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REVIEW ARTICLE

Astragalus Polysaccharide in Digestive Health: A Review of Mechanisms, Applications, and Therapeutic Potential

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ABSTRACT: Astragalus polysaccharides (APS) have attracted increasing attention for their potential benefits in digestive health due to their wide range of biological activities, including immune modulation, anti-tumor effects, and enhancement of digestive functions. This review focuses on summarizing recent research regarding the mechanisms, applications, and therapeutic potential of APS in digestive health. APS has been shown to enhance digestive enzyme activities, improve intestinal structure, and regulate gut microbiota. Specifically, APS significantly increases the activity of trypsin, lipase, and amylase, leading to improved nutrient absorption. Moreover, APS promotes intestinal health by increasing villus height and the villus-to-crypt ratio, contributing to a more efficient intestinal environment. Additionally, APS exhibits prebiotic effects, fostering the growth of beneficial gut bacteria while inhibiting harmful pathogens, thus supporting gut development and mucosal immune function. Although APS shows promising therapeutic potential, further studies are needed to elucidate its precise mechanisms and confirm its clinical efficacy in treating digestive disorders. This review aims to provide valuable insights and research references for the future application of APS in digestive health therapies.

Keywords: Astragalus Polysaccharides, Digestive Enzymes, Gut Microbiota, Digestive System

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1. INTRODUCTION

Gastrointestinal diseases, including gastritis, peptic ulcers, and inflammatory bowel disease (IBD), pose significant challenges to public health on a global scale [1]. As reported in the literauture, these conditions not only adversely affect the quality of life for millions but also impose a substantial economic burden on healthcare systems worldwide [2]. While traditional therapeutic approaches are diverse, many of these diseases continue to present issues such as limited treatment efficacy, high recurrence rates, and notable side effects.

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The complexity and heterogeneity of gastrointestinal disorders underscore the critical need for early diagnosis and effective intervention in clinical practice. For certain conditions, such as autoimmune gastritis, existing treatment modalities have yet to adequately address the underlying pathophysiological mechanisms, highlighting an urgent need for the exploration of novel therapeutic strategies and pharmacological agents.

In this context, Astragalus polysaccharide (APS) has garnered significant attention as a natural compound with a wide range of pharmacological activities. APS is an active component extracted from the Astragalus plant, and in addition to its well-established anti-inflammatory and antioxidant properties, it also exhibits notable immunomodulatory and antitumor effects [2]. Research indicates that APS can enhance immune function and modulate immune responses, thereby supporting the body in combating inflammation and pathological changes within the gastrointestinal system [3]. Furthermore, its antitumor characteristics have been demonstrated to play a role in inhibiting the onset and progression of gastrointestinal tumors [4].

Recent studies have increasingly suggested that APS may have a beneficial impact on the treatment of gastrointestinal diseases, including alleviating gastritis, promoting gastric mucosal repair [5], and improving intestinal health [6]. However, the specific effects and underlying mechanisms of APS on the gastrointestinal system remain to be systematically reviewed. Therefore, this review aims to summarize and explore the role of Astragalus polysaccharide (APS) in the gastrointestinal tract, evaluating its potential in improving gastrointestinal diseases. By integrating findings from recent research, we hope to elucidate the mechanisms of action of APS and provide new insights and scientific rationale for the treatment of gastrointestinal disorders.

Gastrointestinal diseases, such as gastritis, peptic ulcers, and inflammatory bowel disease (IBD), continue to pose significant public health challenges globally, affecting millions and placing a heavy burden on healthcare systems. Traditional treatments often face limitations in efficacy, recurrence, and side effects, particularly for complex conditions like autoimmune gastritis. In this context, Astragalus polysaccharide (APS), a bioactive compound with known anti-inflammatory, antioxidant, and immunomodulatory properties, has garnered attention for its potential therapeutic benefits in gastrointestinal disorders. Recent research highlights APS's ability to support immune function, combat inflammation, promote gastric mucosal repair, and enhance intestinal health. This review aims to explore APS's mechanisms of action and its potential as a novel treatment for gastrointestinal diseases, providing valuable insights into its role in improving clinical outcomes.

2. CHEMICAL STRUCTURE AND PHARMACOLOGICAL EFFECTS OF APS

Astragalus (Astragalus spp.) is first documented in the ancient Chinese medical text Shen Nong Ben Cao Jing (The Divine Farmer's Materia Medica). The roots of this herb are derived from two species of leguminous plants: Astragalus *membranaceus* Bge. var. mongholicus (Bge.) Hsiao, and A. *membranaceus* (Fisch.) Bge [7]. Astragalus is characterized by its sweet and slightly warm nature, and it primarily enters the lung and spleen meridians, exerting a range of therapeutic effects including qi tonification, exterior reinforcement, yang elevation, diuresis, pus expulsion, wound healing, and muscle generation [8]. In traditional medicine, Astragalus is considered a herb of significant medicinal value. Astragalus polysaccharides (APS) are one of the key active components of Astragalus [9]. Recently, APS has garnered considerable attention due to its pharmacological activities, which include immunomodulation, antitumor, hypoglycemic, anti-aging, and anti-inflammatory effects. In contemporary research, driven by increasing interest in health and natural medicine, the potential applications of APS in the treatment of digestive system disorders have become a focus of interest.

As an important natural polysaccharide, APS exhibits a complex chemical structure, predominantly composed of various monosaccharides such as glucose, arabinose, xylose, and galactose [8]. This structural diversity endows APS with multiple biological activities, including immunomodulatory, antioxidant, anti-inflammatory, and antiviral properties. Owing to these activities, APS has been widely utilized in traditional Chinese medicine, particularly in enhancing immune function and managing chronic diseases. In recent years, research on APS has increasingly concentrated on its effects on the digestive system, highlighting its potential therapeutic value in this area.

2.1. Chemical Structure of APS

Astragalus Polysaccharides (APS) is a significant natural polysaccharide formed by various monosaccharides, including glucose, arabinose, xylose, and galactose, linked through different glycosidic bonds to create a complex structure. This diversity in monosaccharide composition and linkage patterns endows APS with unique chemical properties and multiple biological activities. Studies have shown that the main chain of APS consists primarily of α-D-(1-4) glucose, with a single-chain height of 0.552 nm and a length of 27 nm [8]. These structural features contribute to its role as a hetero-polysaccharide with various biological functions in the body. For example, the unique structure of APS allows it to bind to specific receptors, thereby modulating the immune system and enhancing anti-inflammatory and antitumor effects. Advanced analytical techniques such as high-performance liquid chromatography (HPLC) and mass spectrometry can further elucidate the specific structure of APS and its component ratios, providing a foundation for investigating its biological activities.

2.2. Pharmacological Effects of APS

Astragalus Polysaccharides (APS), as a natural active component, exhibits a wide range of pharmacological effects, including immunomodulatory, antitumor, anti-inflammatory, and antioxidant properties [8]. These characteristics suggest the potential application of APS in the treatment and management of digestive system diseases

2.2.1. Immunomodulatory Effects

The immunomodulatory effects of APS are particularly notable, especially in enhancing immune system function and improving digestive system health.

