Future Foods 12 (2025) 100684

Contents lists available at ScienceDirect

Future Foods

journal homepage: www.elsevier.com/locate/fufo

A review on anti-aging actions of plant polysaccharides

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ARTICLE INFO

Keywords:
Aging mechanism
Plant polysaccharide
Antisenescence

ABSTRACT

Aging can lead to a decline in the biological functions of the body's cells and tissues, triggering various chronic diseases, including cardiovascular disease, diabetes, and neurodegenerative disorders. This gradual weakening of the body increases the risk of mortality. With societal advancements and improvements in modern medical standards, there is a growing focus on anti-aging research, prompting an urgent search for effective anti-aging therapies. Plant polysaccharides possess numerous natural pharmacological effects, including anti-aging, anti-inflammatory, immune regulation, anti-tumor properties, and blood sugar reduction. Additionally, plant polysaccharides are associated with minimal toxic side effects and high safety profiles, while being widely sourced from various plants. Owing to these natural advantages, plant polysaccharides have become a research hotspot across multiple fields. Specifically, plant polysaccharides can modulate aging through mechanisms such as enhancing antioxidant enzyme activity, regulating inflammatory factors, promoting cell autophagy and division, improving mitochondrial function, increasing telomerase activity, and regulating gut microbiota. Thus, they play a significant role and hold an important position in the field of anti-aging research. This article briefly reviews the mechanisms of aging and the progress made in understanding the anti-aging effects of plant polysaccharides, providing a reference for further investigation in this area.

1. Introduction

Aging is a cellular response that can induce stable growth arrest, which is characterized by progressive dysfunction of tissue function (McHugh and Gil, 2018). According to the "World Population Prospects 2022" report released by the United Nations, the global population aged 60 and older accounts for over 10% of the total population in the 21st century (Hong et al., 2023). Population aging has become a significant issue for societal development, imposing a significant burden on ever more strained health systems (Chen et al., 2023).

Although aging is inevitable, it can be managed and delayed (da Costa et al., 2016). Common anti-aging drugs, including rapamycin, metformin, and aspirin (Piskovatska et al., 2019) may have side effects, such as gastric ulceration, hallucinations, and leukopenia (Blagosklonny, 2019), which can lead to undesirable treatment experiences for patients. In contrast, plant polysaccharides have the characteristics of wide sources, low toxicity or side effects (Dong et al., 2021) and excellent anti-aging effects (Wang et al., 2022a), which has become a new focus in current research on anti-aging drugs.

Polysaccharides are macromolecular carbohydrates formed by condensation of multiple monosaccharides, with a wide variety and complex molecular structure (Huang and Huang, 2020a). This paper primarily addresses non-starch polysaccharides. Notably, plant polysaccharides composed of different monosaccharides can exhibit varied

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https://doi.org/10.1016/j.fufo.2025.100684
Received 9 April 2025; Received in revised form 9 June 2025; Accepted 13 June 2025
Available online 14 June 2025
2666-8335/

biological activities. For instance, Chen discovered through experiments that the separation and purification of mulberry leaf polysaccharides could yield MLP-1, which contains xylose, and MLP-2 without xylose, with MLP-2 showing higher immunoreactivity than MLP-1 (Chen et al., 2019). Furthermore, the connection mode and quantity of monosaccharides are various, resulting in diverse polysaccharide microstructures (Huang and Huang, 2020b). It has been noted that monosaccharides can be connected into polysaccharides through glycosidic bonds, and α-1,4-, β-1,4-and α-1,6-glycosidic bonds are common glycosidic bonds (Feng et al., 2022). Among them, the α-1, 4-glycosidic bond and the β-1,4-glycosidic bond are generally connected to the linear chain, and the alpha-1,6-glycosidic bond is generally the connection point. The structural differences in polysaccharides are closely related to the different biological characteristics. For example, inulin is considered as an indigestible polysaccharide, which may be due to its unique β-(2,1)-glycosidic bond (Du et al., 2023). Most of the polysaccharides with a β-helix structure exhibit strong biological functions, while macromolecular polysaccharides usually have high biological activities (Yin et al., 2019). Numerous studies have indicated that plant polysaccharides exhibit diverse physiological activities, including antioxidant, anti-tumor, glucose-lowering, and immune-regulating properties, demonstrating significant therapeutic effects in many fields. As shown in Figure 1, various plant polysaccharides have rich pharmacological effects. For instance, Zeng and others have highlighted the excellent effects of *Lycium barbarum* polysaccharide (LBP) in improving liver damage, retinal degeneration, brain ischemia-reperfusion injury, stroke, and Alzheimer's disease (Zeng et al., 2019). *Angelica sinensis* polysaccharide (ASP) exhibit a variety of biological activities, including anti-aging, immune regulation, anti-oxidation, hematopoiesis (Nai et al., 2021), and the ability to protect the liver and gastrointestinal tract, as well as improve diabetes. Ginseng polysaccharides display outstanding antioxidant stress-relieving effects, along with anti-tumor and immune-regulating properties, making them potential immune modulator (Tao et al., 2023). Radix *astragali* polysaccharide is an immunomodulatory substance, presenting activities such as anti-aging, antioxidant, antiviral, and anti-tumor effects (Tang and Huang, 2022). *Cistanche deserticola* polysaccharides possess antioxidant and hepatoprotective properties, can alleviate age-related inflammation, and exhibit anti-aging activity (Takaya et al., 2023). Currently, plant polysaccharides such as those from *Angelica sinensis, Cistanche deserticola*, and *Astragalus* have been found to exhibit anti-aging biological activities, playing crucial roles in anti-aging. This article provides a comprehensive review of the mechanisms of aging and the anti-aging effects of plant polysaccharides, offering insights for further research on anti-aging polysaccharides and the development of novel anti-aging formulations to prolong lifespan and alleviate age-related diseases.

2. *Absorption of polysaccharides*

Due to their high molecular weight, polysaccharides were once widely believed to be difficult for the human body to digest and absorb orally, and the mechanism by which polysaccharides exert effects throughout the body was not well understood (Nagamine et al., 2014). The human genome encodes only a small number of digestive glycoside hydrolases which are responsible for breaking down sucrose, lactose, and starch. However, Kaoutari's group demonstrated that the digestion of many complex polysaccharides in our diet mainly relies on some specific enzymes from the gut microbiome, such as polysaccharide lyases, which decompose complex carbohydrates via elimination reactions. As a result, polysaccharides are broken down into monosaccharides that can be absorbed and utilized by the human body (Kaoutari et al., 2013). In the process of polysaccharide decomposition, not only are the large intestine cells nourished, but the proliferation of harmful bacteria is effectively inhibited, thereby enhancing the intestinal barrier function (Xue et al., 2024). This process is essential for

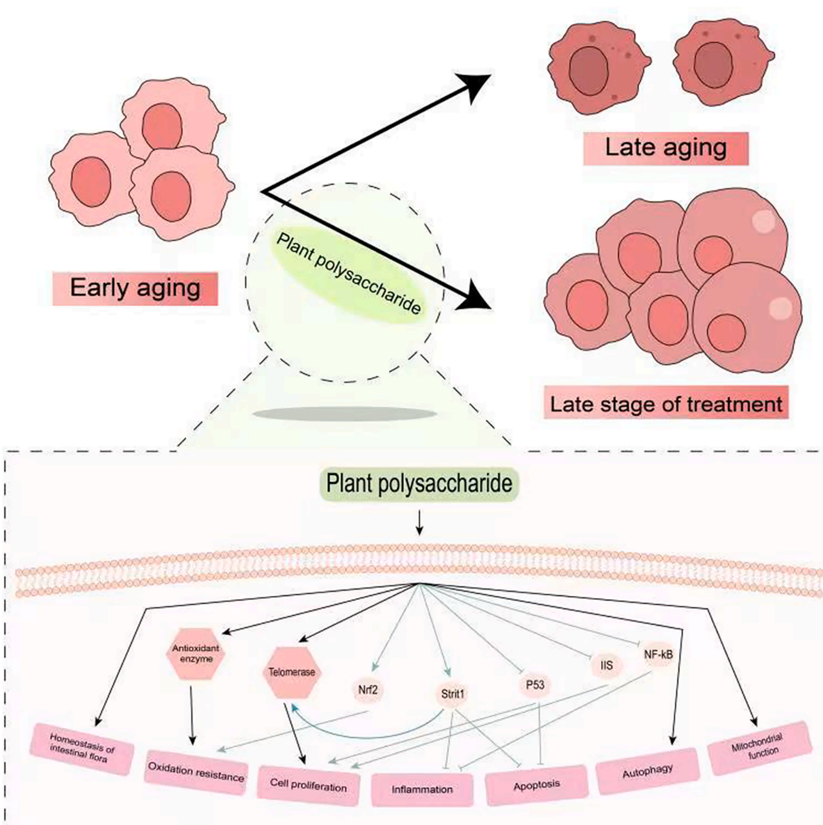

Figure 1. Various plant polysaccharides have rich pharmacological effects.

maintaining the stability of the internal environment and regulating the health of the body. At the same time, much literature emphasizes that oral polysaccharides can be absorbed in various ways, including the endocytosis of intestinal epithelial cells (mediated by macrophages, clathrin, and caveolin-related pathways), paracellular pathways, and absorption mediated by microfolded cells (M cells) and Peyer's patches (Zheng et al., 2022). These mechanisms play an important role in the absorption of oral polysaccharides. A mouse study showed that *Ganoderma* polysaccharides are absorbed in small intestine in a time-dependent manner, and a study of Caco-2 cells further indicate their uptake via endocytosis (Wang et al., 2018). Although there are differences in the absorption of oral fucoidan between the jejunum and ileum, evidence suggests that oral fucoidan can be absorbed through the small intestine, possibly via transporter proteins or phagocytosis (Nagamine et al., 2014). It is worth noting that polysaccharides are likely to be absorbed into the blood circulation system after oral administration. A mice study showed that pumpkin polysaccharide was absorbed by the jejunum and ileum, but some was distributed to the spleen and pancreas, suggesting that the polysaccharide can enter different organs through blood flow (Yu et al., 2019). Using the sandwich ELISA method, it was observed that the serum levels of orally administered fucoidan in healthy volunteers increased after 6 and 9 hours, with results indicating an absorption rate of 0.6% in the intestines (Tokita et al., 2010). Tea polysaccharides are negatively charged and bulky, with a molecular weight between 10^4-10^6 g mol^{-1}, resulting in extremely low absorption rate (Mao et al., 2021). It can be seen that most polysaccharides can be absorbed by oral administration, but it is undeniable that the absorption of some polysaccharides is not ideal.

The differences in absorption effects are mainly influenced by factors such as charge characteristics, molecular weight, complex spatial structure, and varying intake doses of polysaccharides (Zheng et al., 2022). Understanding these factors is crucial for developing strategies to enhance the absorption efficiency of polysaccharides, thereby maximizing their potential health benefits, such as anti-aging. The dosage of polysaccharides is relatively easy to adjust and control. In the concentration range of 75-300 μg / mL, a neutral heteropolysaccharide from *Halenia elliptica D. Don* can significantly increase the activities of superoxide dismutase (SOD), catalase (CAT) and glutathione peroxidase (GSH-Px) in a dose-dependent manner, thus showing a significant anti-aging effect (Zhou et al., 2023). At the same time, in the high-dose group of 1000 μg / mL, *Gracilaria lemaneiformis* polysaccharide can increase the average life span of *Caenorhabditis elegans* by more than 16.47% (Wang et al., 2019b). This phenomenon indicates that in a specific concentration range, the anti-aging effect will increase with the increase of dose. However, it is worth noting that the concentration at which different plant polysaccharides exert the best anti-aging effect in the human body is not clear. The absorption of polysaccharides by the body is a crucial prerequisite for the anti-aging effects, which may be enhanced by optimizing the properties of polysaccharides and also regulated by adjusting the dosage concentration and administration routes.

