqueous extraction followed by ethanol precipitation, which remains a widely used and technically straightforward method (20). Pharmacological evidence indicates that AST can downregulate p21 and Bcl-xL, and upregulate Caspase-3 and cleaved PARP. It mainly exerts its antitumor effects by inhibiting tumor cell proliferation and inducing cell apoptosis (21). APS also displays a broad range of biological activities, including antitumor, anti-aging and antiviral effects (22-24). These actions are mediated through multiple mechanisms, such as modulation of immune responses, promotion of apoptotic signaling, and inhibition of tumor invasion and metastasis (25).

Clinical indications of Astragalus membranaceus. Astragalus membranaceus has traditionally been used to enhance immune function and support overall physiological homeostasis. In contemporary oncology, it is increasingly applied as an adjuvant therapy, with particular relevance to the management of common malignancies in women, such as breast, cervical and ovarian cancers (26). A pharmacological study indicates that bioactive constituents of *Astragalus*, such as astragaloside III, exert bidirectional immunomodulatory actions by activating immune effector cells, including lymphocytes and natural killer (NK) cells, thereby strengthening antitumor immunity. These constituents may also mitigate immunosuppressant-associated myelosuppression, which can improve therapeutic efficacy and reduce treatment-related adverse effects (27). In addition, APS has been reported to upregulate IL-12, TNF-α, Bax and Caspase-3, and downregulate Bcl-2, thereby exerting antitumor activities through immune regulation, induction of tumor cell apoptosis, and inhibition of invasion and migration (28,29).

Clinical evidence further suggests that APS can enhance treatment responses and improve immune status in patients with cancer. Compared with radiotherapy alone, combined radiotherapy and APS has been associated with an increased $CD4^+$ to $CD8^+$ ratio in breast cancer and other malignancies, which may contribute to improved clinical outcomes (30). However, clinical studies specifically evaluating AST and APS remain limited. Most available evidence derives from investigations of *Astragalus* as a whole herb or from traditional Chinese medicine formulas in which *Astragalus* is a principal component. This pattern reflects current clinical practice, where compound prescriptions are commonly used, and findings from formula-based studies are more readily translatable to real-world application. For example, clinical data indicate that *Astragalus*-based formulas combined with chemotherapy can reduce post-chemotherapy adverse reactions and chemotherapy-associated hepatorenal toxicity in cervical cancer while improving overall efficacy (31). Additional clinical studies have reported that *Astragalus* may alleviate common cancer-related complications and improve patient quality of life (32).

Beyond oncology, *Astragalus* has shown beneficial effects in anti-inflammatory, antioxidant and anti-infective settings (33-35). Accordingly, its use in patients with cancer is primarily supported by its roles in immunoregulation and functional support. In this population, *Astragalus* may help

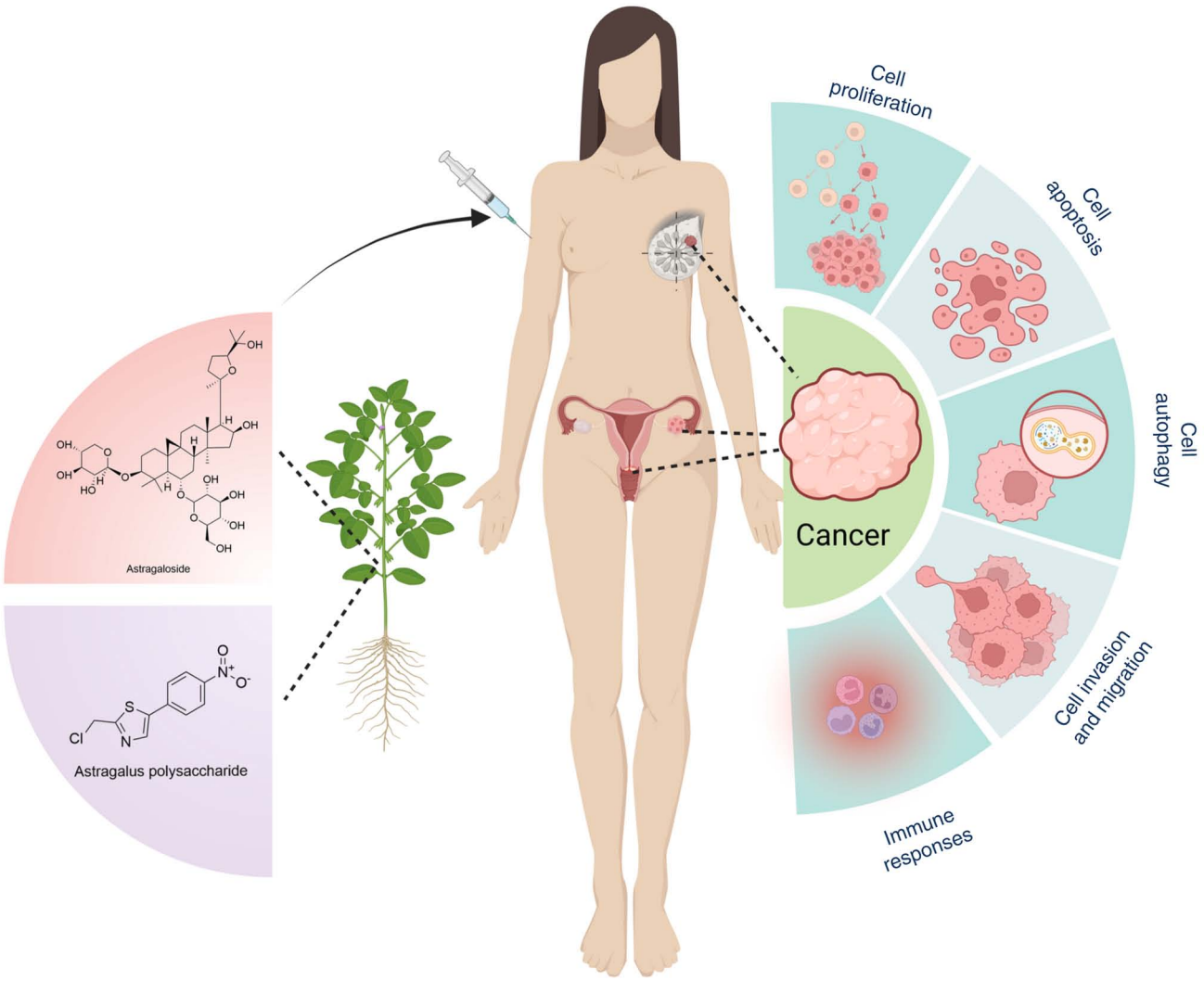

Figure 1. Astragalosides and *Astragalus* polysaccharides in the treatment of gynecological tumors and breast cancer.

relieve frequent symptoms such as fatigue (36), anorexia (37) and vomiting (38), while enhancing immune competence and improving quality of life (39). Therefore, in the clinical management of female malignancies, *Astragalus* and its preparations are widely used as adjunctive interventions to improve treatment tolerance, support therapeutic response and potentially enhance prognosis.

3. Mechanisms of Astragalus active constituents in female malignancies

Mechanisms of Astragalus constituents in breast cancer

Mechanisms of APS in breast cancer. Disruption of cellular homeostasis is a fundamental driver of tumor initiation and progression. Uncontrolled tumor cell proliferation frequently results from impaired apoptosis, a form of programmed cell death that is essential for maintaining tissue integrity. Programmed cell death not only shapes the immunosuppressive tumor microenvironment but also markedly influences therapeutic responses to anticancer treatments (40). Li *et al* (41) reported that APS activates RAW264.7 macrophages and increases the production of nitric oxide (NO) and tumor necrosis factor alpha (TNF-α), thereby inducing apoptosis and inhibiting the proliferation of breast cancer cells. In a related study, Li *et al* (42) showed that APS increased ANXA1 mRNA and protein expression while reducing epidermal growth factor receptor (EGFR) mRNA levels in GFP-4T1 cells, suggesting that APS may promote programmed cell death through coordinated upregulation of ANXA1 and suppression of EGFR signaling.

Advances in drug delivery have further expanded the therapeutic potential of APS. A dual-targeted nanodelivery system based on quercetin 3 prime,3 prime dithiodipropionic acid, APS, and folate, termed Nano Pomegranate, effectively induced programmed cell death in breast cancer cells and demonstrated improved antitumor efficacy with fewer adverse effects compared with free curcumin, highlighting its translational promise (43). In triple negative breast cancer (TNBC) 4T1 cells, Sun *et al* (44) found that 24 h co-treatment with APS and cisplatin significantly enhanced apoptosis by downregulating Bcl-2 and Bcl-xL and upregulating PUMA, cleaved caspase 3, and cleaved PARP. The combination also increased E-cadherin expression. Because E-cadherin is central to cell-cell adhesion, its loss is closely associated with epithelial mesenchymal transition (EMT), enhanced invasiveness, and poor prognosis across multiple cancers (45). Consistently,

Yang *et al* (46) reported that APS treatment for 24 h reduced Snail and vimentin expression, decreased Wnt1 and β-catenin levels, and increased E-cadherin expression in MCF 7 and MDA MB 231 cells, supporting inhibition of Wnt/β-catenin signaling and suppression of breast cancer cell proliferation, invasion, and migration.