Enhancing Immune Organ Function: Research by Chen et al. has demonstrated that APS can significantly enhance the function of immune organs, such as the thymus and spleen, with results shown in Table 1 [10]. Li et al. found that APS could increase the thymus and spleen indices in mice, improving the structural integrity and function of these organs, thereby enhancing immune response capability [11]. In another study, APS significantly enhanced the function of immune organs related to the digestive tract, such as mesenteric lymph nodes, which play a key role in the immune defense of the digestive tract [12]. By promoting lymphocyte proliferation and macrophage phagocytic activity, APS helps strengthen the digestive tract's defense against infections and pathogens [13]. To the best of our knowledge, previous studies have not explored the immune modulatory effects of APS combined with an inactivated IHNV vaccine on rainbow trout. In this study, we purified a novel APS from Astragalus extract, primarily composed of mannose, glucosamine, glucose, galactose, and arabinose units. Using this APS (P-APS) as an adjuvant, we developed an inactivated IHNV vaccine to enhance immune responses in rainbow trout, as illustrated in Figure 1 [14]. Furthermore, RNA-seq analysis of the head kidney revealed the mechanisms through which P-APS enhances the efficacy of inactivated vaccines. This research provides a promising strategy for preventing viral diseases in fish while deepening our understanding of the synergistic mechanisms between adjuvants and inactivated vaccines.

Table 1. Comparison of thymus index and spleen index in rats of each group (x±s, n=10).

Groups	Thymus Index(mg/g)	Spleen Index(mg/g)
Groups M	1.85±0.43	5.16±1.51
Groups S	1.22±0.48*	4.01±1.09*
Groups APSH	2.33±0.33*#	7.49±1.15*#
Groups APSM	2.06±0.18*#	6.12±1.22*#
Groups APSL	1.88±0.20#	5.22±1.09#
F	12.284	11.230
P	<0.001	<0.001

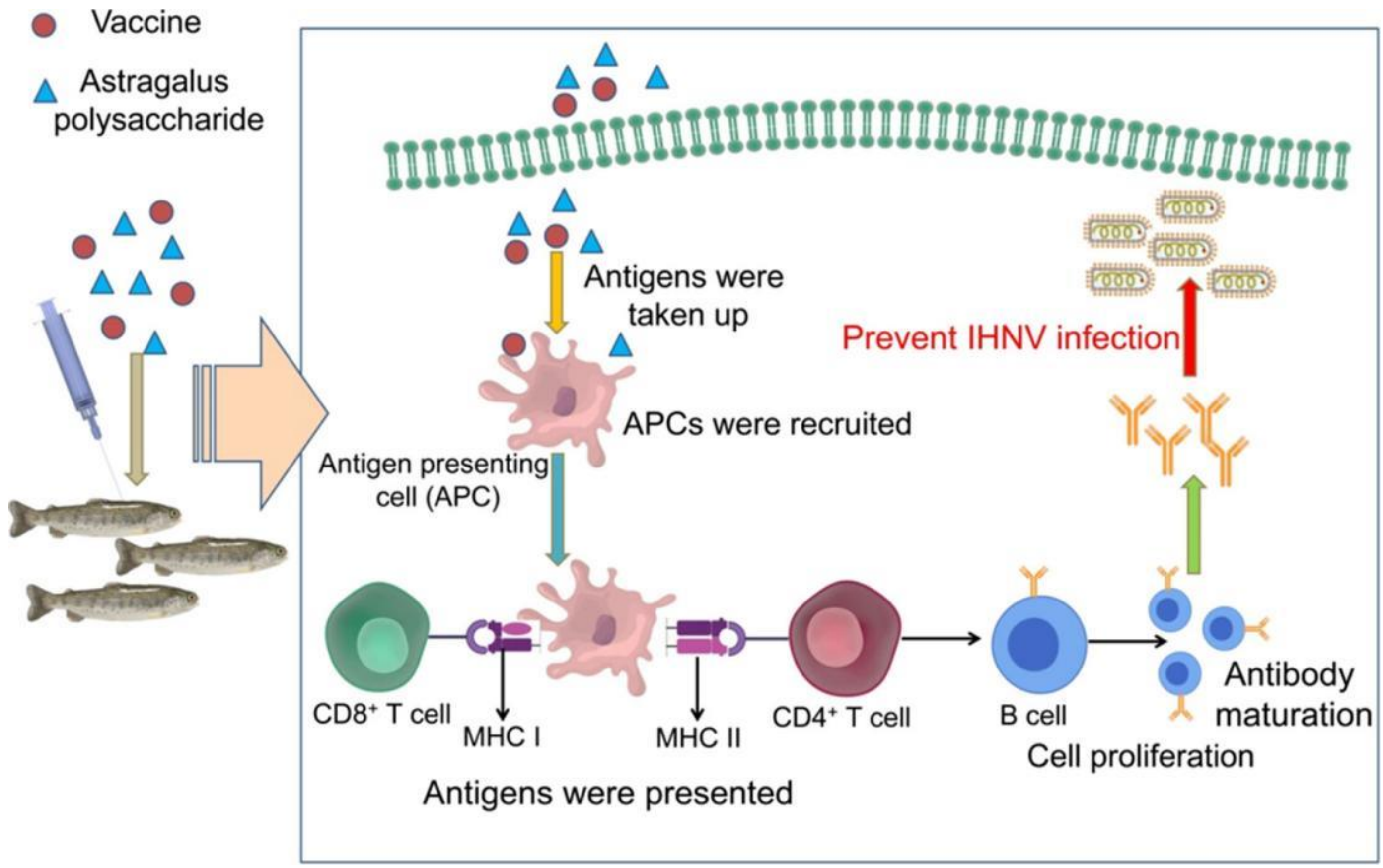

Fig. 1. Mechanism of action of the vaccine.Reprinted with permission from ref. [18], Pan, Yucai, Zhe Liu, Jinqiang Quan, Wei Gu, Junwei Wang, Guiyan Zhao, Junhao Lu, and Jianfu Wang. "Purified Astragalus Polysaccharide Combined with Inactivated Vaccine Markedly Prevents Infectious Haematopoietic Necrosis Virus Infection in Rainbow Trout (Oncorhynchus mykiss)." *ACS Biomaterials Science & Engineering* 10, no. 11 (2024): 6938-6953. Copyright © American Chemical Society.