3. Exploration of plant polysaccharides by modern analytical techniques

3.1. Application of metabolomics in studying plant polysaccharides

Metabolomics is qualitative and quantitative analysis of metabolites in biological samples, which is commonly used in food science such as plant polysaccharides (Fraga-Corral et al., 2022). By using metabolomics in a mice study, scientists have demonstrated that *Dendrobium officinale* polysaccharide (DOP) can effectively alleviate acute ulcerative colitis by improving intestinal health and inducing antioxidant capacity coupled with decreased in inflammatory cytokine levels (Zeng et al., 2024). Another metabolomic study further suggested that the combining use of DOP and spermidine mediated lipid metabolic processes to exhibit anti-aging effects (Duan et al., 2024). A metabolomic study in Alzheimer's disease (AD) rat model shown that *Schisandra chinensis* polysaccharide can effectively reduce gut microbiota dysbiosis and neuroinflammatory responses, promoting the efficiency of AD treatment (Fu et al., 2023). So, cumulating metabolomic study have demonstrated the changes in multiple metabolic pathways during the aging process, providing a novel direction for aging research (Tian et al., 2022). Metabolomics not only explore the potential functions of plant polysaccharides but also delineated the anti-aging mechanisms, promising the anti-aging functions of plant polysaccharides.

3.2. Application of proteomics in studying plant polysaccharides

Proteomics is a unbiased and holistic investigation of all proteins within sample (Buhimschi and Buhimschi, 2012; Cookson, 2019). A proteomic studies has revealed that *Dictyophora* polysaccharide exhibited neuroprotective effect by regulating the expression of oxidative stress and mitochondrial dysfunction related proteins in arsenic-induced nerve injury in rats (Zhang et al., 2023b). Proteomics was also used for discovery of aging-related biomarkers in clinical research on aging interventions (Basisty et al., 2020). Proteomics may be able to analyze the pathogenesis of aging and to unfold the anti-aging mechanism of plant polysaccharides.

3.3. Application of gut microbiota sequencing in studying plant polysaccharides

Recent research has demonstrated the correlation between the gut microbiota and the central nervous and immune systems through targeting different metabolic pathways, which are contributed to the aging processes (Sonnenburg and Sonnenburg, 2019). For example, a study using *in vitro* microbiome assays coupled with fecal microbiota transplantation has demonstrated that Astragalus polysaccharides (APS) can reduce pathogenic bacteria including *Escherichia coli-Shigella* and *Enterococcus*, leading to restoration of polyunsaturated fatty acid metabolism (Wang et al., 2024). By using intestinal flora analysis and immunofluorescence staining, researchers have showed that *Poria cocos* polysaccharides can modulate intestinal floral structure and body metabolism, improving intestinal microecology and host physiological function (Xu et al., 2023a). The combined analysis of intestinal flora and metabolomics also shows that *Rehmannia glutinosa* polysaccharides can significantly increase the abundance of the Lachnospiraceae _ NK4B4 _ group through regulating amino acid metabolism (Liang et al., 2023), suggesting that *Rehmannia glutinosa* polysaccharides might play a role in delaying aging by regulating probiotic communities and key metabolic pathways. Researchers may utilize multiple omics approaches to explore how plant polysaccharides alter the gut microbiota structure and theirs associated products which have anti-aging effects, demonstrating the potential therapeutic value of plant polysaccharides in anti-aging mechanisms.

4. The mechanism of plant polysaccharides in anti-aging action

The aging mechanism of the organism is extremely complex, involving loss of proteostasis, chronic inflammation, cellular senescence, mitochondrial dysfunction, genomic instability, telomere attrition, and dysbiosis (López-Otín et al., 2023). At the same time, as shown in Figure 2, plant polysaccharides may regulate the aging organism through various pathways, such as increasing antioxidant enzyme activity, regulating inflammatory factors, controlling cellular autophagy and division, improving mitochondrial dysfunction, enhancing telomerase activity, and regulating intestinal flora, thereby exhibiting superior anti-aging effects. Many plant polysaccharides can exert anti-aging effects through different mechanisms (Table 1).

4.1. Aging mechanism

Currently, there is a deep understanding of aging, characterized by a wide variety of interconnected aging mechanisms. Factors such as cellular aging (Cheng et al., 2017), stem cell exhaustion, genomic

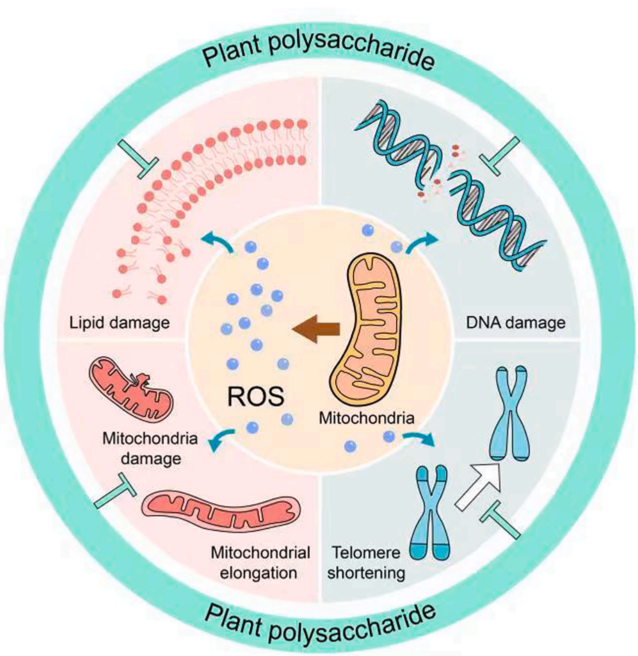

Figure 2. Plant polysaccharides achieve anti-aging through a variety of ways. Plant polysaccharides enhance cellular antioxidant capacity and proliferation ability by increasing the activities of antioxidant enzymes and telomerase; activate Nrf2 to improve cellular antioxidant capacity; activate Sirt1 to inhibit cell inflammation and apoptosis; inhibit P53 to promote cell proliferation and inhibit cell apoptosis; inhibit NF-kB to suppress inflammation; can also work through multiple pathways such as regulating the homeostasis of intestinal flora, activating cellular autophagy, and improving mitochondrial dysfunction to alleviate aging. See text for details.

instability, protein imbalance, mitochondrial dysfunction, telomere erosion, and changes in intercellular communication drive aging to a certain extent (Li et al., 2024b). Among these, cell cycle arrest and typically irreversible cell senescence are key factors in inducing aging (Zhang et al., 2022). Figure 3 illustrates this process. Damage to large molecules like DNA activates proteins $p21^{CIP1}$ and cell cycle inhibitory factor $P16^{INK4a}$, inhibitory cell cycle proteins CDK4 and CDK6 that are necessary for cell cycle progression, ultimately leading to proliferation arrest (Birch and Gil, 2020). Literature has indicated that the generation of mitochondrial free radicals is a highly regulated mechanism that determines lifespan (Gómez et al., 2023). ROS are primarily generated by the mitochondrial (Andrieux et al., 2021). After ROS reacts with nitrogenous bases and deoxyribose in DNA, significant oxidative reactions occur, potentially causing mutations, apoptosis, necrosis, and genetic diseases (Juan et al., 2021). The pathways to regulate aging are not singular. They work collectively and sometimes even interact with each other. Plant-derived polysaccharides exhibit potent anti-aging properties through manipulation of multiple aging-related biological mechanisms and functions antioxidation, immunity, autophagy, apoptosis, promoting cell division and proliferation, mitochondrial function, telomerase activity as well as.

4.2. Plant Polysaccharides Improve Antioxidant Capacity

With the onset of aging, the activity of antioxidant enzymes in the body gradually decreases (Thiab et al., 2015; Tian et al., 1998). Antioxidant enzymes can scavenge free radicals effectively; however, when antioxidant enzymes are impaired, the changes they trigger can lead to oxidative damage (Roy et al., 2023) Oxidative damage occurs when the balance between the production of free radicals and the cell defense mechanism is destroyed, which may damage the cell structure (Saleh et al., 2023). Oxidative damage, as an important marker in the process of aging, has been verified early (Haenold et al., 2005). We speculate that plant polysaccharides may enhance the activity of antioxidant enzymes such as GPx, SOD, and CAT, thereby improving the ability of aging cells to clear free radicals and prevent their excessive accumulation. This aids in maintaining redox homeostasis within cells, slowing down oxidative damage, and inhibiting aging. Study has shown that supplementing feed with *Eucommiae* polysaccharides can increase the expression of antioxidant enzymes GSH-Px and T-SOD in Drosophila, effectively alleviating age-related oxidative stress and prolonging the life span of *Drosophila melanogaster* (Wei et al., 2023). A fern polysaccharide from *Alsophila spinulosa* leaf can enhance the activity of SOD and CAT antioxidant enzymes, reduce levels of reactive oxygen species (ROS) and malondialdehyde (MDA), exhibit fantastic antioxidant and anti-aging activities (Pei et al., 2022). The Polyphenol–Polysaccharide complex extract from Hizikia fusiforme attenuated D-gal-induced senescence, which was achieved by activating Nrf2, thereby affecting the expression levels of various antioxidant enzymes in mice (Li et al., 2023a). Additionally, *polygonatum sibiricum* polysaccharides have been found to reduce ROS and MDA levels, increase SOD levels, and inhibit lipid peroxidation and DNA damage in the hearts of aging mice induced by D-galactose, suggesting that *polygonatum sibiricum* polysaccharides alleviate cardiac aging by inhibiting oxidative stress (Ma et al., 2021).

Insulin signaling (IIS) plays a pivotal role in regulating aging and longevity (Sasako and Ueki, 2016). Neutral polysaccharides from *Rehmannia glutinosa* can inhibit the expression of DAF-2, weaken the inhibitory effect on daf-16, and continuously stimulate IIS, thereby enhancing the antioxidant stress capacity of *Caenorhabditis elegans* and extend their lifespan (Yuan et al., 2019). The Kelch-like ECH-associated protein 1 (*Keap1*)–nuclear factor erythroid 2-related factor 2 (*Nrf2*) pathway regulates many antioxidant genes that maintain cellular homeostasis during oxidative stress responses (Wei et al., 2023). Wei et al. found that eucommia polysaccharides upregulated the antioxidant-related Keap1-Nrf1 pathway genes in aged Drosophila while increasing the activity of antioxidant enzymes, which resulted in the alleviation of oxidative stress and the extension of lifespan. Some plant polysaccharides exhibit significant biological activity by effectively enhancing the activity of antioxidative enzymes in the body, thereby improving the overall antioxidant defense mechanism. This process may not only help to resist damage from free radicals and reduce oxidative stress reactions but also significantly enhance the body's anti-aging ability.