Beyond direct cytotoxicity, APS also exerts immunomodulatory and synergistic anticancer effects. Zhou *et al* (47) showed that APS stimulates RAW264.7 macrophages to secrete immunoregulatory mediators including NO, TNF-α, IL-1β, and IL-6 through activation of the Toll-like receptor 4- and MyD88-dependent pathways, thereby enhancing antitumor immunity. Moreover, Bao *et al* (48) demonstrated that APS attenuates paclitaxel-induced cytotoxicity in RAW264.7 cells by downregulating phospho-histone H2A (P-HA), PARP, checkpoint kinase 1, p53 and p21 while upregulating Bcl-xL and Mcl-1. This selective protection of immune cells may improve the therapeutic index of paclitaxel in breast cancer treatment.

Mechanisms of AST in breast cancer. Accumulating evidence indicates that ASTs, particularly astragaloside IV (AS-IV), exert robust antitumor effects through multiple mechanisms (49). Because chemoresistance remains a major barrier to effective cancer therapy (50), a study has investigated the potential of AS-IV to restore treatment sensitivity. Lou *et al* (51) reported that AS-IV upregulates Nrf2 and increases intracellular ATP levels, thereby enhancing the efflux function of breast cancer resistance protein (BCRP). Huang *et al* (52) showed that AS-IV markedly reduces the stemness of breast cancer stem cells and reverses paclitaxel resistance in MCF7-derived cancer stem cells by modulating the (hypoxia-inducible factor) HIF-1α/HIF-2α axis and inhibiting Notch, PI3K/Akt/mTOR and JAK/STAT3 signaling. Caveolin-1, a membrane protein linked to metastasis and drug resistance (53), has also been reported to be downregulated by AS-IV in a dose-dependent manner. This change activates the endothelial nitric oxide (NO) synthase (eNOS)/NO/peroxynitrite ($ONOO^-$) pathway, promotes oxidative damage, and increases paclitaxel sensitivity in MCF 7 and MDA MB 231 cells (54). In addition, a liposomal co-delivery system incorporating oxymatrine and AS-IV suppresses cancer-associated fibroblast activation and increases tumor-infiltrating lymphocytes, thereby potentiating the efficacy of programmed cell death protein 1 inhibitors and supporting the potential utility of AS-IV-based strategies in breast cancer immunotherapy (55).

Beyond chemosensitization, AS-IV also inhibits invasion and metastasis through modulation of tumor and microenvironmental signaling. Yu *et al* (56) found that AS-IV downregulated TGF-β and suppressed Akt/forkhead box protein (FOX)O1 signaling in THP-1-derived macrophages. This effect reduced M2 polarization and decreased the expression of IL-10, MMP-9, CD206, CD163 and TGF-β, which in turn limited macrophage-mediated breast cancer cell proliferation, invasion and migration. Vav3, a guanine nucleotide exchange factor that promotes tumor proliferation and invasion when overexpressed (57), has been identified as another target of AS-IV. Jiang *et al* (58) reported that AS-IV downregulated Vav3 and its downstream effectors, ERK1/2, JNK, MMP-2 and MMP-9, thereby reducing Rac1 activation and inhibiting breast cancer cell viability and motility. Similarly, Hu *et al* (59) demonstrated that AS-IV induced the long non-coding RNA TRHDE-AS1 in MCF-7 and MDA-MB-231 cells in a dose- and time-dependent manner, leading to reduced proliferation and invasion *in vitro* and *in vivo*. Moreover, Yang *et al* (60) demonstrated that AS-IV activated the transcription factor FOXA1 and upregulates galactose-3-O-sulfotransferase 1, thereby suppressing proliferation and viability in obesity-associated triple negative breast cancer by remodeling sphingolipid metabolism.

Collectively, APS related studies in breast cancer have primarily employed RAW264.7 macrophages and TNBC 4T1 cells, with an emphasis on inhibiting proliferation, inducing apoptosis, modulating immunity and enhancing chemotherapeutic efficacy (41-44,46-48). By contrast, studies of AS-IV have largely relied on MCF-7 and MDA-MB-231 models and have highlighted regulation of Akt/FOXO1, eNOS/NO/ONOO and Rac1/MAPK signaling, together with their associated molecular targets (51,52,54-56,58-60), as summarized in Fig. 2.

Mechanisms of Astragalus active constituents in ovarian cancer

Mechanisms of APS in ovarian cancer. APS are natural compounds with strong immunomodulatory and antitumor properties (61) and have gained attention as potential therapeutic agents for ovarian cancer. Growing evidence indicates that APS suppresses tumor growth by inhibiting cancer cell proliferation and promoting apoptosis. Guo *et al* (62) reported that APS reduced microRNA (miR)-27a expression in a dose-dependent manner, which increased the expression of the tumor suppressor FBXW7 and consequently inhibited proliferation while inducing apoptosis in the human ovarian cancer cell line OV-90. Consistently, Li *et al* (63) showed that APS combined with cisplatin markedly decreased SKOV3 cell viability and enhanced apoptosis by downregulating Bcl-2, upregulating Bax and caspase-3, and activating JNK1/2 signaling. This synergistic interaction increased cisplatin sensitivity and strengthened its antitumor activity in ovarian cancer.

Cancer stem cells are closely linked to recurrence and chemoresistance (64). Peng *et al* (65) demonstrated that APS downregulates PTEN-induced kinase 1 (PINK1) and suppresses mitochondrial autophagy through the PINK1/Parkin pathway, thereby increasing the sensitivity of ovarian cancer stem cells to poly (ADP-ribose) polymerase inhibitors. This combination promoted apoptosis and reduced both viability and self-renewal capacity of ovarian cancer stem cells.

APS also modulates immune responses relevant to ovarian cancer. Shokati *et al* (66) found that 7 day exposure of peripheral blood mononuclear cells to APS significantly increased cell proliferation, reduced the proportion of regulatory T cells in the T cell population, decreased expression levels of anti-inflammatory mediators including IL-10, TGF-β and VEGF-A, and increased the levels of proinflammatory cytokine IL-6, collectively supporting enhanced antitumor immunity. In addition, Liu *et al* (67) developed an APS-based micellar delivery system modified with methotrexate and podophyllotoxin. This formulation increased TNF-α and

