Acupuncture and Herbal Medicine

Chemical structure and beneficial roles of active biomacromolecules from Ginseng: a narrative review

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Abstract

Biomacromolecules derived from plant-based traditional Chinese medicines play a pivotal role in natural drug research. Ginseng, the root of *Panax ginseng* C.A. Meyer, has attracted significant attention due to its diverse pharmacological activities and broad therapeutic applications. This review focuses on specific active macromolecules obtained from ginseng, including pectin, exosomes, proteins, and dietary fibers. These components possess unique structural characteristics and biological activities that offer novel insights into the multifaceted applications of ginseng. To systematically assess this field, we reviewed literature published over the past 60 years and identified 119 relevant studies investigating the structural composition, pharmacological activity, and potential applications of *P. ginseng* biomacromolecules. By highlighting their crucial role in promoting health and enhancing disease resistance, this review synthesizes the latest research findings on ginseng's pharmacological effects, providing new perspectives and strong theoretical support for clinical drug development.

Keywords: Dietary fiber, Exosomes, Ginseng, Pectin, Proteins, Review

Introduction

Chinese herbal medicine, a critical component of traditional medicine, comprises a wide range of bioactive compounds that play important roles in promoting health and treating diseases. Ginseng (*Panax ginseng* C. A. Mey.), often referred to as the "King of Medicines"[1], exhibits broad pharmacological effects[2], including enhanced immunomodulatory activity, antioxidant effects, and anti-proliferative action against tumor cells. These activities are attributed to its diverse bioactive components, including acidic polysaccharides[3], exosomes[4], and other biologically active substances. Such compounds are essential for regulating physiological functions, enhancing immune defense, and promoting overall health. Consequently, ginseng is not only a prominent research focus in the medical field but also an important resource for clinical applications and related product development.

Among the various bioactive components in ginseng, polysaccharides stand out as a major class with significant pharmacological potential. These include pectin, dietary fiber, and other heteropolysaccharides, which have received extensive attention due to their structural diversity and multifaceted pharmacological effects. Ginseng polysaccharides are typically categorized into water-soluble and insoluble forms, exhibiting immunomodulatory, hypoglycemic, antioxidant, and anti-tumor activities. Their biological functions are closely related to structural features such as glycosidic bond types, molecular weight, and monosaccharide composition. Recent studies have also investigated the synergistic effects of polysaccharides with other ginseng constituents, such as ginsenosides, underscoring their potential as multi-target therapeutic agents. This review focuses on pectin and dietary fiber as representative polysaccharides and emphasizes the need for systematic research on the broader polysaccharide family in ginseng.

Previous studies have comprehensively analyzed active components of ginseng, such as ginsenosides and polypeptides, elucidating their potential value in promoting health and combating diseases[5–6]. In recent years, research on other biological substances in ginseng, including pectin, exosomes, proteins, and dietary fibers, has increased, further underscoring their pharmacological significance. The pharmacological activities of these substances highlight their importance in various physiological processes, and they are now increasingly recognized for their potential in clinical applications and

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health product development. Continued investigation into their properties and activities will advance the modernization of Traditional Chinese Medicine and contribute to global health.

This article systematically reviews 60 years of research on bioactive substances in ginseng, analyzing 119 published studies to summarize their structural characteristics, biological activities, and potential applications. This review aims to enhance understanding of ginseng's role in various health conditions and to encourage further research and applications, thereby providing valuable references to support its broader integration into modern medicine and healthcare.

Research progress of ginseng pectin

Ginseng pectin[7] is an important acidic polysaccharide primarily located in the cell walls and membranes of *Panax ginseng*. Its polyhydroxy structure facilitates the formation of high-molecular-weight polysaccharides, thereby playing a key role in regulating physiological functions. Previous studies have demonstrated that ginseng pectin significantly reduces blood glucose and lipid levels and may serve as an adjuvant therapeutic agent for patients with diabetes and hyperlipidemia[8]. In addition, ginseng pectin exhibits diverse biological activities, including immune system regulation, inhibition of tumor cell migration, and antioxidant effects[9]. These activities underscore its potential in promoting health and provide a scientific basis for understanding the broader medicinal value of ginseng. Studies have reported that the primary purification method for ginseng pectin is column chromatography, and on a dry-weight basis, ginseng pectin constitutes approximately 20% of the total polysaccharides[10]. The main functions of ginseng pectin are summarized in Table 1, offering new insights for researchers to better understand its medicinal value and establishing a foundation for future studies.

Characterization of the structure of ginseng pectin

Plant pectin macromolecules are generally recognized to consist of three main regions: homogalacturonan (HG), rhamnogalacturonan I (RG-I), and RG-II[16]. The backbone of ginseng pectin is primarily composed of galacturonic acid residues linked by α-1,4-glycosidic bonds. Various monosaccharides, including galactose, arabinose, and mannose, are typically attached as side chains through β-1,2-, β-1,3-, or β-1,6-glycosidic bonds[17]. Consequently, the molecular weight of ginseng pectin is generally high. However, its specific structure, composition, and degree of polymerization may vary depending on the source and extraction method used. Chen et al.[18] compared the bioactive components of ginseng samples

Table 1

Bioactivity corresponding to ginseng pectin structure and its possible mechanism

Ginseng pectin extract	Main structure	Model	Extraction method	Effective dose	Weight	Biological activity	Mechanism	References
WGPE, EGP, WGP; WGP, WGPE	RG-I, HG, AG	Male ICR mice	60°C, 3 h (EDTA)/100°C for 30 min (water), then 50°C for 24 h (α-amylase-assisted)	50 mg/kg/day	20 ± 2g	Immunoregulatory	Stimulate the proliferation of T and B lymphocytes	[11–12]
GPW-1, GPR-1, GPS-1	RG, HG, AG	Male ICR mice	100°C, 4 h (water), then 4 h, 95% ethanol	100 mg/kg/day	20 ± 2g	Hypoglycemic	Increase liver glycogen and insulin levels while reducing TG and TC levels	[13]
GPW-1, GPR-1, GPS-1	RG, HG, AG	Male ICR mice	100°C, 4 h (water), then 4 h, 95% ethanol	100 mg/kg/day	20 ± 2g	Antioxidant	Increase the content of non-enzymatic antioxidants and enhance the activity of antioxidant enzymes	[13]
WGPA-1-HG,WGPA-4-HG; WGPA-3-RG,WGPA-4-RG	RG-I, HG	L-929 cells, HT-29 cells	100°C, 4 h (water), then 4 h, 95% ethanol	0.015 mg/mL/day	Not reported	Anti-tumor	Inhibits cell adhesion and tumor cell migration; induces apoptosis by activating caspase-3	[14]
RG-I-4	RG-I	Galectin-3–mediated HT-29 cell adhesion	120°C, 4 h (sodium borate buffer)	Not reported	Not reported	Anti-tumor	Binding and inhibition of galectin-3	[15]

