Current Trends in Biotechnology and Pharmacy
Vol. 17(Supplementary issue - 3B) 1327-1339,September 2023, ISSN 0973-8916 (Print), 2230-7303 (Online)
10.5530/ctbp.2023.3s.67

Analyzing the Active Constituents of *Astragalus*: A Salient Element in Human Health

Rudra Awdhesh Kumar Mishra[1], Rujuta Vijay Thorat[1], Smruti Mahapatra[1], Shweta Priyadarshini Dash[1], Sarah Louis Dharmaji[1], Nalini Easwaran[1], Rama Jayaraj[2, 3], Gothandam Kodiveri Muthukaliannan[1*]

[1]Department of Biotechnology, School of Bio Sciences and Technology, Vellore Institute of Technology, Vellore - 632 014. Tamil Nadu, India
[2]Jindal Institute of Behavioral Sciences, Jindal Global Institution of Eminence Deemed to Be University, Sonipat 131001, India[3]Director of Clinical Sciences, Northern Territory Institute of Research and Training, Darwin, NT 0909, Australia
*Corresponding author: gothandam@gmail.com

Abstract

Astragalus used mainly in Chinese traditional medicine, and in some parts of other Asian countries like Japan. It is one of the fundamental herbs found among medicinal and food plants. The plant contains various beneficial compounds, which provide enormous benefits to human health, such as the improvisation of the immune system, and it prevents and helps in the treatments of many diseases. These compounds act against various diseases like cancer, heart disease, a neurodegenerative disorder, and kidney and urinary-related problems. These elements also perform some crucial activities like anti-microbial activity, anti-oxidative activity, anti-hypertensive effect, etc., which is the precursor for the cause of various diseases. The dried root or the root powder of the plant is widely used as a nutrient supplement and used in foodstuffs includes ice cream, jelly, mayonnaise, syrups, sauce, candies, etc. The bark, root, flower, and stem extracts used widely in cosmetics, such as skin protection and skin whitening. *Astragalus membranaceus* (AM) is a natural substitute for food, medicine, and cosmetic ingredients as it is always good to replace synthetic ones with natural compounds. Therefore, this review describes the importance of its biologically active molecules and their applications in different health benefits in various aspects.

Keywords: *Astragalus membranaceus,* Polysaccharides, dietary supplement, Neurodegenerative disorder, Cosmetic industry, Anti-aging

Introduction

In the family *Fabaceae*, *Astragalus* is a floral herb. It is one of the 50 essential herbs in Chinese herbal medicine (1). The efficacy of China's herbal medicine is poorly investigated, and endorsed, and most of its therapeutic applications do not have a proper mechanism of action (2). In China, over 3 million tonnes of herbal medicines are processed in traditional Chinese medicine, and their medicinal parts are consumed (3). *Astragalus membranaceus* is used as an effective adaptogenic Qi tonic in traditional Chinese medicine (4). In several other countries, the dried root part of *Astragalus membranaceus* is used as an ethnopharmacological herb (5). In Shennong's Materia Medica Classic, *Astragali Radix* was first documented in Qin or Han Dynasty (221 BC-220 AD) (6). *A. Radix* is one of the key and widely used herbs, which facilitate metabolism, and the physiological role of the human body. It also acts as an immune-regulatory and anti-oxidant in treating various diseases (7). *A. Radix* has the characteristics of enhancing the reticuloendothelial system of phagocytosis. Thus, it restores the formation of

Vol. 17(Supplementary issue - 3B) 1327-1339,September 2023, ISSN 0973-8916 (Print), 2230-7303 (Online)
10.5530/ctbp.2023.3s.67

red blood cells in the bone marrow by inducing the activity of the adrenal cortical mechanism. It has also been known for its antibiotic, antiperspirant, anti-inflammatory, diuretic and tonic effects (8). Certain other species of these plants are used as a replacement for coffee, and tea, and as substitutes for vegetable gums in foods, and medicinal items. It is used frequently in the cosmetics industry because it includes chemical compounds that can strengthen hair follicles, avoid fungal infections and encourage hair growth. *Astragalus* taxonomy and phylogeny have been widely mistaken. Various authors tried to distinguish *Astragalus* through morphological characters in the hope of obtaining a natural subgeneric classification. Among them, Bunge›s genus classification was commonly used (9). The primary component of the *Astragalus* taxa, which is used widely in the world, Gum tragacanth and Iran provide most of it, 70 per cent of the typically used tragacanth gum. Given the widespread ethnobotanical knowledge of this genus around the world, its effective applications have not mentioned separately, and most publications dispersed widely. Moreover, there are also too limited findings of this genus on photochemistry and pharmacology. This study, therefore, aims at incorporating the results on ethnobotanical aspects of *Astragalus* to endorse adequate baseline evidence for future works and commercial exploitation.

Chemical composition

Astragalus Polysaccharides (APS) have the immense potential to develop or cure multiple disorders. It is a water-soluble bioactive molecule belonging to the heteropolysaccharides group isolated from stems and root parts of *A. membranaceus*. It consists of monomers of polymeric carbons which are primarily interconnected by glycosidic α-type linkage. *Astragalu*s Polysaccharides is the most used because of its less toxic nature, minimal side effects, and non-residuality. The immunomodulatory behaviour is shown in this chemical compound. Polysaccharides D are regarded as heteropolysaccharides and polysaccharides A, B & C are regarded as glucans (10).