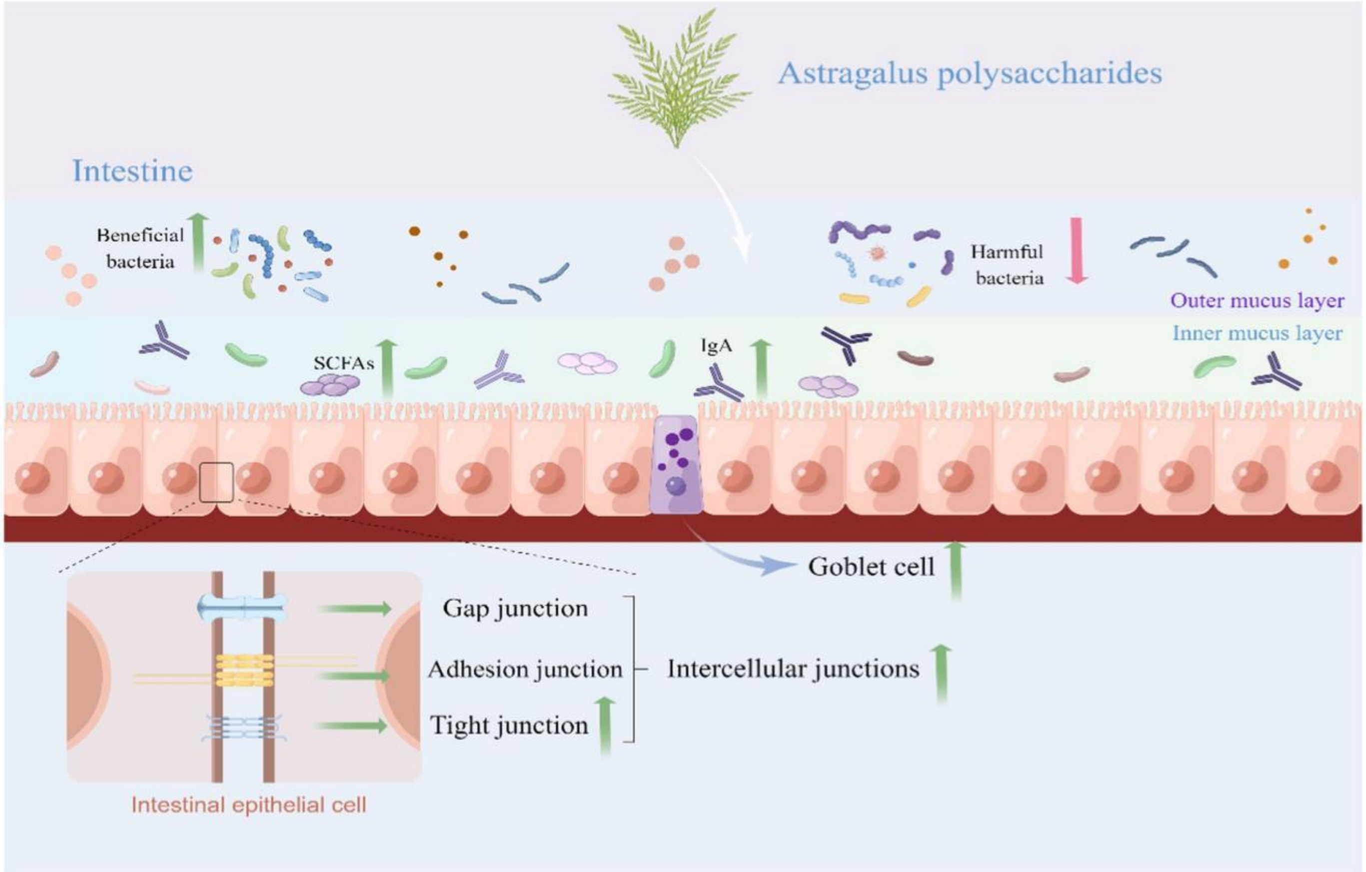

Fig. 2. Schematic representation of the protective effects of Astragalus polysaccharide (APS) on intestinal health, including barrier integrity, immune response, and microbiota regulation. Reprinted with permission from ref. [22], Liang, H., Tao, S., Wang, Y., Zhao, J., Yan, C., Wu, Y., Liu, N. and Qin, Y., 2024. Astragalus polysaccharide: implication for intestinal barrier, anti-inflammation, and animal production. *Frontiers in Nutrition*, *11*, p.1364739. Copyright © Frontiers Media S.A.

Promoting Immune Cell Proliferation and Function: Immune cells play a crucial role in the prevention and treatment of digestive system diseases. APS has been found to significantly promote the proliferation and activation of various immune cells, such as dendritic cells and T cells [13]. Hwang et al. showed that APS could increase the number of dendritic cells in mesenteric lymph nodes and enhance their function by upregulating the expression of CC-chemokine receptor 7 [14]. This action not only improves the immune surveillance capability of the intestine but also further strengthens the defense against digestive tract pathogens by activating natural killer cells and T cells.

Modulating Cytokine Secretion: APS has a significant impact on cytokine secretion, which plays a crucial role in immune modulation in digestive system diseases. Research indicates that APS can upregulate the levels of several cytokines that help enhance immunity and have anti-inflammatory effects, such as IL-2, IL-6, and TNF-α [15]. For example, in a study on inflammatory bowel disease (IBD), APS reduced the production of pro-inflammatory cytokines (such as IL-6 and TNF- α) in the intestine while increasing the levels of anti-inflammatory cytokines (such as IL-10), significantly alleviating IBD symptoms [16]. These findings suggest that APS has the potential to modulate digestive tract immune responses and mitigate inflammation.

Influencing Immunoglobulin Secretion: Immunoglobulins play a vital role in mucosal immunity in the digestive tract. Studies have shown that APS can promote the secretion of immunoglobulins such as IgA, IgG, and IgM, thereby enhancing humoral immune responses [17]. For instance, in a study on gastrointestinal infections, APS significantly increased IgA levels in the mouse intestine, which is crucial for neutralizing pathogens and toxins in the gut [18]. Additionally, APS can further promote intestinal health and immune homeostasis by modulating the balance of intestinal microbiota [19].

Protecting Intestinal Barrier Function: APS has also been shown to protect intestinal barrier function. The intestinal barrier, composed of epithelial cells and tight junctions, prevents harmful substances and pathogens from entering the body. Studies have found that APS can enhance the integrity and function of the intestinal barrier by regulating the expression of tight junction proteins such as ZO-1 and Occludin [20]. This effect is significant for the prevention and alleviation of digestive system diseases such as IBD and irritable bowel syndrome [21]. As illustrated in Figure 2, Astragalus polysaccharide (APS) exerts a multifaceted protective role in intestinal health. APS strengthens the intestinal barrier by upregulating tight junction proteins like ZO-1 and Occludin, while also increasing the number of goblet cells that secrete protective mucus. Moreover, APS enhances the intestinal immune response by promoting the secretion of secretory immunoglobulin A (sIgA), regulating cytokine production, and supporting the proliferation and differentiation of immune cells. In addition, APS maintains the biochemical barrier of the intestine by modulating gut microbiota composition and structure, as well as increasing the levels of short-chain fatty acids (SCFAs), which are essential for gut health and metabolic balance. These integrated effects make APS a key agent in supporting intestinal health and immune homeostasis [22].

2.2.2. Antitumor Effects

APS also demonstrates notable antitumor effects, particularly in the prevention and treatment of digestive system tumors. *Inhibiting Tumor Cell Proliferation*: APS inhibits tumor cell proliferation through multiple mechanisms. For example, studies have shown that APS can inhibit the proliferation and migration of colorectal cancer cells by regulating the miR-195-5p signaling pathway [22]. Additionally, APS may prevent gastric cancer cell division and proliferation by influencing cell cycle regulatory proteins [23, 24]. As depicted in Figure 3, polysaccharide metal complexes, including those derived from APS, enhance bioactivity across various domains. These complexes exhibit significant biological activities, such as antitumor, antioxidation, ant radiation, antibacterial, immune regulation, hypoglycemic, and blood lipid-lowering effects. By leveraging such properties, polysaccharide metal complexes hold promise for applications in food, pharmaceuticals, and bioactive materials [25, 26]. These enhanced effects suggest that the integration of APS with metal ions may further potentiate its antitumor mechanisms by modulating oxidative stress and immune responses, providing a novel approach for cancer treatment.