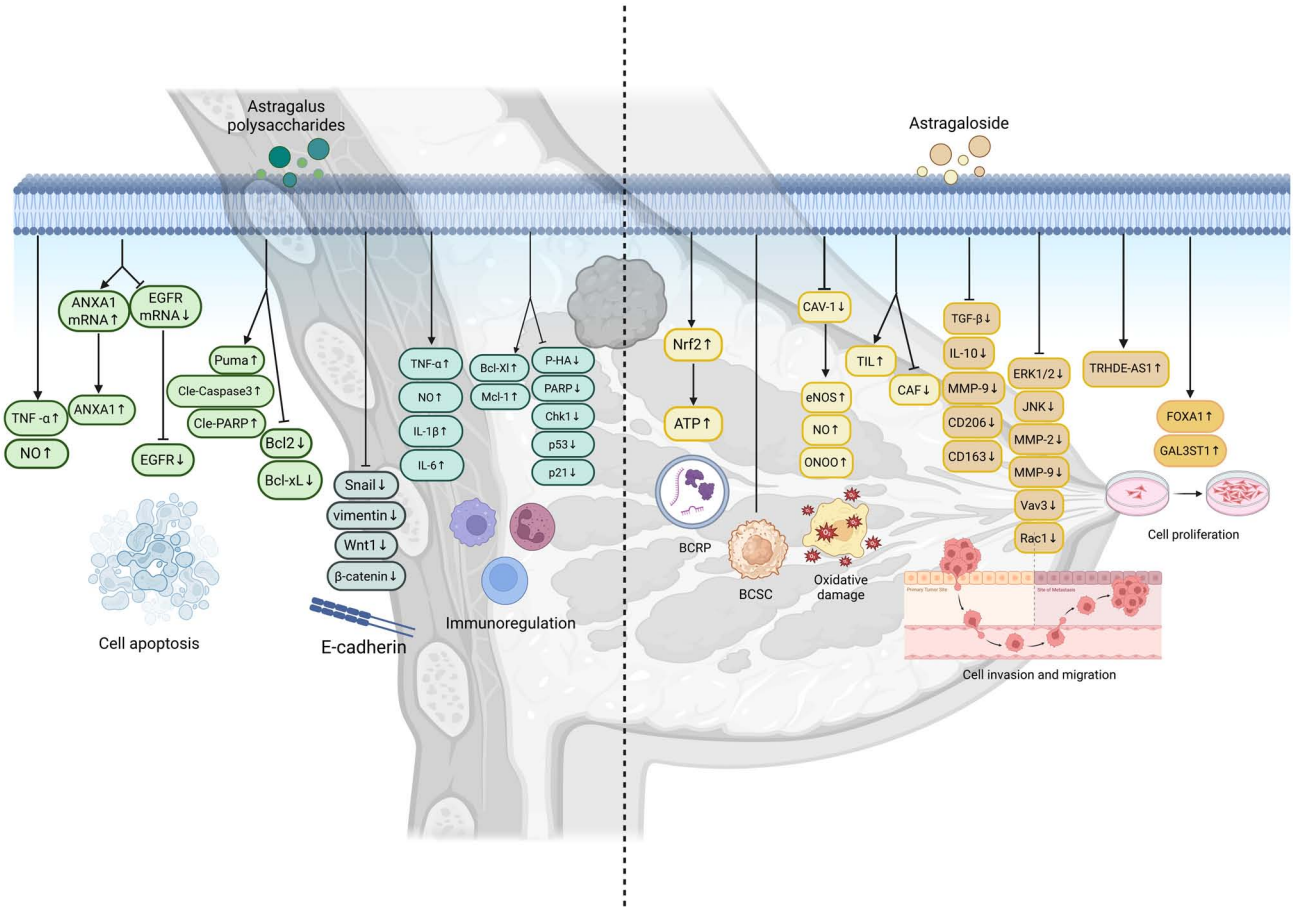

Figure 2. Mechanism of action of *Astragalus* polysaccharides and astragalosides in treating breast cancer. ANXA, annexin A1; NO, nitric oxide; P-HA, phospho-histone H2A; Chk1, checkpoint kinase 1; BCRP, breast cancer resistance protein; BCSC, breast cancer stem cells; ONOO, peroxynitrite; eNOS, endothelial nitric oxide synthase; CAV-1, caveolin-1; TIL, tumor-infiltrating lymphocytes; CAF, cancer-associated fibroblasts; TRHDE-AS1, the lncRNA of TRHDE antisense RNA 1; FOXA1, forkhead box A1; GAL3ST1, galactose-3-o-sulfotransferase 1.

IL-12p40 levels while reducing IL-4 and TGF-β1 expression levels, and it promoted repolarization of tumor associated macrophages from an M2-like state toward an M1-like phenotype, supporting immune mediated targeting of ovarian cancer.

Mechanisms of AST in ovarian cancer. Given the high rates of chemoresistance and recurrence in ovarian cancer, natural products with intrinsic antitumor activity, including AST, are increasingly investigated as potential adjunctive therapies. Zhang *et al* (68) demonstrated in both *in vitro* and *in vivo* models that astragaloside II enhances cisplatin efficacy by downregulating multidrug resistance protein 1 (MDR1), the cell cycle regulator cyclin D1 and proliferating cell nuclear antigen, while upregulating apoptosis-associated proteins PARP and caspase-3. This coordinated regulation promoted apoptosis and inhibited ovarian cancer cell proliferation, thereby increasing cisplatin sensitivity. AS-IV has also been reported to influence ovarian cancer progression through immune microenvironment modulation. Wang *et al* (69) treated IL-4/IL-13-induced THP-1 derived macrophages with AS-IV and found that it suppressed the overexpression of high mobility group box 1 (HMGB1) and Toll-like receptor 4 (TLR4), reduced the secretion of M2-associated factors including TGF-β, MMP-9 and IL-10, and inhibited ovarian cancer cell proliferation, invasion and migration by promoting macrophage repolarization. In addition, Dekinash *et al* (70) profiled methanolic *Astragalus* extracts using HPLC-MS/MS and identified six saponins and five flavonoids with moderate cytotoxic activity against SKOV3 ovarian cancer cells, as reflected by reduced cell viability, which supports a direct antiproliferative potential of the extract.

Collectively, APS-related studies in ovarian cancer, which primarily use human cell lines such as OV-90 and SKOV3, have focused on mechanistic axes including miR-27a/FBXW7, JNK1/2 and PINK1/Parkin. These findings suggest that APS inhibits proliferation, induces programmed cell death, regulates immune responses, modulates macrophage polarization and can synergize with chemotherapeutic agents to enhance efficacy while reducing toxicity. The development of APS-based delivery systems further supports translational potential (62,63,65-67). By contrast, studies on AST have mainly examined their roles in suppressing proliferation, promoting apoptosis, improving chemosensitivity and reshaping macrophage polarization, with particular emphasis on HMGB1-TLR4 signaling (68-70), as summarized in Fig. 3.

Mechanisms of Astragalus bioactive constituents in cervical cancer

Mechanisms of APS in cervical cancer. As principal bioactive constituents of *Astragalus membranaceus*, APS have potential

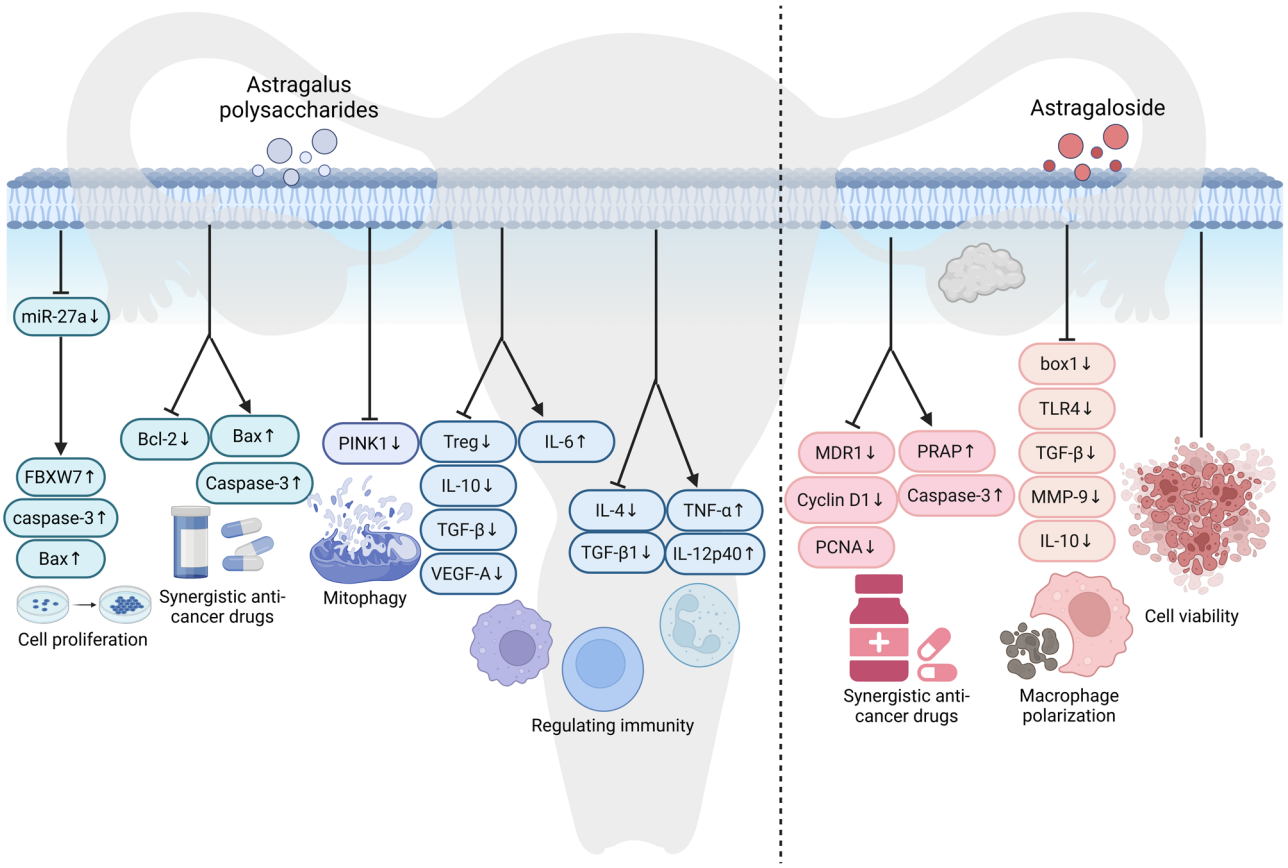

Figure 3. Therapeutic mechanism of *Astragalus* Polysaccharides and astragalosides against ovarian cancer. miR, microRNA; FBXW7, F-box and WD-40 domain protein 7; PINK1, PTEN-induced kinase 1; Treg, regulatory T cells; MDR1, multidrug resistance protein 1; PCNA, proliferating cell nuclear antigen; box1, high mobility group box 1; TLR4, toll-like receptor 4.

therapeutic value in cervical cancer. Liu *et al* (71) reported that 24 h treatment of cisplatin-resistant cervical cancer cells with APS increased peroxisome proliferator-activated receptor δ (PPARD) expression, which in turn suppressed CDC20 transcription and inhibited Wnt/β-catenin signaling. This regulatory effect markedly enhanced cisplatin sensitivity, reduced proliferative capacity, and promoted apoptosis. These findings suggest that APS may exert antitumor activity in cervical cancer by modulating cell cycle regulation and reversing chemoresistance.