Saponins

Because of their unexplored diversity, saponins are crucial resources in medical fields for various applications. It has several ecological roles, such as disease protection, herbivores protection of plants, and allelopathic agents. It has been reported to have immunomodulatory activity. Astragaloside IV a saponin isolated from the Astragalus enhances the proliferation mechanism of murine B and T lymphocytes cells, and cardio-protective properties (11, 12). Another study has reported that APS have anti-tumorigenic activity against colorectal cancer and inhibits tumour growth during xenograft transplantation. It inhibits the proliferation mechanism in cancer cells by arresting the phase-specific cell cycle process and facilitating the caspase-dependent apoptosis mechanism, and finally suppresses the cancer cell growth. Saponins derived from *A. Radix* can be used as an effective therapeutic molecule for the treatment of gastric cancer and act by enhancing the apoptosis mechanism and inhibiting the cell proliferation cycle in invitro and in-vivo experiments. This indicates the potential for *Astragalus* to be further developed as an experimental drug or maybe used as an adjuvant chemotherapy agent for gastric cancer treatment (13).

Flavonoids

Flavonoid classes are one of the principal bioactive metabolites in *Astragalus* as they intensely show many biological activities like anti-allergic, anti-inflammatory, antitumor, anti-viral, antioxidant, anti-carcinogenic, pro-differentiation activity etc. All the flavonoids, especially phytoalexins protect the immune system from viral infections. Many isoflavones have reported having estrogenic activity, and their different combinations were clinically used to reduce vascular fragility. These flavonoids have been further categorized and graded into petrocarpans, flavonols, flavanones, flavano4-ols, isoflavones and isophlavans. The most important isolated compounds are flavonols.

Vol. 17(Supplementary issue - 3B) 1327-1339,September 2023, ISSN 0973-8916 (Print), 2230-7303 (Online)
10.5530/ctbp.2023.3s.67

The higher number of *Astragalus* species mainly contain quercetin, kaempferol, and their glycosides. The only recorded *Astragalus* species to possess flavanones are *Astragalus sinicus*. From this *Astragalus* species, plantampelopsin and its 3',-glucoside and 3'-xyloside compounds are isolated (14). The isoflavonoids, which are isolated, are mostly a glycones than glycosides. The isoflavones and isoflavanes are two separate classes. Many of the *Astragalus* species isoflavonoids have become novel compounds (15). Another two unique isoflavones that are astragaluquinone and eight methoxyvestitol are isolated from *Astragalus Alexandrinus* and *Astragalus trigonus* roots (16). The latest isoflavone found in the aerial portion of *Astragalus peregrinus* is 7-hydroxy-3, 5›-dimethoxyisoflavone (17). It has been reported to have various anti-oxidant activities and can also serve as the function of singlet oxygen, Chalcone and Isoflavan, both of which are derived from *Astragalus surgeons* and which show antibacterial activity with phytopathogens against five bacterial strains including *Escherichia coli, Staphylococcus aureus, Erwinia carotovora,* and *Bacillus subtilis* (18).

Essential oils

It has been reported that 17 compounds were present of essential oils obtained from stems, flowers and leaves of *A. schahrudensis*. The main compounds included were germacrene D and germacrene B from the flowers part, β-selinene, δ-guaiene, α-guaiene, and α- selinene from stem parts and α-pinene, bornyl acetate, and limonene from leaves. The flower and stem oils of *A. schahrudensis* are mostly comprised of sesquiterpenes, whereas in leaves parts monoterpenes were found in abundance in comparison to sesquiterpenes. In another study, it has been reported that the essential oils from the aerial parts of *A. microcephalus* wild species, which was purified using Gas chromatography and characterized with GC-MS. The main components found were hexadecanoic acid, α-cadinene, tridecanol benzyl benzoate etc. (19). Pomel, which is one of the Astragalus sp., is a desert plant and is of medium recurrence, because of the more volatile compounds toxic for livestock. The essential oil of the Pomel plant was extracted and analysed. The oils were refined by distillation method out of various parts of the plants and studied using different analytical techniques such as GC-MS (Gas Chromatography–Mass Spectrometry), NMR (Nuclear Magnetic Resonance) and HPLC-MS (High-Performance Liquid Chromatography). The main components obtained were the phytol dillapiole, hexadecanoic acid, etc. Other volatiles were identified like their antioxidant compound - benzeneacetonitrile, butylated hydroxytoluene and caprolactam (20).

Other constituents

Various other phyto-compounds were isolated from the roots includes an essential oil, phytosterols and certain other metabolites like gamma-aminobutyric acid (GABA) and L-canavanine. In the *Astragalus* root, traces of several elements have been found includes tantalum, hafnium, europium, thorium, manganese, calcium, zinc, iron, copper, magnesium, potassium, chrome, vanadium, tin, sodium, cobalt, rubidium, molybdenum and silver. Choline, betaine, laconic acid, β-sitosterols, linoleic acid, α-aminobutyric acid, and asparagine are actively present in the roots of the *Astragalus* genus (9).

Effect of APS on human health

The APS is the natural and essential active metabolite in *A. membranaceus* and has several pharmacological effects. The scientific basis for the therapeutic use of APS has proven to have pharmacologic effects. Several factors influence the amount of APS production in *A. membranaceus. Factors include* the plants producing part, the fundamental origins, the development site, the plantation system and the year of development (Table 1). Through metabolomics profiling, it has been found that *A. membranaceus* has a higher content of mannose, xylose and other soluble sugar molecules in comparison to *A. mongholicus* (17). The Gansu region has the highest APS content among four locations in China that are Heilongjiang, Inner Mongolia, Shanxi and Gansu. The contents of polysaccharides are considered the highest in the annual growth of *Astragali radix*. The polysaccharide content steadily declines with time. The molecular weight of APS was reported to be between 10 – 50 KDa (Kilo Dalton). It used to be in white powder form when it is isolated from the plant. Out of 24 polysaccharides isolated from A. *membranaceous,* most are heteropolysaccharides. Heteropolysaccharides weight varies from 8.7–4,800 kDa, consisting of numerous monosaccharides, including L-rhamnoses, L-arabinose, D-xylose, L-xylose, and D-ribose (19).