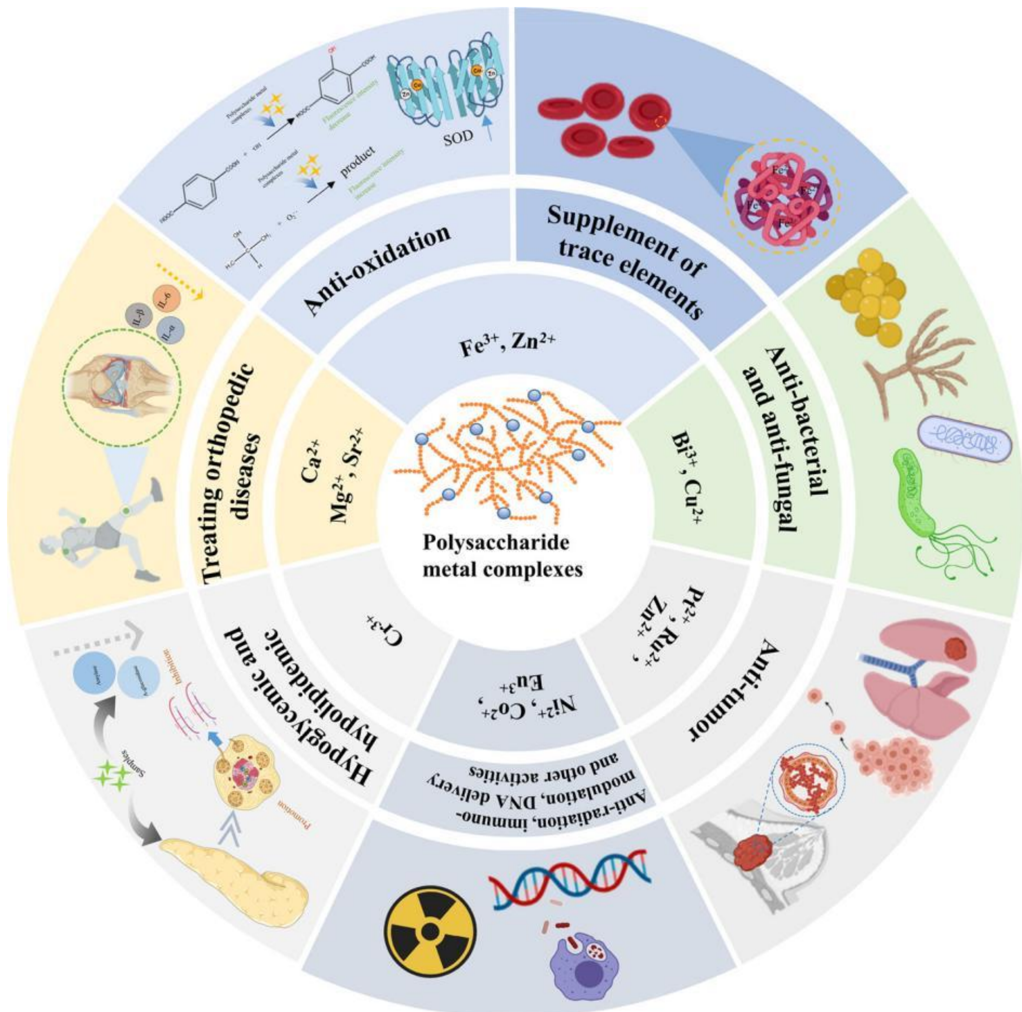

Fig. 3. Bioactivity of polysaccharide metal complexes. Reprinted with permission from ref. [25], Li, X., Jiang, F., Liu, M., Qu, Y., Lan, Z., Dai, X., Huang, C., Yue, X., Zhao, S., Pan, X. and Zhang, C., **2022.** Synthesis, characterization, and bioactivities of polysaccharide metal complexes: a review. *Journal of Agricultural and Food Chemistry*, *70*(23), pp.6922-6942. Copyright © American Chemical Society.

Inducing Tumor Cell Apoptosis: APS can induce apoptosis in digestive system tumor cells, thereby inhibiting tumor growth. Research has found that APS induces apoptosis in gastric and liver cancer cells by regulating the expression of Bax/Bcl-2 and caspase family proteins [10, 25-31]. This mechanism provides potential applications for APS in the treatment of digestive system tumors.

Astragalus isoflavonoids enhance intracellular antioxidant defenses by increasing the activity of key enzymes such as SOD, CAT, and GSH-Px, which scavenge reactive oxygen species (ROS) and mitigate oxidative stress. In high-glucose conditions, these isoflavonoids restore antioxidant enzyme activity, reducing oxidative damage in mesangial cells, as shown in Figure 4 [32-35]. This highlights their potential as catalytic antioxidants for managing diabetes-induced oxidative stress.

Inhibiting Tumor Cell Metastasis and Invasion: APS also possesses the ability to inhibit tumor cell metastasis and invasion. Studies have demonstrated that APS can reduce the migration and invasion abilities of gastric and colorectal cancer cells by inhibiting the epithelial-mesenchymal transition (EMT) process [33-38]. This effect is associated with the inhibition of key signaling pathways, such as Wnt/β-catenin and NF-κB, highlighting its potential as an anti-metastatic agent. Furthermore, epigenetic mechanisms appear to play a role in APS's broad health-promoting effects. As shown in Figure 5, 4.0-4.3% of differentially methylated sites (DMSs) were located in CpG islands (CGI), and 5.5-5.6% were found in the promoter-transcription start site (TSS) region, with most DMSs residing in CGI open sea or intergenic regions. Methylation in the promoter-TSS region, which is rich in CpG dinucleotides, often inhibits transcription factor binding and downregulates gene expression. However, the functional implications of methylation in other gene regions remain unclear [39, 40].

Figure 6 further highlights the versatile health-promoting effects of APS mediated through epigenetic and molecular mechanisms. APS has demonstrated efficacy in preventing diabetes by attenuating insulin resistance, improving insulin sensitivity, and participating in insulin-related processes such as secretion and signaling. Additionally, APS shows antiviral properties by regulating viral replication, enhancing host virus clearance, and preventing viral entry through immunomodulation.

Epigenetic analysis has also revealed APS's role in wound healing, influencing five processes involving 183 genes, and suggested its pleiotropic potential in mitigating heart diseases, neurological disorders, reproductive problems, and olfactory dysfunction through gene set enrichment analysis (GSEA). Remarkably, 97 of the 111 olfaction-associated genes identified were olfactory receptor genes, underscoring APS's potential to improve olfactory abilities. Moreover, APS modifies various immunological processes, emphasizing its broad therapeutic applications and its potential to influence multiple pathways for health improvement.

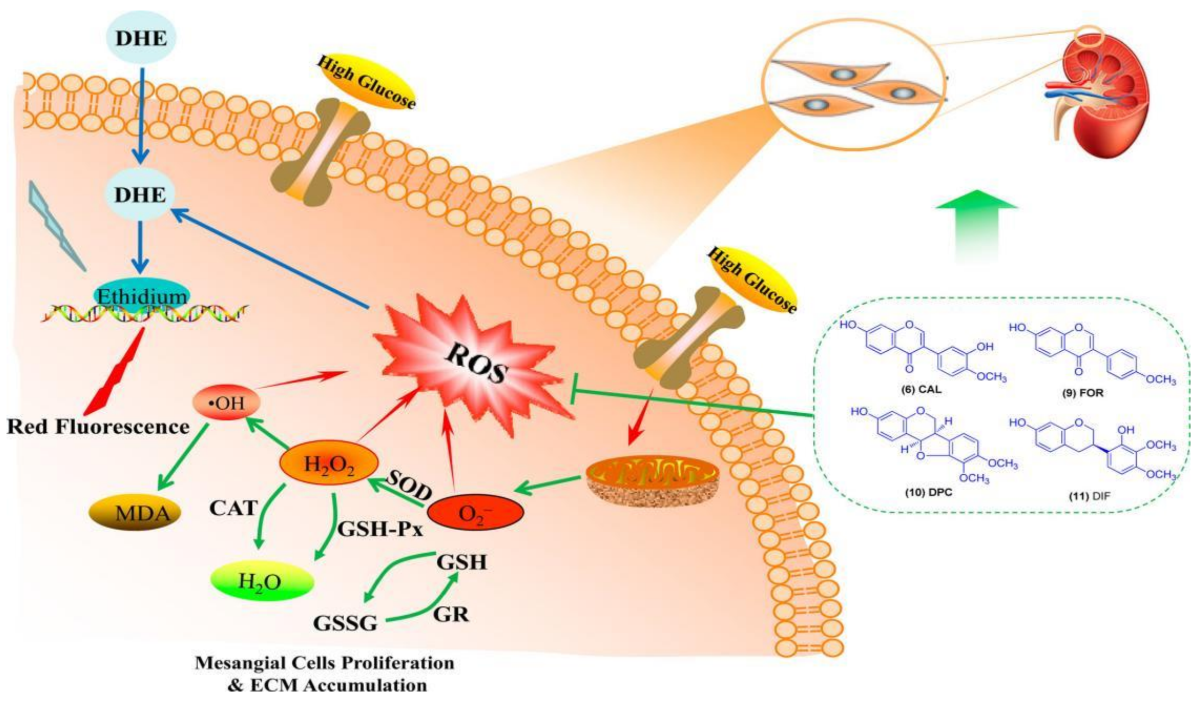

Fig. 4. Possible intracellular antioxidant detoxifying mechanisms of Astragalus isoflavonoids that attenuate high-glucose-induced oxidative stressthrough inhibition of ROS generation. Reprinted with permission from ref. [32], Tang, D., Shen, Y.B., Wang, Z.H., He, B., Xu, Y.H., Nie, H. and Zhu, Q., **2018.** Rapid Analysis and Guided Isolation of Astragalus Isoflavonoids by UHPLC–DAD–MS n and Their Cellular Antioxidant Defense on High-Glucose-Induced Mesangial Cell Dysfunction. *Journal of Agricultural and Food Chemistry*, *66*(5), pp.1105-1113.Copyright © American Chemical Society.