Mechanisms of AST in cervical cancer. Clarifying the mechanisms through which AST regulate cervical cancer progression is essential for defining their clinical potential. Available evidence indicates that AST can inhibit cervical cancer cell invasion and migration through multiple signaling pathways. Xia *et al* (72), using integrated *in vitro* and *in vivo* assays together with quantitative proteomics, reported that AS-IV increased Atg12 expression and upregulated mRNA-decapping enzyme 1A and Thymosin β-4, thereby inducing autophagy and suppressing cervical cancer cell proliferation and invasion. EMT is a critical process that promotes tumor cell invasion and migration (73). Zhang *et al* (74) found that 24 h AS-IV treatment reduced TGF-β1 expression and increased E-cadherin levels, while inhibiting phosphorylation of MAPK and PI3K. These effects were associated with EMT suppression and reduced invasive and migratory capacity of cervical cancer cells. Macrophages, which are abundant stromal components within the tumor microenvironment, also contribute to cancer progression through polarization-dependent functions (75). Shen *et al* (76) demonstrated that AS-IV downregulated TGF-β and decreased phosphorylated Smad2 and Smad3 in cervical cancer cells. Inhibition of TGF-β/Smad2/3 signaling reduced macrophage M2 polarization and consequently restrained EMT progression, migration and angiogenesis.

Overall, the study of APS in cervical cancer has focused primarily on enhancing chemosensitivity, suppressing proliferation and inducing programmed cell death through pathways involving PPARD, CDC20 and Wnt/β-catenin signaling (71). Research on AST, largely conducted in SiHa cervical cancer cells and macrophage models, has emphasized regulation of MAPK/PI3K signaling and the TGF-β/Smad2/3 axis (72,74,76). Reported mechanisms include inhibition of EMT, suppression of invasion and migration, and induction of autophagy (72,74,76), as summarized in Fig. 4.

In summary, the antitumor mechanisms of APS across breast, ovarian and cervical cancers are most consistently linked to immunomodulation and apoptosis induction, with frequent involvement of JNK1/2, Wnt/β-catenin and PINK1/Parkin signaling, as well as downstream effectors including TNF-α, IL-6, IL-1β, NO, Bcl-2 and Bax. By contrast, the predominant actions of AST involve reversal of drug resistance, enhancement of chemosensitivity, and inhibition of invasion and metastasis. These effects are largely mediated through

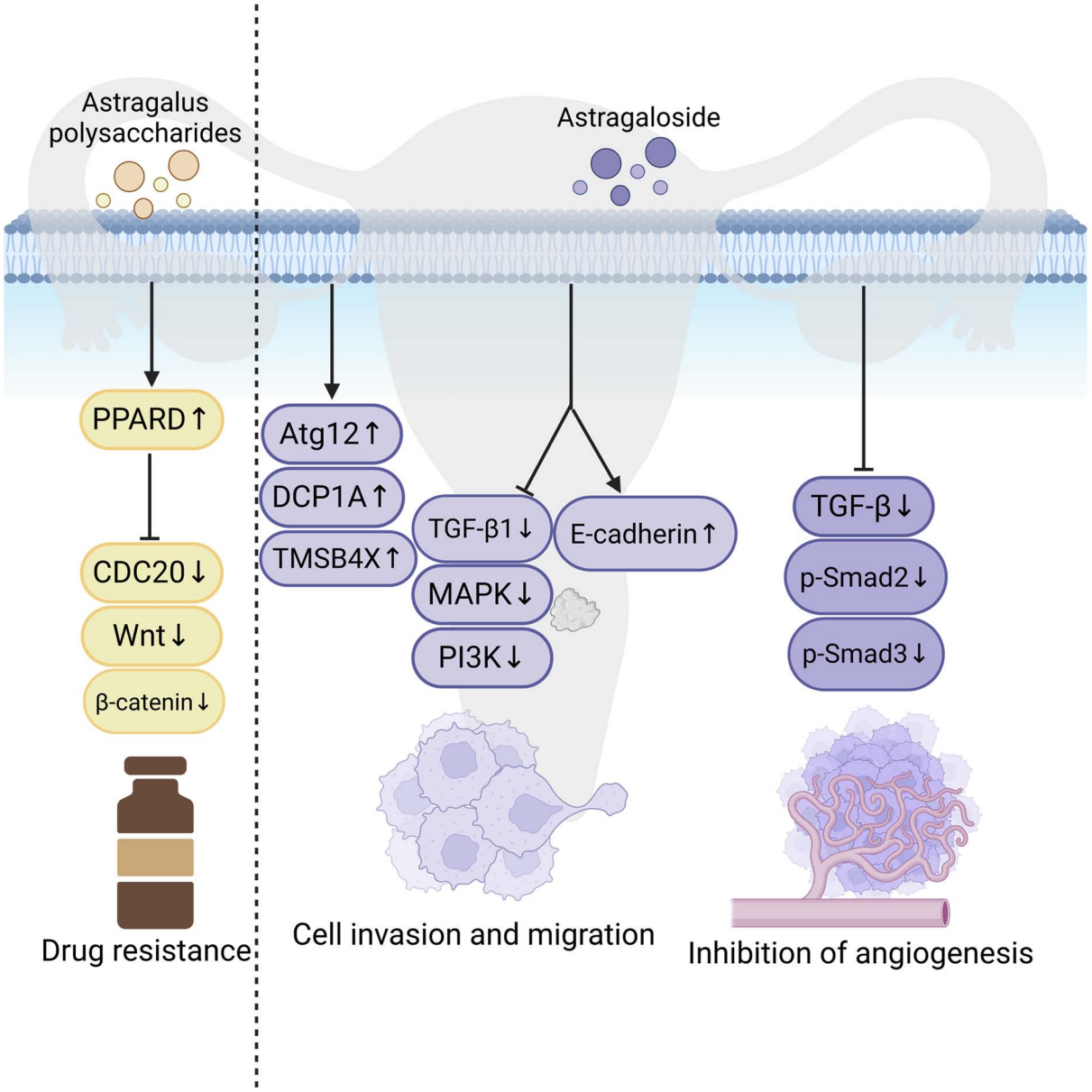

Figure 4. Mechanisms by which *Astragalus* polysaccharides and astragalosides act against cervical cancer. PPARD, peroxisome proliferator-activated receptor δ; DCP1A, mRNA-decapping enzyme 1A; TMSB4X, thymosin β-4; p-, phosphorylated.

the PI3K/Akt/mTOR, TGF-β/Smad, eNOS/NO/ONOO and Rac1/MAPK pathways, highlighting the multitarget antitumor potential of *Astragalus* bioactive constituents in gynecological malignancies, as summarized in Table I.

4. Discussion

APS and AST show therapeutic potential against breast, ovarian and cervical cancers by acting on diverse molecular targets and signaling pathways. The present review systematically synthesizes the antitumor mechanisms of APS and AST, the major bioactive constituents of *Astragalus membranaceus*, in gynecological malignancies and delineates their key targets and regulatory networks. These insights provide a mechanistic rationale for the clinical use of *Astragalus* as an adjuvant therapy in breast, ovarian and cervical cancers. Notably, because intratumoral heterogeneity is substantial across malignancies, the biological effects of *Astragalus* constituents are likely to vary among tumor subtypes. In clinical practice, breast cancer is commonly classified according to molecular features and biological behavior (77) into Luminal A, Luminal B, HER2-enriched and TNBC (78). The studies included in the current review placed particular emphasis on TNBC, where APS and AST most consistently suppress tumor cell proliferation and promote apoptosis, thereby offering mechanistic support and new directions for therapeutic development in this refractory subtype. By contrast, subtype-specific evidence in ovarian and cervical cancers remains limited. A number of studies have treated these malignancies as single disease entities in mechanistic investigations, and the present review reflects the current evidence base. This gap highlights the need for future research integrating refined pathological and molecular subtyping to better define subtype dependent responses and therapeutic potential.