Table 1. Plant parts of *Astragalus* membranaceus and their uses in different health conditions

Plant part used	Uses
Leaves, gummy exudation	Kidney diseases, hypertension, burns
Root	Stomach pain, flu, analgesic
Whole plant	Galactogogue of animals
Root	Astringent
Root, seed	Leishmaniasis against helminthes
Root	Diabetes
Manna	Digestion
Seed	Cold
Aerial part	Sedative and tonic
Gum	Cough
Stem	Tooth ache, tighten the roots of teeth
Flower	Powdered flowers given in strangury
Root	Ulcer
Leaf, flower	Belly ache

Several studies have reported that APS can affect different immune molecules to boost the immune system and index, therefore encouraging partial visceral organ development. In combination with probiotics, APS greatly strengthened the lymphocytes producing lymphoid organ systems such as the spleen, bursa of *Fabricius* and thymus. APS could facilitate immune organ maturation (20) by effectively enhancing the immune system and thereby improving its functions. It majorly increases the cell proliferation process and differentiation of B and T cell lymphocytes. It also modulates the function of T lymphocytes, Natural killer cells (NK cells), and macrophages. To activate the immune response, dendritic cells (DCs) are essential; they can significantly stimulate dendritic cells originating from bone marrow production and maturation. T cells are activated by APS, which contributes to DCs differentiation (21).

In different conditions, APS has different effects on cytokines. It can stimulate cytokine development and increase immunity under normal physiological conditions, whereas with a slight increase in the response of cytokines, the inflammatory reaction takes place in the body. However, it can also alter the different factors, which affect the inflammatory response and thereby protect the different cells of the body. However, APS can reduce inflammatory response factors and protect the cells or the body, following an increase in cytokines because of an inflammatory reaction. By stimulating the development of IL in the human body, APS facilitates immune control. Dose-dependent development of IL10, IL12 and IL2 was observed in contrast with negative control after the application of APS (22). APS in Ig plays a significant part in the mediation of immunity by IgA, IgG and IgM. APS improved IL2 expression, IL3 expression, IL4 expression, IFNg expression, IgM expression as well as IgG expression while the IgE expression decreases (23).

APS induces an anti-ageing effect by antioxidants and improves another metabolic process in various trials. Increased in vivo free radicals can contribute to the peroxidation of lipids. APS has oxidation resistance and is capable of scavenging free radicals, oxidising stress improvement, lipid peroxidation inhibition and ion chelation in vitro. APS also improves peroxide dismutase while blocking the development of malondialdehyde (24). Thus, increases the

Vol. 17(Supplementary issue - 3B) 1327-1339,September 2023, ISSN 0973-8916 (Print), 2230-7303 (Online)
10.5530/ctbp.2023.3s.67

glutathione secretion and overall antioxidant potential while eliminating radical hydroxyl activity (25). It can also use to control telomerase, control or modify telomerase-binding proteins and prevent the end of the chromosomal fragment from being shortened (38). In addition, BMSC ageing caused by ferric ammonium citrate can be effectively prevented by APS (26).

An important Qi-reinforcing herb *Astragalus membranaceus* indeed have a preventive impact on general gastrointestinal disorders like ulcerative colitis, irritable bowel syndrome and diarrhoea (27). Nucleotide oligomerization domain (NOD)-like receptor protein 3 inflammasome serves particularly a crucial role in the pathophysiology of inflammatory bowel disease. It is generally known to alter the inflammatory and immune response after infections. There is not much information regarding the function of NOD-like receptor protein 3 inflammasome and its mechanism of action. A study has been done to evaluate the effect of APS against inflammatory bowel disease, where it has reduced the Disease Activity Index (DAI) in comparison to the colitis model group of mice. The expression of the NOD-like receptor protein 3, a c-terminal caspase domain, caspase-1, interleukin (18,1β) is inhibited strongly by the effect of A*stragalus* polysaccharide, which could be measured by ELISA or RT-PCR technique. (Table 2) In dextran sulphate sodium-induced colitis. It is capable of exerting a medicinal potential that will be able to inhibit the activation of NOD-like receptor protein 3 inflammasome, which can function to limit the development of inflammatory mediators. Several previous studies have reported that in both the models of humans and animals, it has been linked with cytokine imbalances resulting in the disruption and damage of tissue within the gut. Therefore, it can be inferred that the inflammatory mediators play a crucial role in the pathogenesis of Ulcerative colitis (28).

Table 2: Active Constituents of *Astragalus* used as Medicines for various diseases.