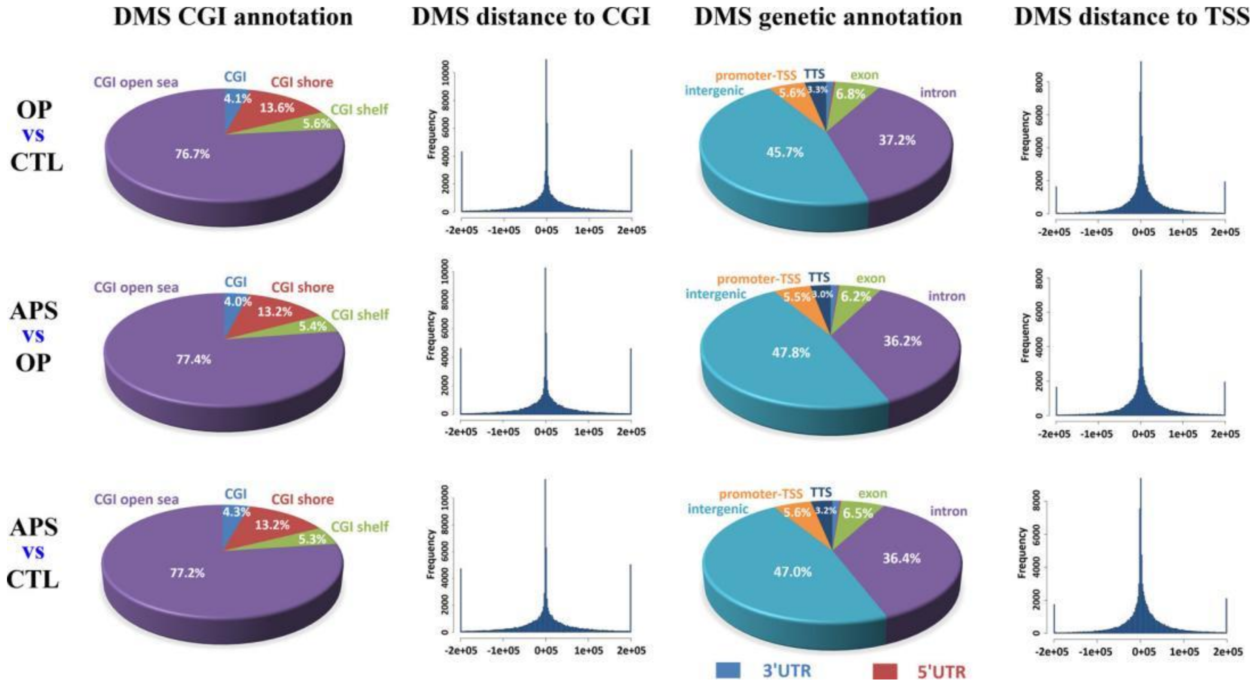

Fig. 5. Annotation of 5mC to CpG island (CGI) and the transcription start site (TSS). Reprinted with permission from ref. [39], Liu, J., Liu, J., Duan, S., Liu, L., Zhang, G. and Peng, X., 2020. Reprogrammed epigenetic landscape-prophesied functions of bioactive polysaccharides in alleviating diseases: a pilot study of DNA methylome remodeling in Astragalus polysaccharide (APS)-Improved osteoporosis in a rat model. *Journal of Agricultural and Food Chemistry*, *68*(52), pp.15449-15459. Copyright © American Chemical Society.

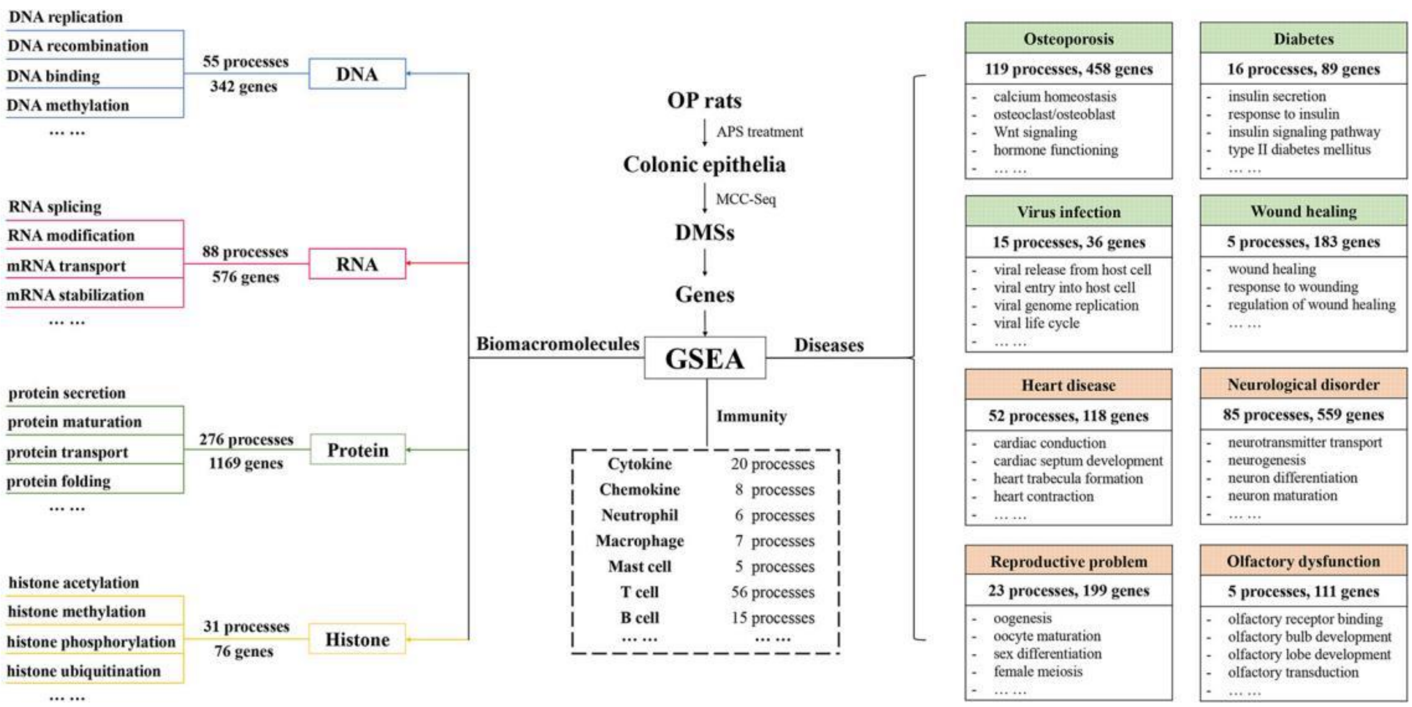

Fig. 6. APS-participated processes based on DNA methylomic analysis. Based on the annotation of the differentially methylated sites (DMSs), the involved genes were identified for gene set enrichment analysis (GSEA). The processes associated with biomacromolecules, diseases, and immunity were presented. Reprinted with permission from ref. [39], Liu, J., Liu, J., Duan, S., Liu, L., Zhang, G. and Peng, X., 2020. Reprogrammed epigenetic landscape-prophesied functions of bioactive polysaccharides in alleviating diseases: a pilot study of DNA methylome remodeling in Astragalus polysaccharide (APS)-Improved osteoporosis in a rat model. *Journal of Agricultural and Food Chemistry*, *68*(52), pp.15449-15459. Copyright © American Chemical Society.