Table I. Mechanism of *Astragalus* polysaccharides and astragalosides in gynecological tumors and breast cancer.

A, Breast cancer (treated with APS)

Experimental models (animal/cell)	Possible mechanisms	Targets	Doses	(Refs.)
Cell: MCF-7, RAW264.7	Induce apoptosis in tumor cells and inhibit tumor cells proliferation	NO↑, TNF-α↑	1,000 μg/ml	(41)
Animal: BALB/c mice Cell: GFP-4T1	Induce programmed cell death in tumor cells and inhibit tumor cells proliferation	ANXA1 mRNA↑, ANXA1↑, EGFR mRNA↓, EGFR↓	200 mg/kg	(42)
Cell: MCF-7	Induce programmed cell death in tumor cells	NA	20 mg/ml	(43)
Cell: TNBC 4T1 Animal: BALB/c mice	Synergistic cisplatin, induce apoptosis in tumor cells	Bcl2↓, Bcl-xL↓, Puma↑, Cle-Caspase3↑, Cle-PARP↑	2.5 mM, 100 mg/kg	(44)
Cell: MCF7, Mda-MB-231	Inhibit tumor cells proliferation, invasion, and migration	Snail↓, vimentin↓, Wnt1↓, β-catenin↓	800 μg/ml	(46)
Cell: RAW264.7	Regulate immunity	NO↑, TNF-α↑, IL-1β↑, IL-6↑	400 μg/ml	(47)
Cell: 4T1 mouse breast cancer cell lines, RAW 264.7 Animal: BALB/c mice	Synergistic paclitaxel, regulate immunity	P-HA↓, PARP↓, Checkpoint kinase 1↓, p53↓, p21↓, Bcl-Xl↑, Mcl-1↑	50 μg/ml, 40 mg/kg	(48)

B, Breast cancer (treated with AST)

Experimental models (animal/cell)	Possible mechanisms	Targets	Doses	(Refs.)
Animal: Male C57BL/6 mice, Male Nrf2-/- C57BL/6 mice Cell: HepG2	Enhance the efflux activity of breast cancer resistance protein	Nrf2↑, ATP↑	150 mg/kg, 25 μM	(51)
Cell: MCF7-CSCs48 Animal: 5-week-old Balb/c-nu/nu female mice	Synergistic paclitaxel, reduce the stemness of breast cancer stem cells	NA	60 nM, 40 mg/kg	(52)
Cell: MCF-7, MDA-MB-231	Enhance sensitivity to the chemotherapy drug paclitaxel	CAV-1↓, eNOS↑, NO↑, ONOO↑	30 μM	(54)
Animal: BALB/c mice Cell: 4T1-luc, CTLL-2	Synergistically enhance the antitumor efficacy of programmed cell death protein-1 inhibitors	CAF↓, TIL↑	1.5 mg/kg	(55)
Cell: THP-1	Inhibit tumor cells proliferation, invasion, and migration	TGF-β↓, IL-10↓, MMP-9↓, CD206↓, CD163↓	50 μM	(56)
Cell: MDA-MB-231	Inhibit tumor cells invasion and migration	ERK1/2↓, JNK↓, MMP-2↓, MMP-9↓, Vav3↓, Rac1↓	40 μg/ml	(58)
Cell: MCF-7, MDAMB-231 Animal: BALB/c mice	Inhibit tumor cells proliferation, invasion, and migration	TRHDE-AS1↑	80 μg/ml, 20 mg/kg	(59)
Cell: MDA-MB-231, MDA-MB-468, MCF-10A	Inhibit tumor cells proliferation and viability	FOXA1↑, GAL3ST1↑	60 μM	(60)

C, Ovarian cancer (treated with APS)

Experimental models (animal/cell)	Possible mechanisms	Targets	Doses	(Refs.)
Cell: OV-90, SKOV-3, HEK 293T	Induce apoptosis in tumor cells and inhibit tumor cells proliferation	miR-27a↓, FBXW7↑, caspase-3↑, Bax↑	1 mg/ml	(62)
Cell: SKOV3	Inhibit tumor cells viability, promote tumor cells apoptosis, and enhance sensitivity to the chemotherapy drug cisplatin	Bcl-2↓, Bax↑, Caspase-3↑	800 μg/ml	(63)
Cell: 3AO, SKOV3	Induce tumor cells apoptosis and enhance sensitivity to PARPi	PINK1↓	200 mg/l	(65)

Table I. Continued.

C, Ovarian cancer (treated with APS)

Experimental models (animal/cell)	Possible mechanisms	Targets	Doses	(Refs.)
Cell: PBMC, A2780	Regulate immunity	Treg↓, IL-10↓, TGF-β↓, VEGF-A↓, IL-6↑	1,000 μg/ml	(66)
Cell: ID8, RAW264.7, SKOV3 Animal: Female C57BL/6 mice	Regulate immunity	TNF-α↑, IL-12p40↑, IL-4↓, TGF-β1↓	30 μM, 80 mg/kg	(67)

D, Ovarian cancer (treated with AST)

Experimental models (animal/cell)	Possible mechanisms	Targets	Doses	(Refs.)
Cell: A2780, SKOV3	Promote tumor cells apoptosis, inhibit tumor cells proliferation, and enhance sensitivity to the chemotherapy drug cisplatin	MDR1↓, Cyclin D1↓, PCNA↓, PARP↑, Caspase-3↑	160 μM, 320 μM	(68)
Cell: THP-1, SKOV3	Inhibit tumor cells proliferation, invasion and migration	Box1↓, TLR4↓, TGF-β↓, MMP-9↓, IL-10↓	100 μg/ml	(69)
Cell: SKOV-3	Reduce tumor cells viability	NA	100 μg/ml	(70)

E, Cervical cancer (treated with APS)

Experimental models (animal/cell)	Possible mechanisms	Targets	Doses	(Refs.)
Cell: Hela, SiHa, HCerEpics	Promote tumor cells apoptosis, inhibit tumor cells proliferation, and enhance sensitivity to the chemotherapy drug cisplatin.	PPARD↑, CDC20↓, Wnt↓, β-catenin↓	3 mg/ml	(71)

F, Cervical cancer (treated with AST)

Experimental models (animal/cell)	Possible mechanisms	Targets	Doses	(Refs.)
Cell: SiHa, HeLa	Inhibit tumor cells proliferation, invasion and migration	Atg12↑, DCP1A↑, TMSB4X↑	25 μM	(72)
Cell: SiHa	Inhibit tumor cells invasion and migration	TGF-β1↓, E-cadherin↑, MAPK↓, PI3K↓	800 μg/ml	(74)
Cell: THP-1, HeLa, SiHa, HUVECs	Inhibit macrophage M2 polarization, inhibit tumor cells migration, inhibit angiogenesis	TGF-β↓, p-Smad2↓, p-Smad3↓	20 μmol/l, 40 μmol/l	(76)