Astragalus	**Plant Part**	**Active Constituent**	**Model Organism**	**Assay/ Techniques**	**Functions**	**Effect**
Astragalus membranaceus	Root	saponins, isoflavones and polysaccharides	NA	Western blot analysis, Cell cycle analysis, ELISA	Inhibited protein tyrosine phosphorylase and protein kinase C activation, as well as improving F-actin rearrangements, thereby altering insulin sensitivity	Antidiabetic effects: can lower blood glucose
Astragalus membranaceus	Root	polysaccharides	Streptozotocin (STZ)-treated rats	ELISA, RT-PCR, Radioimmuno-assay	Mediated by inhibition of NF -kappa-B activation and mRNA expression	Anti-inflammatory activity
Astragalus membranaceus	Astragalus extract (from root)	Polysaccharide fractions	NA	DNA hybridization technique, Virus isolation method	Induce endogenous interferon production in animals and humans and to potentiate the actions of interferon in viral infections	Antimicrobial activity

Vol. 17(Supplementary issue - 3B) 1327-1339,September 2023, ISSN 0973-8916 (Print), 2230-7303 (Online)
10.5530/ctbp.2023.3s.67

Astragalus membranaceus	*Astragalus* extract	Polysaccharides, saponin	NA	Western immunoblottin, RT-PCR, luciferase reporter assay and electrophoretic mobility shift assay	Used to ameliorate the side effects of antineoplastic drugs because of its immune-modulating nature	Anticancer effect
Astragalus membranaceus	Root	Flavonoids, poly-saccharide, saponins	NA	DPPH Assay, Folin -Denis Method	Exert significant cellular antioxidant effects that could help to develop more efficient material in functional food	Antioxidant effects
Astragalus mongh olicus	Root	Flavonoids, saponins	Rats	Immunohistochemica l staining, in situ hybridization staining	*Astragalus* reduced arterial pressure, stimulate angiogenesis and revascularization in ischemic myocardium and amnion	Cardiovascular effects
Astragalus membranaceus	Root	polysaccharide fractions	NA	TMMR Method	increased in vitro sperm motility and viability	Hormonal/reproductive effects
Astragalus membranaceus	Root	polysaccharide, triterpene, and its flavonoid fractions	Mice	Colorimetric assay, RT-PCR, ELISA	Used as a tonic herb in treating immunosuppressive diseases.	Immune system effects and its regulating actions
Astragalus. Propinquus, Astragalus membranaceus	Root	Polysaccharides	NA	HPLC, ELISA, Flow Cytometry	Prevent the recurrence of asthma by modulating Th1/Th2 cytokines	Asthma & Allergic Airway Disease (Seasonal Allergies
Astragalus membranaceus, Astragalus hamosus and Astragalus tribuloides	Root	Polysaccharides	Mouse models	luciferase reporter assay	Mediated by inhibition of NF-kappaB activation and mRNA expression	Auto-Inflammatory Destruction of the Pancreas
Astragalus membranaceus	Root	Polysaccharides	Mouse models	Immunosorbent assay, PCR	Suppress iron overload in the cerebral cortex and improve spatial learning and memory disorders in Alzheimer's disease	Brain Protection

Vol. 17(Supplementary issue - 3B) 1327-1339,September 2023, ISSN 0973-8916 (Print), 2230-7303 (Online)
10.5530/ctbp.2023.3s.67

A clinical study has performed with 30 patients' samples where the therapeutic effect of herbal formulations was able to control the levels of TNF-α and interleukin – 8 (IL-8) in the case of ulcerative colitis. In diabetic rats, *Astragalus membranaceus* showed a major ulcer-healing effect. Polysaccharides derived from organic resources have been found in the last two decades to have beneficial effects on inflammation of the gastric or colonic mucous membrane, diarrhoea and ulceration in animal models. The mechanisms remain, however, vague (29). Mechanically, decreased NF-kB DNA phosphorylation activity and lowered TNF-a, IL-1β, IL-6, IL-17 and myeloperoxidase (MPO) forms are significantly associated with the advancement in APS-treated mice when colitis observation was done, thereby, contributing to the increase in the DAI (colitis disease activity index. Another analysis of *Astragalus* polysaccharides (APS) in an exceeding rat colitis model mediated by *trinitrobenzene sulfonic* acid (TNBS) further revealed that the therapeutic benefits included regulating the expression of TNF-alpha, IL-1β and NFATc4 (30).

There is a lack of studies regarding Parkinson's disease (PD) therapy with APS. A research study was carried out to evaluate the effects of APS against Parkinson's disease for the protection of neurons and mitochondria in the nerve cells, as well as the analyses of the mitochondrial structure and transmembrane potential (44). In addition, another investigation was done on the effect of *Astragalus* polysaccharides on injury-induced due to hypoxia conditions in the neural stem cells (NSCs). The process of transfection with the miR-138 inhibitor blocked miR-138 expression, and by qRT-PCR, the miR-138 level was determined. Hypoxia-induced cell injury was attenuated by APS pre-treatment, as demonstrated by an increase in the viability of the cells, significant reduction in the apoptotic cells, suppression of pro-apoptotic factors, and strengthening of anti-apoptotic factors expression. The regulatory mechanism has regulated by the expression of miR-138 and inhibition of JNK, p38 and MAPK-regulated signalling pathways (31).

Antitumor effect

The anti-tumour activity of *Astragalus membranaceus* has drawn worldwide attention from researchers recently. It has also the ability that can help to boost humoral and cellular immunity, thereby enhancing the effect of inhibition on anti-tumour cells and thereby stimulating apoptotic cell death, through using different cancer models and cell lines. It can also lessen the damage to the immune system through radiation therapy; on the other hand, it involves the balance of tumour adjunctive chemotherapy (32). Research findings have shown that to minimize complications and prevent chemotherapy-induced side effects, the compounds of AM coupled with chemotherapy can improve anti-tumour effects in people with cancer. In addition, AM enhances immunosuppression by stimulating the tumour-kill role of M1 macrophages and in the tumour microenvironment (TME) of T cells (33). Researchers developed gene expression profiling data for laryngeal cancer, whereas the samples were obtained from 109 cancer patients. Reports of GSEA enrichment revealed that they have been predominantly active in various tumour-regulated pathways such as interplay with extracellular matrix components receptors and leukaemia. Therefore, providing a tentative long-term analysis for the therapy of laryngeal cancer as well as providing insights for drug development (34). Effects of *Astragalus* polysaccharide against breast cancer were studied on the MCF-7 cell line, where cancer cells were targeted by enabling macrophage cells. APS activated the regulation of the TNF- α mediated macrophage process, which kills the cancer cells. In addition to this, it can also up-regulate the expression of IL-2, TNF- α and IFN-γ and thereby be effective against breast cancer (34).