AG: Arabinogalactans; EGP: EDTA-soluble Ginseng Polysaccharide; GPR: Ginseng pectin from red ginseng; GPS: Ginseng pectin from steamed ginseng; GPW: Ginseng pectin from white ginseng; HG: Homogalacturonan; RG-I: Rhamnogalacturonan-I; WGP: Water-soluble Ginseng Polysaccharide; WGPA: Water-soluble ginseng pectin acid; WGPE: Water-soluble Ginseng Polysaccharide.

of different ages and plant parts and found that ginseng pectin content was approximately 4.6 mg/g in the main roots of 5-year-old ginseng and about 7 mg/g in the leaves of 5-year-old ginseng. For example, pectin extracted by heat treatment undergoes structural changes and has been shown to exhibit significant hypoglycemic activity, indicating that the extraction method substantially influences both the structural characteristics and biological activity of ginseng pectin[13].

Biological activity of ginseng pectin

Immunoregulatory activity

As an important acidic polysaccharide, ginseng pectin has demonstrated considerable potential in immunomodulation[19]. Studies have indicated that its immunomodulatory function has a clear structural basis. For example, Gao et al.[20] found that non-branched galacturonic acid residues on the RG-I backbone of ginseng pectin significantly reduced the anti-complement activity of processed ginseng leaf pectin, thereby providing structural evidence for its immunomodulatory effects. Further studies have shown that ginseng pectin can effectively activate the complement system, leading to stimulated macrophages producing increased levels of cytokines such as interleukin (IL)-6, IL-2, and tumor necrosis factor-alpha (TNF-α)[21]. Moreover, literature reports indicate that ginseng acidic polysaccharide, a precursor isolated from ginseng pectin, can activate the Toll-like receptor 2, trigger the extracellular signal-regulated kinase/c-Jun N-terminal kinase (ERK/JNK) signaling pathway, and subsequently activate the nuclear transcription factors nuclear factor kappa-light-chain-enhancer of activated B cells (NF-κB) and activator protein 1. This activation upregulates the expression of inducible nitric oxide synthase, increases nitric oxide production, and enhances macrophage phagocytic activity[22]. It can also directly activate monocytes and Tamm-Horsfall protein (THP)-1 cells, promote IL-8 production, and recruit neutrophils and T cells to the site of inflammation, thereby enhancing anti-infective responses[23]. These findings suggest that ginseng pectin may share similar mechanisms of immune activity with acidic polysaccharides, making this an important direction for future research.

Anti-tumor effect

Research on the anti-tumor effects of ginseng pectin has increased steadily in recent years. Literature reports indicate that ginseng pectin inhibits the growth of various cancer cell types, including lung, liver, and breast cancer cells[24]. Multiple studies have shown that ginseng pectin exerts anti-tumor effects through different mechanisms, such as inducing apoptosis[25] and inhibiting cell migration[14]. For example, in 2011, Cheng et al.[26] found that HG-type pectin from ginseng significantly inhibited the proliferation of human colorectal adenocarcinoma cells (Figure 1A), suggesting its potential as an adjuvant treatment. In 2019, Xue et al.[27] demonstrated in an *in vivo* study that the ginseng pectin derivatives water-soluble ginseng pectin acid (WGPA)-UD and RG-I-4 effectively inhibited the growth of sarcoma-180 tumors by modulating galectin-3-mediated T-cell activation and apoptosis (Figure 1B). These findings suggest that ginseng pectin may hold therapeutic potential in cancer treatment. Furthermore, the combination of Pectasol-C modified citrus pectin and paclitaxel has been shown to enhance anti-tumor efficacy and reduce toxicity through a synergistic formulation rather than a simple mixture[28]. Such synergy between pectin and chemotherapeutic agents opens new avenues for cancer prevention and treatment[29]. Collectively, these studies indicate that ginseng pectin shows promising potential in anti-tumor therapy. Future research should elucidate its mechanisms of action and explore its clinical applications to provide more effective treatment options for patients with cancer.

Antioxidant activity and anti-aging properties

The antioxidant activity of ginseng pectin is closely associated with its molecular characteristics. For example, a decrease in molecular weight markedly improves its solubility, thereby enhancing antioxidant capacity through more efficient free radical scavenging[11]. The antioxidant effects of ginseng pectin are likely related to the structure of GalA and other reducing sugar residues. This property enables ginseng pectin to scavenge free radicals, inhibit oxidative stress, and consequently reduce oxidative damage to cells. Such mechanisms contribute to delaying the aging process and may aid in the prevention of chronic diseases, including cardiovascular disease and diabetes. In addition, pectin rich in RG-I and HG[30] domains exhibits significant anti-aging biological activity. For instance, Wang et al.[31] investigated RG pectin from ginseng acidic polysaccharide-1 and its RG-dependent endocytosis, as well as its effects on the nuclear accumulation of transcription factors such as FOXO/DAF-16 and Nrf2/SKN-1. In summary, the antioxidant and anti-aging properties of ginseng pectin represent promising strategies for promoting health and preventing disease. Further research should elucidate the specific mechanisms of action and explore its potential roles in delaying aging and improving health outcomes.

Blood glucose regulation

Numerous studies have confirmed that ginseng polysaccharides possess significant hypoglycemic activity, and ginseng pectin, as an acidic polysaccharide, shares this characteristic. For example, Sun et al.[32] demonstrated that oral administration of WGPA to streptozotocin-induced diabetic mice effectively lowered blood glucose levels. The primary mechanisms involve enhancing insulin sensitivity and promoting glycogen synthesis[33]. This dual action contributes to regulating blood glucose levels and offers a potential approach to diabetes management. In addition, ginseng pectin has been shown to regulate lipid metabolism[34] and inhibit obesity[35]. By modulating intestinal flora and activating the AMP-activated protein kinase signaling pathway, ginseng pectin inhibits fat synthesis, promotes fat breakdown, and improves lipid metabolism disorders in type 2 diabetic and obese rats. These effects provide a basis for the development of