↓, downregulation; ↑, upregulation; NO, nitric oxide; TNF-α, tumor necrosis factor-α; ANXA1 mRNA, annexin A1 mRNA; EGFR mRNA, epidermal growth factor receptor mRNA; Bcl-2, B-cell lymphoma 2; Bcl-xL, B-cell lymphoma-extra large; Puma, p53 upregulated modulator of apoptosis; Cle-Caspase3, cleaved caspase-3; Cle-PARP, cleaved poly(ADP-ribose) polymerase; Snail, snail family transcriptional repressor 1; Wnt1, Wnt family member 1; IL-1β, interleukin-1β; IL-6, interleukin-6; P-HA, phospho-histone H2A; PARP, poly(ADP-ribose) polymerase; p53, tumor protein p53; p21, cyclin-dependent kinase inhibitor 1A; Mcl-1, myeloid cell leukemia 1; Nrf2, nuclear factor erythroid 2-related factor 2; ATP, adenosine triphosphate; CAV-1, caveolin-1; eNOS, endothelial nitric oxide synthase; ONOO, peroxynitrite; CAF, cancer-associated fibroblasts; TIL, tumor-infiltrating lymphocytes; TGF-β, transforming growth factor-β; IL-10, interleukin-10; MMP-9, matrix metalloproteinase 9; CD206, cluster of differentiation 206; CD163, cluster of differentiation 163; ERK1/2, extracellular signal-regulated kinase 1/2; JNK, c-Jun N-terminal kinase; MMP-2, matrix metalloproteinase 2; Vav3, vav guanine nucleotide exchange factor 3; Rac1, Rac family small GTPase 1; TRHDE-AS1, the lncRNA of TRHDE antisense RNA 1; FOXA1, forkhead box A1; GAL3ST1, galactose-3-O-sulfotransferase 1; miR-27a, microRNA-27a; FBXW7, F-box and WD-40 domain protein 7; caspase-3, cysteine-aspartic protease 3; Bax, Bcl-2-associated X protein; PINK1, PTEN-induced kinase 1; Treg, regulatory T cells; VEGF-A, vascular endothelial growth factor A; IL-12p40, interleukin-12 subunit p40; IL-4, interleukin-4; MDR1, multidrug resistance protein 1; PCNA, proliferating cell nuclear antigen; Box1, high mobility group box 1; TLR4, toll-like receptor 4; PPARD, peroxisome proliferator-activated receptor δ; CDC20, cell division cycle 20; Wnt, wingless-type MMTV integration site family; Atg12, autophagy-related gene 12; DCP1A, mRNA-decapping enzyme 1A; TMSB4X, thymosin β-4; E-cadherin, epithelial cadherin; MAPK, mitogen-activated protein kinase; PI3K, phosphoinositide 3-kinase; p-Smad2, phosphorylated Smad2; p-Smad3, phosphorylated Smad 3.

Emerging evidence also indicates that the pharmacological actions of *Astragalus* extend beyond gynecological oncology to common non-neoplastic disorders of the female reproductive system. For example, AS-IV has been reported to activate peroxisome proliferator-activated receptor-γ (PPARγ), induce autophagy, suppress granulosa cell proliferation and promote apoptosis, suggesting potential relevance to polycystic ovary syndrome (PCOS) (79). Similarly, APS ameliorates PCOS-like phenotypes in mice by improving serum metabolic profiles, increasing gut microbiome diversity, and reducing insulin resistance and oxidative stress (80). In addition, aqueous extracts of *Astragalus* roots, in which AST are major constituents, upregulated uterine and ovarian PPARα mRNA and increased mitochondrial 2,4-dienoyl-CoA reductase expression, thereby suppressing estrogen-dependent uterine hyperplasia (81). APS has also been shown to alleviate bovine mammary fibrosis through reduction of reactive oxygen species, inhibition of NLRP3 and modulation of EMT (82). Collectively, these findings suggest that *Astragalus* bioactive compounds exert broad regulatory effects across female reproductive disorders and may help maintain reproductive axis homeostasis through multi-target and multi-level mechanisms.

Despite encouraging preclinical evidence, important challenges remain for the clinical translation of APS and AST in gynecological oncology. Current knowledge of their *in vivo* metabolism, bioavailability and interactions with the tumor microenvironment remains incomplete, and the mechanisms that determine efficacy across distinct subtypes of female malignancies require further clarification. Although available studies suggest that APS and AST can influence drug disposition and therapeutic response by regulating metabolic enzymes and transporters such as BCRP and MDR1, systematic characterization of absorption, distribution, metabolism and excretion profiles remains insufficient. Clinical development is further constrained by poor water solubility, low oral bioavailability and suboptimal tissue distribution, which limit accumulation at tumor sites. Advanced delivery platforms including lipid based carriers, polymeric micelles and nanoparticle formulations may improve bioavailability, enable controlled release and reduce adverse effects, yet barriers related to formulation complexity, large scale manufacturing and safety evaluation continue to impede translation (83). In addition, chemotherapy remains a cornerstone of treatment for breast, ovarian and cervical cancers, but its effectiveness is frequently limited by resistance and dose-limiting toxicities that reduce adherence and quality of life. Building on the immunomodulatory and cytoprotective properties of APS and AST, future studies should develop natural immunomodulatory adjuvants with improved bioactivity and tumor targeting capacity to mitigate chemotherapy-related toxicities and enhance therapeutic outcomes. Notably, most existing evidence is derived from cellular and animal models, and high quality clinical data remain scarce regarding long-term efficacy, optimal dosing and rational combination strategies. Future work should prioritize multidisciplinary collaboration to clarify molecular mechanisms, optimize delivery technologies, conduct rigorous clinical trials and establish standardized quality control systems, thereby accelerating clinical translation and maximizing the therapeutic potential of *Astragalus* in gynecological malignancies.

Acknowledgements

Not applicable.

Funding

This work was supported by the Shandong Province Collaborative Innovation Center for Classic Traditional Chinese Medicine Formulas (grant no. 2019KFY12) and the National College Students' Innovation and Entrepreneurship Training Program (grant no. 202510441006).

Availability of data and materials

Not applicable.

Authors' contributions

RL wrote the manuscript and drew the pictures. ZL and YL collected and organized literature and participated in the revision of the manuscript. YC and ZG proofread the manuscript. ZX is responsible for the study designing, research fields, drafting and finalizing the manuscript. All authors read and approved the final version of the manuscript. Data authentication is not applicable.

Ethics approval and consent to participate

Not applicable.

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

References

1. Jha AK, Mithun S, Sherkhane UB, Jaiswar V, Osong B, Purandare N, Kannan S, Prabhash K, Gupta S, Vanneste B, *et al*: Systematic review and meta-analysis of prediction models used in cervical cancer. Artif Intell Med 139: 102549, 2023.
2. Olusola P, Banerjee HN, Philley JV and Dasgupta S: Human papilloma virus-associated cervical cancer and health disparities. Cells 8: 622, 2019.
3. Gupta KK, Gupta VK and Naumann RW: Ovarian cancer: Screening and future directions. Int J Gynecol Cancer 29: 195-200, 2019.
4. Kossaï M, Leary A, Scoazec JY and Genestie C: Ovarian cancer: A heterogeneous disease. Pathobiology 85: 41-49, 2018.
5. Menon U, Karpinskyj C and Gentry-Maharaj A: Ovarian cancer prevention and screening. Obstet Gynecol 131: 909-927, 2018.
6. Xiong X, Zheng LW, Ding Y, Chen YF, Cai YW, Wang LP, Huang L, Liu CC, Shao ZM and Yu KD: Breast cancer: Pathogenesis and treatments. Signal Transduct Target Ther 10: 49, 2025.
7. Anastasiadi Z, Lianos GD, Ignatiadou E, Harissis HV and Mitsis M: Breast cancer in young women: An overview. Updates Surg 69: 313-317, 2017.
8. Jabbour HN, Sales KJ, Catalano RD and Norman JE: Inflammatory pathways in female reproductive health and disease. Reproduction 138: 903-919, 2009.
9. Rayburn WF: Gynecologic cancer care: Innovative progress. Obstet Gynecol Clin North Am 46: xiii-xiv, 2019.