Growing evidence from the study of immune modulation results has led to a profound outcome, including that polysaccharide with

Vol. 17(Supplementary issue - 3B) 1327-1339,September 2023, ISSN 0973-8916 (Print), 2230-7303 (Online)
10.5530/ctbp.2023.3s.67

evolutionary preserved structural-related properties. It does not directly target cancerous cells and has been known to primarily invoke the antitumor effects by triggering a humoral and cell-mediated immune response to the cells. Thereby completely able to suppress the assembly of immunosuppressive cytokines, Natural Killer (NK) cells, macrophages, and dendritic cells. APS when treated with cancer cells enhances the T-cell proliferation, enhances the cytotoxicity of T lymphocytes (35). The antiproliferative effect of APS on Hepatocellular carcinoma (HCC) cells is investigated in vivo, where it plays a major role in anti-tumour by causing tumour cell apoptosis by encouraging the Bax protein expression and minimizing Bcl-2 gene expression levels. This significantly leads to boosting the Bax and Bcl-2 ratio after a flow cytometry measurement (36). A novel finding indicated that APS might effectively increase spleen lymphocyte proliferation and hence, maximise the peritoneal macrophage phagocytosis in mice. In addition, it is also effective within the peripheral blood expression upregulation of the Interleukin-2, TNF-α and Interferon-γ (37).

APS inhibits the proliferation of erythroleukemia K562, by downregulating the cyclin B and cyclin E production and increasing the expression of p21. The mechanism involves blocking MKN45 cells in the G0-G1 stage, which affects the cell cycle (38). The apoptosis of tumour cells can be greatly promoted by APS. Study experiments have shown that apoptosis of MCF-7 and 4T1 cells can be triggered by APS by stopping a cell cycle at stage G1 (39). Moreover, the migration and invasive potential of cervical cancer cells C-4I was substantially inhibited by APS; this result could contribute to E-cadherin expression upregulations and MMP2 activities inhibitions (40).

For diabetes

Upon treatment with APS, it has been observed that Type 1 Diabetes mellitus occurrence has been reduced in non-obese diabetic mice. Other symptoms, which were improved, were the deferration of disease, reduction of islets inflammation, and the cellular ultra-structuring has been protected. APS also increases Galectin 1 expression in T1DM mice, which causes CD8+T cell apoptosis. APS can indeed effectively protect islet b cells and suppress sugar levels and fast insulin in T2DM rats (11). It reduces serum triglyceride levels in T2DM rats and stimulates the metabolism of body fat (41). Another study has reported that APS helps to lower the blood glucose level by reducing ER tension in Type II Diabetes mellitus patients, thereby enhancing insulin sensitivity (42).

For wound healing

It has been reported that APS has the property of inducing reepithelialisation, revascularization, and cytokine secretion. When studies were carried out on the skin healing process, and the replication cycle of the cell cycle. The process, which takes place in the healing, involves resurfacing the wound on the epithelial cells, sealing the wounded area of the tissues, restoring the circulation of the blood in that area and regulating the TGF-β1 signalling pathway (43). It was studied by downregulating the cyclin D1 protein that involves in the development of the cell cycle (44). It has been observed that APS has decreased collagen synthesis in the skin, treated with bleomycin and antagonised prostaglandin-induced fibrotic disease (59). After X-ray irradiation and nuclear and chromosomal damage, the APS is found to be able to mitigate DNA damage within BMSC (45).

Conclusion and future perspectives

There are several traditional medicinal plants that has been reported to have various therapeutic potentials such as for the control of glucose regulation in diabetes, anti-cancer activity, etc. (46-48). In this review, we have discussed the importance of *the Astragalus* plant›s three key applications - Improvement of the immune system and anti-inflammatory activity, for diabetes and wound healing as well as antitumor property. *Astragalus* is also an antibacterial and antiviral agent and helps in the management of blood glucose levels. *Astragalus* also has numerously diverse medicinal properties such as adaptogen, cardiotonic, hypotonic, hypoglycaemic, circulatory stimulant, vasodilator, and antifatigue. In addition to the mechanism, and how these compounds influence different biochemical processes in the body, the exact impact of multiple A*stragalus* components on a single organ should be investigated in future research. However, more clarifications are required regarding its processes of lowering blood pressure, fibrosis antagonisms, and bacteriostatic/bactericidal and antiviral activity. APS from the *A. membranaceous* almost has no harmful side effects in avoiding and curing infections, the dose-response interaction is a significant aspect. Thus, effective monitoring of APS dosages needs further study when taking into account its various pharmacological consequences. In the APS study, the main current challenge is to isolate its basic elements and establish its specific goals. APS is a naturally complex compound. A detailed detection of the goals of the APS would offer further guidance in the therapeutic application of an APS, as well as a demonstration of the excellent results. While over 200 substances, including saponins and flavonoids in the form of cyclobutane, were obtained, systematic research into photochemistry should be enhanced. In addition, while several analytical studies for flavonoids and saponins were performed qualitatively and quantitatively research against the inflammatory action of flavonoids was unusual so the improvement was needed in this area. Further clinical testing is expected to classify different molecules or secondary metabolites, which are responsible for the cure or the treatment of diseases.