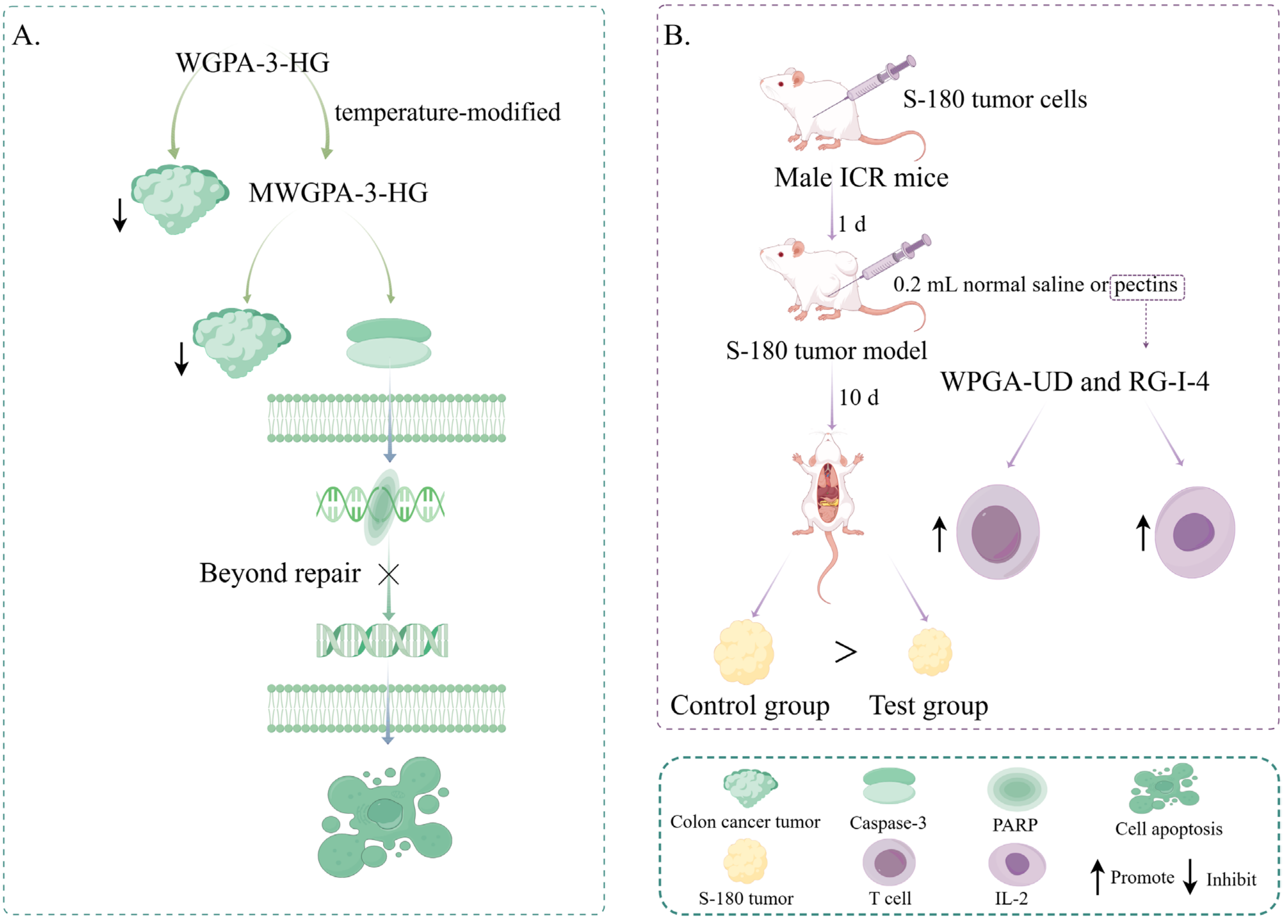

Figure 1. Anti-tumor activity of ginseng pectin. (A) WGPA-3-HG can resist tumor proliferation. Moreover, the MWGPA-3-HG obtained by denaturating this pectin after heating treatment can not only resist tumor proliferation but also inhibit cell apoptosis. (B) WPGA-UD and RG-I-4 can effectively inhibit the growth of sarcoma-180 tumors by modulating GAL-3-mediated T cell and IL-2 activation. GAL-3: Galectin-3; HG: Homogalacturonan; IL: Interleukin-2; RG: Rhamnogalacturonan; WPGA: Water-soluble Ginseng pectin acid.

related functional foods or pharmaceuticals. Collectively, these findings suggest new avenues for dietary and therapeutic interventions in diabetes management, potentially leading to more effective clinical strategies to improve the quality of life for patients with diabetes. Therefore, large-scale clinical trials are warranted to comprehensively elucidate its mechanisms of action and therapeutic efficacy.

Other biological activities

In addition to the biological activities discussed above, ginseng pectin also exhibits anti-inflammatory[36], anti-fatigue[37], neuroprotective[38], antiviral[39], radioprotective[40], cytoprotective[41], anti-ulcer[42], antidepressant[43], and antibacterial adhesion properties[44]. Furthermore, chemically modified pectin has demonstrated significant retinoprotective effects *in vivo* without markedly altering blood glucose levels[45]. This finding suggests that ginseng pectin may have therapeutic potential, particularly in the treatment of diabetes-related retinopathies. However, despite these promising preliminary findings, further studies are required to elucidate the precise mechanisms of action of ginseng pectin and to evaluate its clinical efficacy. In summary, the diverse biological activities of ginseng pectin highlight its potential for disease prevention and treatment, emphasizing the need for future research to establish a more robust theoretical basis for its clinical applications.

Application prospects of ginseng pectin

Pharmaceutical applications

The pharmacological activities of pectin macromolecules extracted from ginseng have been well documented in the literature. Notably, ginseng pectin has been shown to be an effective drug carrier due to its excellent biocompatibility. For example, studies have demonstrated that ginseng pectin can significantly improve drug release characteristics and enhance drug bioavailability, thereby increasing therapeutic efficacy while reducing potential adverse effects[46]. These findings indicate that ginseng pectin holds potential for pharmaceutical and clinical applications; however, data on its safety profile remain limited, warranting further investigation.

