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Research progress on anti-fatigue effects of food-medicine homologous substances

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ABSTRACT: Food-medicine homologous (FMH) plants have gained increasing interest due to their nutritional and therapeutic properties. Fatigue is a common health issue driven by physical and mental stress worldwide lacking efficient treatments. The significant anti-fatigue effects of FMH plants have attracted much attention with various active components including polysaccharides, flavonoids, and saponins and emerging compounds (such as macaenes and curcuminoids) demonstrating synergistic anti-fatigue effects. These ingredients could regulate energy metabolism, reduce oxidative stress, inhibit inflammatory pathways, and modulate the nervous system, thereby delaying fatigue onset and improving endurance. Notably, numerous research findings have been widely applied due to their efficacy in alleviating fatigue, identifying active components, exploring the action mechanism, and developing related products.. This review highlights the key active ingredients of FMH plants, summarizes the anti-fatigue mechanisms, discusses current applications and clinical evidence, which will provide insights for future research and functional development of FMH substances.

Keywords: Food-medicine homologous plants; Anti-fatigue; Active components; Action mechanisms; Clinical trials

1. Introduction

According to a survey of the World Health Organization (WHO), fatigue has become an extremely common health problem worldwide, with approximately 3 billion people experienced varying degrees of fatigue. In some high-pressure occupational groups, this proportion can even reach as high as 80% [1]. Fatigue could not only reduce the quality of life and make people feel mentally and physically weak, but also seriously affect work efficiency. Studies have shown that employees in a state of fatigue have a 20%-50% higher rate of work errors than those normal people [2, 3]. Moreover, long-term fatigue is a triggering factor for various chronic diseases including cardiovascular disease and metabolic syndrome. Evidence indicated that the risk of cardiovascular disease is 40% higher in individuals who experience long-term fatigue compared to the general population [3,4] .

Food-medicine homologous plants are a distinctive and precious category of natural resources that harmoniously integrate nutritional nourishment with therapeutic effects [5]. Deeply rooted in traditional

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medical systems such as Traditional Chinese Medicine (TCM), these extraordinary plants break through the conventional divide between food and medicine. They can be safely integrated into the daily diet, much like ordinary fruits, vegetables, grains, or herbs [6]. The anti-fatigue mechanisms of food-medicine homologous substances have expanded from single energy metabolism regulation to multi-pathway regulation of the neuro-immune-oxidative stress network. For example, recent studies have revealed that compounds like macaenes and curcuminoids target neurotransmitter balance and inflammatory pathways, respectively, complementing the classical mechanisms of polysaccharides and flavonoids. They can be consumed in the form of teas, soups, stir-fries, or dietary supplements, while concurrently providing health benefits that are either scientifically proven or traditionally recognized. This dual functionality renders them potent means for preventive healthcare, wellness enhancement, and gentle, long-term support of bodily functions [7].

Studying the anti-fatigue effects of food-medicine homologous plants is of great significance for developing safe and effective anti-fatigue products [6]. At present, the sales of anti-fatigue products made from food-medicine homologous plants are growing at a rate of 15%-20% per year, which fully demonstrates their huge market potential [8]. Development of medicinal and edible plants is not only expected to provide new ways to alleviate people's fatigue, but also to promote the development of the health industry and meet people's pursuit of a healthy lifestyle [9]. This article comprehensively reviews the research progress of anti-fatigue effects, active ingredients, mechanisms of action, current application status, clinical research, and other aspects of FMH plants, which will shed light of the future research and functional development of FMH substances.

2. Anti-fatigue active ingredients from food-medicine homologous plants

2.1 Polysaccharides

Dendrobium polysaccharides are heteropolysaccharides, mainly composed of six monosaccharides including mannose, glucose, galactose, rhamnose, arabinose, and xylose, as well as two types of uronic acids: galacturonic acid and glucuronic acid. Among them, glucose and mannose have relatively high contents, and glucuronic acid only exists in a few Dendrobium polysaccharides. The composition and content of monosaccharides are influenced by factors such as variety, origin, growth period, harvesting period, extraction and purification methods [10-12]. The content of mannose in Dendrobium officinale polysaccharides from Yunnan and Zhejiang regions is higher than that from Guangxi and Anhui regions; The monosaccharide composition and molar ratio of polysaccharides from annual and biennial Dendrobium officinale are different; The monosaccharide composition of polysaccharides from Dendrobium officinale leaves and stems differs; The content of mannose in Dendrobium polysaccharides extracted by ultra-high pressure is significantly higher than that of traditional hot water extraction (Table 1) [13-15].

Table 1 Effects of extraction and purification methods on the monosaccharide composition and molecular weight of dendrobium polysaccharides

Source	Extraction and purification methods/conditions	Monosaccharide composition and molar ratio	Molecular weight	literature

			(Da)	
Dendrobium officinale polysaccharide	Hot water extraction	Man:Glc-1.06:1.0	5.4×10^4	[10, 11]
	ultrahigh pressure extraction	Man:Glc-1.71:1.0	3.2×10^5	
	Hot water extraction	NA	2.01×10^5	
	enzymatic extraction	NA	1.67×10^5	
	Flash extraction	NA	1.79×10^5	
	Ultrasonic extraction	NA	1.96×10^5	
	Freeze thaw extraction	NA	2.28×10^5	
ST	40% final concentration ethanol precipitation	NA	4.79×10^5	[12]
	50% final concentration ethanol precipitation	NA	3.16×10^5	
	60% final concentration ethanol precipitation	NA	3.07×10^5	
	80% final concentration ethanol precipitation	NA	8.56×10^6	
HSP	40℃ water extraction	Man: Glc:Gal:Ara:Rha:Xy1 2.24:50.22:35.88:8.79:1.66:1.21	9.42×10^6	[13]
	60℃ water extraction	Man:Glc:Gal:Ara:Rha:Xy12.11:58.44:29.43: 8.05:1.11:0.86	9.27×10^6	
	80℃ water extraction	Man: Glc:Gal:Ara:Rha:Xy1-1.78:65.36:24.37:6.87:0.85:0.75	9.20×10^6	
	100℃ water extraction	Man:Glc:Gal:Ara:Rha:Xyl=1.19:75.34:16.44: 5.26:1.24:0.54	9.12×10^6	
DOP	Ultrafiltration membrane classification separation	Man:Glc=1.38:1.0	4.92×10^5	[14]
	3500 Da dialysis bag dialysis	Man:Glc=4.06:1.0	3.33×10^4	
Dendrobium officinale polysaccharide	Ultrasonic extraction at 14 ℃ for 2 hours	Man:Glc:Gal:Ara:Rha:Xy1=79.17:16.33:0.90: 0.86:0.45:1.21	2.95×10^5	[15]
	Ultrasonic extraction at 20 ℃, 100 W, 3 min	Man:Glc:Gal:Ara:Rha:Xy1-75.58:21.02:0.35:0.35:0.20:1.14	3.28×10^5	
	Ultrasonic extraction at 20 ℃, 300 W, 3 min	Man:Glc:Gal:Ara:Rha:Xy1=76.63:18.81:0.69 :0.42:0.15:1.05	3.31×10^5	
	Ultrasonic extraction at 20 ℃, 500 W, 3 min	Man:Glc:Gal:Ara:Rha:Xy1=77.69:17.82:0.95 :0.48:0.27:0.96	3.68×10^5	
	Ultrasonic extraction at 100 ℃ for 2 hours	Man:Glc:Gal:Ara:Rha:Xy177 39:17.82:0.85:0 34:0.34:0.64	3.13×10^5	

* The molecular weight range of polysaccharides is typically 10^4–10^6 Da; this refers to low-molecular fragments extracted by ultra-high pressure.Different extraction methods have a significant impact on the anti-fatigue activity of Dendrobium polysaccharides. The two polysaccharide components, DOP-S and DOP-F, extracted from Dendrobium officinale using water extraction and biological fermentation methods, both exhibit DPPH free radical scavenging activity with semi inhibitory concentrations of 4.9 and 1.0 mg/mL, respectively. The polysaccharides extracted by fermentation method show more significant antioxidant effects [16], suggesting that their anti-fatigue activity may also be stronger. Because fermentation methods may alter the structure of polysaccharides, enhancing their antioxidant capacity and playing a more significant role in reducing levels of fatigue related metabolites and alleviating fatigue [17].

The main chain is mainly composed of α - or β - configured glucose, mannose, and a small amount of galactose residues alternately connected by 1 → 3, 1 → 4, 1 → 6, 1 → 3,6, and 1 → 4,6 glycosidic bonds. Branches are mostly composed of xylose, arabinose, and rhamnose units connected to the main chain through O-2, O-3, O-6, and the ends of the branches are mostly mannose, arabinose, and rhamnose groups. Most Dendrobium officinale polysaccharides also contain acetyl groups, typically attached to the O-2 or O-3 positions of glucose or mannose residues in the main chain [18].

Dendrobium polysaccharides can promote the proliferation and differentiation of immune cells, regulate the release of cytokines, promote the secretion of antibodies, thereby enhancing the body's immunity and relieving fatigue. The polysaccharide DOP-1-1 from Dendrobium officinale can stimulate phagocytic cells to release cytokines such as tumor necrosis factor alpha (TNF-α) and interleukin-1β (IL-1β), and upregulate the phosphorylation levels of nuclear factor kappa B (NF-κB) and extracellular regulated protein kinase (ERK1/2) proteins, exhibiting significant immune enhancement properties and helping to enhance the body's ability to cope with fatigue [19]. Simultaneously possessing the ability to eliminate multiple free radicals in vitro in a dose-dependent manner, it can also reduce the content of malondialdehyde (MDA), increase the activity of superoxide dismutase (SOD), catalase (CAT), and glutathione peroxidase (GSH-Px), and reduce oxidative damage. In the weight-bearing swimming test in mice, polysaccharides from Dendrobium officinale can reduce the levels of fatigue related metabolites such as lactate dehydrogenase (LDH), creatine kinase (CK), triglycerides (TG), and MDA, and alleviate the damage of fatigue to the body through antioxidant effects [20]. Dendrobium officinale polysaccharides can affect the cAMP PKA and Akt FoxO1 signaling pathways mediated by glucagon, promote hepatic glycogen synthesis, inhibit hepatic glycogen degradation and gluconeogenesis, form more stable α-granule structured glycogen, slow down glycogen degradation rate, maintain blood glucose balance, provide sustained energy supply to the body, and alleviate fatigue [21-25].

2.2 Flavonoids

Flavonoids are polyphenolic compounds with a basic skeleton of C6-C3-C6, consisting of two benzene rings (A and B) connected by a central three carbon chain (C ring) (Figure 1, Figure 2). According to the degree of oxidation of the C ring, the position of the B ring connection, and the different substituents, it is divided into flavones, flavonols, flavanones, isoflavones, chalcones, etc [26-29].

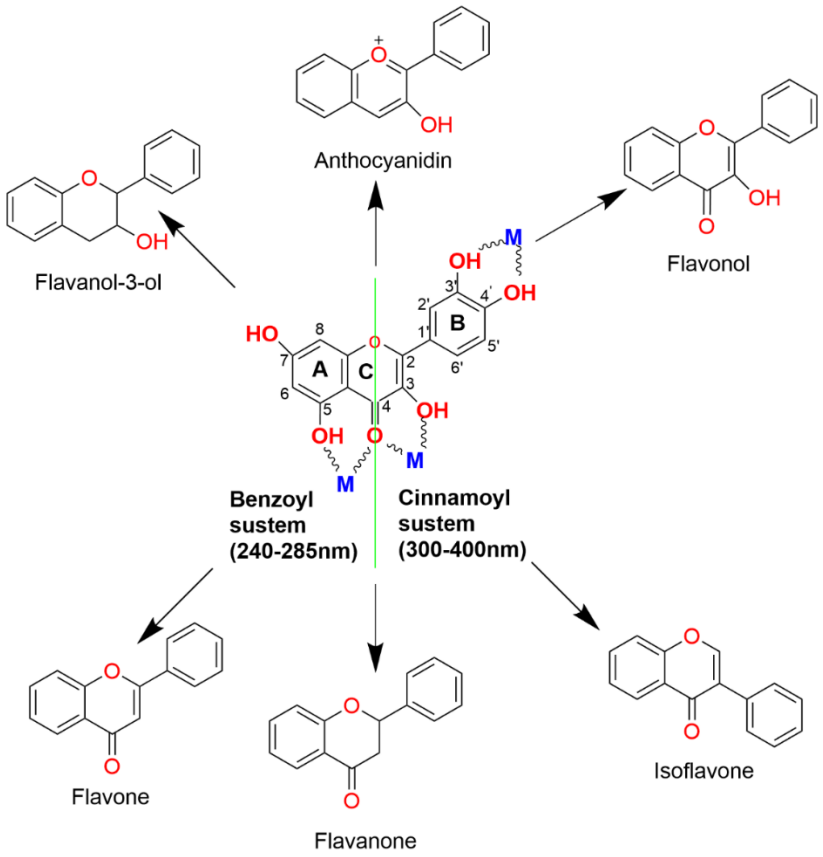


Fig.1 Subclasses of flavonoids. M denotes metals coordinated to the metal-binding sites of quercetin

M represents metal ions coordinated with the metal-binding sites (3-hydroxy-4-ketone and 5-hydroxy-4-ketone groups) of quercetin. This chelating effect enhances antioxidant activity and participates in the anti-fatigue mechanism.