10. Li X, Qu L, Dong Y, Han L, Liu E, Fang S, Zhang Y and Wang T: A review of recent research progress on the astragalus genus. Molecules 19: 18850-18880, 2014.
11. Ma XQ, Shi Q, Duan JA, Dong TT and Tsim KW: Chemical analysis of radix astragali (Huangqi) in China: A comparison with its adulterants and seasonal variations. J Agric Food Chem 50: 4861-4866, 2002.
12. Auyeung KK, Han QB and Ko JK: Astragalus membranaceus: A review of its protection against inflammation and gastrointestinal cancers. Am J Chin Med 44: 1-22, 2016.
13. Tian J, Huo R, Wang Y, Wang J, Fang F and Fang C: Astragalus polysaccharide alleviates cognitive decline in D-galactose-induced aging. Biol Pharm Bull 48: 523-536, 2025.
14. Wang X, Liu Y, Peng N, Yu H, Ma Y, Zhang M, Wang Y, Wang Y and Gao W: Allelopathy and identification of volatile components from the roots and aerial parts of astragalus mongholicus Bunge. Plants (Basel) 13: 317, 2024.
15. Li J, Niu Y, Yuan L, Jiang W, Jiao T, Dou H and Nan Y: Research progress in the medicine-food dual use of astragalus for gastrointestinal tumors. J Med Food 27: 1145-1157, 2024.
16. Li S, Sun Y, Huang J, Wang B, Gong Y, Fang Y, Liu Y, Wang S, Guo Y, Wang H, *et al*: Anti-tumor effects and mechanisms of Astragalus membranaceus (AM) and its specific immunopotentiation: Status and prospect. J Ethnopharmacol 258: 112797, 2020.
17. Tan B, Li Z, Chen S, Wan Q, Jiang C, Fu Y, Su W and Wan X: Advances in molecular mechanisms of anti-tumor bioactive constituents from Astragalus membranaceus: A comprehensive review. J Ethnopharmacol 356: 120744, 2026.
18. Dong M, Li J, Yang D, Li M and Wei J: Biosynthesis and pharmacological activities of flavonoids, triterpene saponins and polysaccharides derived from astragalus membranaceus. Molecules 28: 5018, 2023.
19. Nafti K, Giacinti G, Marghali S and Raynaud CD: Screening for astragalus hamosus triterpenoid saponins using HPTLC methods: Prior identification of Azukisaponin isomers. Molecules 27: 5376, 2022.
20. Tian H, An L, Wang P, Zhang X, Gao W and Li X: Review of Astragalus membranaceus polysaccharides: Extraction process, structural features, bioactivities and applications. Chin Herb Med 17: 56-69, 2025.
21. Tin MMY, Cho CH, Chan K, James AE and Ko JK: Astragalus saponins induce growth inhibition and apoptosis in human colon cancer cells and tumor xenograft. Carcinogenesis 28: 1347-1355, 2007.
22. Li W, Hu X, Wang S, Jiao Z, Sun T, Liu T and Song K: Characterization and anti-tumor bioactivity of astragalus polysaccharides by immunomodulation. Int J Biol Macromol 145: 985-997, 2020.
23. Yan X, Miao J, Zhang B, Liu H, Ma H, Sun Y, Liu P, Zhang X, Wang R, Kan J, *et al*: Study on semi-bionic extraction of Astragalus polysaccharide and its anti-aging activity in vivo. Front Nutr 10: 1201919, 2023.
24. Zeng P, Li J, Chen Y and Zhang L: The structures and biological functions of polysaccharides from traditional Chinese herbs. Prog Mol Biol Transl Sci 163: 423-444, 2019.
25. Zheng Y, Ren W, Zhang L, Zhang Y, Liu D and Liu Y: A review of the pharmacological action of astragalus polysaccharide. Front Pharmacol 11: 349, 2020.
26. Tang Z and Tian X: Astragalus membranaceus: A Traditional Chinese medicine with multifaceted impacts on breast cancer treatment. Biomolecules 14: 1339, 2024.
27. Wang S, Long S, Deng Z and Wu W: Positive role of Chinese herbal medicine in cancer immune regulation. Am J Chin Med 48: 1577-1592, 2020.
28. Qin ZT, Wu ZH, Wang CM, Xie XC and Wang YH: Astragalus polysaccharide as a potential antitumor immunomodulatory drug (Review). Mol Med Rep 32: 341, 2025.
29. Duya PA, Chen Y, Bai L, Li Z, Li J, Chai R, Bian Y and Zhao S: Nature products of traditional Chinese medicine provide new ideas in γδT cell for tumor immunotherapy. Acupuncture and Herbal Medicine 2: 78-83, 2022.
30. Li Q, Li J, Wang Y, Wu F and Li T: Efficacy and safety of astragalus polysaccharides in patients with malignant tumors: A systematic review and meta-analysis. Naunyn Schmiedebergs Arch Pharmacol 398: 11705-11732, 2025.
31. Shen L, Gwak SR, Cui ZY, Joo JC and Park SJ: Astragalus-Containing Chinese herbal medicine combined with chemotherapy for cervical cancer: A systematic review and meta-analysis. Front Pharmacol 12: 587021, 2021.
32. Sheng X, Yang L, Huang B, Lin G, Wang Y, Wu X and Lin R: Efficacy of Astragalus Membranaceus (Huang Qi) for cancer-related fatigue: A systematic review and meta-analysis of randomized controlled studies. Integr Cancer Ther 24: 15347354241313344, 2025.
33. Chen G, Jiang N, Zheng J, Hu H, Yang H, Lin A, Hu B and Liu H: Structural characterization and anti-inflammatory activity of polysaccharides from Astragalus membranaceus. Int J Biol Macromol 241: 124386, 2023.
34. Shahzad M, Shabbir A, Wojcikowski K, Wohlmuth H and Gobe GC: The antioxidant effects of Radix Astragali (Astragalus membranaceus and Related Species) in protecting tissues from injury and disease. Curr Drug Targets 17: 1331-1340, 2016.
35. Li CX, Liu Y, Zhang YZ, Li JC and Lai J: Astragalus polysaccharide: A review of its immunomodulatory effect. Arch Pharm Res 45: 367-389, 2022.
36. Zhang C, Guo W, Yao X, Xia J, Zhang Z, Li J, Chen H and Lin L: Database mining and animal experiment-based validation of the efficacy and mechanism of Radix Astragali (Huangqi) and Rhizoma Atractylodis Macrocephalae (Baizhu) as core drugs of Traditional Chinese medicine in cancer-related fatigue. J Ethnopharmacol 285: 114892, 2022.
37. Huang WC, Kuo KT, Bamodu OA, Lin YK, Wang CH, Lee KY, Wang LS, Yeh CT and Tsai JT: Astragalus polysaccharide (PG2) ameliorates cancer symptom clusters, as well as improves quality of life in patients with metastatic disease, through modulation of the inflammatory cascade. Cancers (Basel) 11: 1054, 2019.
38. Chen MH, May BH, Zhou IW, Zhang AL and Xue CC: Integrative medicine for relief of nausea and vomiting in the treatment of colorectal cancer using oxaliplatin-based chemotherapy: A systematic review and meta-analysis. Phytother Res 30: 741-753, 2016.
39. Zhang X, Qiu H, Li C, Cai P and Qi F: The positive role of traditional Chinese medicine as an adjunctive therapy for cancer. Biosci Trends 15: 283-298, 2021.
40. Liu J, Hong M, Li Y, Chen D, Wu Y and Hu Y: Programmed cell death tunes tumor immunity. Front Immunol 13: 847345, 2022.
41. Li W, Song K, Wang S, Zhang C, Zhuang M, Wang Y and Liu T: Anti-tumor potential of astragalus polysaccharides on breast cancer cell line mediated by macrophage activation. Mater Sci Eng C Mater Biol Appl 98: 685-695, 2019.
42. Li W, Hu X, Li Y and Song K: Cytotoxicity and growth-inhibiting activity of Astragalus polysaccharides against breast cancer via the regulation of EGFR and ANXA1. J Nat Med 75: 854-870, 2021.
43. Wang B, Guo C, Liu Y, Han G, Li Y, Zhang Y, Xu H and Chen D: Novel nano-pomegranates based on astragalus polysaccharides for targeting ERα-positive breast cancer and multidrug resistance. Drug Deliv 27: 607-621, 2020.
44. Sun LI, Zhuo S, Li X, Kong H, DU W, Zhou C and Huang J: Astragalus polysaccharide enhances the therapeutic efficacy of cisplatin in triple-negative breast cancer through multiple mechanisms. Oncol Res 33: 641-651, 2025.
45. Al Kassam D, Marcos CA, Blanco I, de Los Toyos JR and Llorente JL: Diagnostic value of E-cadherin, MMP-9, activated MMP-13 and anti-p53 antibodies in squamous cell carcinomas of head and neck. Med Clín (Barc) 129: 761-765, 2007 (In Spanish).
46. Yang S, Sun S, Xu W, Yu B, Wang G and Wang H: Astragalus polysaccharide inhibits breast cancer cell migration and invasion by regulating epithelial-mesenchymal transition via the Wnt/β-catenin signaling pathway. Mol Med Rep 21: 1819-1832, 2020.
47. Zhou L, Liu Z, Wang Z, Yu S, Long T, Zhou X and Bao Y: Astragalus polysaccharides exerts immunomodulatory effects via TLR4-mediated MyD88-dependent signaling pathway in vitro and in vivo. Sci Rep 7: 44822, 2017.
48. Bao WR, Li ZP, Zhang QW, Li LF, Liu HB, Ma DL, Leung CH, Lu AP, Bian ZX and Han Q: Astragalus Polysaccharide RAP selectively attenuates paclitaxel-induced cytotoxicity toward RAW 264.7 cells by reversing cell cycle arrest and apoptosis. Front Pharmacol 9: 1580, 2019.
49. Sheng F, Yang S, Li M, Wang J, Liu L and Zhang L: Research progress on the anti-cancer effects of astragalus membranaceus saponins and their mechanisms of action. Molecules 29: 3388, 2024.
50. Lin-Rahardja K, Scarborough J and Scott JG: Evolution-informed strategies for combating drug resistance in cancer. Int J Mol Sci 24: 6738, 2023.
51. Lou Y, Guo Z, Zhu Y, Zhang G, Wang Y, Qi X, Lu L, Liu Z and Wu J: Astragali radix and its main bioactive compounds activate the Nrf2-mediated signaling pathway to induce P-glycoprotein and breast cancer resistance protein. J Ethnopharmacol 228: 82-91, 2019.