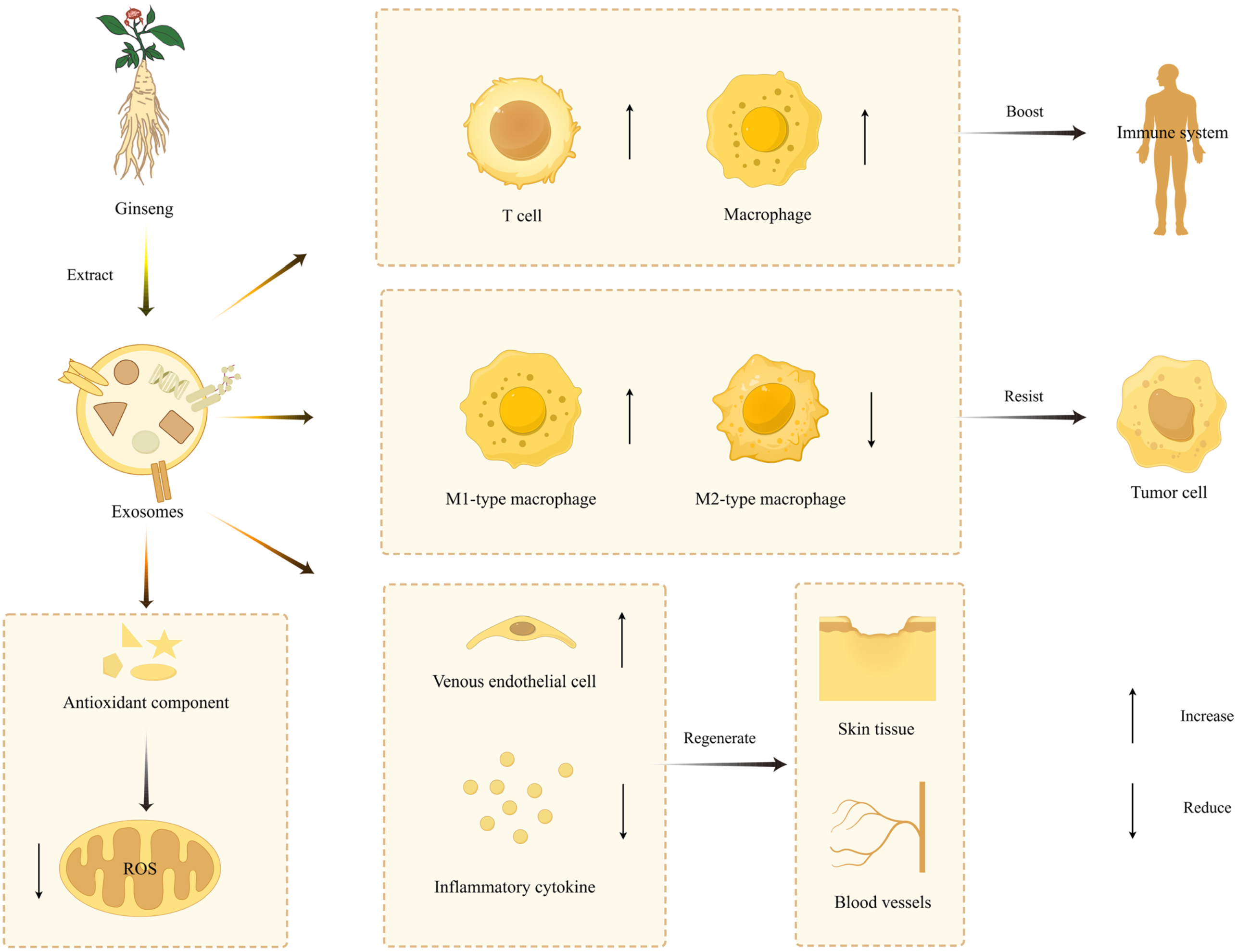

Figure 2. Biological activities of ginseng exosomes. Exosomes extracted from ginseng can ROS and thereby exert antioxidant effects. It can mediate T cells and macrophages, thereby strengthening the human immune system. It can increase M1-type macrophages and reduce M2-type macrophages, thereby combating tumor cells. It can increase venous endothelial cells and reduce inflammatory cytokines, thereby enabling the regeneration and repair of skin tissue and blood vessels. ROS: Reduce oxidative stress.

Functional food and healthcare applications

Ginseng pectin is a natural plant-derived polysaccharide that is non-toxic and free from adverse reactions, making it highly suitable for applications in the food and healthcare sectors. In addition, ginseng pectin can act as a natural thickener and stabilizer, with applications in products such as jams, juices, and dairy products. Residues from the ginseng extraction process are also rich in pectin, which enhances their functional properties. An experimental study demonstrated that these residues can be effectively recycled for use as fruit coatings[47], thereby improving fruit preservation and extending shelf life. This approach simultaneously reduces waste and mitigates environmental pollution. Such sustainable utilization reflects environmental protection principles while opening new avenues for innovation and development in the food industry, contributing to the growth of a green economy. Therefore, the comprehensive use of ginseng pectin and its byproducts offers not only economic benefits but also environmental advantages, demonstrating practical value in a mutually beneficial outcome.

Research progress of ginseng exosomes

Plant exosomes are nanovesicles secreted by plant cells[48], enriched with a diverse array of bioactive molecules that serve as critical mediators of intercellular communication. These vesicles contain DNA, small RNAs, proteins, and lipids, all of which play essential roles in signaling between cells[49]. As a type of plant-derived exosome, ginseng exosomes share these characteristics. They facilitate intrinsic signal transmission and may also contribute to the plant's interactions with its environment. Notably, the biomolecules contained in ginseng exosomes are closely associated with the pharmacological activities of ginseng (Figure 2). This association offers novel research directions and provides a framework for further investigations into ginseng's therapeutic potential and underlying mechanisms. Systematic study of ginseng exosomes and the bioactive molecules they transport is expected to elucidate the traditional medicinal value of ginseng and foster the development of innovative exosome-based therapies or health products. This emerging research area holds considerable theoretical significance for both plant biology and pharmacology.

Structural characteristics and composition of ginseng exosomes

Previous studies have suggested that ginseng exosomes are nanosized vesicles secreted by ginseng cells through exocytosis, with diameters typically ranging from 30 to 150 nm. Electron microscopy observations by Ma et al.[50] revealed that ginseng root exosomes possess a characteristic bilayer membrane structure, primarily composed of phospholipids and cholesterol, which contributes to their stability and biocompatibility. This specific size range and membrane composition are important for their biological functions. The exosome membrane contains various specific membrane proteins, including CD63 and TSG101, which play crucial roles in exosome formation, release, and signal transduction[51]. Ginseng exosomes carry diverse bioactive molecules, including ginsenosides[52], mRNA, miRNA, proteins (such as heat shock proteins), and lipids, all of which contribute to their functional roles. Specific microRNA (miRNAs), such as miR-166a and miR-319c, are enriched and play key roles in intercellular communication and the regulation of gene expression[53]. For example, miRNAs can regulate gene expression by binding to target mRNA, while heat shock proteins can modulate cellular stress responses[54]. In addition, ginseng exosomes may also contain polysaccharides and small-molecule metabolites. The interactions among these components form a strong biological basis for the diverse functions of exosomes, including intercellular communication and immune regulation.