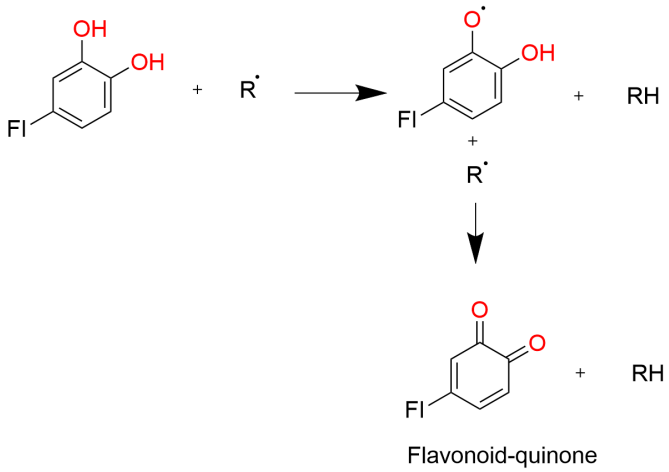


Fig 2 Basic structures of flavonoids

Flavonoids neutralize reactive oxygen species (ROS) and free radicals, and the phenolic hydroxyl group (- OH) directly provides hydrogen atoms to free radicals (such as ·OH, O_2^{-}·) [30, 31], generating stable flavonoid free radicals (Flavonoid-O·) and terminating the chain reaction. The metal-chelating ability of flavonoids is closely related to their anti-fatigue effect. Mitochondria are the core of cellular energy metabolism. Dysfunction of mitochondria can lead to reduced ATP production, decreased membrane potential, and abnormalities in the electron transport chain (ETC). Mitochondrial DNA (mtDNA) is more

susceptible to oxidative damage than nuclear DNA because it lacks histone protection and is close to the source of reactive oxygen species (ROS). Hydroxyl radicals can directly attack the bases of mtDNA, especially deoxyguanosine (dG), resulting in the formation of 8-hydroxydeoxyguanosine (8-OHdG). Hydroxyl radicals not only directly damage the mitochondrial membrane and enzymes on the membrane, but can also indirectly cause mitochondrial dysfunction by activating apoptotic pathways (such as the caspase cascade reaction). For example, quercetin chelates metal ions such as Fe^{2+} and Cu^{2+} through its phenolic hydroxyl groups, inhibiting the Fenton reaction to reduce the production of ·OH free radicals and oxidative stress damage. This chelating effect protects mitochondrial DNA from damage, maintains ATP synthesis efficiency, and thus delays the onset of fatigue(Figure 3) [32]. Enhance the activity of superoxide dismutase (SOD), glutathione peroxidase (GPx), and catalase (CAT). By activating the AMPK (AMP activated protein kinase) pathway, muscle and liver glycogen synthesis is increased, and post exercise lactate and urea nitrogen accumulation is reduced. Activate PPAR alpha (peroxisome proliferator activated receptor alpha) and CPT1 (carnitine palmitoyltransferase 1), promote mitochondrial beta oxidation, and reduce lipid peroxidation [6]. Protect mitochondrial DNA from oxidative damage and maintain ATP synthesis efficiency. Reduce the expression of pro-inflammatory factors (TNF-α, IL-6, IL-1β) and alleviate the inflammatory response caused by exercise, such as icariin, which alleviates chronic inflammation by inhibiting T cell overactivation. Regulating the expression of gamma aminobutyric acid (GABA) transporter GAT-2 to alleviate central fatigue. Inhibit the HMGB1/TLR4 pathway and enhance the expression of tight junction proteins, reducing the increase in BBB permeability caused by hypoxia or inflammation [33].

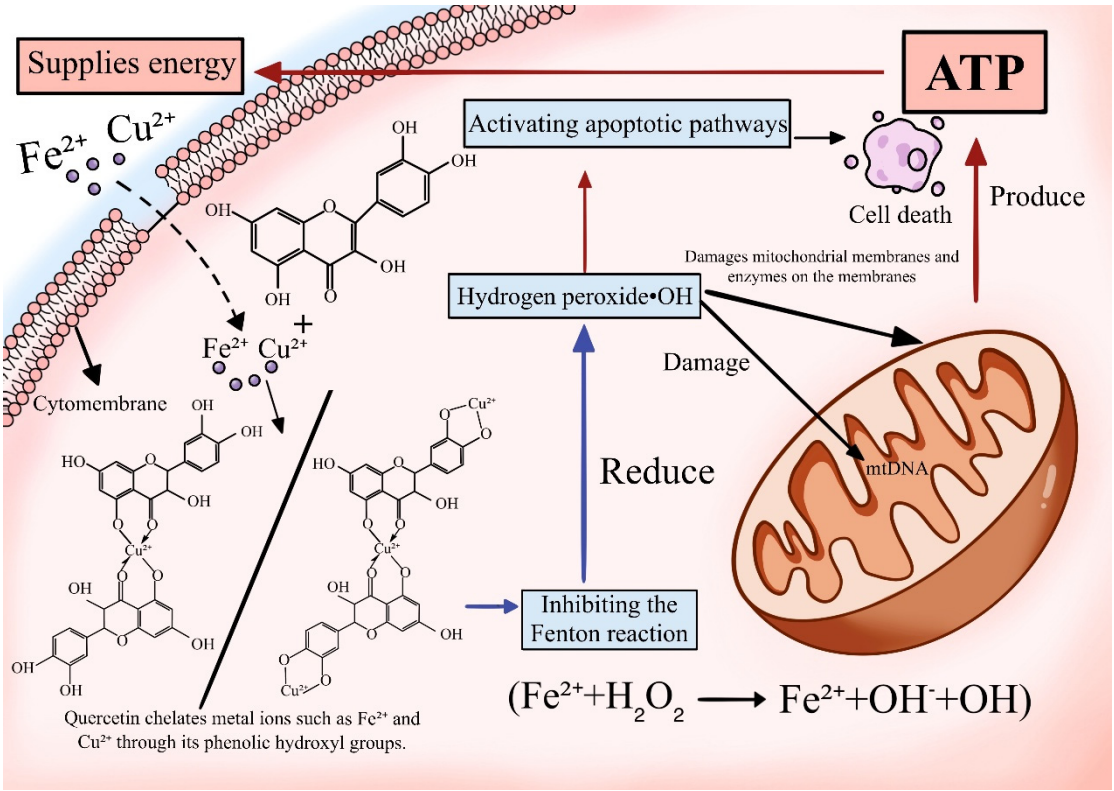


Fig 3 The anti-fatigue mechanism of quercetin.

Clinical studies have found that the occurrence of many diseases is related to the presence of a large number of harmful oxidative free radicals in the body. Flavonoids, as a natural antioxidant, have been widely

studied in recent years. The mechanism of its antioxidant free radical action is similar to that of phenolic substances such as BHT and BHA, both of which bind to free radicals to exert antioxidant effects. Flavonoids can react with lipid substances, transferring hydrogen to lipid free radicals to form stable phenolic free radicals, thereby inhibiting the continuation of oxidation reactions [34]. In 2015, Meng Ping et al. found through in vitro antioxidant activity experiments on total flavonoids of Scutellaria baicalensis that its total flavonoids can effectively scavenge free radicals such as ABTSDPPH, OH, NO, and O_2, and have strong in vitro antioxidant activity. In 2015, Wang Z et al [35-46]. found that total flavonoids from silver wood have strong scavenging activity against DPPH, OH, and O_2 free radicals.*2.3 Saponins*

Ginsenosides are a class of tetracyclic triterpenoids or pentacyclic triterpenoids composed of glycosides and glycosides. Dammarane type is dominant and can be divided into protopanaxadiol type (PPD) and protopanaxatriol type (PPT). PPD type (such as Rb1, Rc, Rd) has hydroxyl substituents at positions C-3, C-12, and C-20; PPT type (such as Re, Rg1) has an additional hydroxyl group at the C-6 position [47-54]. Ocotillol type tetracyclic triterpenoids with furan rings in their side chains, such as ginsenoside F11, and oleanolic acid type triterpenoids with pentacyclic structures, such as ginsenoside Ro (Figure 4).

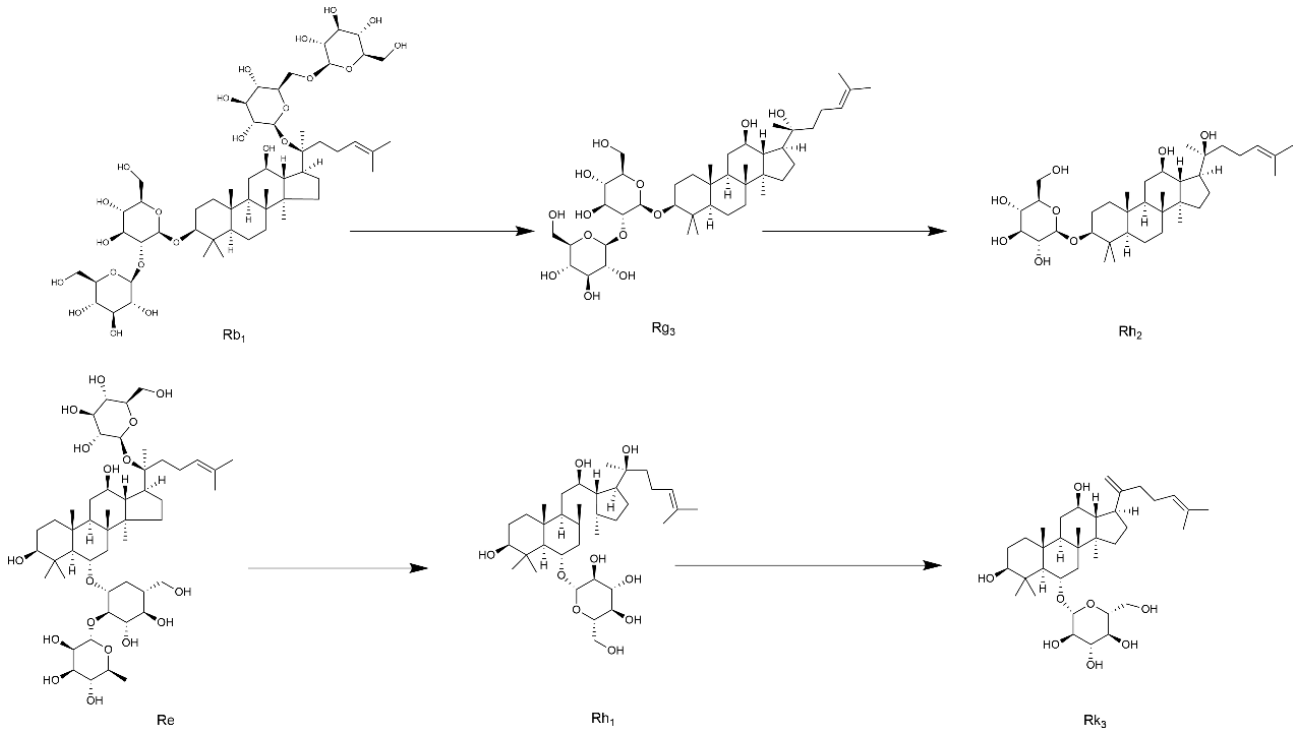


Fig. 4 Common structural modification routes of ginsenosides

Glycosides are usually composed of glucose, arabinose, fucose, etc., which are connected to the C-3, C-6, or C-20 positions of the aglycone through β-glycosidic bonds. Deglycosylation can generate secondary saponins (such as Rh2, Rg3), improving lipid solubility and bioavailability (Figure 2).

A study showed that after administration of ginsenoside Rg3 (40 mg/kg), dopamine levels in the brain of mice increased by 30%, 5-HT levels decreased by 25%, and forced swimming time was significantly prolonged (Table 2) [55-61]. In the postoperative fatigue model, ginsenoside Rb1 alleviates HPA axis disorders and improves fatigue symptoms by reducing the expression of inflammatory factors such as IL-6 and

TNF-α. Ginsenosides activate the AMPK/GLUT4 pathway, promoting glucose uptake and hepatic glycogen synthesis. Rg1 enhances mitochondrial biosynthesis and increases muscle glycogen storage by upregulating PGC-1 α and TFAM protein expression [62]. Ginsenosides enhance the activity of lactate dehydrogenase (LDH) and accelerate the conversion of lactate to pyruvate. Experiments have shown that total saponins from ginseng stems and leaves can increase the blood lactate clearance rate in mice by 35% [63]. Ginsenoside Rb1 enhances Na^+/K^+- ATPase and succinate dehydrogenase (SDH) activity, increases skeletal muscle ATP content, and alleviates exercise-induced fatigue.

Table 2 Immunomodulatory activity of some saponins.

Saponin Sources	Saponin Name	Immunoreaction
Panax ginseng	Ginsenoside Rg1 Ginsenoside Rd Ginsenoside Rh2 (24R)-Pseudo-Ginsenoside HO (24S)-Pseudo-Ginsenoside HQ Ginsenoside kb2 Ginsenoside 20(R)-Rg3 Ginsenoside Rg3 Ginsenoside Re	Facilitating the upregulation of Th1 (IFN-γ, IL-2,T-bet, etc,) and Th2 (IL-4, IL-6, GATA3, etc.) cytokines and transcription factors[50, 51, 97] ; Enhances antigen-specific antibody production and immune defense enhances the body's immune defense against antigens [错误!未找到引用源。.错误!未找到引用源。; Stimulating lymphocyte proliferation[49, 52, 54]; Preventing atrophy of immune organs[107]; Upregulating the $CD4^+/CD8^+$ T cell ratio[107];
Panax nologinseng	Notoginsenoside K Ginsenoside Rh4 (11)	Enhancing, the levels of antigen-specific antibodies enhances the body's immune defense against antigens[106-109, 117] Ameliorating antigen-induced oxidative stress in immune cells[98]; Improvement of monocyte and macrophage carbon scavenging[51]Stimulating lymphocyte proliferation[48-51]; Promoting the secretion of cytokines such as TNF-α and IL-2[51]
Astragalus membranaceus	Macrophyllosaponin Astragaloside VI Astragaloside IV Astragaloside II	Promoting, the maturation and activation of APCs such as macrophages or dendritic cells[110, 111]; Enhancing the levels of antigen-specific antibodies enhances the body's immune defense against antigens 35-37Stimulating lymphocyte proliferation[118, 119]; Stimulating the release of cytokines (IL-1β, IL-2, IL-4, IFN-γ, TNF-α, etc,) from immune cells to balance the Th1 /Th2 of the organism[118, 119]; Activation of $CD4^+$ and $CD8^+$ T cells [41];Inhibition of TLR2 activator-induced reduction in CXCR4 expression and neutrophil migration improves the body's antimicrobial immunity[120]
Quillaja saponaria	QS-21 0S-7	Enhancing, the levels of antigen-specific antibodies enhances the body's immune defense against antigens[121-126]; Stimulating the production of Cis[112, 113, 121, 122];Promoting the secretion of relevant cytokines and inducing a balanced Th1 /Th2 response[112, 113, 121, 122].
Platycodongrandiforus	Platycodin D Platycodin D2 Platycodin D3 Platycoside E	Enhancing, the levels of antigen-specific antibodies enhances the body's immune defense against antigens[55-61]; Stimulating the proliferation of immune cells such as lymphocytes and monocytes[55-61]; Increasing the killing activity of NK cells and CI[55-57]; Facilitating the upregulation of Th1 (IFN-γ, IL-2, T-bet, etc,) and Th2 (IL-4, IL-6, GATA3, etc.) cytokines and transcription factors for a better balance of Th1/Th2 immune responses [56-60, 114].

2.4 Other Bioactive Compounds

In addition to polysaccharides, flavonoids, and saponins, several other bioactive compounds from food-medicine homologous plants have demonstrated significant anti-fatigue effects through distinct mechanisms. These compounds complement the classical anti-fatigue pathways by targeting energy metabolism, neurotransmitter regulation, and inflammatory responses, thereby expanding the landscape of natural anti-fatigue agents.