4.3. Plant Polysaccharides Improve Immunity

Aging is characterized by chronic inflammation (Li et al., 2023b), with a decline in immune system function (Cisneros et al., 2022). Article has shown that with the continuous growth of the body's age, the immune function is impaired, inflammatory factors and senescent cells continue to accumulate, causing immune aging and increasing the risk of various elderly-related diseases (Li et al., 2024a). Plant polysaccharides serve as effective immune modulators that can enhance immunity (Zhao et al., 2023). They can also promote the expression of anti-inflammatory factors while inhibiting the expression of pro-inflammatory factors, thereby reducing inflammation (Zhang et al., 2023c). Both APS and the polysaccharide of *Atractylodes macrocephala Koidz* (PAMK) possess the ability to inhibit the transcription of pro-inflammatory cytokines, thereby exerting immunomodulatory effects (Zhao et al., 2023). Specifically, APS acts through the MDA5/NF-κB signaling pathway to inhibit the production of pro-inflammatory cytokines, while PAMK can not only exert this effect but also activate T lymphocytes in the thymus through the novel_mir2/CTLA4/TCR and novel_mir2/CTLA4/CD28 signaling pathways. Research has shown that the levels of TNF-α, IL-1β, and IL-6 in neural stem cells (NSCs) of aged mice increase, whereas in those treated with ASP, the levels of these inflammatory cytokines in NSCs decrease. (Cheng et al., 2019). This

Table 1
The potential anti-aging mechanism of plant polysaccharides.

Plant Polysaccharides	Bioactivity	Potential Mechanism of Anti-aging	Reference
Angelica sinensis polysaccharide	Anti-aging, immune regulation, anti-oxidation, anti-inflammation, hematopoiesis, anti-tumor, hepatoprotective effects, heart protection, anti-virus, hypoglycemia	Increase the cell proliferation; decrease the number of SA-β-gal stained neurons; increase the activity of SOD and T-AOC, decreasing the content of malondialdehyde (MDA); decrease the levels of IL-1b,IL-6,TNF-a and ROS, up-regulate p53/p21 signaling pathway in neural stem cells.	(Cheng et al., 2019) (Nai et al., 2021)
Radix *astragali* polysaccharide	Anti-aging, anti-oxidation, antiviral, anti-tumor effects, immune regulation	Inhibit the apoptosis and senescence of bone marrow mesenchymal stem cells, reduce mitochondrial ROS production, promote the expression of miR-124, inhibit the expression of activating ATF-6, promote the expressions of dFoxO and 4E-BP, regulate the insulin /IGF-1 signaling pathway.	(Tang and Huang, 2022)
Cistanche deserticola polysaccharides	Anti-oxidation, anti-aging, anti-inflammation, hepatoprotective properties,	Alleviate H_2O_2-induced oxidative stress, mitigate ROS formation via the nuclear factor erythroid 2-related factor/ heme oxygenase-1 pathway, suppress p-extracellular signal-regulated kinase.	(Takaya et al., 2023)
Halenia elliptica neutral heteropolysaccharide	Anti-oxidation, anti-aging	Increase the activities of SOD, CAT and GSH-Px, inhibit MDA formation via the activation of the PI3K/Akt and Nrf2/HO-1 signalling pathways.	(Zhou et al., 2023)
Gracilaria lemaneiformis polysaccharide	Anti-oxidation, hepatoprotective properties, anti-inflammation, anti-aging anti-tumor, anti-virus, immune regulation, anti-allergic, hypoglycemic and antidiabetic activities	Induce the insulin pathway DAF-16 nuclear translocation. Downregulate the expression of p21 and p53, influence the cell cycle, promote cell division and proliferation, and delay cell aging induced by H_2O_2.	(Wang et al., 2019b) (Wang et al., 2022b)
Rehmannia glutinosa polysaccharides	Anti-oxidation, anti-inflammation, anti-aging, blood glucose lowering	Increase the abundance of the *Lachnospiraceae* NK4B4 group, enhance the antioxidant enzyme system, diminish lipofuscin and reactive oxygen species levels, up-regulate the expression of daf-16, skn-1 and their downstream genes, and down-regulate the expression of age-1.	(Liang et al., 2023)
		Inhibit the expression of DAF-2, weaken the inhibitory effect on daf-16, and continuously stimulate IIS.	(Yuan et al., 2019)
Eucommiae polysaccharides	Anti-oxidation, immune regulation, anti-aging, antifatigue effects	Increase the expression of antioxidant enzymes GSH-Px and T-SOD in Drosophila, suppress *Gluconobacter, Providencia*, and Enterobacteriaceae in aged Drosophila, improve .gut dysbiosis.	(Wei et al., 2023)
Alsophila spinulosa leaf polysaccharide	Anti-oxidation, immune regulation, anti-aging, antimicrobial, anti-tumor	Enhance the activity of SOD and CAT antioxidant enzymes, reduce levels of ROS and MDA	(Pei et al., 2022)
Polygonatum sibiricum polysaccharides	Anti-oxidation, immune regulation, anti-aging, anti-tumor, reduce blood lipids, promote osteoblastic differentiation	Reduce ROS and MDA levels, increase SOD levels, and inhibit lipid peroxidation and DNA damage in the hearts of aging mice induced by D-galactose	(Ma et al., 2021)
Rehmannia glutinosa neutral polysaccharides	Anti-oxidation, anti-inflammation, anti-aging, anti-bacterial, anti-tumor, protect cardiovascular function	Inhibit the expression of DAF-2, weaken the inhibitory effect on daf-16, and continuously stimulate IIS	(Yuan et al., 2019)
Astragalus polysaccharide	Anti-oxidation, anti-inflammation, anti-aging, anti-hypertensive, anti-tumor	Promote the formation of autophagosomes by activating the PI3K/AKT/mTOR pathway, enhancing cell viability and autophagic levels	(Tan et al., 2020)
		Activate the autophagy signal through the AMPK/mTOR pathway	(Yao et al., 2022a)
Atractylodes macrocephala Koidz polysaccharides	Immunomodulation, anti-tumor, anti-aging, anti-inflammation, neuroprotective and hypoglycemic effects	Resist oxidative stress and promote the proliferation and differentiation of osteoblasts, slow apoptosis and alleviate cell senescence	(Wang et al., 2025)
Lycium barbarum polysaccharides	Anti-oxidation anti-inflammation, anti-aging, neuroprotection	Downregulate the expression levels of mRNA and protein related to the TLR4/NF-kB signaling pathway,	(Zheng et al., 2021)
		Decrease the expression of P53 and P21 genes	(Xia et al., 2014)
		Increase the antioxidant markers SOD and GSH-Px, decrease MDA	(Amagase et al., 2009)
Rhizoma Dioscoreae polysaccharides	Anti-oxidation, anti-aging	Improve the viability of hypoxic neuronal cells, and the expression levels of apoptosis-regulating protein, decrease the expression levels of Bax and caspase-3, increase expression levels of Bcl-2 in hypoxic neurons.	(Xiang et al., 2015)
Maca polysaccharide	Anti-oxidation, anti-aging, anti-hemolytic effect	Increase GSH-Px activity, reduce MDA levels, alleviate cell cycle arrest, and downregulate the expression of cleaved caspase 3 and P53 protein expression.	(Zhou et al., 2022)
Spirulina polysaccharides	Anti-oxidation, anti-aging, anti-cancer, anti-bacterial effect	Upregulate SOD2 in aging fibroblasts, stimulate ER protein folding by upregulating ER chaperones expression.	(Machihara et al., 2023)
Dendrobium officinale polysaccharide	Hypoglycemia, anti-inflammation, anti-aging, metabolism regulation, neuroprotective effect	Restore gut microbial homeostasis and decrease the abundance ratio of *Firmicutes* to *Bacteroidetes.*	(Xu et al., 2023a)
Aronia melanocarpa polysaccharide	Anti-oxidation, anti-aging, anti-tumor, anti-inflammation, anti-viral,anti-microbial, hepatoprotective effect	Regulate the AMPK/SIRT1/NF-κB and Nrf2/HO-1 signaling pathways, improve the composition of intestinal flora and abundance of beneficial bacteria.	(Zhao et al., 2021)
Ganoderma lucidum polysaccharides	Immune regulation, anti-virus, anti-tumor, anti-oxidation, anti-aging, anti-fatigue, metabolism regulation	Enhance the Krebs cycle dehydrogenases, CDH, a-KGDH, SDH, MDH and mitochondrial electron transport chain complex IV activities in aged rats.	(Sudheesh et al., 2009)
Schisandra chinensis polysaccharide	Anti-oxidation, anti-inflammation, anti-aging, hepatoprotective and neuroprotective effects	Inhibit the expression of inflammatory factors, β-galactosidase activity, and down-regulate of reactive oxygen species in RAW 264.7 and aged HDF cells.	(Kim et al., 2019)

(*continued on next page*)

Table 1 (*continued*)

Plant Polysaccharides	Bioactivity	Potential Mechanism of Anti-aging	Reference
Chrysanthemum morifolium polysaccharide	Anti-oxidation, anti-inflammation, anti-aging, anti-tumor, antibacterial and hepatoprotective effects	Reduce malondialdehyde level and increased activities of endogenous antioxidant enzymes in fruit flies	(Wang et al., 2021, Jing Feng et al., 2022)
		Inhibit the expression of MAPK, activate Nrf2/ARE pathway in mice.	(Xu et al., 2024)
Poria cocos polysaccharides	Antitumor, anti-aging, anti-inflammatory, antioxidant, immunomodulatory and hepatoprotective effect	Increase the activities of SOD and CAT, reduce the content of MDA, downregulate the expression of the branched-chain amino acid transferase-encoding gene (bcat)	(Zhu et al., 2025)
Bletilla striata polysaccharide	Anti-oxidation anti-inflammation, immune regulation, anti-aging	Downregulate Mal-A1, Amy-d, Men-b, Pgm-1, Mdh1, and Hex-C, upregulate CG32026, CG11291, and Ald2	(Hafeez et al., 2025)
Premna microphylla turcz polysaccharides	Anti-oxidation, anti-aging, anti-inflammation, antibacterial activity	Increase protein levels of Nrf2, Keap1, Maf, HO-1, and the expression of antioxidant enzymes including SOD, CAT, and GSH-Px, decrease the protein levels of NF-κB, IKKβ, COX-2, and pro-inflammatory cytokines	(Chen et al., 2022)
Pectic polysaccharide	Anti-oxidation, antitumor, prebiotic, immune regulation	Modulate gut microbiota in a positive way and regulate autophagy associated genes	(Gullón et al., 2013; Kapoor and Dharmesh, 2017).

4E-BP, eukaryotic translation initiation factor 4E-binding protein; Akt, protein kinase B; AMPK, AMP-activated protein kinase; ARE, antioxidant response element; ATF-6, transcription factor 6; a-KGDH, alpha-ketoglutarate dehydrogenase; Bax, BCL2-associated X protein; CAT, catalase; CDH, cadherin; COX-2, cyclooxygenase-2; DAF-2, dauer formation abnormal-2; daf-16, dauer formation abnormal-16; dFoxO, Drosophila forkhead box O; ER, endoplasmic reticulum; GSH-Px, glutathione peroxidase; HO-1, heme oxygenase 1; IGF-1, insulin-like growth factor 1; IKKβ, inhibitor kappa B kinase β; IL-1β, interleukin 1 beta; IL-6, interleukin 6; Keap1, Kelch-like ECH-associated protein 1; Maf, macrophage-activating factor; MAPK, mitogen-activated protein kinase; MDH, malate dehydrogenase; MDA, malondialdehyde; Men-b, menaquinone biosynthesis protein B; mTOR, mammalian target of rapamycin; mRNA, messenger ribonucleic acid; NF-κB, nuclear factor-kappa B; Nrf2, nuclear factor erythroid 2-related factor 2; P21, cyclin-dependent kinase inhibitor 1A; P53, tumor protein p53; Pgm-1, phosphoglucomutase 1; PI3K, phosphatidylinositol 3-kinase; ROS, reactive oxygen species; SIRT1, sirtuin 1; SDH, succinate dehydrogenase; SOD, superoxide dismutase; T-AOC, total antioxidant capacity; T-SOD, total superoxide dismutase; TLR4, toll-like receptor 4; TNF-α, tumor necrosis factor alpha.