Biological function of ginseng exosomes

Immunomodulatory and anti-tumor effects

Ginseng exosomes enhance the immune response by regulating immune cell functions, such as activating T cells and macrophages, thereby improving resistance to pathogens[55]. This immunomodulatory activity is particularly valuable in tumor therapy. Cao et al.[56] demonstrated that ginseng-derived nanoparticles (GDNPs) significantly inhibit the growth of glioma and melanoma by regulating the polarization of tumor-associated macrophages, increasing the proportion of M1-type macrophages in tumor tissues, and suppressing the activity of tumor-promoting M2-type macrophages. In addition, studies have reported that GDNPs inhibit melanoma progression in mouse models and exhibit synergistic effects with anti-cancer drugs[57]. These findings suggest that GDNPs enhance the anti-tumor immune response by modulating the immunosuppressive tumor microenvironment. Furthermore, ginseng exosomes may indirectly influence systemic immune homeostasis by regulating the composition of the gut microbiota[58]. This dual regulatory effect—direct immune activation and microenvironment remodeling—offers new opportunities for their application in immune-related diseases such as cancer and chronic infections. For example, their therapeutic potential in acute lung injury[50] and inflammatory bowel disease[59] is closely associated with immune regulation. In summary, ginseng exosomes not only enhance innate and adaptive immunity but also provide innovative anti-tumor strategies by targeting the tumor microenvironment.

Anti-inflammatory, wound healing, and neuroprotective effects

Ginseng exosomes alleviate chronic inflammation by inhibiting the release of inflammatory mediators such as TNF-α and IL-6[60]. This anti-inflammatory activity is particularly important during wound healing, as modulation of the inflammatory phase directly influences tissue repair efficiency. Yang et al.[61] and Tan et al.[62] reported that ginseng exosomes promote the proliferation and migration of fibroblasts and stem cells. These effects accelerate angiogenesis and tissue regeneration by activating the ERK and protein kinase B/mechanistic target of rapamycin (AKT/mTOR) signaling pathways. Consequently, ginseng exosomes significantly enhance chronic skin wound healing through these mechanisms, highlighting their potential in regenerative medicine. Furthermore, anti-inflammatory activity is closely associated with neuroprotection. Ginseng exosomes may slow the progression of neurodegenerative diseases, including Alzheimer and Parkinson disease[63], by inhibiting neuroinflammation and oxidative stress while preserving neuronal function. In addition, their ability to promote nerve regeneration further supports their potential in neurological disease treatment. Future studies should clarify specific molecular mechanisms, such as the targets of particular miRNAs within exosomes and their roles in neural differentiation. Existing evidence suggests that ginseng exosomes offer an integrated therapeutic strategy for multisystem diseases through synergistic anti-inflammatory, pro-repair, and neuroprotective activities.

Antioxidant activity

As carriers of bioactive components, ginseng exosomes play an important role in modulating various intracellular processes, particularly antioxidant responses. Their antioxidant constituents can effectively scavenge free radicals and mitigate cell damage caused by oxidative stress[64]. Choi et al.[65] reported that ginseng exosomes significantly reduce intracellular reactive oxygen species levels by delivering active antioxidant molecules, such as ginsenosides. This action enhances overall antioxidant capacity and reduces cellular damage induced by free radicals. These properties show promise for applications in anti-aging and the prevention of age-related diseases[66]. In addition, studies have demonstrated that GDNPs exhibit anti-osteoporosis potential by inhibiting osteoclast differentiation[67]. This suggests that ginseng exosomes contribute to cellular protection and may serve as effective therapeutic agents for osteoporosis. Overall, as multifunctional bioactive carriers enriched with antioxidant components, ginseng exosomes represent a novel approach for disease prevention and treatment.

Potential applications and future research directions

Ginseng exosomes show considerable potential as both therapeutic agents and drug delivery carriers, with promising efficacy in the treatment of cancer[68], immune disorders[69], and other diseases[70–71]. They can enhance the bioavailability of ginseng's active components[72], thereby increasing the value of health products and contributing to overall human health. In addition, ginseng exosomes have demonstrated effectiveness in skin trauma repair, postoperative recovery, and tissue regeneration. They are also enriched with small RNA molecules that support gene therapy and targeted disease treatment[64]. Compared with other plant-derived exosomes[73], ginseng exosomes possess unique advantages due to their high content of bioactive compounds, such as ginsenosides and specific small RNAs, which enhance stability, bioavailability, and precise gene regulation in target cells—potentially improving therapeutic outcomes. Nevertheless, several challenges remain. The mechanisms and kinetics underlying their delivery capabilities are not yet fully understood, and large-scale extraction and purification remain difficult and costly. Future research should focus on elucidating their therapeutic mechanisms, optimizing delivery systems, and developing efficient, cost-effective extraction and purification methods to facilitate practical clinical and commercial applications.

Research progress of ginseng proteins

Proteins are important natural bioactive components of *Panax ginseng*, playing pivotal pharmacological roles that cannot be replaced by other constituents. In recent years, advancements in biotechnology and proteomics have increased scientific interest in ginseng proteins. These proteins exhibit a wide range of biological activities, including immune system regulation, antioxidant activity, and anti-inflammatory effects. They also show potential for promoting cell growth and repair, as well as for enhancing physical strength and endurance. These distinct biological features place ginseng proteins at the forefront of current pharmacological and nutritional research. Consequently, studies on ginseng proteins have increasingly focused on their composition, biological functions, and specific applications.

Composition and classification of ginseng proteins

Ginseng proteins primarily originate from the roots of *Panax ginseng* and are characterized by a complex and diverse structural profile. They contain both essential and non-essential amino acids, and their unique composition and structure confer significant biological activity. The specific arrangement of amino acids determines the functions[74] and properties of ginseng proteins. Quantitative analyses indicate notable differences in protein content among ginseng of different ages and plant parts: approximately 170 mg/g in 6-year-old roots, up to 225 mg/g in 5-year-old flowers, about 127 mg/g in 5-year-old leaves, and the lowest level in 6-year-old stems at approximately 86 mg/g (dry weight)[18]. With advances in biotechnology, ginseng proteins have been classified into several categories according to their distinct functions. These include RNase-like proteins, ribonucleases, saponin synthesis-related enzymes, chitin-binding proteins, and xylanases. Each of these protein types plays a crucial role in the plant's physiological processes, including stress resistance, metabolic regulation, and other biological functions, as illustrated in Table 2. As research progresses, the importance of these bioactive constituents is being increasingly recognized for their potential benefits to both animal and human health.