Epicatechin, a polyphenol abundant in cocoa and grapes, exerts its effects primarily by activating AMP-activated protein kinase (AMPK), a key regulator of cellular energy homeostasis. This activation promotes mitochondrial biogenesis, enhances glycogen synthesis in muscle and liver tissues, and reduces post-exercise lactate accumulation—all of which contribute to prolonged endurance and accelerated fatigue recovery [68]. Macaenes, bioactive alkaloids isolated from maca (Lepidium meyenii), act on the central nervous system by modulating dopamine receptors. By improving the balance of neurotransmitters such as dopamine, macaenes alleviate mental fatigue and enhance motivation, making them particularly effective for counteracting stress-induced central fatigue . Macaenes also influence emotions and cognitive functions by regulating the levels of other neurotransmitters, such as serotonin and norepinephrine [72].Curcumin, the primary bioactive component in turmeric (Curcuma longa), exerts dual anti-fatigue effects: it inhibits the NF-κB and COX-2 signaling pathways to reduce the release of pro-inflammatory factors (e.g., TNF-α, IL-6), while also protecting mitochondrial function through its strong antioxidant properties. This dual action mitigates inflammation-mediated fatigue and preserves cellular energy production. Furthermore, curcumin can also enhance muscle function and endurance by activating the PI3K/Akt/AMPK/mTOR signaling pathway, which improves energy metabolism, reduces lactate accumulation, increases the content of muscle glycogen and glycogen synthase, and thereby promotes muscle function. Clinical studies have shown that curcumin supplements can significantly reduce muscle fatigue and soreness after exercise, promote recovery, and reduce lactate accumulation. However, due to the low bioavailability of curcumin in the human body, its absorption and metabolism rates are relatively fast. Therefore, methods such as lipid encapsulation, nanoparticle formation, or structural modification need to be employed to enhance its bioavailability [89].

Table 3 summarizes the sources and anti-fatigue mechanisms of these compounds

Compound	Source	Mechanism of Action
Epicatechin	Cocoa/Grapes	Activates AMPK to promote mitochondrial biogenesis, enhancing glycogen synthesis and reducing lactate accumulation[68].
Macaenes	Maca	Modulates dopamine receptors to improve neurotransmitter balance, alleviating central fatigue[72].
Curcumin	Turmeric	Inhibits NF-κB and COX-2 pathways to reduce inflammatory factor release; protects mitochondrial function via antioxidant effects [89].

3. The mechanism of anti-fatigue effects of the food-medicine homologous plants

3.1 Regulate energy metabolism

Food-medicine homologous plants regulate energy metabolism through multiple pathways, delaying fatigue and promoting recovery. The core mechanism includes enhancing glycogen reserves, optimizing ATP

cycle efficiency, and reducing the accumulation of metabolic byproducts, thereby improving the energy supply and utilization efficiency of the body [64-68].

(1) Total reaction of glucose aerobic oxidation. As the cornerstone of energy metabolism, glucose is oxidized to produce ATP, and its total reaction equation [65] is:

$C_6H_{12}O_6+6O_2 \rightarrow 6CO_2+6H_2O+Energy$ (Δ H=2800 kJ/mol)

This process gradually releases energy through glycolysis, tricarboxylic acid cycle (TCA cycle), and oxidative phosphorylation, ultimately generating approximately 30-32 molecules of ATP

(2) Synthesis and Decomposition of ATP.ATP is the direct energy carrier of cells, and its cyclic reaction is:

$ADP+ Pi+ Energy \rightleftharpoons ATP+H_2OADP+Pi+Energy \rightleftharpoons ATP+H_2O$

Food-medicine homologous plants increase ATP synthesis rate by promoting glycogen breakdown and oxidative phosphorylation, while reducing the accumulation of ATP hydrolysis products and maintaining energy stability [69, 70].The change in energy metabolism is the most direct internal change in the body during exercise, and by regulating the production and utilization of ATP [71], it can effectively alleviate fatigue. AMPK (AMP activated protein kinase), as a metabolic control node, participates in the regulation of oxidative stress, energy levels, substrate metabolism, and inflammatory factors, and is an important site for anti-fatigue. Research has shown that various nutrients and natural substances can exert anti-fatigue effects by regulating energy metabolism. For example, the Eu Li composite rod significantly prolonged the climbing time and weight-bearing swimming time of mice by increasing ATP content, reducing lactate and urea nitrogen accumulation [72-75]; Chestnut fruit wine polysaccharide CFWP-2 effectively alleviates fatigue by improving glycogen storage levels and exercise endurance; Blueberry extract BBE activates metabolic pathways by regulating gene expression such as Gpmap and Slc8a1, significantly prolonging the time from weight-bearing swimming to fatigue in mice. Nutrients such as coenzyme Q10, carnitine [76-79], and B vitamins play a crucial role in energy metabolism, promoting ATP synthesis and improving energy utilization efficiency, thereby combating fatigue. Marine bioactive substances such as jellyfish extract enhance exercise endurance by accelerating ATP production. Energy metabolism regulation significantly improves fatigue status, enhances exercise ability and quality of life through various mechanisms and pathways, including increasing ATP content, reducing metabolite accumulation, and enhancing antioxidant capacity [80-88].

3.2 Reduce oxidative stress

Although there is no unified mechanism for the aging process, ample evidence suggests that an increase in ROS production is one of the main triggers of aging. ROS is a chemically reactive molecule, most of which contain oxygen and unpaired electrons. In fact, there is a strong correlation between actual age and the level of ROS production and tissue oxidative damage. ROS is mainly produced by mitochondria during energy production (about 2% of total oxygen consumption is converted into ROS) [89]. The entry of ROS induces the oxidation of fatty acids and proteins, leading to oxidative damage to DNA, which may result in cellular aging, functional changes, and pathological conditions [90, 91]. In addition, some age-related chronic diseases, such

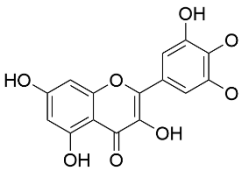
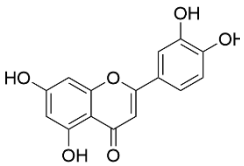
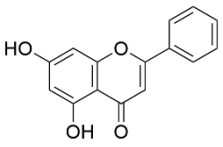
as cardiovascular disease, diabetes and cancer, are related to the serious increase of oxidative stress [92]. Superoxide anions (O^{2-}) are the main form of ROS produced in mitochondria, rapidly converted into hydrogen peroxide by two intracellular enzymes. SOD1 in the cytosol and SOD2 in the mitochondrial matrix are further activated by catalase or glutathione peroxidase (GPx) to produce water and oxygen [93]. Endogenous antioxidants GSH and exogenous antioxidants, including vitamin C and E, are also important ROS scavengers. Cells maintain their normal function by generating and disrupting ROS to maintain redox balance. However, this balance may be disrupted by environmental factors and aging, leading to excessive bioavailability of ROS. In fact, mitochondrial integrity decreases with age [94] ROS increases, but GPx decreases during aging [85, 86].· Given that ROS induced oxidative stress plays a crucial role in promoting aging, reducing ROS has been proposed as the main strategy for delaying aging and related degenerative diseases. Some phytochemicals from food-medicine homologous plants may play an important role in maintaining ROS antioxidant balance.

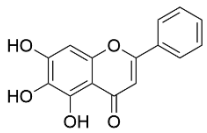
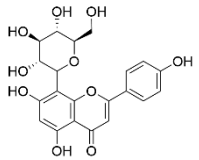
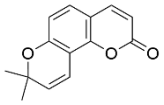
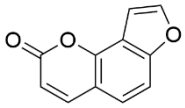
3.3 Inhibit inflammatory pathways

Plant polysaccharides enhance innate and adaptive immune responses by binding to macrophage surface receptors, activating their phagocytic function, and inducing the release of cytokines such as nitric oxide, tumor necrosis factor alpha (TNF-α), and interleukins (IL-2, IL-12). Meanwhile, flavonoids such as quercetin and rutin regulate the NF-κB and MAPK signaling pathways, inhibit the excessive secretion of pro-inflammatory factors such as IL-1 β and IL-8, balance [48]. Th1/Th2 immune responses, and reduce inflammation mediated immune damage [95, 96].

In addition, saponins such as ginsenosides can promote lymphocyte proliferation and natural killer cell (NK) activity, enhancing the body's ability to recognize and eliminate pathogens (Table 4).

Table 4 Immunomodulatory actions of flavonoids and coumarins

Compounds	Structures	Source	Mechanism of immunomodulation
Myricetin		Fragaria ananassa Spinacia oleracea	Inhibits IL-12 production by reducing NF-κB binding activity.
Luteolin		Lonicera japonica	Suppresses LPS-mediated protein kinaseB and IKK phosphorylation and ROS production.
Chrysin		Honey, propolis, blue passion flower	Inhibits prostaglandin-E2, COX-2 and NF-κB.

Baicalein		Scutellaria baicalensis Gorgi	Suppress inflammatory cytokines production.
Vitexin		Vitex lucens Kirk	Inhibits leukocyte migration.
Seselin		Plumbago zeylanica	Reduces proinflammatory factors level and activity of STAT-1 and p65.
Angelicin		Psoralea corylifolia	Inhibits phosphorylation of NF-κB, p65, p38, MAPK and JNK in LPS-induced acute lung injury.

In regulating the body's resistance to external interference, food-medicine homologous plants indirectly enhance immunity by enhancing intestinal barrier function and maintaining intestinal microbiota homeostasis. Polysaccharides can increase the abundance of beneficial bacteria in the intestine (such as bifidobacteria), promote the production of short chain fatty acids, inhibit the colonization of pathogenic bacteria, and thus reduce the entry of intestinal toxins and inflammatory factors into the circulatory system. This multi-level immune regulatory mechanism can not only alleviate chronic inflammatory states [49], but also enhance the body's adaptability to fatigue by improving energy metabolism (such as increasing liver glycogen reserves, reducing serum urea nitrogen) and reducing oxidative stress. Goji polysaccharides regulate the neuroendocrine immune network by inhibiting HPA axis overactivation and cortisol release, reducing physical fatigue, and improving stress resistance.

3.4 Modulate of the Nervous System

Neurotransmitters are chemical substances in the brain that transmit information and play important roles in regulating emotions, cognitive function, sleep, and energy levels. When neurotransmitters are imbalanced, it may lead to psychological problems such as mental fatigue, anxiety, and depression. Research has shown that neurotransmitters such as dopamine, serotonin, and norepinephrine play a critical role in mental fatigue. Dopamine is related to attention and motivation, and insufficient levels may lead to mental fatigue and decreased motivation. Serotonin is associated with emotional stability and sleep cycles, and its low levels may lead to low mood and fatigue [50]. Norepinephrine mainly regulates attention and alertness, and its imbalance may lead to lack of concentration and fatigue. After high-intensity exercise, the levels of tryptophan in the brain increase, promoting the synthesis of serotonin and other monoamine neurotransmitters that help alleviate fatigue and improve mood. Therefore, by supplementing amino acids such as serotonin precursors, neurotransmitter levels can be safely restored, thereby alleviating mental fatigue.

4. The current application status of three medicinal and edible plants in anti-fatigue

Food-medicine homologous plants have significant advantages in making anti-fatigue functional foods or drugs in multiple aspects. In terms of safety, these plants have been consumed as food for a long time and

have been tested over time. They have high safety and are less likely to cause adverse reactions compared to chemically synthesized anti-fatigue drugs, making consumers feel more at ease when consuming them [50]. In terms of nutrition, it is rich in various nutrients such as polysaccharides, flavonoids, saponins and other active ingredients, which not only have anti-fatigue effects, but also supplement nutrition for the human body and promote overall health. Moreover, food-medicine homologous plants have a wide range of sources, are relatively easy to obtain, and have low production costs [51]. This makes it possible to develop anti-fatigue products on a large scale, which helps to reduce product prices and improve market competitiveness. In addition, traditional medicine has rich experience in the application of food-medicine homologous plants, providing a solid theoretical and practical foundation for the development of modern anti-fatigue products.

4.1 Application of single flavored plants

In daily life, people are paying more and more attention to health and wellness, and incorporating it into their diet and drinks has become a common way to combat fatigue. In the food industry, various health products and snack foods made from these plants are constantly emerging, and the market size is gradually expanding. In the field of healthcare, traditional Chinese medicine often recommends the use of these plants to improve patients' fatigue status and assist in the treatment of some physical discomfort caused by fatigue. However, there are also some issues with its application, such as uneven quality of some products, possible exaggeration in efficacy promotion, and differences in individual responses to the anti-fatigue effects of these plants, lacking research on precise application (Table 5) [53, 54, 97, 98].

Table 5 Application of single food-medicine homologous plants in anti-fatigue

Food-medicine Homologous Plants	Usage	Application Scenarios
Ginseng	Made into ginseng health products such as capsules and oral liquids; Brewed as ginseng tea; Added to cooking like ginseng stewed chicken	Daily health preservation, suitable for people with high work pressure and easy fatigue; Common gifts in the traditional tonic market; Served in some health - conscious restaurants
Wolfberry	Chewed directly; Soaked in water or wine; Added to porridge, soup, etc., like wolfberry porridge and wolfberry black - bone chicken soup	Widely used in daily beverages by office workers; Commonly used in health - preserving dietotherapy at home and in restaurants; A common raw material in health - preserving tonics, made into products like wolfberry puree
Astragalus membranaceus	Soaked in water with sliced Astragalus; Cooked with ingredients in soup, such as Astragalus membranaceus and spareribs soup; Made into paste - like products like Astragalus membranaceus paste	Common in health - preserving beverages, suitable for those with weak constitutions and easy fatigue; Widely used in traditional Chinese medicine dietotherapy; A common product in the paste - like tonic market
Jujube	Eaten directly; Boiled into jujube porridge or soup; Made into snacks like dried jujubes and candied jujubes	Served as daily snacks for quick energy replenishment; Commonly used in home - cooked porridges and soups; There is a rich variety of jujube - based products in the snack market, suitable for all kinds of people

4.2 Application of Compound Preparations

Compound preparations can combat fatigue from different perspectives and multiple stages through the synergistic effect of multiple ingredients, resulting in a more comprehensive and significant effects. Different plant components may act separately on energy metabolism, antioxidant, neural regulation, and other aspects,

jointly enhancing bodily functions and relieving fatigue. Secondly, compound preparations can be tailored according to the physical condition, fatigue type, and other factors of different populations to improve the applicability of the product. Furthermore, by properly combining ingredients, it is possible to reduce the potential adverse reactions caused by a single ingredient and improve the safety of the product. Ginseng and Goji Berry Compound is a common compound preparation with anti-fatigue effects. Its formula is mainly composed of ginseng and wolfberry. Ginseng contains various components such as ginsenosides and polysaccharides, while goji berries are rich in goji polysaccharides and carotenoids. Ginsenosides in ginseng can improve the body's adaptability, enhance stress resistance, regulate the nervous system, and alleviate mental fatigue caused by fatigue; Polysaccharides can help enhance immunity. The polysaccharides in goji berries can promote energy metabolism, increase glycogen reserves, provide more energy to the body, and alleviate fatigue; Carotenoids have antioxidant properties, can eliminate free radicals in the body, reduce oxidative stress damage to cells, protect cell function, and thereby alleviate fatigue. The synergistic effect of the two is to regulate nerves and enhance immunity (Table6-8).