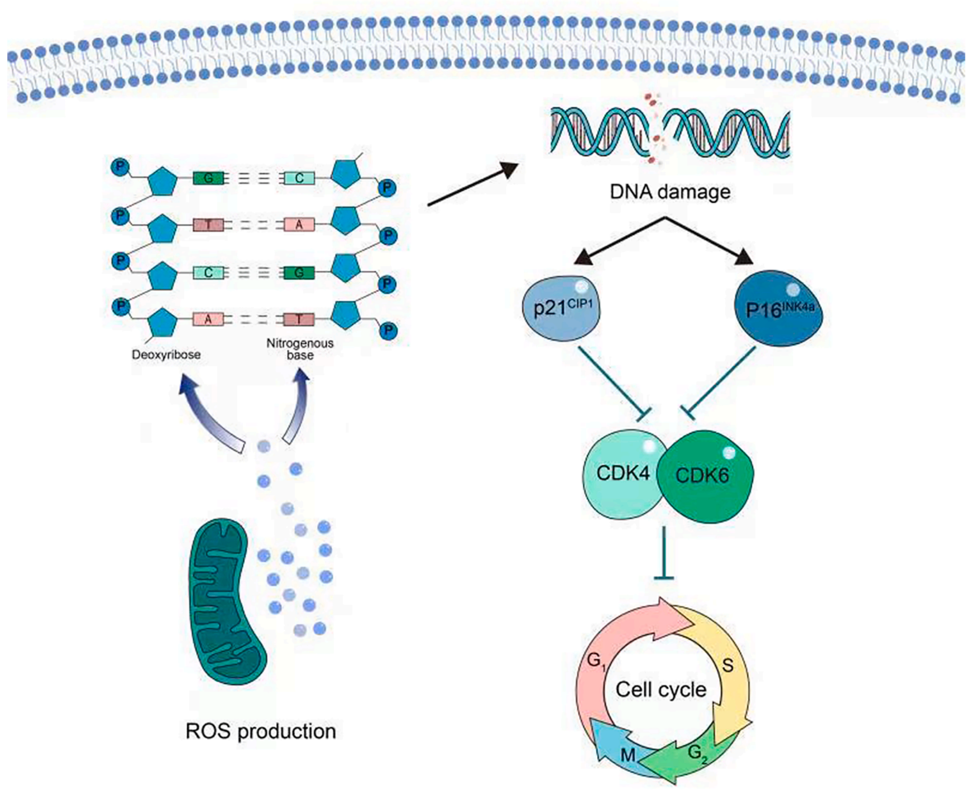

Figure 3. Aging-related mechanism. Most ROS are generated by mitochondria. After ROS reacts with nitrogenous bases and deoxyribose in DNA, obvious oxidative reactions can occur, causing damage to DNA. Damage to large molecules such as DNA activates the $p21^{CIP1}$ and cell cycle inhibitory protein $P16^{INK4a}$, which inhibits cell cycle protein-dependent kinases CDK4 and CDK6 necessary for cell cycle progression, ultimately leading to proliferation arrest.

indicates that ASP protects NSCs by regulating inflammatory factors and other pathways, thereby achieving the effect of slowing down the aging process. *Premna microphylla* Turcz, a plant with high medicinal and edible value, has polysaccharides that can enhance inflammation defense and extend the lifespan of fruit flies (Song et al., 2021).

Plant polysaccharides may regulate different signaling pathways to enhance immune function and overall immunity. Among them, the transcription factor nuclear factor kappa B (NF-kB) family plays an important role in regulating inflammation, immunity, and death (Zinatizadeh et al., 2021). LBP downregulates the expression levels of mRNA related to the TLR4/NF-kB signaling pathway, reducing inflammation in mice undergoing ovariectomy, and exhibiting anti-inflammatory bioactivity (Zheng et al., 2021). *Bletilla striata* polysaccharide can enhance immune function, which may be caused by the activation of NF-κB and MAPK signaling pathways (Niu et al., 2022). *Morchella esculenta (L.) Pers* contains various biologically active substances, polysaccharides extracted from Se-enriched *Morchella mycelium (L.) Pers* exert immunomodulatory functions by activating the TLR4-TRAF6-MAPKs-NF-kB signaling pathway, showing great development potential (Qian et al., 2023). Although enhancing immunity does not directly equate to extending lifespan, certain polysaccharides have the effect of boosting immunity, which may reduce the risk of diseases in the elderly, thereby indirectly promoting the extension of lifespan to some extent.

4.4. Plant polysaccharides increase activity

4.4.1. Activate autophagy

Cellular autophagy can eliminate damaged proteins and organelles, renew cellular components (Wang and Xu, 2020). In addition, cellular autophagy participates in the organism's immune regulatory function, which is essential for maintaining cell survival and homeostasis (Chang, 2020). However, with age, the expression of autophagy-related genes such as ATG5, ATG7, and BECN1 declines, indicating a decrease in autophagy activity (Aman et al., 2021). Kitada and Koya also mentioned that there is a negative correlation between autophagic activity and age in many species, and enhanced autophagy usually improves metabolic health and prolongs lifespan (Kitada and Koya, 2021). Hence, moderately increasing autophagy may be an important mechanism for anti-aging in the body. In a Parkinson's disease model induced by 6-hydroxydopamine (6-HODA), it was found that APS promote the formation of autophagosomes by activating the PI3K/AKT/mTOR pathway, enhancing cell viability and autophagic levels, thus treating Parkinson's disease (Tan et al., 2020). Yao and others discovered that APS increased p-AMPK levels and reduced p-mTOR expression, indicating that APS can activate the autophagy signal through the AMPK/mTOR pathway, eliminating activated mitochondria, helping regulate oxidative metabolism, and delaying cell aging (Yao et al., 2022a). In addition to APS, a variety of plant polysaccharides, including *Lycium barbarum* polysaccharides, *Ganoderma lucidum* polysaccharides and *Laminaria japonica* polysaccharides, have the function of regulating autophagy (Li et al., 2024c). However, autophagy may play different roles in different cellular environments and stages of disease progression. Autophagy shows a double-edged sword effect during ischemia-reperfusion injury, and excessive autophagy may lead to neuronal death (Hou et al., 2019). In conclusion, some plant polysaccharides may achieve the effect of extending lifespan by moderately promoting cellular autophagy. However, attention should be paid to preventing excessive autophagy to avoid potential adverse effects.

4.4.2. Regulation of apoptosis

Cell apoptosis is a multi-gene-regulated process of programmed cell death (Yao et al., 2022a; Ye et al., 2024). Cell apoptosis can eliminate damaged or dysfunctional cells, maintaining internal environmental homeostasis (Salminen et al., 2011). During the process of liver aging, insufficient apoptosis of cells can lead to abnormal cell accumulation, which may promote the formation of malignant cells (Hu et al., 2019). However, excessive apoptosis-induced cell death can lead to abnormal cell loss, thereby affecting tissue function, while inhibiting apoptosis can extend the lifespan of mice and *Drosophila melanogaster* (Kidera et al., 2020). The apoptosis of different cells and rates produces different effects (Goldblatt et al., 2021). Thus, accurate regulation of apoptosis is crucial for the organism. The sulfate oligosaccharides from green algae *Ulva lactuca* and *Enteromorpha prolifera* up-regulate the Sirt1 gene, deacetylate p53 and FOXO1 to regulate the cell cycle and inhibit cell apoptosis, achieving the goal of alleviating aging (Liu et al., 2019). *Rhizoma Dioscoreae* polysaccharides may increase the Bcl-2:Bax ratio in hypoxic neurons and other ways to inhibit cell apoptosis induced by hypoxia in vitro, suggesting that these polysaccharides can be used for the prevention and treatment of ischemic brain diseases and aging (Xiang et al., 2015).

There are many Sirtuins in the genome of multicellular organisms, and Sirt1, a member of the Sirtuin family, is a recognized longevity gene (Lee et al., 2019). Sirt1 can alleviate aging, inhibit cell apoptosis, regulate metabolism, and suppress inflammation (Shi et al., 2024; Zia et al., 2021). Biochemical and histological analysis showed that *Ganoderma lucidum* polysaccharides may affect inflammatory response, apoptosis, and proliferation by activating SIRT1 (Xu et al., 2022). Although excessive inhibition of apoptosis may lead to adverse effects similar to autophagy, some plant polysaccharides may alleviate aging by inhibiting apoptosis.

4.4.3. Promote cell division and proliferation

Normal cell division and proliferation serve as the foundation for biological inheritance, growth, and development. They enable the transmission of genetic material to the next generation of daughter cells, ensuring the continuation of biological species and replenishing aging or dying cells within the organism. This process represents an essential characteristic of life. Aging is triggered by molecular damage-induced cellular stress responses. Damage to large molecules, such as DNA, activates the $p53/p21^{CIP1}$ and $P16^{INK4a}/RB$ tumor suppressor pathways, inhibiting cell proliferation (Birch and Gil, 2020). Promoting cell proliferation and division in aging organisms may increase cell numbers and, to some extent, delay aging. *Gracilaria lemaneiformis* polysaccharides can downregulate the expression of p21 and p53, influence the cell cycle, promote cell division and proliferation, and delay cell aging induced by H_2O_2 (Wang et al., 2022b). Research has shown that a Chinese herbal compound polysaccharide composed of *Angelica sinensis* and *astragalus membranaceus* can accelerate the transition of the cell cycle from the G1 phase to the S phase in aging rats, promoting cell division and proliferation, and alleviating aging (Pu et al., 2020). As age increases, P53, P21, and other genes continue to accumulate, impeding the cell cycle transition from the G1 phase to the S phase, causing cell cycle arrest and eventually leading to cell senescence. Studies have indicated that LBP can decrease the expression of P53 and P21 genes, inhibiting aging (Xia et al., 2014). *Maca* polysaccharide can alleviate cell cycle arrest, and downregulate the expression of cleaved caspase 3 and P53 protein expression, exhibiting good neuroprotective effects (Zhou et al., 2022). By studying plant polysaccharides such as *Lycium barbarum* polysaccharide and *Maca* polysaccharide, we can conclude that some plant polysaccharides may regulate gene expression, actively stimulating cell division and proliferation activities, thereby exhibiting remarkable anti-aging effects in organisms.