Biological functions of ginseng protein

Immunomodulatory and anti-inflammatory and antibacterial activities

Specific proteins present in ginseng extracts can significantly enhance immune system function[76]. These proteins also stimulate macrophage activity, increasing their phagocytic capacity and efficiency in eliminating pathogens. In addition to regulating immune function, ginseng proteins exhibit notable anti-inflammatory and antibacterial activities[75]. Their anti-inflammatory effects are primarily achieved by inhibiting inflammatory responses and reducing tissue damage caused by inflammation, thereby contributing to the treatment of various inflammatory diseases. Regarding antibacterial activity, Colzani et al.[83] used a combined proteomics and peptidomics approach to investigate total ginseng proteins and their hydrolyzed products. Their simulated gastrointestinal digestion experiments demonstrated that these proteins and peptides possess substantial antibacterial properties. This finding advances our understanding of the biological activities of ginseng proteins and provides a valuable reference for developing new antibacterial agents.

Other biological activities

The literature indicates that glycoproteins from ginseng and certain proteins with specific functions possess notable antioxidant properties, effectively scavenging free radicals and protecting cells from oxidative damage[84]. This protective activity not only slows the aging process but also enhances cell survival under oxidative stress, thereby maintaining normal cellular functions. Accordingly, ginseng's total protein and its glycoproteins may contribute to delaying aging and promoting cell health by mitigating the harmful effects of oxidative stress[85–86]. Zhang et al.[79] demonstrated that ginsenoside-β-glucosidase derived from ginseng can selectively hydrolyze Rg3 to generate Rh2, which has stronger anticancer activity. This finding suggests that the enzyme plays a key catalytic role in the "saponin–protein synergy" anti-tumor pathway. In addition, numerous studies have reported that specific proteins from ginseng may protect the nervous system[87], enhance cognitive function[88–89], and potentially slow the progression of neurodegenerative diseases, including Alzheimer disease and Parkinson disease[90]. Notably, a ribonuclease-like storage protein isolated from mountain ginseng has been shown to exert significant protective effects on cardiomyocytes, whereas the homologous protein from garden ginseng does not, indicating that cultivation methods or genetic background can influence protein functional specificity[80]. Furthermore, Wang et al.[82] identified a novel protein, quinqueginsin, from American ginseng, which exhibits both antiviral and transcriptional inhibitory activities, providing a new target for the development of broad-spectrum antiviral agents and gene expression regulators. Collectively, these findings indicate that ginseng proteins can enhance the survival and function of neurons and cardiomyocytes through multiple mechanisms, including antioxidation, enzyme catalysis, organ-specific protection, and the activity of novel functional proteins, thereby supporting their potential

Table 2
Functional classification of ginseng proteins

Source	Ginseng protein type	Purification method	Quantity currently isolated	Relative molecular mass	Activity	References
Ginseng root	Ribonuclease	$(NH_4)_2SO_4$ precipitation + ion exchange	1	2.6×10^4	Antifungal, antiviral, transcriptional inhibiting and ribonuclease activities	[75]
Ginseng root	RNA-like endoribonuclease protein	$(NH_4)_2SO_4$ precipitation + ion exchange	1	2.8×10^4	Anti-complementary activity	[76]
Ginseng flower buds	Ribonuclease	DEAE-cellu-lose +Affi-gel blue gel +CM-cellulose	1	2.3×10^4	No antifungal, antiviral, or proliferation-inhibiting activity	[77]
Ginseng callus	Ribonuclease	$(NH_4)_2SO_4$ precipitation + gel filtration + affinity chromatography	2	1.8×10^4	Not a clear statement	[78]
Ginseng root	Saponin synthesis-related enzymes	Column of DEAE-cellulose DE-52 (Whatman)	1	5.9×10^4	Hydrolyzing Rg3 yields the anti-cancer substance Rh2	[79]
Mountain-cultivated ginseng's root	Ribonuclease-like storage protein	Not reported	1	2.62×10^4	Protective effect on cardiomyocytes	[80]
Garden-cultivated ginseng's root	Ribonuclease-like storage protein	Not reported	1	2.42×10^4	No protective effect on cardiomyocytes	[80]
Ginseng leaf	Cyclophilins	Not reported	Not reported	1.87×10^4	Antifungal	[81]
Ginseng root	Ribonuclease	DEAE-cellu-lose + Affi-gel blue gel + CM-cellulose	Not reported	5.3×10^4	Antifungal, antiviral, transcriptional inhibiting and ribonuclease activities	[82]

CM: Carboxymethyl; DEAE: Diethylaminoethyl.

applications in preventing and treating nervous system disorders, cardiovascular diseases, and cancers.

Application prospects

The diverse biological activities of ginseng proteins support their potential development into novel immune-regulating and anti-inflammatory drugs. These functional proteins may also be incorporated into health products and food additives to enhance the quality of life and improve the nutritional value of food. This dual role addresses both the health and nutritional needs of modern society. With the advent of proteomics technology[91], researchers have integrated mass spectrometry and bioinformatics to systematically identify and quantify multiple proteins in ginseng. This approach provides a comprehensive understanding of how ginseng protein profiles change under different growth environments, varieties, and extraction methods[92]. In conclusion, in-depth analysis of the composition and functional roles of ginseng proteins will help clarify their biological characteristics and provide a solid scientific basis for applications in pharmacology and nutrition. With ongoing advancements in research, ginseng proteins are expected to contribute to the development of new therapeutic approaches, stimulate progress in the health product industry, and improve public health outcomes.

Research progress of ginseng dietary fiber

Dietary fiber is an essential nutrient abundantly present in many natural food sources, particularly plant-based foods. Owing to its unique physical and chemical properties, dietary fiber can adsorb cholesterol, metal ions, and various other harmful substances[93–94]. This capacity plays an important role in maintaining intestinal health, preventing constipation, regulating blood glucose levels, and supporting overall metabolic well-being. In recent years, researchers have identified dietary fiber in ginseng. This section of the review discusses the diversity, structural characteristics, functional activities, and other relevant aspects of ginseng dietary fiber[95].