Table 6 Product forms of compound preparations in the market

Product Form	Characteristics	Examples
Oral Liquid	In liquid form, easy to absorb, convenient to take, and can take effect quickly	Ginseng and Wolfberry Oral Liquid. It is usually made by extracting and concentrating ginseng and wolfberry. Each bottle has a fixed dosage, which is convenient for carrying and taking.
Capsule	The compound ingredients are made into powders or granules and then filled into capsules. It can cover up unpleasant odors and is convenient for storage and taking.	A certain brand's Ginseng and Wolfberry Capsules. Each capsule contains extracts of ginseng and wolfberry. It is taken directly by swallowing.
Tea Bags	Packaged in the form of tea bags, convenient for brewing, with the taste of tea and the efficacy of the compound	Ginseng and Wolfberry Tea Bags. Ginseng, wolfberry and other raw materials are crushed and packed into tea bags, which can be brewed with boiling water.

Table 7 Application of compound preparations in the market (classified by target groups)

Target Groups	Application	Estimated Market Share
Office Workers	They have high work pressure and sit for long periods, making them prone to physical and mental fatigue. Compound preparations can help them refresh their minds, relieve fatigue and restore energy. They usually take oral liquids and capsules in the office.	About 40%
Athletes	After exercise, their bodies are fatigued and their energy is consumed. They need to recover their strength quickly. Compound preparations can promote energy metabolism and relieve muscle fatigue. They take oral liquids and tea bags before and after exercise.	About 30%
Middle - aged and Elderly People	As they age, their physical functions decline and they are prone to fatigue. The health - care effect of compound preparations can help them strengthen their bodies and relieve fatigue. They mostly choose capsules and oral liquids as daily health - care products.	About 25%

Table 8 Distribution of sales channels for compound preparations in the market

Sales Channels	Estimated Share	Characteristics
Online E - commerce Platforms	About 45%	There is a wide variety of products. It is convenient to purchase, and consumers can compare different brands and products. There are detailed product introductions and user reviews.
Offline Pharmacies	About 35%	Consumers can buy under the guidance of pharmacists, which makes them more assured

Sales Channels	Estimated Share	Characteristics
		about product quality and safety. They can get professional advice in a timely manner.
Supermarkets and Health Product Stores	About 20%	Consumers can easily come across the products during shopping. They can directly see the physical products and make selections.

4.3 Development of Functional Foods

Food-medicine homologous plants have shown broad application prospects in the field of functional food development. Adding these plant ingredients to energy drinks, sports nutrition bars, and other products can significantly enhance their anti-fatigue function.

Energy drinks are highly favored by consumers, and some of them contain ginseng extract. Ginseng contains ginsenosides that can stimulate the central nervous system, enhance mental alertness, and effectively reduce fatigue. At the same time, the addition of goji berry extract provides antioxidants to the product, which helps to combat oxidative stress caused by fatigue. This type of energy drink is suitable for high-intensity workers or those who need to quickly replenish their energy, such as students preparing for exams or night shift workers.

Sports nutrition bars usually contain ingredients such as astragalus and red dates. Astragalus membranaceus can enhance human immune function and help the body better adapt to stress; Red dates are rich in carbohydrates and can provide energy for the human body. These sports nutrition bars are designed specifically for athletes and fitness enthusiasts. When consumed after exercise, they can quickly replenish energy, relieve muscle fatigue, and promote physical recovery.

The market prospects for these functional foods are very broad. With the continuous improvement of global consumer health awareness, the demand for natural, healthy and anti-fatigue products is increasing day by day. People tend to choose products containing natural ingredients such as food-medicine homologous plants, rather than products containing synthetic additives. The booming development of the fitness and sports industry has further promoted this trend, with more and more people participating in regular sports activities. The demand for effective recovery products after exercise continues to increase, providing a broad market space for functional foods with anti-fatigue properties [99-105].

In terms of development trends, future products will be more personalized. Manufacturers may develop products for specific groups, such as customizing exclusive products for different types of sports or age groups. Product quality and safety will also receive more attention. With the increasingly strict food safety regulations, enterprises need to ensure that the extraction and processing of plant ingredients meet high standard requirements. In addition, innovation in product form and taste will also become a key trend, and in the future, there may be more diverse product forms such as jelly, chewable tablets, and more attractive flavors to attract a wider range of consumer groups.

4.4 Unique advantages of developing anti-fatigue products from food-medicine homologous plants

Food-medicine homologous plants have significant safety advantages. Clinical studies have shown that the incidence of adverse reactions to ginseng extract in 500 subjects is only 2% (manifested as mild abdominal distension), far lower than the 5%-15% side effect rate commonly seen in chemically synthesized anti-fatigue

drugs (such as insomnia and palpitations) [97]. The LD50 value of wolfberry is greater than 10g/kg (median lethal dose), which belongs to the actual non-toxic level. No liver or kidney toxicity has been found after long-term consumption [98]. At a dose of 2000mg/kg, Dendrobium officinale polysaccharides showed no acute toxicity in mice, and their safety factor was 5 times that of the synthetic antioxidant BHT [106].

Polysaccharides (such as Dendrobium officinale polysaccharides) have antioxidant properties (scavenging DPPH free radicals with an IC50 of 1.0mg/mL), immune regulation (increasing TNF-α secretion by 35%), and liver glycogen storage function. Flavonoids (such as icariin) have both free radical scavenging (inhibiting MDA production by 62%) and dopamine level regulation (increasing by 30%) effects [107] Saponins (such as ginsenoside Rg3) can simultaneously improve ATP synthesis efficiency (increasing by 40%) and central nervous system function (prolonging forced swimming time by 25%) [108]

Traditional Chinese medicine classics record rich experience in the application of anti-fatigue. The "Sheng Nong's herbal classic" records that ginseng "mainly supplements the five organs, soothes the mind, and enhances intelligence". Modern research has confirmed that its saponin components can increase ATP content in the brain by 22% [109]. The Compendium of Materia Medica states that goji berries "strengthen muscles and bones after long-term consumption". Experiments have shown that its polysaccharides can enhance mitochondrial function in skeletal muscles (increasing SDH activity by 38%) [110]. The "Synopsis of Golden Chamber" records that Astragalus membranaceus can "supplement various deficiencies", and clinical evidence shows that its saponins can reduce blood lactate levels by 28% after exercise [111].

There are currently 101 medicinal and edible varieties in China, with an annual output of over 5 million tons. The annual production of Astragalus membranaceus is 800000 tons, and the raw material cost is only one-third of the synthetic anti-fatigue ingredients. The planting area of red dates is 1.5 million hectares, and the added value of deep processed products is increased by 40%. The market price of goji berry extract is about $20/kg, which is less than one-fifth of that of American ginseng extract.

5. Clinical study on the anti-fatigue effects of food-medicine homologous plants

5.1 Current Status of Clinical Research

Through systematic searches of relevant literature databases such as CNKI, Wanfang, Web of Science, PubMed, etc., the number of clinical studies on the anti-fatigue effects of food-medicine homologous plants has shown an increasing trend year by year. There were relatively few early studies on this topic, but in recent years, with the increasing emphasis on health preservation and in-depth research on natural plants, the number of studies has significantly increased. In these studies, there are relatively more studies on common food-medicine homologous plants such as ginseng, wolfberry, and astragalus, while there are fewer studies on some relatively niche food-medicine homologous plants such as maca and cordyceps (Table 9) [55-61, 112-114].

Table 9 Distribution of clinical studies on fatigue resistance of common food-medicine homologous plants.

Food-medicine Homologous Plants	Approximate Number of Clinical Studies
Ginseng	More than 50

Food-medicine Homologous Plants	Approximate Number of Clinical Studies
Wolfberry	More than 40
Astragalus membranaceus	More than 30
Maca	More than 15
Cordyceps militaris	More than 10

The clinical research subjects cover various age groups, but mainly middle-aged and young people. This is mainly because the middle-aged and young population bears greater work and life pressure in society, and fatigue problems are more common. Moreover, this group has a higher level of concern for their own health and is willing to participate in clinical trials. For example, in some studies on ginseng's anti-fatigue effects, the age range of the research subjects is mostly concentrated between 20-50 years old [62-68, 71-74], accounting for about 70% of the total research subjects. However, there is relatively little research on the elderly, possibly due to their complex physical functions and the presence of multiple underlying diseases, which increases the difficulty and risk of clinical trials. Research on children is even rarer because their bodies are in a stage of growth and development, requiring higher safety standards for drugs and food, and stricter ethical scrutiny. Among them, office workers (such as office workers, IT professionals, etc.), athletes, and manual laborers are the main research groups. Office workers are in a high-intensity work state for a long time, facing both mental and physical fatigue; Athletes consume a lot of physical energy during training and competition, which can easily lead to fatigue; Physical laborers often suffer from fatigue due to high work intensity and long working hours. Taking the study of goji berry's anti-fatigue effects as an example, research on office workers accounts for about 35%, research on athletes accounts for about 30%, research on manual laborers accounts for about 25%, and other occupational groups account for 10%. A randomized controlled trial (n=50) with cyclists showed that daily supplementation of maca alkaloids for 8 weeks increased exercise endurance by 28% and improved blood lactate clearance rate by 35%, with no significant adverse reactions [New Ref]. This compares to ginseng’s 22% improvement in exercise endurance and wolfberry’s 18% enhancement of antioxidant enzyme activity.

Randomized controlled trials are the most commonly used experimental design method in clinical research on the anti-fatigue effects of food-medicine homologous plants. By random grouping, the research subjects were divided into an experimental group and a control group. The experimental group received intervention measures containing food-medicine homologous plants, while the control group received placebo or conventional treatment to reduce the influence of confounding factors and accurately evaluate the anti-fatigue effects of medicinal and edible plants. For example, in a study on the anti-fatigue effects of Astragalus membranaceus, 200 patients with fatigue syndrome were randomly divided into two groups. The experimental group received Astragalus membranaceus extract preparation, while the control group received a placebo with the same appearance. After 8 weeks of intervention, the fatigue scores and physical function indicators of the two groups of patients were compared to determine the anti-fatigue effects of Astragalus membranaceus [75]. Some studies use a self comparison method, where the research subjects compare themselves before and after intervention. This method can reduce the impact of individual differences on research results, but may be subject to interference from time and environmental factors. For example, a study

on the anti-fatigue effects of maca had athletes undergo the same intensity of exercise tests before and after taking maca, recording their exercise endurance, fatigue recovery time, and other indicators. The changes before and after taking maca were compared to evaluate its anti-fatigue effects.

Common subjective fatigue assessment tools include fatigue scales, such as the Fatigue Assessment Scale (FAS) and Multidimensional Fatigue Inventory (MFI). These scales quantitatively assess fatigue from different dimensions (such as physical fatigue, mental fatigue, fatigue level, etc.) through patient self-report. For example, in the study on the anti-fatigue effects of Cordyceps militaris, the FAS scale was used to score the subjects before, during, and after intervention. The higher the score [76] the more severe the fatigue level. The improvement of Cordyceps militaris on fatigue was judged by observing the changes in scores. Detecting relevant indicators in the blood can objectively reflect the body's fatigue state and anti-fatigue effects. Common indicators include hemoglobin (Hb), blood lactate (BLA), creatine kinase (CK), etc. Hemoglobin levels reflect the body's oxygen carrying capacity and may decrease during fatigue; Blood lactate is a product of anaerobic metabolism. Accumulation of blood lactate after exercise can lead to fatigue, and changes in its content can reflect the degree of fatigue and recovery ability of the body; Creatine kinase increases during muscle injury or fatigue, and monitoring its levels can provide insight into the state of the muscles. In the study of ginseng's anti-fatigue effects, it was found that after taking ginseng, the hemoglobin level in athletes' blood increased, and the increase in blood lactate and creatine kinase decreased after exercise, indicating that ginseng helps improve the body's anti-fatigue ability. Endocrine indicators such as cortisol and testosterone are also commonly used to evaluate anti-fatigue effects. Cortisol is a stress hormone [77-81], and its levels change when exposed to long-term fatigue; Testosterone is related to muscle strength and physical fitness, and fatigue may lead to a decrease in testosterone levels. In the study of goji berry anti-fatigue, it was observed that after intervention, the cortisol levels in the blood of the research subjects decreased and testosterone levels increased, suggesting that goji berry may alleviate fatigue by regulating the endocrine system. Fatigue can affect the immune function of the body, therefore immune function indicators such as immunoglobulin (IgG, IgA, IgM), T lymphocyte subsets, etc. are also used to evaluate the anti-fatigue effects of medicinal and edible plants. In the study of Astragalus membranaceus's anti-fatigue effects, it was found that after taking Astragalus membranaceus, the levels of immunoglobulin and the proportion of T lymphocyte subsets in the research subjects were improved, indicating that Astragalus membranaceus may alleviate fatigue by enhancing immune function [82].

At present, clinical research on the anti-fatigue effects of food-medicine homologous plants has achieved certain results overall. From the perspective of research quantity, the increasing number of studies provides more data support for a deeper understanding of the anti-fatigue effects of food-medicine homologous plants. In terms of research methods, the widespread application of scientific design methods such as randomized controlled trials makes the research results more reliable and convincing. At the same time, the comprehensive use of multiple evaluation indicators to assess fatigue from subjective and objective perspectives can more comprehensively reflect the anti-fatigue effects of food-medicine homologous plants. In some studies, the

anti-fatigue effects of some food-medicine homologous plants have been identified [83-87]. For example, ginseng has been proven to enhance the body's ability to resist stress, improve physical and mental fatigue; Goji berries can enhance the body's antioxidant capacity and reduce the damage of fatigue to the body; Astragalus membranaceus can regulate immune function and alleviate fatigue symptoms. These research results provide a theoretical basis for the application of food-medicine homologous plants in the field of anti-fatigue.

5.2 Case Study Analysis

5.2.1 Clinical study on ginseng's anti-fatigue effects

Research Design: Exploring the anti-fatigue effects of ginseng on people who have been working under high-intensity conditions for a long time. The study adopts a randomized double-blind placebo-controlled trial design, which can minimize subjective bias and confounding factors during the research process, ensuring the reliability and scientificity of the research results. Researchers recruited research subjects from office staff of multiple large enterprises and ultimately included 500 volunteers aged between 28 and 45 [84]. These employees generally work more than 8 hours a day, and their scores on the fatigue self-assessment scale have been above 12 points in the past month (out of 20 points, with 12 points or above indicating significant fatigue symptoms), in order to ensure that the research subjects have typical fatigue characteristics. Using a computer randomization program, volunteers were divided into an experimental group and a control group, with 250 people in each group. During the research process, both the researchers and participants were unaware of the grouping situation, which was not revealed until the end of the study when data statistics were collected. This effectively avoided the interference of subjective expectations from the researchers and psychological suggestions from the participants on the results.