52. Huang P, Li H, Ren L, Xie H, Chen L, Liang Y, Hu Y, Selistre-de-Araujo HS, Boussios S, Jhawar SR, *et al*: Astragaloside IV enhances the sensitivity of breast cancer stem cells to paclitaxel by inhibiting stemness. Transl Cancer Res 12: 3703-3717, 2023.
53. Wang Y, Li Y, Zhong J, Li M, Zhou Y, Lin Q, Zong S, Luo W, Wang J, Wang K, *et al*: Tumor-derived Cav-1 promotes pre-metastatic niche formation and lung metastasis in breast cancer. Theranostics 13: 1684-1697, 2023.
54. Zheng Y, Dai Y, Liu W, Wang N, Cai Y, Wang S, Zhang F, Liu P, Chen Q and Wang Z: Astragaloside IV enhances taxol chemosensitivity of breast cancer via caveolin-1-targeting oxidant damage. J Cell Physiol 234: 4277-4290, 2018.
55. Wei L, Wang H, Ye X, Yue J, Guo H, Mao D, Li X, Sun Y, Liu C, Liu Y and Chen Y: Oxymatrine and astragaloside IV co-loaded liposomes: Scale-up purposes and their enhancement of anti-PD-1 efficacy against breast cancer. Mater Today Bio 32: 101634, 2025.
56. Yu Y, Hao J, Wang L, Zheng X, Xie C, Liu H, Wu J, Qiao S and Shi J: Astragaloside IV antagonizes the malignant progression of breast cancer induced by macrophage M2 polarization through the TGF-β-regulated Akt/Foxo1 pathway. Pathol Res Pract 249: 154766, 2023.
57. Al-Hawary SIS, Altalbawy FMA, Jasim SA, Jyothi SR, Jamal A, Naiyer MM, Mahajan S, Kalra H, Jawad MA and Zwamel AH: VAV3 in human cancers: Mechanism and clinical implication. Pathol Res Pract 248: 154681, 2023.
58. Jiang K, Lu Q, Li Q, Ji Y, Chen W and Xue X: Astragaloside IV inhibits breast cancer cell invasion by suppressing Vav3 mediated Rac1/MAPK signaling. Int Immunopharmacol 42: 195-202, 2017.
59. Hu S, Zheng W and Jin L: Astragaloside IV inhibits cell proliferation and metastasis of breast cancer via promoting the long noncoding RNA TRHDE-AS1. J Nat Med 75: 156-166, 2020.
60. Yang Y, Lu J, Zhu Y, Chen D, Tang J, Zhang M, Lu J, Yang Y, Tian S and Zhao H: Astragaloside IV inhibits the growth of obesity-associated triple-negative breast cancer by activating FOXA1 transcription factor to regulate GAL3ST1-GalCer signaling and remodel sphingolipid metabolism. Phytomedicine 144: 156907, 2025.
61. Li X, Gong C, Naeem A, Liu J, Yang M, Zhang J and Shang H: Priming immunity via herbal components and their nanomedicines for the treatment of cancer. Acupuncture and Herbal Medicine 4: 436-462. 2024.
62. Guo Y, Zhang Z, Wang Z, Liu G, Liu Y and Wang H: Astragalus polysaccharides inhibit ovarian cancer cell growth via microRNA-27a/FBXW7 signaling pathway. Biosci Rep 40: BSR20193396, 2020.
63. Li C, Hong L, Liu C, Min J, Hu M and Guo W: Astragalus polysaccharides increase the sensitivity of SKOV3 cells to cisplatin. Arch Gynecol Obstet 297: 381-386, 2017.
64. Najafi M, Mortezaee K and Majidpoor J: Cancer stem cell (CSC) resistance drivers. Life Sci 234: 116781, 2019.
65. Peng Q, Yu Y, Ye L, Zhang S, Li Y, Hua X, Shen S, Hu D and Lu W: Astragalus polysaccharides sensitize ovarian cancer stem cells to PARPi by inhibiting mitophagy via PINK1/Parkin signaling. iScience 27: 110376, 2024.
66. Shokati E, Motalebnezhad M and Safari E: Astragalus polysaccharide mediates immunomodulatory effects on crosstalk between human peripheral blood mononuclear cells and ovarian cancer cell line. Iran J Allergy Asthma Immunol 22: 172-182, 2023.
67. Liu M, Zhang ZX, Wang JH, Guo RB, Zhang L, Kong L, Yu Y, Zang J, Liu Y and Li XT: Immunomodulatory and anti-ovarian cancer effects of novel astragalus polysaccharide micelles loaded with podophyllotoxin. Int J Biol Macromol 290: 138960, 2025.
68. Zhang L, Liu Y, Lei X, Liu X, Sun H and Liu S: Astragaloside II enhanced sensitivity of ovarian cancer cells to cisplatin via triggering apoptosis and autophagy. Cell Biol Int 47: 1600-1613, 2023.
69. Wang X, Gao S, Song L, Liu M, Sun Z and Liu J: Astragaloside IV antagonizes M2 phenotype macrophage polarization-evoked ovarian cancer cell malignant progression by suppressing the HMGB1-TLR4 axis. Mol Immunol 130: 113-121, 2021.
70. Dekinash MF, Okda TM, Elmahallawy EK, El-Fiky FK, Omran GAEH, Svajdlenka E, Dahran N, El-Khadragy MF, Al-Megrin WA and El Naggar EMBA: Insights into HPLC-MS/MS analysis, antioxidant and cytotoxic activity of astragalus fruticosus against different types of cancer cell lines. Pharmaceuticals (Basel) 15: 1406, 2022.
71. Liu W, Fu Y, Jiang X, Tan J, Zhang Y and Zhang L: Astragalus polysaccharide regulates the cervical cancer cell cycle and inhibits cisplatin resistance by blocking the Wnt/β-catenin pathway through the PPARD/CDC20 axis. Cytotechnology 77: 126, 2025.
72. Xia C, He Z and Cai Y: Quantitative proteomics analysis of differentially expressed proteins induced by astragaloside IV in cervical cancer cell invasion. Cell Mol Biol Lett 25: 25, 2020.
73. Lu W and Kang Y: Epithelial-mesenchymal plasticity in cancer progression and metastasis. Dev Cell 49: 361-374, 2019.
74. Zhang L, Zhou J, Qin X, Huang H and Nie C: Astragaloside IV inhibits the invasion and metastasis of SiHa cervical cancer cells via the TGF-β1-mediated PI3K and MAPK pathways. Oncol Rep 41: 2975-2986, 2019.
75. Boutilier AJ and Elsawa SF: Macrophage polarization states in the tumor microenvironment. Int J Mol Sci 22: 6995, 2021.
76. Shen L, Li Y, Hu G, Song X, Wang X, Li X and Xu X: Astragaloside IV suppresses the migration and EMT progression of cervical cancer cells by inhibiting macrophage M2 polarization through TGFβ/Smad2/3 signaling. Funct Integr Genomics 23: 133, 2023.
77. Waks AG and Winer EP: Breast cancer treatment: A review. JAMA 321: 288-300, 2019.
78. Holliday DL and Speirs V: Choosing the right cell line for breast cancer research. Breast Cancer Res 13: 215, 2011.
79. Wen M, Chen W, Zhou Q and Dou X: Astragaloside IV regulates autophagy-mediated proliferation and apoptosis in a rat model of PCOS by activating the PPARγ pathway. Iran J Basic Med Sci 25: 882-889, 2022.
80. Li R, Hu R, Huang Y, Li D, Ma X and Yang Y: Astragalus polysaccharide alleviates polycystic ovary syndrome by reducing insulin resistance and oxidative stress and increasing the diversity of gut microbiota. Endocrine 83: 783-797, 2023.
81. Orkhon B, Kobayashi K, Javzan B and Sasaki K: Astragalus root induces ovarian β-oxidation and suppresses estrogen-dependent uterine proliferation. Mol Med Rep 18: 5198-5206, 2018.
82. Zhang J, Liu K, Yang T, Duan H, Xiao L, Zhang Q, Zhang Y, Dong W and Zhao X: Mechanism of Astragalus Polysaccharide in alleviating bovine mammary fibrosis through ROS/NLRP3 inhibition and EMT regulation. Antioxidants (Basel) 14: 503, 2025.
83. Prakash S: Nano-based drug delivery system for therapeutics: A comprehensive review. Biomed Phys Eng Express 9: 10.1088/2057-1976/acedb2, 2023.


Copyright © 2026 Liu et al. This work is licensed under a Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International (CC BY-NC-ND 4.0) License.