Acknowledgement

We would like to thank Vellore Institute of Technology, Vellore, Tamil Nadu, India for providing the facilities to carry out this work.

Disclosure statement

The authors of the article have no conflict of interest to declare.

References

1. Ullah, S., Rashid Khan, M., Ali Shah, N., Afzal Shah, S., Majid, M., & Asad Farooq, M. (2014) Ethnomedicinal plant use value in the Lakki Marwat District of Pakistan. J Ethnopharmacol, 158, 412–422. https://doi.org/10.1016/j.jep.2014.09.048

2. Shang, A., Huwiler, K., Nartey, L., Juni, P., & Egger, M. (2007) Placebo-controlled trials of Chinese herbal medicine and conventional medicine comparative study. Int J Epidemiol, 36(5), 1086–1092. https://doi.org/10.1093/ije/dym119

3. Zhang, Y., Li, X., Ruan, J., Wang, T., Dong, Y., Hao, J., Wang, T. (2016) Oleanane type saponins from the stems of Astragalus membranaceus (Fisch.) Bge. var. mongholicus (Bge.) Hsiao. Fitoterapia, 109, 99–105. https://doi.org/10.1016/j.fitote.2015.12.006

4. Liu, P., Zhao, H., & Luo, Y. (2017) Anti-Aging Implications of Astragalus Membranaceus (Huangqi): A Well-Known Chinese Tonic. Aging Dis, 8(6), 868. https://doi.org/10.14336/ad.2017.0816

5. Chen, Z., Liu, L., Gao, C., Chen, W., Vong, C. T., Yao, P., Wang, Y. (2020) Astragali Radix (Huangqi): A promising edible immunomodulatory herbal medicine. J Ethnopharmacol, 258, 112895. https://doi.org/10.1016/j.jep.2020.112895

6. Fu, J., Wang, Z., Huang, L., Zheng, S., Wang, D., Chen, S., Yang, S. (2014) Review of the botanical characteristics, phytochemistry, and pharmacology of *Astragalus membranaceus* (Huangqi). Phytother Res, *28*(9), 1275–1283. https://

doi.org/10.1002/ptr.5188

7. Cho, W. C. S., & Leung, K. N. (2007) In vitro and in vivo immunomodulating and immunorestorative effects of *Astragalus membranaceus*. J Ethnopharmacol, 113(1), 132–141. https://doi.org/10.1016/j.jep.2007.05.020

8. Fathiazad, F., Khosropanah, M. K., & Movafeghi, A. (2010) Cycloartane-type glycosides from the roots of *Astragalus caspicus* Bieb. Nat Prod Res, 24(11), 1069–1078. https://doi.org/10.1080/14786410902975582

9. Zarre, S., & Azani, N. (2013) Perspectives in taxonomy and phylogeny of the genus Astragalus (Fabaceae): a review. Prog Biol Sci, 3(1), 1–6. https://doi.org/10.22059/pbs.2013.32086

10. Zheng, Y., Ren, W., Zhang, L., Zhang, Y., Liu, D., & Liu, Y. (2020) A Review of the Pharmacological Action of Astragalus Polysaccharide. Front. Pharmacol, 11, 349–349. https://doi.org/10.3389/FPHAR.2020.00349/BIBTEX

11. Wang, Y.-P., Li, X.-Y., Song, C.-Q., & Hu, Z.-B. (2002) Effect of astragaloside IV on T, B lymphocyte proliferation and peritoneal macrophage function in mice. Acta Pharmacol Sin, *23*(3), 263–266. https://pubmed.ncbi.nlm.nih.gov/11918853/

12. Zhang, B.-Q., Hu, S.-J., Qiu, L.-H., Shan, Q.-X., Sun, J., Xia, Q., & Bian, K. (2005) Diphasic Effects of *Astragalus membranaceus* BUNGE (Leguminosae) on Vascular Tone in Rat Thoracic Aorta. Biol. Pharm. Bull, 28(8), 1450–1454. https://doi.org/10.1248/bpb.28.1450

13. Tin, M. M. Y., Cho, C.-H., Chan, K., James, A. E., & Ko, J. K. S. (2007) Astragalus saponins induce growth inhibition and apoptosis in human colon cancer cells and tumor xenograft. Carcinogenesis, 28(6), 1347–1355. https://doi.org/10.1093/carcin/bgl238

14. Chen, J., Li, Y., Yang, L.-Q., Li, Y.-Z., Nan, Z.-B., & Gao, K. (2012) Biological activities of flavonoids from pathogenic-infected *Astragalus adsurgens*. Food Chem, 131(2), 546–551. https://doi.org/10.1016/j.foodchem.2011.09.021

15. Teyeb, H., Zouari, S., Douki, W., Najjar, M. F., & Neffati, M. (2010) Essential oils of leaves, flowers and fruits of *Astragalus gombiformis* Pomel *(Fabaceae*). Acta Hortic, *835*(853), 263–268. https://doi.org/10.17660/actahortic.2010.853.30

16. Bone, K., & Mills, S. (2012) Principles and practice of phytotherapy: Modern herbal medicine. Princ. Pract. Phytother. Second Ed, 1–1051. https://doi.org/10.1016/C20090487257