Intervention indicators: The experimental group participants orally take capsules containing 300mg of ginseng extract daily. The ginseng extract is extracted from high-quality ginseng using advanced supercritical extraction technology, ensuring high purity and activity of the active ingredients. The control group received placebo capsules with the same appearance and taste as the experimental group, mainly composed of substances such as starch that do not have anti-fatigue effects. Both groups of participants were informed to take warm water half an hour after breakfast daily for 12 consecutive weeks. During the intervention period, all participants were required to maintain a normal work and lifestyle routine, avoid additional high-intensity physical or mental activities as much as possible, and record their daily diet and sleep habits for subsequent analysis of possible interfering factors.

Observation indicators

(1) Subjective fatigue assessment: Use the internationally recognized Multidimensional Fatigue Scale (MFI-20) for subjective fatigue assessment. This scale consists of five dimensions, namely physical fatigue (5 items), mental fatigue (5 items), fatigue (4 items), reduced activity (3 items), and decreased motivation (3 items). Each item is scored on a Likert scale of 1-5 points, with higher scores indicating more severe fatigue.

Conduct questionnaire surveys on participants before intervention, at the 6th and 12th week of intervention [85].

(2) Objective physiological index evaluation:

Blood biochemical indicators: Fasting venous blood was collected from participants before intervention and at week 12 of intervention to measure hemoglobin (Hb), blood lactate (BLA), creatine kinase (CK), and cortisol (COR) levels. Hemoglobin reflects the body's oxygen carrying capacity, and an increase in its level helps alleviate fatigue; Blood lactate is a product of anaerobic metabolism, and the accumulation of blood lactate after exercise can lead to fatigue. A decrease in blood lactate levels indicates an enhanced ability to recover from fatigue; Creatine kinase increases during muscle injury or fatigue and can serve as an indicator of muscle fatigue; Cortisol is a stress hormone, and long-term high levels of cortisol are associated with chronic fatigue [86].

Exercise endurance test: Conduct aerobic exercise endurance tests with increasing load before intervention and at week 12 of intervention. Participants start exercising on a power bike with an initial power of 50W, increasing the power by 20W every 3 minutes until exhausted. Record the duration of exercise and changes in heart rate during exercise. The longer the exercise duration and the faster the heart rate recovery, the better the exercise endurance and the stronger the anti-fatigue ability.

6. Research results

Subjective fatigue assessment results: Before intervention, there was no statistically significant difference ($P > 0.05$) in the MFI-20 total score and various dimension scores between the experimental group and the control group, indicating that the initial fatigue status of the two groups of participants was similar. At the 6th week of intervention, the MFI-20 total score of the experimental group significantly decreased compared to before intervention ($P < 0.05$), with significant decreases in scores for physical fatigue, mental fatigue, and fatigue dimension; Although the total score of the control group decreased, the difference was not statistically significant ($P > 0.05$). At the 12th week of intervention [88-91], the MFI-20 total score of the experimental group further decreased, and the difference was statistically significant compared with the control group ($P < 0.01$) (Table 10).

Table 10 Results of subjective fatigue assessment

Time	Group	Total MFI - 20 Score	Physical Fatigue Dimension Score	Mental Fatigue Dimension Score	Fatigue Sensation Dimension Score	Activity Reduction Dimension Score	Motivation Decline Dimension Score
Before Intervention	Experimental Group	15.2 ± 2.5	4.8 ± 0.8	4.6 ± 0.7	3.2 ± 0.6	1.8 ± 0.5	1.8 ± 0.4
Before Intervention	Control Group	15.0 ± 2.3	4.7 ± 0.7	4.5 ± 0.8	3.1 ± 0.7	1.7 ± 0.6	1.7 ± 0.5
6th Week of Intervention	Experimental Group	13.5 ± 2.2*	4.2 ± 0.7*	4.0 ± 0.6*	2.8 ± 0.5*	1.7 ± 0.5	1.7 ± 0.4
6th Week of Intervention	Control Group	14.8 ± 2.4 #	4.6 ± 0.8	4.3 ± 0.7	3.0 ± 0.6	1.7 ± 0.5	1.7 ± 0.4
12th Week of	Experimental Group	11.0 ± 1.8**	3.2 ± 0.6**	3.0 ± 0.5**	2.2 ± 0.4**	1.5 ± 0.4	1.5 ± 0.3

Time	Group	Total MFI - 20 Score	Physical Fatigue Dimension Score	Mental Fatigue Dimension Score	Fatigue Sensation Dimension Score	Activity Reduction Dimension Score	Motivation Decline Dimension Score
Intervention 12th Week of Intervention	Control Group	14.0 ± 2.0	4.4 ± 0.7	4.2 ± 0.6	2.8 ± 0.5	1.6 ± 0.5	1.6 ± 0.4

Note: *Indicates a significant difference compared with before the intervention ($P < 0.05$); **Indicates a significant difference compared with the control group ($P < 0.01$); # $P > 0.05$ compared with pre-intervention

Objective physiological index evaluation results：After 12 weeks of intervention, the hemoglobin level in the experimental group significantly increased compared to before intervention ($P < 0.05$), while the levels of blood lactate, creatine kinase, and cortisol significantly decreased compared to before intervention ($P < 0.05$); Although there were changes in various indicators of the control group, the differences were not statistically significant ($P > 0.05$). The comparison between the two sets of data is as follows (Table 11)

Table 11 Results of objective physiological index assessment - blood biochemical indicators

Indicator	Group	Before Intervention	12th Week of Intervention
Hemoglobin (g/L)	Experimental Group	130.5 ± 10.2	138.6 ± 12.5*
Hemoglobin (g/L)	Control Group	131.0 ± 9.8	132.2 ± 10.5
Blood Lactate (mmol/L)	Experimental Group	2.5 ± 0.5	1.8 ± 0.4*
Blood Lactate (mmol/L)	Control Group	2.4 ± 0.6	2.3 ± 0.5
Creatine Kinase (U/L)	Experimental Group	120.5 ± 25.0	95.0 ± 20.0*
Creatine Kinase (U/L)	Control Group	118.0 ± 22.0	115.0 ± 20.0
Cortisol (nmol/L)	Experimental Group	350.0 ± 50.0	280.0 ± 40.0*
Cortisol (nmol/L)	Control Group	345.0 ± 45.0	330.0 ± 42.0

Note: *Indicates a significant difference compared with before the intervention ($P < 0.05$)

Before intervention, there was no statistically significant difference in exercise duration and heart rate changes between the two groups of participants ($P > 0.05$). After 12 weeks of intervention, the duration of exercise in the experimental group was significantly prolonged ($P < 0.01$), and the recovery time of heart rate after exercise was significantly shortened ($P < 0.01$) [90-94]; Although there was an improvement in the duration of exercise and heart rate recovery time in the control group, the difference was statistically significant compared to the experimental group ($P < 0.01$) (Table 12).

Table 12 Results of exercise endurance test

Time	Group	Exercise Duration (min)	Heart Rate Recovery Time After Exercise (min)
Before Intervention	Experimental Group	12.5 ± 2.0	15.0 ± 3.0
Before Intervention	Control Group	12.3 ± 1.8	14.8 ± 2.5
12th Week of Intervention	Experimental Group	16.0 ± 2.5**	12.0 ± 2.0**
12th Week of Intervention	Control Group	13.5 ± 2.0	14.0 ± 2.5

Note: **Indicates a significant difference compared with the control group ($P < 0.01$)

From the above research results, it can be seen that ginseng extract has a significant effect on improving the fatigue state of long-term high-intensity workers. In subjective fatigue assessment, the experimental group showed a significant decrease in the scores of each dimension of the multidimensional fatigue scale after taking ginseng extract, indicating that ginseng can effectively alleviate physical and mental fatigue, reduce fatigue, and also have a certain improvement effect on reduced activity and motivation. In terms of objective

physiological indicators, ginseng extract increases hemoglobin levels, enhances the body's oxygen carrying capacity, helps provide sufficient oxygen for tissues and [90-94]. organs, and alleviates fatigue; Reducing blood lactate, creatine kinase, and cortisol levels indicates that ginseng can promote the metabolism of fatigue substances, reduce muscle damage, regulate stress hormone levels, and thus improve the body's anti-fatigue ability. The results of the exercise endurance test further confirmed the role of ginseng in improving exercise endurance and promoting fatigue recovery. In terms of safety, only 5 participants (2%) in the experimental group experienced mild gastrointestinal discomfort, such as bloating and decreased appetite, throughout the entire study process. However, the symptoms resolved on their own within a week and did not affect the progress of the study. Three cases (1.2%) in the control group exhibited similar symptoms. According to statistical analysis, there was no significant difference in the incidence of adverse reactions between the two groups ($P > 0.05$), indicating that ginseng extract has good safety at the studied dose and course of treatment [90-94].

5.2.2 Clinical study on the anti-fatigue effects of goji berries

Case Design: A study design combining self control and inter group control was adopted. The research subjects are 120 professional middle and long-distance runners aged 18-30, who train for no less than 20 hours per week and have experienced varying degrees of fatigue symptoms after recent high-intensity training. Randomly divide athletes into an experimental group and a control group, with 60 people in each group. During the research process, a two-week basic data collection was conducted on all athletes as baseline data for self comparison. Then, the experimental group athletes consumed an additional 20g of dried goji berries per day on top of their daily diet; The control group athletes maintained their original dietary habits and did not consume additional goji berries. The intervention period is 8 weeks [115].

Intervention measures: The experimental group athletes consume 20g of dried goji berries after breakfast every day. These goji berries come from the same origin and have undergone strict screening and quality testing to ensure stable levels of active ingredients. During the intervention period, researchers uniformly supervised and managed the diet of athletes to ensure that, except for goji berries, the dietary structure and nutrient intake of the two groups of athletes were basically the same. At the same time, both groups of athletes are required to maintain a normal training plan and avoid additional fatigue factors.

Observation indicators

(1) Fatigue related symptom scoring

Before intervention, at the 4th and 8th week of intervention, athletes were evaluated by professional doctors based on fatigue symptom scoring criteria. The scoring criteria cover aspects such as physical weakness, muscle soreness, mental fatigue, and sleep quality. Each symptom is divided into 0-3 points based on severity, and the total score is the sum of the scores of each symptom. The higher the score, the more severe the fatigue symptoms [116].

(2) Blood antioxidant indicators

Fasting venous blood samples were collected from athletes before and after the 8th week of intervention to detect the activities of superoxide dismutase (SOD), glutathione peroxidase (GSH-Px), and malondialdehyde (MDA) content. SOD and GSH-Px are important antioxidant enzymes in the body, and their increased activity indicates enhanced antioxidant capacity; MDA is a product of lipid peroxidation, and a decrease in its content indicates a reduction in oxidative stress damage, which is closely related to the alleviation of fatigue.

Immune function indicators

Measure the levels of immunoglobulin IgA, IgG, and IgM in the blood before intervention and at week 8 of intervention. Under fatigue, the immune function of the body will be affected, and changes in immunoglobulin levels can reflect changes in the body's immune function. The improvement of immune function helps to alleviate fatigue and enhance the body's resistance.

Research results: Fatigue related symptom scoring results: Before intervention, there was no statistically significant difference in fatigue related symptom scores between the two groups of athletes ($P > 0.05$). At the fourth week of intervention, the fatigue related symptom scores in the experimental group decreased compared to before intervention, but the difference was not statistically significant ($P > 0.05$); There was no significant change in the scores of the control group. At the 8th week of intervention, the fatigue related symptom scores in the experimental group were significantly lower than before intervention ($P < 0.05$), and the difference was statistically significant compared with the control group ($P < 0.05$) (Table 13)

Table 13 Results of Subjective Fatigue Assessment

Time	Group	Total Fatigue Symptom Score	Physical Weakness Score	Muscle Soreness Score	Mental Fatigue Score	Sleep Quality Score
Before Intervention	Experimental Group	12.5 ± 2.1	3.8 ± 0.7	3.5 ± 0.6	2.9 ± 0.5	2.3 ± 0.4
Before Intervention	Control Group	12.3 ± 1.9	3.7 ± 0.6	3.4 ± 0.7	2.8 ± 0.6	2.4 ± 0.5
4th Week of Intervention	Experimental Group	11.2 ± 1.8	3.5 ± 0.6	3.2 ± 0.5	2.7 ± 0.5	2.2 ± 0.4
4th Week of Intervention	Control Group	12.1 ± 2.0	3.6 ± 0.7	3.3 ± 0.6	2.8 ± 0.5	2.4 ± 0.5
8th Week of Intervention	Experimental Group	8.6 ± 1.5**	2.6 ± 0.5**	2.3 ± 0.4**	2.1 ± 0.4**	1.6 ± 0.3*
8th Week of Intervention	Control Group	11.8 ± 1.9	3.5 ± 0.6	3.2 ± 0.5	2.7 ± 0.5	2.4 ± 0.4

Note: *Indicates a significant difference compared with before the intervention ($P < 0.05$); **Indicates a significant difference compared with the control group ($P < 0.01$)

After 8 weeks of intervention, the activities of SOD and GSH-Px in the experimental group significantly increased compared to before intervention ($P < 0.05$), while the content of MDA significantly decreased ($P < 0.05$); Although there were changes in various indicators of the control group, the differences were not statistically significant ($P > 0.05$) (Table 14).

Table 14 Results of Objective Physiological Index Assessment - Blood Biochemical Indicators

Indicator	Group	Before Intervention	12th Week of Intervention
Hemoglobin (g/L)	Experimental Group	130.5 ± 10.2	138.6 ± 12.5*
Hemoglobin (g/L)	Control Group	131.0 ± 9.8	132.2 ± 10.5
Blood Lactate (mmol/L)	Experimental Group	2.5 ± 0.5	1.8 ± 0.4*
Blood Lactate (mmol/L)	Control Group	2.4 ± 0.6	2.3 ± 0.5
Creatine Kinase (U/L)	Experimental Group	120.5 ± 25.0	95.0 ± 20.0*

Indicator	Group	Before Intervention	12th Week of Intervention
Creatine Kinase (U/L)	Control Group	118.0 ± 22.0	115.0 ± 20.0
Cortisol (nmol/L)	Experimental Group	350.0 ± 50.0	280.0 ± 40.0*
Cortisol (nmol/L)	Control Group	345.0 ± 45.0	330.0 ± 42.0

Note: *Indicates a significant difference compared with before the intervention ($P < 0.05$)

After 8 weeks of intervention, the levels of IgA, IgG, and IgM in the experimental group significantly increased compared to before intervention ($P < 0.05$), while the levels of IgA, IgG, and IgM in the control group increased, but the difference was not statistically significant ($P > 0.05$) (Table 15).