3. EFFECTS OF APS ON DIGESTIVE PROCESSES

APS improves digestive system function through multiple mechanisms, such as regulating the gut microbiota, repairing the intestinal barrier, and promoting nutrient absorption.

3.1. Enhancing Digestive Enzyme Activity

APS can improve digestive enzyme activity and increase digestive absorption efficiency by enhancing cellular function and regulating protein synthesis [39]. Studies have shown that APS can significantly increase the activity of enzymes such as trypsin, lipase, and amylase [40]. For example, Chen et al. (2020) found that APS significantly increased trypsin activity (by approximately 35%) and lipase activity (by about 28%) in a rat model of chronic.

3.2. Gut Microbiota and Immune Regulation

Astragalus Polysaccharides (APS), as a natural plant polysaccharide, exhibit significant biological activities, including antioxidant and immune-regulatory functions. In recent years, the restricted use of antibiotics has drawn attention to natural plant polysaccharides due to their high biodegradability and low toxicity. APS positively impacts the gut microbiota [41, 42] by modulating intestinal immune functions [43]. Specifically, research by Li et al. demonstrated that APS promotes the growth of beneficial bacteria such as Lactobacillus and Bifidobacterium, while inhibiting harmful bacteria like Escherichia coli and Staphylococcus aureus, leading to a significant improvement in microbial balance (with an increase in beneficial bacteria by over 40%) [44]. This action aids in enhancing gut health, strengthening the intestinal barrier, and providing energy to the body. Furthermore, APS enhances anti-inflammatory activity and improves gut micro-ecology by promoting the production of beneficial microbial metabolites like short-chain fatty acids, thus improving the overall function of the digestive system [45].

3.3. Repairing the Intestinal Barrier and Improving Gut Microbiota

APS further enhances intestinal health by repairing the intestinal barrier and improving microbial fermentation processes [46]. The gut, a crucial digestive and immune organ, plays a key role in maintaining the integrity of the intestinal barrier and regulating host physiological functions. It was found that APS significantly increases the expression levels of tight junction proteins in intestinal epithelial cells, such as occludin and claudin-1, by approximately 50% [47], thereby reducing intestinal permeability [48], and inflammatory responses [49]. APS contributes to promoting the growth of beneficial bacteria, inhibiting the growth of harmful bacteria, and improving intestinal barrier functions, thus facilitating nutrient digestion and absorption, and slowing the onset and progression of related diseases. Figure 7 highlights the reduction in crystal adhesion and endocytosis in oxalate-damaged HK-2 cells after repair by Se-APS. Oxalate-induced oxidative stress disrupts the balance between ROS production and antioxidant defenses, causing damage to proteins, DNA, and lipids, which promotes kidney stone formation by enhancing CaOx crystal adhesion to renal epithelial cells. Se-APS mitigates oxidative stress, reducing ROS levels and crystal deposition, offering a potential therapeutic approach for kidney stones caused by high oxalate levels [50-55].

4. POTENTIAL APPLICATIONS OF APS IN ANIMAL DIGESTIVE SYSTEMS

Astragalus Polysaccharides (APS) have been widely studied and applied in animal nutrition and health. Studies have shown that APS not only significantly enhances digestive enzyme activities and digestion absorption efficiency in animals but also improves gut health, thereby boosting animal growth performance [52-55].

4.1. Effects of APS on the Digestive System of Aquatic Animals

Research indicates that APS enhances digestive enzyme activities and improves intestinal structure increasing villus length and number, and muscular layer thickness in the intestines, thereby significantly boosting digestion absorption efficiency and improving growth performance. For instance, it was found that APS effectively promotes the growth and development of Asian swamp eel (Monopterus albus) by improving its digestive system and intestinal structure [56]. Similar effectiveness has been confirmed in other aquatic animals such as fish. For example, it was reported that APS enhances intestinal health by regulating gut microbiota and promoting intestinal mucosal development [57, 58].

4.2. Effects of APS on the Digestive System of Poultry

In poultry farming, APS also demonstrates significant positive effects. Research indicates that adding APS to broiler diets can significantly increase the activities of digestive enzymes such as protease, amylase, and lipase in the digestive tract, improving the digestion and absorption of proteins and energy from feed, thereby enhancing feed utilization efficiency [59, 60]. Further studies showed that APS significantly enhances the activity of digestive enzymes like lipase and protease in broiler intestines, promotes the development of the digestive system, accelerates the maturation of small intestinal mucosal epithelial cells, and increases the secretion of digestive enzymes in the small intestine, thus improving feed digestion and absorption capacity [61]. Moreover, APS improves intestinal morphology, maintains intestinal mucosal integrity, and helps sustain gut microbiota balance, thus boosting the immunity and disease resistance of broilers. Further research shows that adding APS to broiler diets significantly increases pancreatic lipase and protease activities [62]. It was found that adding 2% Astragalus stem and leaf powder and 1% Codonopsis pilosula stem and leaf powder to the diet significantly enhances villus length, villus height/crypt depth ratio in the duodenum, and villus length and crypt depth in the jejunum and ileum of broiler chickens [63]. These findings indicate that APS improves broiler digestion absorption capacity and production performance by enhancing the digestive system and intestinal structure.

4.3. Effects of APS on the Digestive System of Livestock

In livestock, APS demonstrates significant physiological promoting effects. For instance, studies by Feng Shi-bin et al. revealed that APS significantly increases the apparent digestibility of crude protein and crude fat in the diet of Hu sheep lambs. Additionally, APS significantly increases villus height and V/C ratio (villus height to crypt depth ratio) in the duodenum, jejunum, and ileum, although it has no significant effect on crypt depth ($P > 0.05$) [64] (Tables 2). Another study found that APS improves nutrient digestibility and reduces feed conversion ratio in weaned piglets [65]. It was observed that adding APS to piglet diets significantly improves the digestibility of crude protein and crude fat [66]. Similarly, it was indicated that APS increases the apparent digestibility of dry matter and crude protein in the diet of Rex rabbits and improves calcium digestibility [67].

Astragalus (Astragalus membranaceus), a traditional Chinese medicinal herb with over two thousand years of use, contains APS as its main component, which exhibits significant bioactivity and immunomodulatory effects, participating in various immune responses, antitumor, and antioxidant processes [68-70]. Studies have shown that APS enhances overall digestive and absorption capacity in animals by regulating gut microbiota balance, promoting the proliferation of beneficial bacteria, and improving intestinal health, thereby promoting animal health and growth [71].