17. Duan, L.-X., Chen, T.-L., Li, M., Chen, M., Zhou, Y.-Q., Cui, G.-H., Qi, X. (2012) Use of the Metabolomics Approach to Characterize Chinese Medicinal Material Huangqi. Mol Plant, 5(2), 376–386. https://doi.org/10.1093/mp/ssr093

18. Jiang, C. L., Tang, C., Qian, Y., Suo, H. Y., Li, L. (2013) Review on the Immunomodulation of Astragalus Polysaccharide. Food Sci, 34, 327–332. https://doi.org/10.7506/spkx1002-6630-201311069

19. Jin, M., Zhao, K., Huang, Q., & Shang, P. (2014) Structural features and biological activities of the polysaccharides from Astragalus membranaceus. Int J Biol Macromol, 64, 257–266. https://doi.org/10.1016/j.ijbiomac.2013.12.002

20. Shao, P., Zhao, L.-H., Zhi-Chen, & Pan, J.-P. (2006) Regulation on maturation and

function of dendritic cells by *Astragalus mongholicus* polysaccharides. Int Immunopharmacol, *6*(7), 1161–1166. https://doi.org/10.1016/j.intimp.2006.02.009

21. Liu, Q., Yao, Y., Zhang, S., & Sheng, Z. (2011) Astragalus polysaccharides regulate T cell-mediated immunity via CD-11chighCD45RBlow DCs in vitro. J Ethnopharmacol, 136(3), 457–464. https://doi.org/10.1016/j.jep.2010.06.041

22. Yin, J.-Y., Chan, B. C.-L., Yu, H., Lau, I. Y.-K., Han, X.-Q., Cheng, S.-W., Han, Q.-B. (2012) Separation, structure characterization, conformation and immunomodulating effect of a hyperbranched heteroglycan from Radix *Astragali*. Carbohydr Polym, 87(1), 667–675. https://doi.org/10.1016/j.carbpol.2011.08.045

23. Lu, Y., Xing, Q.-Q., Xu, J.-Y., Ding, D., & Zhao, X. (2016). Astragalus polysaccharide modulates ER stress response in an OVA-LPS induced murine model of severe asthma. Int J Biol Macromol, *93*, 995–1006. https://doi.org/10.1016/j.ijbiomac.2016.09.058

24. Huang, W. M., Liang, Y. Q., Tang, L. J., Ding, Y., & Wang, X. H. (2013) Antioxidant and anti-inflammatory effects of Astragalus polysaccharide on EA.hy926 cells. Exp Ther Med, *6*(1), 199–203. https://doi.org/10.3892/etm.2013.1074

25. Tian, C.M., Xing, M.Y., Xia, D.Z., (2018) Optimization of Extraction Process of Astragalus Polysaccharide and Study on Its Antioxidant Activity in Vitro. Lishizhen Med Mater Med Res, 29, 2072–2076. https://doi.org/10.3969/j.issn.1008-0805.2018.09.007

26. Yang, F., Yan, G., Li, Y., Han, Z., Zhang, L., Chen, S., Yang, L. (2016) Astragalus Polysaccharide Attenuated Iron Overload-Induced Dysfunction of Mesenchymal Stem Cells via Suppressing Mitochondrial ROS. Cell Physiol Biochem, *39*(4), 1369–1379. https://doi.org/10.1159/000447841

27. Zhao, L., Wu, H., Zhao, A., Lu, H., Sun, W., Ma, C., Jia, W. (2014) The in vivo and in vitro study of polysaccharides from a two-herb formula on ulcerative colitis and potential mechanism of action. J Ethnopharmacol, *153*(1), 151–159. https://doi.org/10.1016/j.jep.2014.02.008

28. Tian, Z., Liu, Y., Yang, B., Zhang, J., He, H., Ge, H., Shen, Z. (2016) Astragalus Polysaccharide Attenuates Murine Colitis through Inhibition of the NLRP3 Inflammasome. Planta Med, 83, 70–77. https://doi.org/10.1055/s-0042-108589

29. Feng, J., Geng, J., Wu, J., Wang, H., Liu, Y., Du, B., Xiao, H. (2022) A Potential Role of Plant/Macrofungi/Algae-Derived Non-Starch Polysaccharide in Colitis Curing: Review of Possible Mechanisms of Action. Molecules, *27*(19), 6467. https://doi.org/10.3390/molecules27196467

30. Lv, J., Zhang, Y., Tian, Z., Liu, F., Shi, Y., Liu, Y., & Xia, P. (2017) Astragalus polysaccharides protect against dextran sulfate sodium-induced colitis by inhibiting NF-κB activation. Int. J. Biol. Macromol, *98*, 723–729. https://doi.org/10.1016/j.ijbiomac.2017.02.024

31. Liu, H., Chen, S., Guo, C., Tang, W., Liu, W., & Liu, Y. (2018) Astragalus Polysaccharide Protects Neurons and Stabilizes Mitochondrial in a Mouse Model of Parkinson Disease. Med. Sci. Monit, 24, 5192–5199. https://doi.org/10.12659/msm.908021

32. Li, S., Sun, Y., Huang, J., Wang, B., Gong, Y., Fang, Y., Guo, Y. (2020). Anti-tumor effects and mechanisms of *Astragalus membranaceus* (AM) and its specific im-

Vol. 17(Supplementary issue - 3B) 1327-1339,September 2023, ISSN 0973-8916 (Print), 2230-7303 (Online)
10.5530/ctbp.2023.3s.67

munopotentiation: Status and prospect. J. Ethnopharmacol, 258, 112797. https://doi.org/10.1016/j.jep.2020.112797