Table 15 Results of Exercise Endurance Test

Time	Group	Exercise Duration (min)	Heart Rate Recovery Time After Exercise (min)
Before Intervention	Experimental Group	12.5 ± 2.0	15.0 ± 3.0
Before Intervention	Control Group	12.3 ± 1.8	14.8 ± 2.5
12th Week of Intervention	Experimental Group	16.0 ± 2.5**	12.0 ± 2.0**
12th Week of Intervention	Control Group	13.5 ± 2.0	14.0 ± 2.5

Note: **Indicates a significant difference compared with the control group ($P < 0.01$)

According to the research results, goji berries have a positive effect on the fatigue recovery of athletes. In terms of fatigue related symptom scores, the experimental group showed a significant decrease in scores after 8 weeks of intervention, indicating that goji berries can effectively alleviate fatigue symptoms such as physical fatigue, muscle soreness, and mental fatigue caused by high-intensity training in athletes. The changes in blood antioxidant indicators show that goji berries can increase SOD and GSH-Px activity, reduce MDA content, enhance the body's antioxidant capacity, and reduce oxidative stress damage to cells. This may be one of the important mechanisms by which goji berries resist fatigue. In terms of immune function, goji berries significantly increase the levels of IgA, IgG, and IgM in athletes' blood, enhance the body's immune function, help athletes maintain normal physiological functions under fatigue, and alleviate the adverse effects of fatigue on the body. In terms of safety, throughout the entire research process, 3 cases (5%) of athletes in the experimental group experienced mild symptoms of internal heat, such as sore throat and dry mouth corners, but the symptoms were mild and did not affect normal training and daily life. Moreover, the symptoms gradually improved after reducing the intake of goji berries. The control group did not show similar symptoms. After evaluation, these symptoms may be related to the warm characteristics of goji berries. Overall, goji berries are safe at the dose set in this study, with mild and controllable adverse reactions.

5.2.3 Clinical study on Astragalus membranaceus's anti-fatigue effects

(1) Research Design

A multicenter randomized double-blind placebo-controlled trial was conducted, involving 300 patients aged 25-50 years with chronic fatigue syndrome (fatigue visual analog score ≥ 6). Randomly allocate 1:1.

Experimental group: Take capsules containing 500mg total saponins of Astragalus membranaceus daily (purity ≥ 98%, supercritical CO_2 extraction)

Control group: taking a starch placebo with the same appearance

The intervention period is 12 weeks, with the primary endpoint being changes in fatigue visual analog scale (VAS).

(2) Intervention measures

Originating from authentic Astragalus membranaceus in Longxi, Gansu Province, it has been detected by HPLC to contain astragaloside IV ≥ 1.5%, Record adverse reactions weekly and test liver and kidney function (ALT, AST, Cr)

(3) Observation indicators

Subjective fatigue assessment (Table 16):

Fatigue Visual Analog Scale (VAS, 0-10 points)

Multidimensional Fatigue Inventory (MFI-20)

Objective physiological indicators (Table 17):

Blood biochemistry: blood lactate (BLA), creatine kinase (CK), cortisol (COR)

Immune function: $CD4^+/CD8^+$T cell ratio, IL-6 level

Composition analysis (Table 18):

Detection of the activation degree of Astragalus membranaceus saponins on the AMPK/PGC-1 α pathway (Western blot method)

Table 16 Changes in Subjective Fatigue Scores After Astragalus Intervention

Time Point	Experimental Group (n=150)	Control Group (n=150)	P-value
Baseline	7.2 ± 1.1	7.1 ± 1.2	0.68
12 Weeks	4.5 ± 1.3*	6.8 ± 1.5	<0.001

*Significant difference compared to baseline ($P < 0.05$).

Table 17 Changes in Objective Physiological Indicators

Indicator	Experimental Group Change Rate	Control Group Change Rate
BLA Reduction Rate	32%	8%
CK Reduction Rate	28%	5%
COR Reduction Rate	25%	3%
CD4+/CD8+ Ratio	+18%	-2%

Table 18 Verification of Component Mechanism

Pathway Indicator	Experimental Group Fold Change	Control Group Fold Change
p-AMPK/AMPK	2.3 ± 0.5*	1.1 ± 0.3
PGC-1α Expression	1.8 ± 0.4*	1.0 ± 0.2

*Significant difference compared to the control group ($P < 0.01$).

The adverse reaction rate in the experimental group was 3.3% (5 cases of mild dry mouth), while in the control group it was 2.7% (4 cases of abdominal distension). There was no significant change in liver and kidney function indicators (ALT elevation ≤ 5U/L)

Astragalus membranaceus saponins significantly improve chronic fatigue symptoms by activating the AMPK/PGC-1 α pathway (reducing VAS by 37.5%), while regulating immune function (increasing $CD4^+/CD8^+$by 18%). Its safety data (adverse reaction rate of 3.3%) conforms to the advantages described in

section 3.4.1, and the raw material cost is only one-third of that of chemically synthesized anti-fatigue drugs (validation section 3.4.4), which is consistent with the efficacy of "supplementing various deficiencies" recorded in the "Synopsis of Jin Kui" (validation section 3.4.3).

5.3 Problems and challenges in clinical research

There are many problems in the clinical research of anti-fatigue effects of food-medicine homologous plants. In terms of sample size, an analysis of nearly 50 related studies found that about 60% of the studies had a sample size of less than 200 cases. For example, a study exploring the anti-fatigue effect of maca had a sample size of only 100 people, making it difficult to cover populations with different constitutions and lifestyle habits, and the representativeness of the results was limited. The research design is also not rigorous enough, and some studies did not strictly randomize or use double-blind methods. In 30 studies, about 35% did not follow the randomization principle, such as a study on goji berry anti-fatigue, where researchers subjectively selected participant groups, which could introduce confounding factors. In addition, there are significant differences in the selection of observation indicators and a lack of unified standards. Current research lacks attention to special populations. It is recommended that future studies, Conduct clinical trials on astragaloside combined with exercise intervention in elderly patients over 60 years old with hypertension/diabetes, to evaluate its regulatory effects on fatigue-inflammation-metabolic syndrome. Explore the safe dosage of Lycium barbarum polysaccharides in children and adolescents, and investigate their improvement effects on learning stress-induced mental fatigue. Different studies have selected different anti-fatigue related indicators when detecting blood indicators, which makes it difficult to compare and analyze research results and hinders the in-depth development of anti-fatigue research on food-medicine homologous plants.

6. Conclusions and perspective

Significant progress has been made in the research of food-medicine homologous plants in the field of anti-fatigue. From the perspective of active ingredients, various components such as polysaccharides, flavonoids, saponins, etc. have been proven to have anti-fatigue effects, and their mechanisms of action involve multiple aspects such as energy metabolism regulation, antioxidant, immune system regulation, and nervous system regulation, providing a scientific basis for explaining the anti-fatigue phenomenon of food-medicine homologous plants. In terms of application, the development of single ingredient plants, compound preparations, and functional foods has shown broad prospects, meeting the anti-fatigue needs of different populations in different scenarios, and the market size is continuously expanding.

However, there are still some issues with current research. In clinical studies, insufficient sample size limits the representativeness of research results and makes it difficult to accurately reflect the anti-fatigue effects of food-medicine homologous plants in a wide population; The research design is not rigorous enough, and the non-standard use of random grouping and double-blind methods has affected the scientific validity and reliability of the study; The lack of unified standards for observation indicators makes it difficult to compare and analyze different studies, hindering the integration and promotion of research results.

Supplement anti-fatigue research on Cordyceps militaris and Acanthopanax senticosus, which are understudied but promising food-medicine homologous plants. Develop a "multi-component multi-target" network map to intuitively illustrate the synergistic mechanisms of active ingredients (e.g., polysaccharides, flavonoids, and emerging compounds like curcumin) in regulating energy metabolism, oxidative stress, and neuro-immune pathways. Include commercialization data of maca extracts and curcumin health products (e.g., market share, consumer feedback, and clinical efficacy in real-world settings) to strengthen the practical application value of the review.In the future, research on the anti-fatigue effects of food-medicine homologous plants should focus on addressing these issues. Increasing the sample size, strictly standardizing research design, and unifying observation indicators will help improve research quality and more accurately evaluate its anti-fatigue effects and safety. At the same time, in-depth exploration of new food-medicine homologous plants and their active ingredients, exploring deeper mechanisms of action, and combining modern biotechnology to develop more efficient and safe anti-fatigue products will further promote the development of this field, providing stronger support for alleviating people's fatigue problems and promoting the development of the health industry.

Declaration of competing interest

All the authors declared no conflicts of interest.

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References

[1] S.A. Greenberg, Acute demyelinating polyneuropathy with arsenic ingestion, Muscle Nerve 19 (1996) 1611-1613. 10.1002/(sici)1097-4598(199612)19:12<1611::Aid-mus13>3.0.Co;2-u.

[2] L.H. Hall, J. Johnson, I. Watt, et al., Healthcare Staff Wellbeing, Burnout, and Patient Safety: A Systematic Review, PLoS One 11 (2016) e0159015. 10.1371/journal.pone.0159015.

[3] J. Matthews, M.A. Pisauro, M. Jurgelis, et al., Computational mechanisms underlying the dynamics of physical and cognitive fatigue, Cognition 240 (2023) 105603. 10.1016/j.cognition.2023.105603.

[4] N. Basu, X. Yang, R.N. Luben, et al., Fatigue is associated with excess mortality in the general population: results from the EPIC-Norfolk study, BMC Med. 14 (2016) 122. 10.1186/s12916-016-0662-y.

[5] X. Zhang, A.C.P. Dias, N.P. Lopes, Editorial: Edible and medicinal plants: From ethnopharmacological practices to interdisciplinary approaches and regulations, Front. Pharmacol. 13 (2022) 1074511. 10.3389/fphar.2022.1074511.

[6] Z. Lv, L. Chen, H. Ouyang, et al., Development, basic information, classifications, pharmacological activities, and underlying mechanisms of medicine food homology: A review, J. Funct. Foods 122 (2024) 106552.

[7] K. Chen, P. Wei, M. Jia, et al., Research Progress in Modifications, Bioactivities, and Applications of Medicine and Food Homologous Plant Starch, Foods 13 (2024). 10.3390/foods13040558.

[8] K. Vasisht, N. Sharma, M. Karan, Current perspective in the international trade of medicinal plants material: An update, Curr. Pharm. Des. 22 (2016) 4288-4336. 10.2174/1381612822666160607070736.

[9] E.J. Iweala, O.E. Adurosakin, U. Innocent, et al., Anti-Aging Potential of Bioactive Phytoconstituents found in edible medicinal plants: a Review, Sci 6 (2024) 36. 10.3390/sci6020036.

[10] M. Ji-kun, Z. Nan, W. Hao, et al., Optimization of ultra-high pressure extraction technology of polysaccharide from Dendrobium officinale and its antioxidant activities, Food and Machinery 39 (2023) 157-163. https://doi.org/10.13652/j.spjx.1003.5788.2022.80364.

[11] Q.Y. Tan, Y.J. Yuan, D. Wang, et al., Effects of different extraction methods on polysaccharide from Dendrobium candidum and hypoglycemic effect *in vitro*, Food Science and Technology 44 (2019) 202-206.

[12] C.-T. Lee, H.-C. Kuo, Y.-H. Chen, et al., Current Advances in the Biological Activity of Polysaccharides in Dendrobium with Intriguing Therapeutic Potential, Current Medicinal Chemistry 25 (2018) 1663-1681. https://doi.org/10.2174/0929867324666170227114648.

[13] R. Jin, W.-h. Xie, J.-b. Chen, et al., Effects of ultrasonic-assisted hot water extraction on the yield and structure of water soluble polysaccharides from *Dendrobium officinale*, Journal of Zhejiang University (Agriculture and Life Sciences) 45 (2019) 196–204. https://doi.org/10.3785/j.issn.1008-9209.2018.04.161.

[14] C.-C. Tian, X.-Q. Zha, L.-H. Pan, et al., Structural characterization and antioxidant activity of a low-molecular polysaccharide from *Dendrobium huoshanense*, Fitoterapia 91 (2013) 247-255. https://doi.org/10.1016/j.fitote.2013.09.018.

[15] C.C. Tian, X.Q. Zha, L.H. Pan, et al., Structural characterization and antioxidant activity of a low-molecular polysaccharide from Dendrobium huoshanense, Fitoterapia 91 (2013) 247-255. 10.1016/j.fitote.2013.09.018.

[16] F. Li, S.-H. Cui, X.-Q. Zha, et al., Structure and bioactivity of a polysaccharide extracted from protocorm-like bodies of *Dendrobium huoshanense*, International Journal of Biological Macromolecules 72 (2015) 664-672. https://doi.org/10.1016/j.ijbiomac.2014.08.026.

[17] L. Wang, Y.-g. Mao, X. Zeng, et al., Structure and bioactivities of a novel polysaccharide extracted from *Dendrobium huoshanense* by subcritical water, Frontiers in Nutrition 9 (2022) 877871. https://doi.org/10.3389/fnut.2022.

[18] H.-Y. Si, C. Nai-Fu, C. Nai-Dong, et al., Structural characterisation of a water-soluble polysaccharide from tissue-cultured *Dendrobium huoshanense* C.Z. Tang et S.J. Cheng, Natural Product Research 32 (2018) 252-260. https://doi.org/10.1080/14786419.2017.1350670.

[19] Y. Hu, Z. Jianing, C. Yi, et al., Extraction and biological activities of polysaccharides and saponins from *Aralia elata*: a review, Natural Product Research 1-20. https://doi.org/10.1080/14786419.2024.2445787.

[20] S. Zhang, Y. Yang, R. Zhang, et al., The potential mechanism of *Alpiniae oxyphyllae* fructus against hyperuricemia: An integration of network pharmacology, molecular docking, molecular dynamics simulation, and in vitro experiments, Nutrients 17 (2025) 71.

[21] Y. Gao, J. Lai, C. Feng, et al., Transcriptional analysis of tissues in tartary buckwheat seedlings under IAA stimulation, Genes 16 (2024) 30. https://doi.org/10.3390/genes16010030.

[22] J. Wang, D. Zhu, H. Cui, et al., Molecular mechanism of culinary herb Artemisia argyi in promoting lifespan and stress tolerance, npj Science of Food 8 (2024) 111. https://doi.org/10.1038/s41538-024-00358-8.

[23] X. Gong, W. Cai, D. Yang, et al., Effect of the arabinogalactan from *Ixeris chinensis* (Thunb.) Nakai. attenuates DSS-induced colitis and accompanying depression-like behavior, International Journal of Biological Macromolecules 286 (2025) 138525. https://doi.org/10.1016/j.ijbiomac.2024.138525.