Composition and classification of ginseng dietary fiber

In ginseng-related industries, a substantial amount of dietary fiber is derived from industrial residues generated during ginseng processing[96–97]. These residues are often regarded as byproducts of the ginseng production chain. Ginseng dietary fiber exhibits unique pore structures and polysaccharide functional groups that confer excellent physicochemical properties, providing a basis for its potential biological functions and applications[98]. Several studies have reported that the soluble dietary fiber content in ginseng is approximately 8.98%[98], whereas the insoluble dietary fiber content is about 68.61%[93]. This ratio largely determines the mode and intensity of its physiological functions in the body. Ginseng dietary fiber mainly consists of cellulose, hemicellulose, lignin, acidic heteropolysaccharides, and mineral elements, and can be categorized into two primary types: water-soluble and insoluble dietary fiber. Water-soluble fibers, such as acidic heteropolysaccharides, enhance bioavailability due to their higher solubility, which facilitates more efficient absorption and utilization by the body. By contrast, insoluble dietary fiber[99], such as cellulose, plays a crucial role in promoting intestinal motility and improving digestive health. A systematic review of the literature shows that different extraction methods—such as the enzymatic method[100], Viscozyme L–wet ball milling method[101], and alkaline hydrogen peroxide method[102]—can significantly alter the porosity, crystallinity, and degree of exposure of functional groups in ginseng dietary fiber. These changes, in turn, affect its water-holding capacity, adsorption capacity, and fermentation characteristics. For example, Li et al.[103] reported that dietary fiber from directly dried ginseng has a smaller particle size, higher absolute potential energy, and greater emulsifying activity, whereas dietary fiber from steamed ginseng exhibits higher solubility, foaming capacity, and crystallinity. In conclusion, ginseng dietary fiber holds broad potential value in the food and medical fields and offers new avenues for the high-value utilization of ginseng byproducts.

Function of ginseng dietary fiber

Promoting intestinal health

In the human intestinal microecosystem, diverse microbial communities play essential roles. Studies have shown that ginseng dietary fiber significantly improves the composition and function of the intestinal microbiota[104]. This improvement is reflected in enhanced intestinal barrier integrity and increased levels of short-chain fatty acids (SCFAs), such as butyric acid, which serve as energy sources for epithelial cells[105]. SCFAs not only help lower intestinal pH and inhibit the proliferation of harmful bacteria but also strengthen barrier function and modulate immune responses. Water-soluble dietary fiber, in particular, exerts prebiotic effects by promoting the proliferation of beneficial intestinal bacteria and inhibiting pathogens such as *Helicobacter* and *Peptococcus*[106]. For example, it supports the growth of probiotics such as *Bifidobacterium* and *Lactobacillus*[95], thereby improving microbiota balance[107]. Moreover, studies have demonstrated that ginseng soluble dietary fiber can increase the abundance of *Oscillospira* and *Desulfovibrio*[108], which may reduce inflammation risk and confer metabolic benefits. Therefore, increasing the intake of dietary fiber—especially from ginseng-rich foods—has a significant positive impact on maintaining and improving intestinal health (as shown in Figure 3).

Other activities

Ginseng dietary fiber also contributes to regulating blood glucose and cholesterol levels, thereby improving metabolic health. Water-soluble dietary fiber slows digestion primarily by delaying glucose absorption into the bloodstream, which stabilizes blood sugar levels[109–110]. This effect improves glucose tolerance and reduces the risk of type 2 diabetes. In particular, the ability of dietary fiber to modulate postprandial glycemic response further decreases diabetes risk[111]. In addition, studies have shown that ginseng dietary fiber can lower blood pressure[112]. This hypotensive effect is attributed to the reversible ion exchange of ginseng dietary fiber with sodium ions in the gastrointestinal tract, which promotes sodium excretion. This mechanism highlights the potential role of ginseng dietary fiber in preventing hypertension and its associated cardiovascular complications.

Furthermore, reducing the particle size of insoluble dietary fiber in ginseng increases its 2,2-diphenyl-1-picrylhydrazyl free radical scavenging activity[113]. Ginseng dietary fiber has also been reported to enhance serum total antioxidant capacity[98] and reduce concentrations of inflammatory markers linked to various pathological conditions[114]. Sha et al.[115] found that ginseng dietary fiber improves apoptosis regulation in mouse epithelial cells and enhances intestinal adaptive immunity by modulating the mitogen-activated protein kinase (MAPK)/NF-κB signaling pathway, thereby strengthening host immune function. Moreover, ginseng dietary fiber increases circulating levels of insulin-like growth factors (IGF-1 and IGF-2) and immunoglobulins (IgA, IgM, and IgG), which further supports immune system enhancement[108]. Beyond these activities, ginseng soluble dietary fiber has been shown to improve baseline physiological parameters in obese mice, inhibit adipogenesis, and ameliorate lipid metabolism disorders, while also exerting a regulatory effect on intestinal microbiota dysbiosis[116–117]. In conclusion, ginseng dietary fiber demonstrates considerable potential in promoting human health.

Application of ginseng dietary fiber

Given its beneficial effects on intestinal health and its capacity to lower blood glucose and lipid levels, ginseng dietary fiber can be incorporated into high-fiber foods as an additive to enhance both taste and nutritional value[118]. It may also function as an adjuvant therapy for chronic conditions such as diabetes and hyperlipidemia. Notably, consumption of ginseng dietary fiber induces satiety, thereby helping to control food intake. Consequently, it supports effective weight management, making it a valuable ingredient in low-calorie, weight-reduction diets. With the increasing use of probiotics, studies have shown that multilayer coatings can effectively protect them from acid degradation, thereby enhancing their adhesion to and colonization of intestinal epithelial cells and ultimately improving their efficacy[119]. In everyday diets, ginseng dietary fiber can be used as a supplement to promote digestive health, improve quality of life, and strengthen disease resistance. Therefore, ginseng dietary fiber demonstrates substantial potential for development within the functional food sector. This potential not only increases the added value of ginseng but also facilitates the promotion and adoption of healthy eating practices.