33. Dong, K. F., Huo, M. Q., Sun, H. Y., Li, T. K., & Li, D. (2020) Mechanism of *Astragalus membranaceus* in the treatment of laryngeal cancer based on gene co-expression network and molecular docking. Sci Rep, 10(1). https://doi.org/10.1038/s41598-020-68093-0

34. Guo, S.-Q., Li, X.-J., & Jia, Y.-J. (2020). Advances in anti-tumor mechanism and clinical application of *Astragalus* polysaccharides. TMR Cancer, 3(2), 44–51. https://doi.org/10.12032/TMRC201800067

35. Li, W., Song, K., Wang, S., Zhang, C., Zhuang, M., Wang, Y., & Liu, T. (2019) Anti-tumor potential of astragalus polysaccharides on breast cancer cell line mediated by macrophage activation. Mater Sci Eng. C, *98*, 685–695. https://doi.org/10.1016/j.msec.2019.01.025

36. Banerjee, S., Parasramka, M., & Paruthy, Shivani B. (2015) Polysaccharides in Cancer Prevention: From Bench to Bedside. In Ramawat, Kishan Gopal & J. Mérillon (Eds.), Polysaccharides: Bioactivity and Biotechnology (pp. 2179–2214). Cham: Springer International Publishing. https://doi.org/10.1007/9783319162980_26

37. Wan, L.-H., Li, L.-K., Kuang, W.-J., Huang, Y.-F., Xie, H.-H., Chen, G., Wang, B.-R. (2012) Anti-tumor effects of Astragalus on hepatocellular carcinoma in vivo. Ind J Pharmacol, *44*(1), 78. https://doi.org/10.4103/0253-7613.91872

38. Xie, S. R., Shen, H., Zhao, S., Zhang, G. X., 2009. Effects of Astragalus Polysaccharide on Growth Inhibition and Apoptosis of Gastric Cancer Cells. Hebei J Tradit Chin Med, 31, 1373–1375. https://doi.org/10.3969/j.issn.1002-2619.2009.09.064

39. Chao, L., Zhou, J., Zhu, X.X., Ni, W.P., Wang, H.D., Wang, Q., (2012) Effects of Astragalus Polysaccharide on Growth Inhibition and Cell Cycle of Human Gastric Cancer Cell MKN45. J Tradit Chin Med, 30, 2474–2477. https://doi.org/10.13193/j.archtcm.2012.11.108.chaol.034

40. Chen, W., Lai, Y., Wang, L., Xia, Y., Chen, W., Zhao, X., Ye, H. (2015) Astragalus polysaccharides repress myocardial lipotoxicity in a PPARalpha-dependent manner in vitro and in vivo in mice. J Diabetes Complicat, *29*(2), 164–175. https://doi.org/10.1016/j.jdiacomp.2014.11.007

41. Agyemang, K., Han, L., Liu, E., Zhang, Y., Wang, T., & Gao, X. (2013) Recent Advances in Astragalus membranaceus Anti-Diabetic Research: Pharmacological Effects of Its Phytochemical Constituents. Evid Based Complement Altern Med, 654643. https://doi.org/10.1155/2013/654643

42. Luo, M.-J., Wang, Y., Chen, S.-Y., & Yang, Z.-M. (2022) Astragalus Polysaccharides Alleviate Type 2 Diabetic Rats by Reversing the Expressions of Sweet Taste Receptors and Genes Related to Glycolipid Metabolism in Liver. Front Pharmacol, *13*. https://doi.org/10.3389/fphar.2022.916603

43. Mukherjee, P. K., Maity, N., Nema, N. K., & Sarkar, B. K. (2011) Bioactive compounds from natural resources against skin aging. Phytomedicine, *19*(1), 64–73. https://doi.org/10.1016/j.phymed.2011.10.003

44. Zhao, B., Zhang, X., Han, W., Cheng, J., & Qin, Y. (2017) Wound healing effect of an Astragalus membranaceus polysaccharide and its mechanism. Mol Med Rep, *15*(6), 4077–4083. https://doi.org/10.3892/mmr.2017.6488

Vol. 17(Supplementary issue - 3B) 1327-1339,September 2023, ISSN 0973-8916 (Print), 2230-7303 (Online)
10.5530/ctbp.2023.3s.67

45. Zhang, L., Luo, Y., Lu, Z., He, J., Wang, L., Zhang, L., Liu, Y. (2018) Astragalus Polysaccharide Inhibits Ionizing Radiation-Induced Bystander Effects by Regulating MAPK/NF-kB Signaling Pathway in Bone Mesenchymal Stem Cells (BMSCs). Med Sci Monit, *24*, 4649–4658. https://doi.org/10.12659/msm.909153

46. Dakshayani, L., Merchant, N., Smitha, S., et al. (2020) Holy Basil: A Potential Herbal Source for Therapeutic Applications. Curr Trends Biotechnol Pharm, 15(1), 87–100. https://doi.org/10.5530/ctbp.2021.1.10

47. Dash, S., Pattnaik, G., Kar, B., Sahoo, N., & Bhattacharya, S. (2021) An Approach Towards Method Development to Investigate the Anti-Diabetic Activity on Experimental Animals. Curr Trends Biotechnol Pharm, *15*(3), 330–348.

48. Satapathy, B. S., Biswal, S. K., Maharana, L., & Pattnaik, S. (2023) Bioactive Components of piper betel Could be Potential anticancer Agents: A short Review on Pre-clinical Investigations and Practical Challenges. Curr Trends Biotechnol Pharm, *17*(2), 918–929.