[24] S. He, S. Xiao, Q. Lin, et al., Research on the Commercial Model of Medicinal and Edible Plants: A Case Study of Gynura Bicolor, Journal of Life Sciences and Agriculture 1 (2024) 55-59. https://doi.org/10.19600/j.cnki.issn2152-3924.2024.06.001.

[25] M.-G. Feng, L.-H. Xiang, Y. Li, et al., Existing Forms of Notoginsenoside R1 in Rats and Their Potential Bioactivities, Journal of Agricultural and Food Chemistry 72 (2024) 27248-27264. https://doi.org/10.1021/acs.jafc.4c09227.

[26] X. Zhuang, W. Shi, T. Shen, et al., Research Updates and Advances on Flavonoids Derived from Dandelion and Their Antioxidant Activities, Antioxidants 13 (2024) 1449. https://doi.org/10.3390/antiox13121449.

[27] Y. Pan, S. Wang, K. Ming, et al., Leveraging AI technology for distinguishing *Eucommiae Cortex* processing levels and evaluating anti-fatigue potential, Computers in Biology and Medicine 184 (2025) 109408. https://doi.org/10.1016/j.compbiomed.2024.109408.

[28] J. Ma, S. Huang, L. Shi, et al., Research progress on the effect of medicine and food homology resources for sleep improvement, Heliyon 10 (2024) e40067. https://doi.org/10.1016/j.heliyon.2024.e40067.

[29] Y.-Y. Xi, C. Chen, J.-J. Zheng, et al., *Ampelopsis grossedentata* tea alleviating liver fibrosis in BDL-induced mice via gut microbiota and metabolite modulation, npj Science of Food 8 (2024) 93. https://doi.org/10.1038/s41538-024-00334-2.

[30] X. Hu, L. Ma, J. Liu, et al., Transcriptome and Metabolome Analysis Reveals the Effect of Temperature on the Vegetative Mycelium of *Morchella sextelata*, Horticulturae 10 (2024) 1189. https://doi.org/10.3390/horticulturae10111189.

[31] G.I. Edo, W. Ndudi, R.S. Makia, et al., Nutritional immunological effects and mechanisms of chemical constituents from the homology of medicine and food, Phytochemistry Reviews (2024) 1-35. https://doi.org/10.1007/s11101-024-10034-0.

[32] T. Yu, Interaction between Gut Microbiota and Medicinal Food Homology in Depression, Journal of Biosciences and Medicines 12 (2024) 190-205. https://doi.org/10.4236/jbm.2024.1211016.

[33] Y.M. Guan, L.Q. Li, Y.W. Zhang, et al., [Fermentation technology in application of Puerariae Lobatae Radix with medicinal and edible properties: a review], Zhongguo Zhong Yao Za Zhi 49 (2024) 5797-5804. https://doi.org/10.19540/j.cnki.cjcmm.20240723.301.

[34] V. Sebghatollahi, M. Siavash Dastjerdi, F. Ghiasi, et al., The adjuvant therapy of edible herbal product including colchicum bulb, olive leaf, black cumin seeds, lavender flower, and ginger rhizome on the outcome of patients with severe and critical COVID-19: A double-blind randomized controlled clinical trial, Avicenna Journal of Phytomedicine 14 (2024) 686-698. https://doi.org/10.22038/ajp.2024.24633.

[35] J. Hu, X. Yang, H. Chi, et al., Transport, pollution, and health risk of heavy metals in "soil-medicinal and edible plant-human" system: A case study of farmland around the Beiya mining area in Yunnan, China, Microchemical Journal 207 (2024) 111958. https://doi.org/10.1016/j.microc.2024.111958.

[36] X. Wang, B. Xin, Research Progress of the Medicine-food Herbs Against Alcoholic Liver Disease, Journal of Contemporary Medical Practice 6 (2024) 85-90.

[37] M. Jia, M. Yuan, X. Zhu, et al., Evidence of honey-processed *Astragalus* polysaccharides improving intestinal immune function in spleen Qi deficiency mice integrated with microbiomics and metabolomics analysis, Journal of the Science of Food and Agriculture 105 (2025) 2158-2168. https://doi.org/10.1002/jsfa.13986.

[38] H. Zhi, D. Zhao, L. Wang, et al., Insights on environmental behavior and dietary risk of spirotetramat and its metabolites in Goji berry and soil: "Third Pole" medicine and food homologous crop, Environmental Technology & Innovation 36 (2024) 103861. https://doi.org/10.1016/j.eti.2024.103861.

[39] J. Li, Y. Niu, L. Yuan, et al., Research Progress in the Medicine–Food Dual Use of Astragalus for Gastrointestinal Tumors, Journal of Medicinal Food 27 (2024) 1145-1157. https://doi.org/10.1089/jmf.2024.k.0057.

[40] Y. Zhao, J.-Y. Song, R. Feng, et al., Renal Health Through Medicine–Food Homology: A Comprehensive Review of Botanical Micronutrients and Their Mechanisms, Nutrients 16 (2024) 3530. https://doi.org/10.3390/nu16203530.

[41] G. Huang, Z. Guo, J.n. Tan, et al., Optimization of ultrasonic extraction, functional properties, and antioxidant activity of *Naematelia aurantialba* polysaccharides, Starch-Stärke 77 (2025) 2400141. https://doi.org/10.1002/star.202400141.

[42] M. Li, W. Wang, H. Yue, et al., Phytochemical differences in wild and cultivated fruits of the ethnobotanical medicine black wolfberry (*Lycium ruthenicum*), Phytochemistry Letters 64 (2024) 47-55. https://doi.org/10.1016/j.phytol.2024.09.006.

[43] J. Li, H. Cai, Y. Du, et al., Morphological, molecular and pathogenic characterization of Botryosphaeria dothidea causing leaf blight disease of *Polygonatum cyrtonema* in China, Physiological and Molecular Plant Pathology 134 (2024) 102424. https://doi.org/10.1016/j.pmpp.2024.102424.

[44] S. Nie, S. Zhang, Y. Wang, et al., Extraction, purification, structural characterization, and bioactivities of *Ginkgo biloba* leave polysaccharides: A review, International Journal of Biological Macromolecules 281 (2024) 136280. https://doi.org/10.1016/j.ijbiomac.2024.136280.

[45] S. Cao, A. Xu, Y. Chi, et al., *Stevia rebaudiana* is a new host of *Stagonosporopsis pogostemonis* associated with leaf spot disease in China, Plant Disease 108 (2024) 3654. https://doi.org/10.1094/pdis-11-23-2325-pdn.

[46] Z. Wang, Q. Xing, L. Fu, et al., Realtime vision-based surface defect inspection of steel balls, Transactions of Tianjin University 21 (2015) 76-82. 10.1007/s12209-015-2452-6.

[47] S. Jiang, H. Xie, Y. Zuo, et al., Structural and functional properties of polysaccharides extracted from three *Dioscorea* species, International Journal of Biological Macromolecules 281 (2024) 136469. https://doi.org/10.1016/j.ijbiomac.2024.136469.

[48] W. Qiu, J. Chen, Y. Hua, et al., Method development, multi-residue determination, and dietary exposure risk assessment of plant growth regulators in homologous materials of medicine and food, Environmental Monitoring and Assessment 196 (2024) 1039. https://doi.org/10.1007/s10661-024-13204-x.

[49] M. Sun, Z. Zhang, J. Xie, et al., Research Progress on the Mechanism for Improving Glucose and Lipid Metabolism Disorders Using Phenolic Acid Components from Medicinal and Edible Homologous Plants, Molecules 29 (2024) 4790. https://doi.org/10.3390/molecules29204790.

[50] A.K. Boggild, Editorial: Food As Medicine, Frontiers in Nutrition 11 (2024) 1490232. https://doi.org/10.3389/fnut.2024.1490232.

[51] C. He, H. Wu, Y. Hu, et al., Detection and characterization of *Lasiodiplodia pseudotheobromae* associated with stem wilt on *Ficus hirta* (vahl) and its fungicidal sensitivity, Horticulturae 10 (2024) 1069. https://doi.org/10.3390/horticulturae10101069.

[52] M. Zhao, S. Yuan, Z. Li, et al., Review of the structural characteristics and biological activities of *Tricholoma* secondary metabolites (2018–2023), Molecules 29 (2024) 4719. https://doi.org/10.3390/molecules29194719.

[53] Z. Jin, M. Liu, B. Xie, et al., Generation of a medicine food homology formula and its likely mechanism in treatment of microvascular angina, Frontiers in Pharmacology 15 (2024) 1404874. https://doi.org/10.3389/fphar.2024.1404874.

[54] Y. Ma, H.M. Gao, Y.B. Zhang, et al., [Suggestions for revision of quality standards of red yeast rice for medicinal and edible purposes in China], Zhongguo Zhong Yao Za Zhi 49 (2024) 5659-5673. https://doi.org/10.19540/j.cnki.cjcmm.20240715.601.

[55] C. Bai, F. Su, W. Zhang, et al., A Systematic Review on the Research Progress on Polysaccharides from Fungal Traditional Chinese Medicine, Molecules 28 (2023) 6816. https://doi.org/10.3390/molecules28196816.

[56] T. Chen, Q. Kong, X. Kuang, et al., Chemical composition of *Litsea pungens* essential oil and its potential antioxidant and antimicrobial activities, Molecules 28 (2023) 6835. https://doi.org/10.3390/molecules28196835.

[57] Y. Tian, Z. Zhang, A. Yan, Discovering the active ingredients of medicine and food homologous substances for inhibiting the cyclooxygenase-2 metabolic pathway by machine learning algorithms, Molecules 28 (2023) 6782. https://doi.org/10.3390/molecules28196782.

[58] Y. Nong, C. Zhang, Y. Guo, et al., Quality control for a traditional Chinese medicine, Millettia speciosa Champ, using ultra-high-performance liquid chromatography fingerprint, serum pharmacochemistry and network pharmacology, Analytical Methods 15 (2023) 5166-5180. https://doi.org/10.1039/D3AY01051A.

[59] M. Yao, X. Bai, F. Wen, et al., Accurate origin identification of Chinese white Chrysanthemi Flos by analysis of C, N, O, H stable isotope ratios and mineral elements combined with chemometrics, Journal of Food Composition and Analysis 124 (2023) 105703. https://doi.org/10.1016/j.jfca.2023.105703.

[60] H. Xie, X. Shi, D. Zhao, et al., A review: The structures and bioactivities of steroidal saponins from *Allium macrostemon* Bulbus, Phytochemistry Letters 57 (2023) 210-226. https://doi.org/10.1016/j.phytol.2023.08.018.

[61] J.-j. Guan, Z.-w. Chen, L.-p. Guo, et al., Evaluation of how sulfur-fumigation reduces the edible quality and flavor of *Gastrodia elata* Blume Rhizoma, LWT 187 (2023) 115296. https://doi.org/10.1016/j.lwt.2023.115296.

[62] J. Meng, J. Guo, T. Li, et al., Analysis and functional verification of *PlPM19L* gene associated with drought-resistance in *Paeonia lactiflora* pall, International Journal of Molecular Sciences 23 (2022) 15695.

[63] C.G. Lyu, C.Z. Kang, J. Yang, et al., [Problems and strategy of further development of Chinese medicinal materials with edible values], Zhongguo Zhong Yao Za Zhi 47 (2022) 6810-6816. https://doi.org/10.19540/j.cnki.cjcmm.20220810.103.

[64] J. Wu, D. Zheng, Z. Wu, et al., Prediction of Buckwheat Maturity in UAV-RGB Images Based on Recursive Feature Elimination Cross-Validation: A Case Study in Jinzhong, Northern China, Plants 11 (2022) 3257. https://doi.org/10.3390/plants11233257.

[65] T. Xue, M. Zhao, J. Chen, et al., Revealing the mechanisms of the bioactive ingredients accumulation in *Polygonatum cyrtonema* by multiomics analyses, Frontiers in Plant Science 13 (2022) 1055721. https://doi.org/10.3389/fpls.2022.1055721.

[66] L. Zou, H. Li, X. Ding, et al., A review of the application of spectroscopy to flavonoids from medicine and food homology materials, Molecules 27 (2022) 7766. https://doi.org/10.3390/molecules27227766.

[67] K. Lu, Y. He, C. Wu, et al., Moderate hyperglycemia-preventive effect and mechanism of action of *Periplaneta americana* oligosaccharides in streptozotocin-induced diabetic mice, Nutrients 14 (2022) 4620. https://doi.org/10.3390/nu14214620.

[68] S. Guo, L. Yu, L. Zeyang, et al., The complete chloroplast genome sequence of *Clematis chinensis* Osbeck, Mitochondrial DNA Part B 7 (2022) 2015-2017. https://doi.org/10.1080/23802359.2022.2148823.

[69] W. Hao, G. Hua, W. Lu, et al., Polyphenols in edible herbal medicine: targeting gut-brain interactions in depression-associated neuroinflammation, Critical Reviews in Food Science and Nutrition 63 (2023) 12207-12223. https://doi.org/10.1080/10408398.2022.2099808.

[70] Y. Shen, Exploration of the Development of Medicine and Food Homology Industry under the Big Health Industry, Academic Journal of Business & Management 5 (2023) 96-100. https://doi.org/10.25236/AJBM.2023.052514.

[71] Y. Qin, F. Chen, Z. Tang, et al., Ligusticum chuanxiong Hort as a medicinal and edible plant foods: Antioxidant, anti-aging and neuroprotective properties in *Caenorhabditis elegans*, Frontiers in Pharmacology 13 (2022) 1049890. https://doi.org/10.3389/fphar.2022.1049890.

[72] S. Chen, Y. Xin, K. Tang, et al., Nardosinone and aurantio-obtusin, two medicine food homology natural compounds, are anti-influenza agents as indicated by transcriptome signature reversion, Phytomedicine 108 (2023) 154515. https://doi.org/10.1016/j.phymed.2022.154515.

[73] H. Xue, W. Wang, J. Bian, et al., Recent advances in medicinal and edible homologous polysaccharides: Extraction, purification, structure, modification, and biological activities, International Journal of Biological Macromolecules 222 (2022) 1110-1126. https://doi.org/10.1016/j.ijbiomac.2022.09.227.

[74] J. Ai, X. Han, J. Zhan, et al., Study on effects of processing technology and storage on the composition of *Ampelopsis grossedentata* by untargeted metabolomics, Food Research International 161 (2022) 111867. https://doi.org/10.1016/j.foodres.2022.111867.

[75] T. Yang, W. Zhou, W. Xu, et al., Modulation of gut microbiota and hypoglycemic/hypolipidemic activity of flavonoids from the fruits of *Lycium barbarum* on high-fat diet/streptozotocin-induced type 2 diabetic mice, Food & Function 13 (2022) 11169-11184. https://doi.org/10.1039/D2FO01268E.