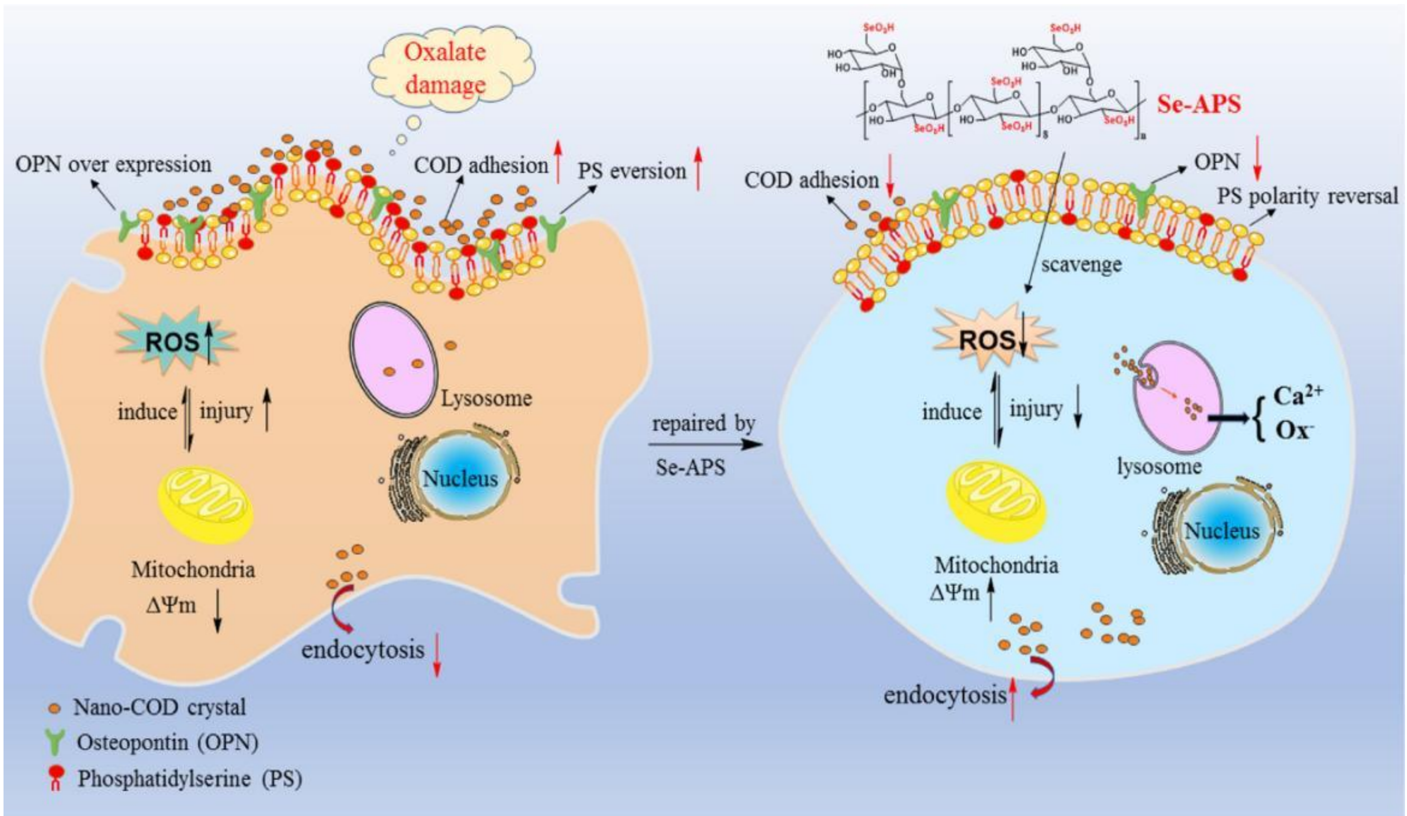

Fig. 7. Schematic diagram of the adhesion and endocytosis of nano-COD crystals in oxalate-damaged HK-2 cells before and after being repaired by APS and Se-APS. Reprinted with permission from ref. [50], Huang, F., Sun, X.Y., Chen, X.W. and Ouyang, J.M., **2021.** Effects of selenized astragalus polysaccharide on the adhesion and endocytosis of nanocalcium oxalate dihydrate after the repair of damaged HK-2 cells. *ACS Biomaterials Science & Engineering*, *7*(2), pp.739-751. Copyright © American Chemical Society.

Table 2. Effects of astragalus polysaccharide on lambs' small intestinal mucosa morphology.

Item		Control Group	Astragalus polysaccharide group
Villus height(ųm)	Duodenum	351.33±6.57 b	364.01±5.59 a
	Jejunum	572.33±6.88b	597.46±14.07a
	Ileum	774.31±19.13b	800.52±8.04a
Crypt depth (μm)	Duodenum	185.25±4.04	184.53±4.79
	Jejunum	299.64±1.37	303.83±7.35
	Ileum	407.31±21.86	393.41±5.61
Villus height/crypt depth (V/C value)	Duodenum	1.89±0.02 b	1.97±0.05 a
	Jejunum	1.91±0.02 b	1.97±0.03 a
	Ileum	1.92±0.07 b	2.03±0.04 a

5. EFFECTS OF APS ON GUT MICROBIOTA

APS significantly influences the structure and function of gut microbiota, improving overall intestinal health by regulating the diversity and metabolic activity of gut microorganisms. Research has shown that APS can significantly inhibit the growth of harmful bacteria in the intestine, increase the number of beneficial bacteria such as Lactobacillus and Bifidobacterium, improve intestinal morphology, and enhance feed utilization [72].

5.1. Effects of APS on Specific Gut Microbiota

Studies show that APS exerts its regulatory effects on gut microbiota primarily through its prebiotic function. It promotes the growth of beneficial bacteria (e.g., Lactobacillus and Bifidobacterium) while inhibiting the proliferation of harmful bacteria (e.g., Escherichia coli and Staphylococcus aureus). For example, in the hindgut of dogs, where microbial diversity is highest, APS can improve intestinal immune function by regulating microbial diversity, thereby affecting overall health [73]. It was reported that APS significantly improves the production performance of livestock and poultry, while also enhancing intestinal development. In mouse models, it was found that APS could restore gut microbiota imbalance induced by a high-fat diet in obese mice [74, 75]. These studies indicate that APS significantly improves intestinal health by regulating the composition and function of gut microbiota.

5.2. Differences in the Effects of Different Types of APS

APS primarily consists of two components: APS-I and APS-II, with molecular weights of $>2\times10^6$ and 1×10^4, and uronic acid contents of 26.25% and 1.62%, respectively [76]. Monosaccharide analysis shows that both APS-I and APS-II are composed of mannose, Rhamnose, Galacturonic acid, Glucose, Galactose, and Arabinose [77, 78], but APS-I has higher proportions of mannose, arabinose, and galactose compared to APS-II [79]. In studies on ulcerative colitis, APS-I showed more significant therapeutic effects [76]. Compared to the model group, APS-I significantly improved clinical symptoms such as shortened colon length, weight loss, increased DAI score, and increased spleen and liver indices ($P < 0.05$, 0.01, 0.001). It alleviated histopathological damage in the colon, reduced MPO activity, and TNF-α and IFN-γ levels in colon tissues ($P < 0.01$, 0.001), and elevated IL-4 and IL-10 levels in colon tissues ($P < 0.05$, 0.01, 0.001). These effects suggest that APS-I is more effective than APS-II in treating ulcerative colitis [79]. Further studies indicate that APS-I is the main active component of APS in treating ulcerative colitis, possibly due to its uronic acid content, polysaccharide type, and glycosidic linkage, and it may exert therapeutic effects by modulating the Th1/Th2 immune balance [80]. Moreover, screening results indicate that APS-II has the strongest immunomodulatory effect both in vivo and in vitro, while APS-I exhibits the strongest anti-inflammatory activity in vitro [79]. It was further confirmed the efficacy of APS in regulating ulcerative colitis [80].