4.4.4. Improve mitochondrial dysfunction

As the primary site for cellular aerobic respiration, mitochondria generate large amounts of ATP, providing the essential energy needed for the vital activities of organisms (Jia et al., 2024). Importantly, mitochondria are also the main site for cytotoxic ROS production (Alan et al., 2022). In the process of aging, mitochondrial dysfunction produces excessive ROS (Lee et al., 2021). The accumulation of ROS damage is an important cause of aging, and the mitochondria that mainly produce ROS have dysfunctional characteristics, such as decreased content and morphological changes in aging organisms (Boengler et al., 2017). As shown in Figure 4, excessive ROS may influence the genome and mitochondrial DNA, causing various types of DNA damage (Kudryavtseva et al., 2016), disrupting telomeres, inhibiting telomerase activity, and resulting in telomere shortening (Lin and Epel, 2022), damaging cellular proteins and lipids, and inducing cell apoptosis. Fortunately, mitochondria can eliminate damaged mitochondria through autophagy and maintain cellular homeostasis (Chen et al., 2020). APS may delay aging by increasing mitochondrial autophagy,

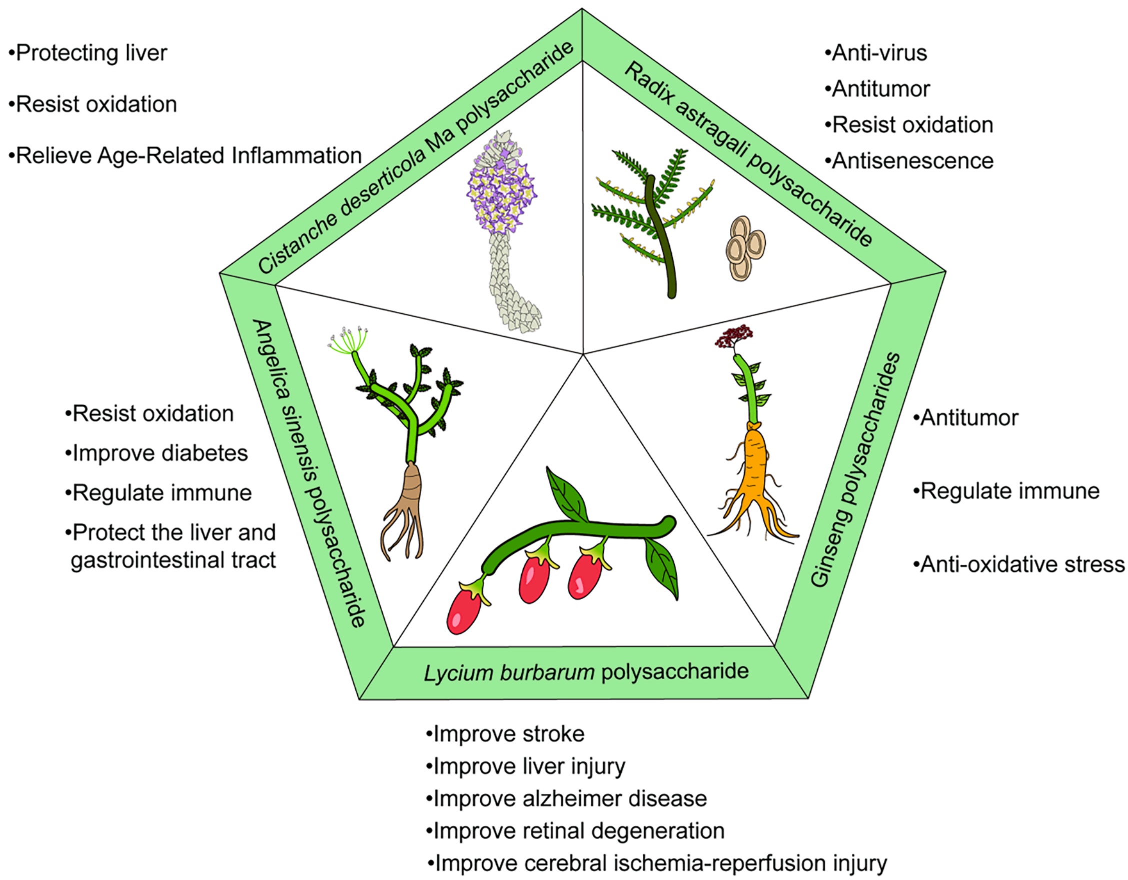

Figure 4. ROS can damage a variety of structures. During the process of aging, the generation of mitochondrial ROS continues to increase. A large amount of ROS may damage the morphology and function of mitochondria, cause various types of DNA damage, result in lipid damage, disrupt telomeres and inhibit telomerase activity, leading to telomere shortening. However, plant polysaccharides can alleviate or repair the aforementioned conditions.

maintaining mitochondrial homeostasis (Yao et al., 2022a). On the other hand, many studies suggest that impaired function of manganese superoxide dismutase 2 (SOD2) can lead to mitochondrial dysfunction, resulting in aging (Liu et al., 2022; Velarde et al., 2012). It has been noted that *spirulina* polysaccharides can upregulate SOD2 in aging fibroblasts to clear superoxide radicals, restore mitochondrial function, and exhibit anti-aging effects (Machihara et al., 2023). Part of plant polysaccharides may improve mitochondrial dysfunction effectively, thereby alleviating oxidative stress. This is beneficial for maintaining cellular and organismal homeostasis, providing an important direction for anti-aging strategies.

4.4.5. Increase telomerase activity

With the continuous increase in cell division cycles, telomere length gradually shortens, leading to a decline in cell division capacity (Dutta, 2023). Simultaneously, oxidative damage also shortens telomere length, and these factors contribute to cell aging and death (Prasad et al., 2017). Telomerase is a reverse transcriptase enzyme that carries its template and can synthesize the required telomere DNA sequence using its RNA as a template, thereby extending telomere length and maintaining chromosomal structural integrity and stability (Osterhage and Friedman, 2009; Wang et al., 2019a; Webb and Zakian, 2016). Research has shown that polysaccharides can enhance telomerase activity, preventing excessive shortening or loss of telomeres, thus enabling normal cell division and delaying aging (Guo et al., 2022). Studies indicate that a traditional Chinese medicine polysaccharide compound composed of *Angelica Sinensis* and *Astragalus membranaceus* can reduce the expression of the P16 protein in brain tissues of D-galactose-induced aging rats, significantly increase telomerase activity, and enhance the activity of SOD, serving as a potential anti-aging agent (Pu et al., 2020). Supplementing a mixture of S-adenosylmethionine (SAMe) and APS extract in the diet can extend telomere length in human lymphocytes, with more significant effects observed in the elderly (M'kacher et al., 2019). Plant polysaccharides demonstrate anti-aging potential, possibly achieved by enhancing telomerase activity, thereby maintaining chromosomal integrity.

4.5. Plant polysaccharides regulate intestinal flora

The composition of the gut microbiota changes with host age, and as the body enters the aging stage, a decrease in beneficial microbes may significantly alter the gut microbiota composition, reduce microbial diversity, disrupt gut microbiota homeostasis, and cause a series of age-related diseases (Badal et al., 2020; Barone et al., 2022). The gut microbiota may also accelerate the development of neurodegenerative diseases by inducing autoimmunity and producing metabolites (Zhu et al., 2021). Consequently, proper regulation of gut microbiota composition may alleviate diseases. Plant polysaccharides act through beneficial gut bacteria to promote the expression of tight junction proteins and repair damaged intestinal barriers; additionally, they regulate the intestinal flora and immune system by increasing the number and type of probiotics in the intestinal microecology (Tang et al., 2022a). Additionally, plant polysaccharides can be degraded by enzymes and gut microbiota in the gastrointestinal tract into short-chain fatty acids, improving immunity (Hu et al., 2023). DOP may restore gut microbial homeostasis and inhibit oxidative damage in neuronal-glial cells of senescent mice by decreasing the abundance ratio of Firmicutes to Bacteroidetes (Xu et al., 2023b). Analysis of mouse feces through 16S rDNA analysis post-treatment with *aronia melanocarpa* polysaccharide showed an increase in the relative abundance of Bacteroidetes and a decrease in Firmicutes, indicating that the treatment improved gut microbiota composition and the abundance of beneficial bacteria, delaying the aging process (Zhao et al., 2021). Age-related gut dysfunction allows microbes (or their derivatives and metabolites) to enter the circulation and reach the liver, leading to a series of liver diseases (Adhikary et al., 2024). Polysaccharide from aerial part of *Chuanminshen violaceum* can regulate gut microbiota composition, restore gut immune barriers, balance disrupted gut microbiota, significantly improve oxidative stress and inflammatory reactions in the intestines and liver of aging mice, and prevent aging (Zou et al., 2023). Notably, the biological activity of polysaccharides in gut microbiota is mediated by their structural features including molecular weight and monosaccharide composition. The accessibility of low-molecular-weight polysaccharides are higher that of high-molecular-weight polysaccharides by intestinal cells. It has been reported that low molecular weight pectic polysaccharide has higher bioactivity as compared to their high molecular weight counterparts (Gullón et al., 2013; Kapoor and Dharmesh, 2017). These plant-derived polysaccharides exhibit diverse pharmacological effects including antioxidant, antitumor, prebiotic, and immunomodulatory effects, promoting gut microbiota composition and function (Li et al., 2023c). On the other hands, this process is also affected by the functional groups of polysaccharides, different monosaccharide compositions can affect the utilization of polysaccharides by intestinal microorganisms (Huang et al., 2020). In an *in vitro* study, the order of monosaccharide utilization of all polysaccharides was suggested to be glucose > galactose > arabinose > galacturonic acid (Li et al., 2022).

5. Application of plant polysaccharides

5.1. Application in clinical practice

With the advantages of excellent immune enhancement, natural sources, low toxicity, and no residue, polysaccharides from traditional Chinese medicine have become a hot research object in the field of vaccine adjuvant research and development. Among them, *Epimedium* polysaccharide, *Ganoderma lucidum* polysaccharide, and *Poria cocos* polysaccharide are excellent vaccine adjuvants (Wan et al., 2022). A clinical trial in healthy Chinese adults (aged 55–72 years) demonstrated that LBP juice increased the antioxidant markers SOD by 8.4% and GSH-Px by 9.9%, while MDA decreased by 8.7%, suggesting that *Lycium barbarum* can improve the body's antioxidant that help to prevent or reduce free radical–related diseases (Amagase et al., 2009). Ensuring the clarity and high purity of the structure of polysaccharides is imperative for advancing their application in the field of clinical therapy, as both the structure and purity of polysaccharides can influence their activity (Wan et al., 2022). However, the complexity of polysaccharide structures, which are more intricate than DNA, inherently presents substantial challenges and difficulties in their chemical structural analysis (Zeng et al., 2019). At the same time, it is worth noting that although polysaccharide extracts from mushrooms have shown immunomodulatory effects in vitro studies, in clinical trials of polysaccharide extracts from *Maitake mushrooms*, the effects of botanical drugs were far more intricate than expected, which may enhance immune function or inhibit immune function (Deng et al., 2009). Plant polysaccharides face many challenges in clinical research, including the difficulty of purification and extraction methods, the complexity of specific mechanisms of action, and the long period required for human anti-aging research.

5.2. Application in the field of cosmetics

With the continuous improvement of living standards, the term "natural health" has become increasingly attractive to people, leading to growing interest in plant-based cosmetics. Plant extracts are among the most common ingredients in cosmetics, known for their wide range of benefits and mild effect (Georgiev et al., 2018). Li et al. noted that globally, herbal cosmetics have captured over 60% of the market share and are showing a growing trend each year, gaining significant popularity (Li et al., 2018). Plant extracts offer high-efficiency skincare benefits, including antioxidant, moisturizing, sun protection, anti-allergy, and anti-aging properties (Georgiev et al., 2018). The polysaccharides derived from Tremella aurantialba are used in high-end skincare and beauty products due to their excellent lubricating, film-forming, moisturizing, and radiation-resistant characteristics, like facial masks and moisturizers (Yan et al., 2022). Lily plays a vital role in cosmetics, being used in creams, masks, lipsticks, shower gels, and more. Lily polysaccharides can be used to develop skin moisturizing products by forming hydrogen bonds with water molecules to enhance hydration, and their antioxidant, antibacterial, anti-inflammatory, and wound-healing properties, leading to skin repair applications (Tang et al., 2022b). In addition, the application of cosmetic products containing plant polysaccharides can diminish signs of skin aging, such as wrinkles and dryness.