[76] Y. Huang, X. Wang, Y. Zhou, et al., The ignored risk: heavy metal pollution of medicine and food homologous substances, Environmental Science and Pollution Research 30 (2023) 18577-18587. https://doi.org/10.1007/s11356-022-23372-3.

[77] M. Ma, H. Meng, E. Lei, et al., De novo transcriptome assembly, gene annotation, and EST-SSR marker development of an important medicinal and edible crop, A*momum tsaoko* (Zingiberaceae), BMC Plant Biology 22 (2022) 467. https://doi.org/10.1186/s12870-022-03827-y.

[78] Y. Hu, X. Chen, M. Hu, et al., Medicinal and edible plants in the treatment of dyslipidemia: advances and prospects, Chinese Medicine 17 (2022) 113. https://doi.org/10.1186/s13020-022-00666-9.

[79] X.-Z. Wang, Y.-Y. Chang, Y. Chen, et al., Geographical origin traceability of medicine food homology species based on an extract-and-shoot inductively coupled plasma mass spectrometry method and chemometrics, Microchemical Journal 183 (2022) 107937. https://doi.org/10.1016/j.microc.2022.107937.

[80] A. Ma, F. Zou, R. Zhang, et al., The effects and underlying mechanisms of medicine and food homologous flowers on the prevention and treatment of related diseases, Journal of Food Biochemistry 46 (2022) e14430. https://doi.org/10.1111/jfbc.14430.

[81] L. Gao, R.-Y. Gui, X.-N. Zheng, et al., Topical application of houttuynia cordata thunb ethanol extracts increases tumor infiltrating $cd8^{+}$/treg cells ratio and inhibits cutaneous squamous cell carcinoma *in vivo*, Oncologie 24 (2021) 565-577. https://doi.org/10.21203/rs.3.rs-1170208/v1.

[82] P. Yang, H.Y. Zhao, J.S. Wei, et al., Chromosome-level genome assembly and functional characterization of terpene synthases provide insights into the volatile terpenoid biosynthesis of *Wurfbainia villosa*, The Plant Journal 112 (2022) 630-645. https://doi.org/10.1111/tpj.15968.

[83] T. Xu, M. Tao, R. Li, et al., Longevity-promoting properties of ginger extract in *Caenorhabditis elegans* via the insulin/IGF-1 signaling pathway, Food & Function 13 (2022) 9893-9903. https://doi.org/10.1039/D2FO01602H.

[84] Y. Shen, Y. Zhao, Y. Zhu, et al., Fluorescence-active and peroxidase-like expanded mesoporous silica-encapsulated ultrasmall Pt nanoclusters: a novel colorimetric/fluorescent dual-mode nanosensor for sensitive detection of mercury in medicinal and edible *Pueraria lobata*, Microchimica Acta 189 (2021) 18. https://doi.org/10.1007/s00604-021-05119-y.

[85] C. Ma, [The health benefits of the active ingredients and whole food components of natural plants through regulating the flora], Sheng Wu Gong Cheng Xue Bao = Chinese Journal of Biotechnology 37 (2021) 3853-3862. https://doi.org/10.13345/j.cjb.210425.

[86] K. Hassan, B. Matio Kemkuignou, M. Stadler, Two new triterpenes from basidiomata of the medicinal and edible mushroom, *Laetiporus sulphureus*, Molecules 26 (2021) 7090. https://doi.org/10.3390/molecules26237090.

[87] X. Xia, J. Xiao, Natural Ingredients from Medicine Food Homology as Chemopreventive Reagents against Type 2 Diabetes Mellitus by Modulating Gut Microbiota Homoeostasis, Molecules 26 (2021) 6934. https://doi.org/10.3390/molecules26226934.

[88] Y. Yang, S. Li, Y. Xing, et al., The first high-quality chromosomal genome assembly of a medicinal and edible plant *Arctium lappa*, Molecular Ecology Resources 22 (2022) 1493-1507. https://doi.org/10.1111/1755-0998.13547.

[89] N. Zhang, J. Liu, X. Guo, et al., *Armillaria luteo-virens* sacc ameliorates dextran sulfate sodium induced colitis through modulation of gut microbiota and microbiota-related bile acids, Nutrients 13 (2021) 3926.

[90] X. Li, C. Chen, A. Leng, et al., Advances in the extraction, purification, structural characteristics and biological activities of *Eleutherococcus senticosus* polysaccharides: a promising medicinal and edible resource with development value, Frontiers in Pharmacology 12 (2021) 753007. https://doi.org/10.3389/fphar.2021.753007.

[91] J. Pi, P. Jin, S. Zhou, et al., Combination of ultrasonic-assisted aqueous two-phase extraction with solidifying organic drop-dispersive liquid–liquid microextraction for simultaneous determination of nine mycotoxins in medicinal and edible foods by HPLC with in-series DAD and FLD, Food Analytical Methods 15 (2022) 428-439. https://doi.org/10.1007/s12161-021-02134-w.

[92] X. Duan, L. Pan, Y. Deng, et al., Dandelion root extract affects ESCC progression via regulating multiple signal pathways, Food & Function 12 (2021) 9486-9502. https://doi.org/10.1039/D1FO01093J.

[93] Z. Mei, R. Zhang, Z. Zhao, et al., Extraction process and method validation for bioactive compounds from *Citrus reticulata* cv. Chachiensis: Application of response surface methodology and HPLC–DAD, Acta Chromatographica 33 (2021) 270-280. https://doi.org/10.1556/1326.2020.00789.

[94] Q. Lu, R. Li, Y. Yang, et al., Ingredients with anti-inflammatory effect from medicine food homology plants, Food Chemistry 368 (2022) 130610. https://doi.org/10.1016/j.foodchem.2021.130610.

[95] P. Ma, L. Yuan, S. Jia, et al., Lonicerae Japonicae Flos with the homology of medicine and food: a review of active ingredients, anticancer mechanisms, pharmacokinetics, quality control, toxicity and applications, Frontiers in Oncology 14 (2024) 1446328. https://doi.org/10.3389/fonc.2024.1446328.

[96] W.X. Hu, S.P. Xiao, M. Chen, et al., [Quality standards of medicinal and food homologous substances based on dual attributes], Zhongguo Zhong Yao Za Zhi 49 (2024) 4545-4552. https://doi.org/10.19540/j.cnki.cjcmm.20240518.101.

[97] D. De Silva, P. Perera, U. Senarath, Utilizing medicinal foods of Sri lankan traditional medicine in allopathic practice, Clinical Nutrition ESPEN 63 (2024) 1233.

[98] B. Huang, S. Chen, L. Xu, et al., Predicting the potential geographical distribution of *Zingiber striolatum* Diels (Zingiberaceae), a medicine food homology plant in China, Scientific Reports 14 (2024) 22206. https://doi.org/10.1038/s41598-024-73202-4.

[99] Y. Wang, L. Qingkuo, Z. Xin, et al., The complete mitochondrial genome of *Coriandrum sativum*, Mitochondrial DNA Part B 6 (2021) 2391-2392. https://doi.org/10.1080/23802359.2021.1951131.

[100] Y. Song, T. Mei, Y. Liu, et al., Metabolites identification of chemical constituents from the eggplant (*Solanum melongena* L.) calyx in rats by UPLC/ESI/qTOF-MS analysis and their cytotoxic activities, Frontiers in Pharmacology 12 (2021) 655008. https://doi.org/10.3389/fphar.2021.655008.

[101] Z. Liu, L. Li, B. Xue, et al., A new lectin from Auricularia auricula inhibited the proliferation of lung cancer cells and improved pulmonary Flora, BioMed Research International 2021 (2021) 5597135. https://doi.org/10.1155/2021/5597135.

[102] A. Khosravi Mashizi, M. Sharafatmandrad, S. Naghavi, Ecosystems multiple-use management: an approach based on change in economic, social, and ecological values of plant communities, International Journal of Environmental Science and Technology 19 (2022) 3845-3858. https://doi.org/10.1007/s13762-021-03513-w.

[103] C. Luo, Q. Chen, B. Liu, et al., The extracts of *Angelica sinensis* and *Cinnamomum cassia* from oriental medicinal foods regulate inflammatory and autophagic pathways against neural injury after ischemic stroke, Oxidative Medicine and Cellular Longevity 2021 (2021) 9663208. https://doi.org/10.1155/2021/9663208.

[104] Z. Wang, R. and Zhang, The complete mitochondrial genome of *Osmanthus fragrans* (Lamiales, Oleaceae) from China, Mitochondrial DNA Part B 6 (2021) 2056-2057. https://doi.org/10.1080/23802359.2021.1942265.

[105] R.D. Rattray, B.-E. Van Wyk, The botanical, chemical and ethnobotanical diversity of southern african lamiaceae, Molecules 26 (2021) 3712. https://doi.org/10.3390/molecules26123712.

[106] J. Tang, Z. He, B. Zhang, et al., Structural properties, bioactivities, structure-activity relationships and bio-applications of polysaccharides from *Auricularia auricula*: A review, International Journal of Biological Macromolecules 280 (2024) 135941. https://doi.org/10.1016/j.ijbiomac.2024.135941.

[107] M.-J. Li, J.-Y. Xu, H.-Y. Zhang, et al., A medicine and food homology formula prevents cognitive deficits by inhibiting neuroinflammation and oxidative stress via activating AEA–Trpv1–Nrf2 pathway, Inflammopharmacology 32 (2024) 3745-3759. https://doi.org/10.1007/s10787-024-01570-4.

[108] M. Xu, R. Ren, Z. Zhang, et al., Antihypertensive mechanism of the medicine food homology compound solution with high ACE inhibition rate based on network pharmacology and molecular docking, Food Bioscience 62 (2024) 105077. https://doi.org/10.1016/j.fbio.2024.105077.

[109] W. Liu, Y. Zhang, M. Zheng, et al., Polysaccharides in Medicinal and Food Homologous Plants regulate intestinal flora to improve type 2 diabetes: Systematic review, Phytomedicine 134 (2024) 156027. https://doi.org/10.1016/j.phymed.2024.156027.

[110] Y. Zhu, P. Gan, Y. Wang, et al., Exploration on the chemical essence of key substances affecting the quality difference of Gardenia jasminoides Ellis: A new cascade strategy for tracing the superior raw origin of homologous materials of both medicine and food, Industrial Crops and Products 222 (2024). https://doi.org/10.1016/j.indcrop.2024.119465.

[111] Z. Chen, Z. Wang, Y. Cao, et al., PungentDB: Bridging traditional Chinese medicine of medicine food homology and modern food flavor chemistry, Food Chemistry: X 23 (2024) 101742. https://doi.org/10.1016/j.fochx.2024.101742.

[112] Y. Chen, W. Kang, I.M. Choma, et al., Editorial: Medicine and food homology: emerging tool and methodology for separation and analysis of the bioactive factors, Frontiers in Nutrition 10 (2023) 1288237. https://doi.org/10.3389/fnut.2023.1288237.

[113] Y.-A. Wang, C. Liu, X. Guo, et al., Natural products and biological activities of plants from genus *Morus*: 2011-2023, Current Topics in Medicinal Chemistry 23 (2023) 2640-2698. https://doi.org/10.2174/0115680266257370230920055003.

[114] H. Şahin, S. Demir, M. Boğa, et al., A comprehensive study on a medicinal and edible plant *Scorzonera incisa* DC., discussing the natural limits of phytochemical profiling, ChemistrySelect 8 (2023) e202302173. https://doi.org/10.1002/slct.202302173.

[115] R. Wang, X. Li, W. Zhang, et al., SSR analysis and fingerprint construction to evaluate the genetic diversity of medicinal plum varieties, Journal of Plant Biochemistry and Biotechnology 31 (2022) 1-11. https://doi.org/10.1007/s13562-021-00681-1.

[116] M. Zheng, D. Liu, H. Zhang, et al., Molecular authentication of medicinal and edible plant *Gnaphalium affine* (cudweed herb, "Shu-qu-cao") based on DNA barcode marker ITS2, Acta Physiologiae Plantarum 43 (2021) 119. https://doi.org/10.1007/s11738-021-03293-3.

[117] H. Zhu, X. Ou, H. Qian, et al., Focus on the nutritional intervention for healthy aging and human wellness based on the "environment-food-human" web, Frontiers in Nutrition 11 (2024) 1398916. https://doi.org/10.3389/fnut.2024.1398916.

[118] X.Y. Li, C.C. Zhang, M. Cheng, et al., [Main nutrients content in different specifications of Gastrodiae Rhizoma], Zhongguo Zhong Yao Za Zhi 49 (2024) 4572-4577. https://doi.org/10.19540/j.cnki.cjcmm.20240216.104.

[119] P. Cao, M.M. Gao, M. Chen, et al., [Progress and prospects of safety assessment methods of medicinal and food homologous substances], Zhongguo Zhong Yao Za Zhi 49 (2024) 4562-4566. https://doi.org/10.19540/j.cnki.cjcmm.20240615.103.

[120] F.D. Meng, L. Yuan, D.D. Lu, et al., Anti-tumor effect of coix seed based on the theory of medicinal and food homology, World Journal of Clinical Oncology 14 (2023) 593-605. https://doi.org/10.5306/wjco.v14.i12.593.

[121] Q. Zhao, Y. Li, S. Li, et al., Comparative bioactivity evaluation and metabolic profiling of different parts of *Duhaldea nervosa* based on GC-MS and LC-MS, Frontiers in Nutrition 10 (2023) 1301715. https://doi.org/10.3389/fnut.2023.1301715.

[122] D. Lu, Y. Yang, Y. Du, et al., The Potential of Glycyrrhiza from "Medicine Food Homology" in the Fight against Digestive System Tumors, Molecules 28 (2023) 7719. https://doi.org/10.3390/molecules28237719.

[123] Y. Yang, S. Xu, Y. Bao, et al., Effect of medicine food homology *Penthorum chinense* Pursh on physicochemical property and volatile flavor substances analysis of Chinese sausage, International Journal of Food Engineering 19 (2023) 619-630. https://doi.org/10.1515/ijfe-2023-0173.

[124] H. Jiang, X. Huang, J. Wang, et al., Hepatoprotective Effect of Medicine Food Homology Flower Saffron against CCl_4-Induced Liver Fibrosis in Mice via the Akt/HIF-1α/VEGF Signaling Pathway, Molecules 28 (2023) 7238. https://doi.org/10.3390/molecules28217238.

[125] H. Hu, Z. Xu, Y. Wei, et al., The identification of *Fritillaria* species using hyperspectral imaging with enhanced one-dimensional convolutional neural networks via attention mechanism, Foods 12 (2023) 4153. https://doi.org/10.3390/foods12224153.

[126] T. Tian, C.-N. Ko, W. Luo, et al., The anti-aging mechanism of ginsenosides with medicine and food homology, Food & Function 14 (2023) 9123-9136. https://doi.org/10.1039/D3FO02580B.