Summary and outlook

Ginseng, a medicinal plant with a long history, continues to be a focal point of research due to its diverse array

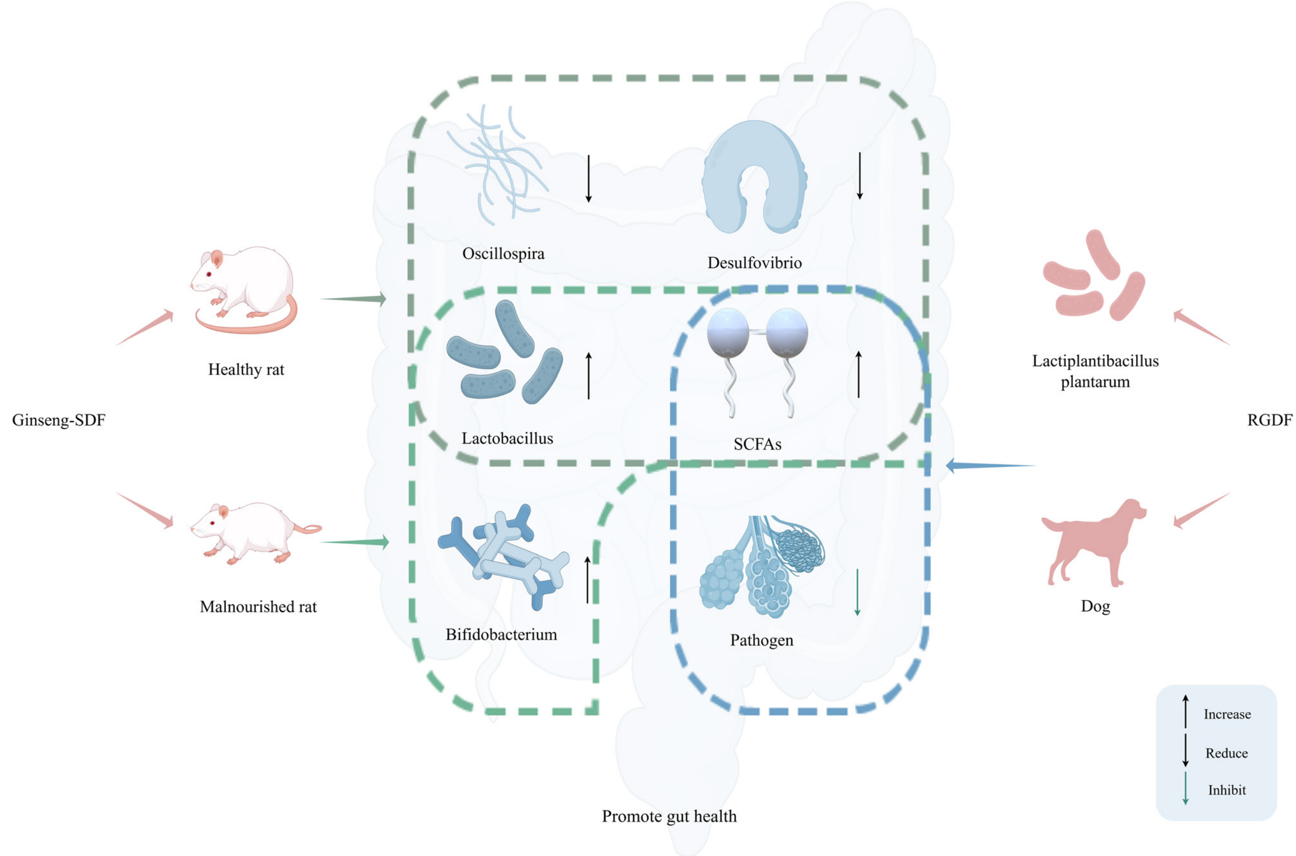

Figure 3. The impact of ginseng dietary fiber on intestinal health. Ginseng SDF has been shown to elevate SCFA levels in the intestines of healthy rats. It also promotes an increase in the abundance of *Lactobacillus* while reducing the populations of *Oscillospira* and *Desulfovibrio*. Similarly, in malnourished rats, Ginseng-SDF enhances SCFAs levels and simultaneously boosts the abundance of beneficial bacteria such as *Lactobacillus* and *Bifidobacterium*. Additionally, RGDF can increase SCFAs concentrations in the intestines of plant-derived lactic acid bacteria and canine subjects, while also exerting inhibitory effects on pathogenic bacteria. RGDF: Red Ginseng dietary fiber; SCFA: Short-chain fatty acids; SDF: Soluble dietary fiber.

of bioactive compounds. While ginsenosides remain the most extensively studied, emerging evidence underscores the importance of other biomolecules—such as proteins, pectin, exosomes, and dietary fiber—in contributing to its pharmacological profile. These biomolecules not only play a crucial role in traditional medicine but also demonstrate broad application prospects and substantial practical value in modern scientific research. Nevertheless, current studies still face significant challenges and limitations. For example, the correlation between the molecular structures of ginseng biomolecules and their pharmacological activities has yet to be fully elucidated, and systematic, in-depth investigations into their underlying mechanisms remain insufficient. Addressing these gaps will be essential for unlocking the full therapeutic potential of ginseng and translating its bioactive components into clinically viable applications. Additionally, the specific content and compositional differences among the four types of ginseng biological macromolecules discussed in this review are scarcely reported in the literature. Therefore, future studies should conduct targeted experiments to address this gap. Moreover, safety and efficacy data supporting their clinical applications remain limited, underscoring the urgent need to establish a more comprehensive clinical trial framework. From a technical perspective, several factors currently hinder their large-scale application. These include the low yield of plant-derived exosomes, the structural heterogeneity of pectin, and the insufficient safety data for proteins. In particular, methods for detecting ginseng exosome content are rare, and existing estimation techniques lack sensitivity, leading to inaccurate results. Thus, the development of standardized, highly sensitive quantitative systems is imperative. Furthermore, there is a notable lack of systematic experimental data on the effects of different processing methods—such as steaming, fermentation, and enzymatic hydrolysis—on the chain length distribution of ginseng pectin, the integrity of exosome membranes, and protein conformation. To date, the literature on these aspects remains largely absent. Future studies should prioritize resolving these technical challenges, achieving large-scale standardized production, and developing more robust characterization methods. In conclusion, the literature reviewed herein demonstrates considerable progress in research on ginseng pectin, exosomes, dietary fiber, and proteins. These studies have expanded our understanding of ginseng's bioactive components and opened new avenues for their application in functional foods and pharmaceutical development. It is anticipated that continued research will further elucidate their potential value, thereby promoting the comprehensive utilization of ginseng and its derivatives for the benefit of a broader population of consumers and patients.

Conflict of interest statement

The authors declare no conflict of interest.

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Author contributions

Shi-Lu Li contributed to conceptualization, data curation, investigation, methodology, writing - original draft. Shuai Zhang contributed to supervision, writing - review & editing. Lu Fu contributed to supervision, writing - review & editing. Chen Chen contributed to supervision, writing - review & editing. Wen-Hui Zhang contributed to supervision, writing - review & editing. Wei Li contributed to conceptualization, writing - review & editing, supervision, funding acquisition. All authors have read and agree to be accountable for all aspects of work, ensuring integrity and accuracy, and publication of the manuscript.

Ethical approval of studies and informed consent

Not applicable.

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None.

Data availability

All data generated or analyzed during this study are included in this published article.

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