5.3. Application in the field of health care products

Plant polysaccharides are considered excellent products for enhancing immunity and delaying aging due to their significant biological activities and widespread application in various health products. Currently, various types of polysaccharide drugs are actively used in clinical practice as therapeutic agents, radiation-resistant beverages, or health products in forms such as chewable tablets and oral liquids (Yao et al., 2022b). Unlike drugs, Calendula polysaccharides, are formulated into nutritional liquids that not only offer a novel taste and vibrant color but also serve as an immune-enhancing and non-toxic health drink with excellent benefits (Yan et al., 2022). Plant polysaccharides-derived health products, owing to their bioactivities in metabolic regulation and immune enhancement, suggesting their highly potential for delaying aging. Also, their diverse formulations could contribute to more convenient solutions for anti-aging interventions.

6. Limitations

Plant polysaccharides, as natural bioactive substances, have shown significant therapeutic effects in various fields and play an important role in anti-aging. However, the application of plant polysaccharides in anti-aging still has many limitations that restrict their further development. Firstly, current extraction and purification methods for plant polysaccharides are still facing many challenges. It includes low extraction efficiency, low purity, high cost, and variations in molecular weights and structures, largely hindering the commercialization of plant polysaccharides (Niyigaba et al., 2021). For example, the extraction and separation methods for tea polysaccharides extracted from tea leaves are greatly limited due to their complex composition, thus constraining their application (Yao et al., 2022b). Secondly, the bioactive mechanisms of plant polysaccharides are not fully understood. While plant polysaccharides can exert anti-aging effects through multiple pathways, their specific target mechanisms remain unclear, and some molecular mechanisms are still poorly understood. Third, their component complexity is also a bottleneck for commercialization of plant polysaccharides. Their bioavailability is also constricted by multiple factors, including effective concentration, structural stability, and targeting ability. All these unpredictable factors pose substantial obstacles to their clinical application. On the other hand, as high-molecular-weight carbohydrates with complex structures of plant polysaccharides exhibit significant variations in monosaccharide composition, glycosidic bond types, and spatial conformations (Zhang et al., 2023a; Zhao et al., 2020), leading to differences in biological activities. Additionally, the synergistic or antagonistic effect of different plant polysaccharides (such as polyphenols) remain largely unknown. Such interacting effects may also affect polysaccharides' functions (Q. Guo et al., 2022). So, some studies have optimized the processes of polysaccharide preparation. For example, the use of Nano-based drug delivery system (NDDS) can effectively enhance the structural stability and bioavailability (Zheng et al., 2020). Fourthly, there is limited clinical research on plant polysaccharides. Currently, most research on the anti-aging effects of plant polysaccharides is limited to animal experiments and lacks clinical studies, deviating from practical applications. *Drosophila melanogaster* and *Caenorhabditis elegans* are often used to construct aging models. Although these aging animal models can simulate the aging state of human body, they still cannot completely replicate the complexity of human aging. There are large metabolic and physiological differences between them and humans, which may affect the conversion of experimental results in different species and cannot be better integrated with human anti-aging strategies. All these limitations restrict the further application of plant polysaccharides and represent urgent problems that need to be addressed.

7. Summary and Prospects

With the increasing aging population, the burden of elderly care and the high incidence of age-related diseases are imposing pressure on families and causing setbacks for society and the economy. In recent years, technologies such as partial reprogramming and senolytics therapy have been applied to anti-aging, providing effective strategies and means to delay aging (Chaib et al., 2022; Puri and Wagner, 2023). At the same time, plant polysaccharides also play a significant role in the field of anti-aging. Current research indicates that plant polysaccharides do not exert anti-aging effects through a single pathway but rather through multiple pathways working together to achieve outstanding anti-aging effects. These pathways include enhancing the body’s antioxidant capacity to effectively remove free radicals, acting as immune modulators to boost the body’s immunity, improving cellular vitality by renewing cell components and enhancing telomerase activity, and regulating intestinal flora to optimize its structure. Unlike other drugs, plant polysaccharides not only exhibit significant anti-aging effects but also have mild effects with minimal toxic side effects. Many regions have abundant reserves of plant resources, serving as a rich source for environment-friendly and safe drug development. However, the molecular mechanisms of plant polysaccharides in anti-aging are not yet fully understood, and future research should focus on clarifying the molecular regulatory effects of plant polysaccharides in organisms to provide a more scientific basis for anti-aging treatments. Plant polysaccharide extracts need to be standardized to enhance the likelihood of exhibiting the anticipated safe and effective biological activities. Plant polysaccharides exhibit compromised biological utilization and clinical efficacy due to insufficient stability, poor targetability, and rapid blood clearance; thus, applying a NDDS in their preparation process emerges as a suitable strategy to enhance polysaccharide stability and biological availability (Zheng et al., 2020). Currently, metagenomic and untargeted metabolomic have been applied to investigate the potential mechanisms of *Sporisorium reilianum* Polysaccharide improving obesity in rats (Guo et al., 2023). A new mechanism of *xylan oligosaccharide* degradation has also been revealed by metagenomics (Armstrong et al., 2018). With the development of new technologies and deeper research on plant polysaccharides, the anti-aging potential of plant polysaccharides will be further explored to contribute more to human health and longevity.

Abbreviation

Abbreviation Full Name
16S rDNA 16S Ribosomal Deoxyribonucleic Acid
4E-BP Eukaryotic translation initiation factor 4E-binding protein
6-HODA 6-Hydroxydopamine
AD Alzheimer’s disease
Akt Protein kinase B
AMPK AMP-activated protein kinase
ARE Antioxidant response element
APS Astragalus polysaccharides
ATF-6 Transcription factor 6
ATG Autophagy-related gene
ATP Adenosine triphosphate
ASP *Angelica sinensis* polysaccharide
Bax BCL2-associated X protein
BECN1 Beclin 1
CAT Catalase
CDK Cyclin-dependent kinase
CDH Cadherin
COX-2 Cyclooxygenase-2
DAF-2 Dauer formation abnormal-2 daf-16 Dauer formation abnormal-16
DNA Deoxyribonucleic acid
DOP *Dendrobium officinale* polysaccharide dFoxO Drosophila forkhead box O
ELISA Enzyme-Linked Immunosorbent Assay
ER Endoplasmic reticulum
FOXO1 Forkhead box protein O1
FABP1 Fatty acid-binding protein 1
GSH-Px Glutathione peroxidase
GHs Glycoside hydrolases
HO-1 Heme oxygenase 1
IGF-1 Insulin-like growth factor 1
IKKβ Inhibitor kappa B kinase β
IL-1β Interleukin-1 beta
IL-6 Interleukin-6
IIS Insulin signaling
Keap1 Kelch-like ECH-associated protein 1
LBP *Lycium barbarum* polysaccharide
Maf Macrophage-activating factor
Abbreviation (continued)
Abbreviation Full Name
MAPK Mitogen-activated protein kinase
MDH Malate dehydrogenase
MDA Malondialdehyde
Men-b Menaquinone biosynthesis protein B
M cells Microfolded cells mTOR Mammalian target of rapamycin
MLP Mulberry leaf polysaccharide mRNA Messenger ribonucleic acid
NF-κB Nuclear factor-kappa B
Nrf2 Nuclear factor erythroid 2-related factor 2
NSCs Neural stem cells
NDDS Nano-based drug delivery system
P21 Cyclin-dependent kinase inhibitor 1A
P53 Tumor protein p53
PAMK Polysaccharide of *Atractylodes macrocephala Koidz*
Pgm-1 Phosphoglucomutase 1
PI3K phosphatidylinositol 3-kinase
ROS Reactive oxygen species
SAMe S-Adenosylmethionine
SIRT1 Silent information regulator type 1
SD Sprague-Dawley
SDH Succinate dehydrogenase
Se Selenium
SOD Superoxide dismutase

Ethical Statement - Studies in humans and animals

Not available.

CRediT authorship contribution statement

Ranran Huang: Writing – original draft, Validation, Software, Resources, Methodology, Formal analysis, Data curation, Conceptualization. **Ruihan Li:** Visualization, Validation, Software, Resources, Methodology, Formal analysis, Data curation. **Meihui Qin:** Visualization, Validation, Software, Methodology, Formal analysis. **Nina Qian:** Visualization, Validation, Software, Formal analysis, Data curation. **Keng Po Lai:** Writing – review & editing, Writing – original draft, Supervision, Project administration, Methodology, Investigation, Conceptualization. **Huiling Lu:** Writing – review & editing, Writing – original draft, Supervision, Project administration, Investigation, Conceptualization. **Rong Li:** Writing – review & editing, Writing – original draft, Supervision, Project administration, Investigation, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

No data was used for the research described in the article.

References

Adhikary, S., Esmeeta, A., Dey, A., Banerjee, A., Saha, B., Gopan, P., Duttaroy, A.K., Pathak, S., 2024. Impacts of gut microbiota alteration on age-related chronic liver diseases. Dig. Liver Dis. Off. J. Ital. Soc. Gastroenterol. Ital. Assoc. Study Liver 56, 112–122. https://doi.org/10.1016/j.dld.2023.06.017.

Alan, P., Vandevoorde, K.R., Joshi, B., Cardoen, B., Gao, G., Mohammadzadeh, Y., Hamarneh, G., Nabi, I.R., 2022. Basal Gp78-dependent mitophagy promotes mitochondrial health and limits mitochondrial ROS. Cell. Mol. Life Sci. CMLS 79, 565. https://doi.org/10.1007/s00018-022-04585-8.

Amagase, H., Sun, B., Borek, C., 2009. *Lycium barbarum* (goji) juice improves in vivo antioxidant biomarkers in serum of healthy adults. Nutr. Res. 29, 19–25. https://doi.org/10.1016/j.nutres.2008.11.005.

Aman, Y., Schmauck-Medina, T., Hansen, M., Morimoto, R.I., Simon, A.K., Bjedov, I., Palikaras, K., Simonsen, A., Johansen, T., Tavernarakis, N., Rubinsztein, D.C., Partridge, L., Kroemer, G., Labbadia, J., Fang, E.F., 2021. Autophagy in healthy aging and disease. Nat. Aging 1, 634–650. https://doi.org/10.1038/s43587-021-00098-4.

Andrieux, P., Chevillard, C., Cunha-Neto, E., Nunes, J.P.S., 2021. Mitochondria as a Cellular Hub in Infection and Inflammation. Int. J. Mol. Sci. 22, 11338. https://doi.org/10.3390/ijms222111338.

Armstrong, Z., Mewis, K., Liu, F., Morgan-Lang, C., Scofield, M., Durno, E., Chen, H.M., Mehr, K., Withers, S.G., Hallam, S.J., 2018. Metagenomics reveals functional synergy and novel polysaccharide utilization loci in the Castor canadensis fecal microbiome. ISME J 12, 2757. https://doi.org/10.1038/s41396-018-0215-9.