5.3 Clinical and Practical Applications of APS

The immunomodulatory effects of Astragalus Polysaccharides (APS) have been extensively studied. In a study involving human colorectal cancer HCT-116 cells, intervention with APS at various concentrations (0.5, 0.75, or 1.0 g/L) resulted in a significant reduction in cell proliferation. This effect may be attributed to APS's modulation of the phosphoinositide 3-kinase (PI3K)/protein kinase B (AKT)/mammalian target of rapamycin (mTOR) signaling pathway [81]. Another study reported that oral administration of APS at doses of 100 or 200 mg/kg body weight to immunosuppressed mice significantly increased the levels of secretory immunoglobulin A (sIgA) in the small intestinal mucosa, indicating APS's significant impact on enhancing immune function [82].

Furthermore, research has shown that APS can regulate the richness and diversity of gut microbiota, increasing the relative abundance of Firmicutes and Bifidobacteria, while decreasing the relative abundance of Bacteroidetes [83]. These results suggest that APS has a modulatory effect on gut microbiota, enhancing immune responses in mice. Additionally, APS exhibits a significant upregulation of Lactobacillus and Bacteroides genera, highlighting its advantages in regulating gut microbiota richness and diversity.

6. EFFECTS OF APS ON DIGESTIVE ENZYMES

6.1. Effects of APS on Digestive Enzymes in Aquatic Animals

Studies confirm that APS (Astragalus Polysaccharides) significantly affects the digestive processes in aquatic species, particularly sea cucumbers, sturgeons, tilapia, and eels. APS has been shown to effectively enhance the activities of trypsin, amylase, and lipase, facilitating more efficient digestion and nutrient absorption, thus improving digestive capacity and growth performance. It was observed that APS significantly increased digestive enzyme activity in sea cucumbers (Apostichopus japonicus), promoting growth [84]. For tilapia (Oreochromis niloticus), it was found that after 14 days of APS feeding, plasma amylase activity was significantly elevated [85]. It was also observed that APS improves trypsin and lipase activity in the intestines of tilapia [86]. These results indicate that APS has a positive effect on digestion in tilapia. In eels (Monopterus albus), researches showed that appropriate levels of APS significantly increased amylase activity in both the liver and intestines, further supporting APS's positive impact on the digestive process [87]. A study on the Yangtze sturgeon (Acipenser dabryanus) showed that APS significantly enhanced lipase and trypsin activities in juvenile sturgeon intestines [88] (Table 3 and 4). These findings are consistent with other research.

6.2. Effects of APS on Digestive Enzymes in Poultry and Livestock

APS (Astragalus Polysaccharides) has shown significant physiological benefits in poultry and ruminants, such as broiler chickens and Hu sheep lambs. Studies indicate that APS enhances digestive enzyme activity in these animals, thereby improving growth performance and immune function.

6.2.1. Application of APS in Broiler Chickens

Research shows that APS significantly increases digestive enzyme activity in broiler chickens. Cao Yong's study found that APS markedly increased the activities of total protease, lipase, and amylase in the intestines of broiler chickens, which helps accelerate growth rates, increase daily weight gain, and significantly improve feed conversion rates and immune function [89]. Further studies by Wei Bingdong et al. indicated that APS significantly enhanced lipase and trypsin activities in the pancreas of 1-14 day-old chicks [90-96].

Table 3. Analysis results of the effects of Astragalus polysaccharides and Wolfiporia cocos polysaccharides on antioxidant, immune anti-stress and digestive capacity of juvenile Acipenser dabryanus.

Item	APS0.1group	APS0.2 group	WCP0.1 group	WCP0.2 group
Antioxiddant	***	*****	*	****
Immunity	**	*******	*	***
Anti-stress	*	*		
Digestive enzymes	*	***		***

Note: * indicates a signilicant change in a relatedindex,the more * indicates a greater number of related indicators that cause a significant change,the higher the degree of impact.

Table 4. Effects of astragalus polysaccharide on lambs' small intestinal mucosa morphology.

Index	Blank control group	APS0.1 group	APS0.2 group	WCP0.1group	WCP0.2group
Intestinal protease/(IU.g-1)	1.14c±0.17	1.68b± 0.14	2.13a±0.25	1. 28c± 0.16	1.67b±0.18
Intestinal lipase /(U · g-1)	3.21b±0.96	4.24b±0.67	5.77c±0.83	3.90b±0.55	5.32ab± 0.88
Intestinal amylase /(IU.g1)	2.22c±0.33	2.47bc±0.34	3.04a±0.37	2.20c±0.22	2.82ab±0.36

These studies demonstrate that APS has a significant effect on increasing digestive enzyme activity during the early stages of broiler chicken development. In a specific experiments, it was investigated that the impact of APS on organ indices in broiler chickens. The results revealed that APS significantly affected the organ indices of 7-day-old chicks but had a lesser impact at 14 days. This may be due to the maturation of the pancreas as the chicks age, which leads to a stabilization in the growth rate of the pancreas despite increased weight. Thus, APS promotes the development of digestive organs in newly hatched chicks, though this effect diminishes as the birds' age and adapt to their environment [97, 98].

6.2.2. Application of APS in Hu Sheep Lambs

In ruminants such as Hu sheep lambs, APS also exhibits significant effects on enhancing digestive enzyme activity. It was observed that APS significantly increased the activity of pancreatic amylase and lipase in Hu sheep lambs, although the increase in trypsin activity was not statistically significant ($P > 0.05$) but showed an upward trend [99, 100]. This indicates that APS positively impacts digestive function in ruminants, particularly for enzymes involved in fat and starch digestion.

7. CONCLUSION AND FUTURE DIRECTIONS

Astragalus Polysaccharides (APS) have demonstrated considerable potential in enhancing digestive processes in aquatic animals. By boosting the activity of digestive enzymes, APS not only improves the digestive efficiency but also supports overall growth and health, leading to better feed utilization and increased production benefits. These findings emphasize APS's role in improving feed conversion rates and growth performance, making it a valuable additive in aquaculture.

In addition, APS, particularly APS-I, has shown significant effects on gut health, immune function, and metabolic regulation. It enhances immune responses, optimizes gut microbiota, and promotes the proliferation of beneficial bacteria, exhibiting multiple biological activities, including anti-inflammatory and antitumor effects. In livestock and poultry, APS has been found to improve the digestibility of key nutrients, such as dry matter, crude protein, and fat, while increasing pancreatic enzyme activity, further supporting its role in promoting nutrient absorption.

While research has highlighted the positive effects of APS on the digestive system, future studies should explore several key areas: determining optimal dosage, assessing long-term safety and efficacy, evaluating its therapeutic potential for specific digestive diseases, and investigating the underlying mechanisms of its effects. Additionally, exploring the synergistic application of APS with other therapeutic methods could lead to more comprehensive treatment strategies. By addressing these areas, future research will not only deepen our understanding of APS but also expand its clinical applications, reinforcing the importance of natural compounds in modern medicine.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interests.

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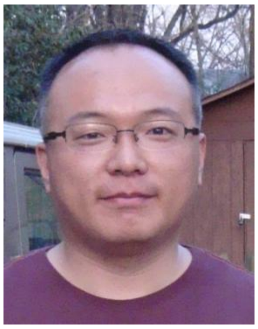

Dr. Kai Song, a Professor at the School of Life Sciences, Changchun Normal University, brings over 14 years of distinguished academic and research expertise. Renowned for his work in nanotechnology and biomaterials, Dr. Song has authored more than 30 high-impact research papers in leading international journals. He has been an integral part of several prestigious research projects funded by the National Natural Science Foundation of China (NSFC) and the Jilin Provincial Department of Science and Technology. His research interests focus on nano-bio interfaces, biomineralization, and environmental nanotechnology, aiming to bridge fundamental science with practical applications. Beyond his research, Dr. Song is deeply committed to nurturing young scientists, fostering innovation, and contributing to advancements in nanomaterials, positioning him as a key figure in his field.