Badal, V.D., Vaccariello, E.D., Murray, E.R., Yu, K.E., Knight, R., Jeste, D.V., Nguyen, T.T., 2020. The Gut Microbiome, Aging, and Longevity: A Systematic Review. Nutrients 12, 3759. https://doi.org/10.3390/nu12123759.

Barone, M., D'Amico, F., Rampelli, S., Brigidi, P., Turroni, S., 2022. Age-related diseases, therapies and gut microbiome: A new frontier for healthy aging. Mech. Ageing Dev. 206, 111711. https://doi.org/10.1016/j.mad.2022.111711.

Basisty, N., Kale, A., Patel, S., Campisi, J., Schilling, B., 2020. The power of proteomics to monitor senescence-associated secretory phenotypes and beyond: toward clinical applications. Expert Rev. Proteomics 17, 297–308. https://doi.org/10.1080/14789450.2020.1766976.

Birch, J., Gil, J., 2020. Senescence and the SASP: many therapeutic avenues. Genes Dev 34, 1565–1576. https://doi.org/10.1101/gad.343129.120.

Blagosklonny, M.V., 2019. Rapamycin for longevity: opinion article. Aging 11, 8048. https://doi.org/10.18632/aging.102355.

Boengler, K., Kosiol, M., Mayr, M., Schulz, R., Rohrbach, S., 2017. Mitochondria and ageing: role in heart, skeletal muscle and adipose tissue. J. Cachexia Sarcopenia Muscle 8, 349–369. https://doi.org/10.1002/jcsm.12178.

Buhimschi, I.A., Buhimschi, C.S., 2012. Proteomics/diagnosis of chorioamnionitis and of relationships with the fetal exposome. Semin. Fetal. Neonatal Med. 17, 36–45. https://doi.org/10.1016/j.siny.2011.10.002.

Chaib, S., Tchkonia, T., Kirkland, J.L., 2022. Cellular senescence and senolytics: the path to the clinic. Nat. Med. 28, 1556–1568. https://doi.org/10.1038/s41591-022-01923-y.

Chang, N.C., 2020. Autophagy and Stem Cells: Self-Eating for Self-Renewal. Front. Cell Dev. Biol. 8, 138. https://doi.org/10.3389/fcell.2020.00138.

Chen, C., Ding, S., Wang, J., 2023. Digital health for aging populations. Nat. Med. 29, 1623–1630. https://doi.org/10.1038/s41591-023-02391-8.

Chen, G., Kroemer, G., Kepp, O., 2020. Mitophagy: An Emerging Role in Aging and Age-Associated Diseases. Front. Cell Dev. Biol. 8, 200. https://doi.org/10.3389/fcell.2020.00200.

Chen, X., Sheng, Z., Qiu, S., Yang, H., Jia, J., Wang, J., Jiang, C., 2019. Purification, characterization and in vitro and in vivo immune enhancement of polysaccharides from mulberry leaves. PLoS ONE 14, e0208611. https://doi.org/10.1371/journal.pone.0208611.

Chen, Y., Liu, X., Lei, X., Lei, L., Zhao, J., Zeng, K., Ming, J., 2022. *Premna microphylla* Turcz pectin protected UVB-induced skin aging in BALB/c-nu mice via Nrf2 pathway. Int. J. Biol. Macromol. 215, 12–22. https://doi.org/10.1016/j.ijbiomac.2022.06.076.

Cheng, L.Q., Zhang, Z.Q., Chen, H.Z., Liu, D.P., 2017. Epigenetic regulation in cell senescence. J. Mol. Med. Berl. Ger. 95, 1257–1268. https://doi.org/10.1007/s00109-017-1581-x.

Cheng, X., Yao, H., Xiang, Y., Chen, L., Xiao, M., Wang, Z., Xiao, H., Wang, L., Wang, S., Wang, Y., 2019. Effect of Angelica polysaccharide on brain senescence of Nestin-GFP mice induced by D-galactose. Neurochem. Int. 122, 149–156. https://doi.org/10.1016/j.neuint.2018.09.003.

Cisneros, B., García-Aguirre, I., Unzueta, J., Arrieta-Cruz, I., González-Morales, O., Domínguez-Larrieta, J.M., Tamez-González, A., Leyva-Gómez, G., Magaña, J.J., 2022. Immune system modulation in aging: Molecular mechanisms and therapeutic targets. Front. Immunol. 13, 1059173. https://doi.org/10.3389/fimmu.2022.1059173.

Cookson, M.R., 2019. Proteomics: Techniques and applications in Neuroscience. J. Neurochem. 151, 394–396. https://doi.org/10.1111/jnc.14867.

da Costa, J.P., Vitorino, R., Silva, G.M., Vogel, C., Duarte, A.C., Rocha-Santos, T., 2016. A synopsis on aging—Theories, mechanisms and future prospects. Ageing Res. Rev. 29, 90–112. https://doi.org/10.1016/j.arr.2016.06.005.

Deng, G., Lin, H., Seidman, A., Fornier, M., D'Andrea, G., Wesa, K., Yeung, S., Cunningham-Rundles, S., Vickers, A.J., Cassileth, B., 2009. A phase I/II trial of a polysaccharide extract from Grifola frondosa (Maitake mushroom) in breast cancer patients: immunological effects. J. Cancer Res. Clin. Oncol. 135, 1215–1221. https://doi.org/10.1007/s00432-009-0562-z.

Dong, X., Zhou, M., Li, Yehong, Li, Yuxin, Ji, H., Hu, Q., 2021. Cardiovascular Protective Effects of Plant Polysaccharides: A Review. Front. Pharmacol. 12, 783641. https://doi.org/10.3389/fphar.2021.783641.

Du, M., Cheng, X., Qian, L., Huo, A., Chen, J., Sun, Y., 2023. Extraction, Physicochemical Properties, Functional Activities and Applications of Inulin Polysaccharide: a Review. Plant Foods Hum. Nutr. Dordr. Neth. 78, 243–252. https://doi.org/10.1007/s11130-023-01066-6.

Duan, H., Yu, Q., Ni, Y., Li, J., Yu, L., Yan, X., Fan, L., 2024. Synergistic anti-aging effect of *Dendrobium officinale* polysaccharide and spermidine: A metabolomics analysis focusing on the regulation of lipid, nucleotide and energy metabolism. Int. J. Biol. Macromol. 278, 135098. https://doi.org/10.1016/j.ijbiomac.2024.135098.

Dutta, S., 2023. Unveiling the telomere-p53-PGC ageing axis. Nat. Rev. Endocrinol. 19, 686. https://doi.org/10.1038/s41574-023-00905-5.

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

Fraga-Corral, M., Carpena, M., Garcia-Oliveira, P., Pereira, A.G., Prieto, M.A., Simal-Gandara, J., 2022. Analytical Metabolomics and Applications in Health, Environmental and Food Science. Crit. Rev. Anal. Chem. 52, 712–734. https://doi.org/10.1080/10408347.2020.1823811.

Fu, J., Li, J., Sun, Y., Liu, S., Song, F., Liu, Z., 2023. In-depth investigation of the mechanisms of *Schisandra chinensis* polysaccharide mitigating Alzheimer's disease rat *via* gut microbiota and feces metabolomics. Int. J. Biol. Macromol. 232, 123488. https://doi.org/10.1016/j.ijbiomac.2023.123488.

Georgiev, V., Slavov, A., Vasileva, I., Pavlov, A., 2018. Plant cell culture as emerging technology for production of active cosmetic ingredients. Eng. Life Sci. 18, 779–798. https://doi.org/10.1002/elsc.201800066.

Goldblatt, Z.E., Cirka, H.A., Billiar, K.L., 2021. Mechanical Regulation of Apoptosis in the Cardiovascular System. Ann. Biomed. Eng. 49, 75–97. https://doi.org/10.1007/s10439-020-02659-x.

Gómez, J., Mota-Martorell, N., Jové, M., Pamplona, R., Barja, G., 2023. Mitochondrial ROS production, oxidative stress and aging within and between species: Evidences and recent advances on this aging effector. Exp. Gerontol. 174, 112134. https://doi.org/10.1016/j.exger.2023.112134.

Gullón, B., Gómez, B., Martínez-Sabajanes, M., Yáñez, R., Parajó, J.C., Alonso, J.L., 2013. Pectic oligosaccharides: Manufacture and functional properties. Trends Food Sci. Technol. 30, 153–161. https://doi.org/10.1016/j.tifs.2013.01.006.

Guo, Luo, J., X, Q., P, Z., Y, A., G, L., W, 2022. The Role and Mechanism of Polysaccharides in Anti-Aging. Nutrients 14. https://doi.org/10.3390/nu14245330.

Guo, Y., Liu, M., Liu, Xin, Zheng, M., Xu, X., Liu, Xiaokang, Gong, J., Liu, H., Liu, J., 2023. Metagenomic and Untargeted Metabolomic Analysis of the Effect of *Sporisorium reilianum* Polysaccharide on Improving Obesity. Foods Basel Switz 12, 1578. https://doi.org/10.3390/foods12081578.

Haenold, R., Wassef, D.M., Heinemann, S.H., Hoshi, T., 2005. Oxidative damage, aging and anti-aging strategies. Age Dordr. Neth. 27, 183–199. https://doi.org/10.1007/s11357-005-2915-0.

Hafeez, E., Du, D., Ni, H., Zhu, K., Hu, F., Zhou, J., Chen, D., 2025. Regulation and mechanism of *Bletilla striata* polysaccharide on delaying aging in *Drosophila melanogaster*. Int. J. Biol. Macromol. 310, 143382. https://doi.org/10.1016/j.ijbiomac.2025.143382.

Hong, C., Sun, L., Liu, G., Guan, B., Li, C., Luo, Y., 2023. Response of Global Health Towards the Challenges Presented by Population Aging. China CDC Wkly 5, 884–887. https://doi.org/10.46234/ccdcw2023.168.

Hou, K., Xu, D., Li, F., Chen, S., Li, Y., 2019. The progress of neuronal autophagy in cerebral ischemia stroke: Mechanisms, roles and research methods. J. Neurol. Sci. 400, 72–82. https://doi.org/10.1016/j.jns.2019.03.015.

Hu, P., Yan, X., Zeng, Y., Jiang, Z., Liu, J., Feng, W.W., 2023. An UPLC-MS/MS method for targeted analysis of microbial and host tryptophan metabolism after administration of polysaccharides from *Atractylodes macrocephala Koidz.* in ulcerative colitis mice. J. Pharm. Biomed. Anal. 235, 115585. https://doi.org/10.1016/j.jpba.2023.115585.

Hu, S.J., Jiang, S.S., Zhang, J., Luo, D., Yu, B., Yang, L.Y., Zhong, H.H., Yang, M.W., Liu, L.Y., Hong, F.F., Yang, S.L., 2019. Effects of apoptosis on liver aging. World J. Clin. Cases 7, 691–704. https://doi.org/10.12998/wjcc.v7.i6.691.

Huang, H., Huang, G., 2020a. Extraction, separation, modification, structural characterization, and antioxidant activity of plant polysaccharides. Chem. Biol. Drug Des. 96, 1209–1222. https://doi.org/10.1111/cbdd.13794.

Huang, H., Huang, G., 2020b. Extraction, separation, modification, structural characterization, and antioxidant activity of plant polysaccharides. Chem. Biol. Drug Des. 96, 1209–1222. https://doi.org/10.1111/cbdd.13794.

Huang, S., Chen, F., Cheng, H., Huang, G., 2020. Modification and application of polysaccharide from traditional Chinese medicine such as *Dendrobium officinale*. Int. J. Biol. Macromol. 157, 385–393. https://doi.org/10.1016/j.ijbiomac.2020.04.141.

Jia, X., Zhu, L., Zhu, Q., Zhang, J., 2024. The role of mitochondrial dysfunction in kidney injury and disease. Autoimmun. Rev. 23, 103576. https://doi.org/10.1016/j.autrev.2024.103576.

Juan, C.A., Pérez de la Lastra, J.M., Plou, F.J., Pérez-Lebeña, E., 2021. The Chemistry of Reactive Oxygen Species (ROS) Revisited: Outlining Their Role in Biological Macromolecules (DNA, Lipids and Proteins) and Induced Pathologies. Int. J. Mol. Sci. 22, 4642. https://doi.org/10.3390/ijms22094642.

Kaoutari, A.E., Armougom, F., Gordon, J.I., Raoult, D., Henrissat, B., 2013. The abundance and variety of carbohydrate-active enzymes in the human gut microbiota. Nat. Rev. Microbiol. 11, 497–504. https://doi.org/10.1038/nrmicro3050.

Kapoor, S., Dharmesh, S.M., 2017. Pectic Oligosaccharide from tomato exhibiting anticancer potential on a gastric cancer cell line: Structure-function relationship. Carbohydr. Polym. 160, 52–61. https://doi.org/10.1016/j.carbpol.2016.12.046.

Kidera, H., Hatabu, T., Takahashi, K.H., 2020. Apoptosis inhibition mitigates aging effects in *Drosophila melanogaster*. Genetica 148, 69–76. https://doi.org/10.1007/s10709-020-00088-1.

Kim, J.S., Takanche, J.S., Kim, J.E., Jeong, S.H., Han, S.H., Yi, H.K., 2019. *Schisandra chinensis* extract ameliorates age-related muscle wasting and bone loss in ovariectomized rats. Phytother. Res. PTR 33, 1865–1877. https://doi.org/10.1002/ptr.6375.

Kitada, M., Koya, D., 2021. Autophagy in metabolic disease and ageing. Nat. Rev. Endocrinol. 17, 647–661. https://doi.org/10.1038/s41574-021-00551-9.

Kudryavtseva, A.V., Krasnov, G.S., Dmitriev, A.A., Alekseev, B.Y., Kardymon, O.L., Sadritdinova, A.F., Fedorova, M.S., Pokrovsky, A.V., Melnikova, N.V., Kaprin, A.D., Moskalev, A.A., Snezhkina, A.V., 2016. Mitochondrial dysfunction and oxidative stress in aging and cancer. Oncotarget 7, 44879–44905. https://doi.org/10.18632/oncotarget.9821.

Lee, S.H., Lee, J.H., Lee, H.Y., Min, K.J., 2019. Sirtuin signaling in cellular senescence and aging. BMB Rep 52, 24–34. https://doi.org/10.5483/BMBRep.2019.52.1.290.

Lee, Y.H., Park, J.Y., Lee, H., Song, E.S., Kuk, M.U., Joo, J., Oh, S., Kwon, H.W., Park, J. T., Park, S.C., 2021. Targeting Mitochondrial Metabolism as a Strategy to Treat Senescence. Cells 10, 3003. https://doi.org/10.3390/cells10113003.

Li, He, Y., Zhong, S., Li, Y., Di, Y., Wang, Q., Ren, D., Liu, S., Li, D., Cao, F., 2023a. Antioxidant and Anti-Aging Properties of Polyphenol–Polysaccharide Complex Extract from Hizikia fusiforme. Foods 12, 3725. https://doi.org/10.3390/foods12203725.

Li, Li, C., Zhang, W., Wang, Y., Qian, P., Huang, H., 2023b. Inflammation and aging: signaling pathways and intervention therapies. Signal Transduct. Target. Ther. 8, 239. https://doi.org/10.1038/s41392-023-01502-8.

Li, Lin, S., Wang, Y., Shi, Y., Fang, X., Wang, J., Cui, H., Bian, Y., Qi, X., 2024a. Immunosenescence: A new direction in anti-aging research. Int. Immunopharmacol. 141, 112900. https://doi.org/10.1016/j.intimp.2024.112900.

Li, Q.Y., Dou, Z.M., Chen, C., Jiang, Y.M., Yang, B., Fu, X., 2022. Study on the Effect of Molecular Weight on the Gut Microbiota Fermentation Properties of Blackberry Polysaccharides In Vitro. J. Agric. Food Chem. 70, 11245–11257. https://doi.org/10.1021/acs.jafc.2c03091.

Li, Tian, X., Luo, J., Bao, T., Wang, S., Wu, X., 2024b. Molecular mechanisms of aging and anti-aging strategies. Cell Commun. Signal. CCS 22, 285. https://doi.org/10.1186/s12964-024-01663-1.

Li, Wang, L., Yang, K., Zhang, G., Li, S., Gong, H., Liu, M., Dai, X., 2023c. Structure characteristics of low molecular weight pectic polysaccharide and its anti-aging capability by modulating the intestinal homeostasis. Carbohydr. Polym. 303, 120467. https://doi.org/10.1016/j.carbpol.2022.120467.

Li, Y., Wang, S., Xin, Y., Zheng, M., Xu, F., Xi, X., Cao, H., Cui, X., Guo, H., Han, C., 2018. *Maca* Cosmetics: A Review on Constituents, Therapeutics and Advantages. J. Oleo Sci. 67, 789–800. https://doi.org/10.5650/jos.ess18012.

Li, Ye, Z., Zheng, G., Su, Z., 2024c. Polysaccharides targeting autophagy to alleviate metabolic syndrome. Int. J. Biol. Macromol. 283, 137393. https://doi.org/10.1016/j.ijbiomac.2024.137393.

Liang, L., Yue, Y., Zhong, L., Liang, Y., Shi, R., Luo, R., Zhao, M., Cao, X., Yang, M., Du, J., Shen, X., Wang, Y., Shu, Z., 2023. Anti-aging activities of *Rehmannia glutinosa* Libosch. crude polysaccharide in Caenorhabditis elegans based on gut microbiota and metabonomic analysis. Int. J. Biol. Macromol. 253, 127647. https://doi.org/10.1016/j.ijbiomac.2023.127647.

Liu, L., Yang, X., Liao, Y., Wang, C., Wang, Y., 2022. Resveratrol alleviates Ang II-induced vascular smooth muscle cell senescence by upregulating E2F1/SOD2 axis. Toxicol. Res. 11, 831–840. https://doi.org/10.1093/toxres/tfac051.

Liu, X.Y., Liu, D., Lin, G.P., Wu, Y.J., Gao, L.Y., Ai, C., Huang, Y.F., Wang, M.F., El-Seedi, H.R., Chen, X.H., Zhao, C., 2019. Anti-ageing and antioxidant effects of sulfate oligosaccharides from green algae *Ulva lactuca* and *Enteromorpha prolifera* in SAMP8 mice. Int. J. Biol. Macromol. 139, 342–351. https://doi.org/10.1016/j.ijbiomac.2019.07.195.

López-Otín, C., Blasco, M.A., Partridge, L., Serrano, M., Kroemer, G., 2023. Hallmarks of aging: An expanding universe. Cell 186, 243–278. https://doi.org/10.1016/j.cell.2022.11.001.

Ma, S, W., W, P., T, S., J, H., R, Y., B, Z., W, L., 2021. Antioxidant Effect of *Polygonatum sibiricum* Polysaccharides in D-Galactose-Induced Heart Aging Mice. BioMed Res. Int. 2021. https://doi.org/10.1155/2021/6688855.

Machihara, K., Oki, S., Maejima, Y., Kageyama, S., Onda, A., Koseki, Y., Imai, Y., Namba, T., 2023. Restoration of mitochondrial function by *Spirulina* polysaccharide via upregulated SOD2 in aging fibroblasts. iScience 26, 107113. https://doi.org/10.1016/j.isci.2023.107113.

Mao, X., Long, L., Shen, J., Lin, K., Yin, L., Yi, J., Zhang, L.M., Deng, D.Y.B., Yang, L., 2021. Nanoparticles composed of the tea polysaccharide-complexed cationic vitamin B12-conjugated glycogen derivative. Food Funct 12, 8522–8534. https://doi.org/10.1039/d1fo00487e.

McHugh, D., Gil, J., 2018. Senescence and aging: Causes, consequences, and therapeutic avenues. J. Cell Biol. 217, 65–77. https://doi.org/10.1083/jcb.201708092.

M'kacher, R., Breton, L., Colicchio, B., Puget, H., Hempel, W.M., Al Jawhari, M., Jeandidier, E., Frey, M., 2019. Benefit of an association of an antioxidative substrate and a traditional chinese medicine on telomere elongation. Cell. Mol. Biol. Noisy–Gd. Fr. 65, 54–58.

Nagamine, T., Nakazato, K., Tomioka, S., Iha, M., Nakajima, K., 2014. Intestinal Absorption of Fucoidan Extracted from the Brown Seaweed, Cladosiphon okamuranus. Mar. Drugs 13, 48–64. https://doi.org/10.3390/md13010048.

Nai, J., Zhang, C., Shao, H., Li, B., Li, H., Gao, L., Dai, M., Zhu, L., Sheng, H., 2021. Extraction, structure, pharmacological activities and drug carrier applications of *Angelica sinensis* polysaccharide. Int. J. Biol. Macromol. 183, 2337–2353. https://doi.org/10.1016/j.ijbiomac.2021.05.213.

Niu, X., Yu, Jiabao, Huang, Q., Yu, Jinjin, Yang, Y., Song, H., Liu, Y., Xiao, X., Cui, L., Li, W., 2022. Immunoenhancement activity of *Bletilla striata* polysaccharide through MAPK and NF-κB signalling pathways in vivo and in vitro. Autoimmunity 55, 650–660. https://doi.org/10.1080/08916934.2022.2103801.

Niyigaba, T., Liu, D., Habimana, J., de, D., 2021. The Extraction, Functionalities and Applications of Plant Polysaccharides in Fermented Foods: A Review. Foods 10, 3004. https://doi.org/10.3390/foods10123004.

Osterhage, J.L., Friedman, K.L., 2009. Chromosome end maintenance by telomerase. J. Biol. Chem. 284, 16061–16065. https://doi.org/10.1074/jbc.R900011200.

Pei, Y.H., Yan, N.N., Zhang, H.F., Zhang, S.T., Tang, Z.Z., Huang, Y., Chen, T., Feng, S.L., Ding, C.B., Yuan, S., Yuan, M., 2022. Physicochemical Characterization of a Fern Polysaccharide from *Alsophila spinulosa* Leaf and Its Anti-Aging Activity in Caenorhabditis elegans. Chem. Biodivers. 19, e202200156. https://doi.org/10.1002/cbdv.202200156.

Piskovatska, V., Strilbytska, O., Koliada, A., Vaiserman, A., Lushchak, O., 2019. Health Benefits of Anti-aging Drugs. In: Harris, J.R., Korolchuk, V.I. (Eds.), Biochemistry and Cell Biology of Ageing: Part II Clinical Science. Springer, Singapore, pp. 339–392. https://doi.org/10.1007/978-981-13-3681-2_13.

Prasad, K.N., Wu, M., Bondy, S.C., 2017. Telomere shortening during aging: Attenuation by antioxidants and anti-inflammatory agents. Mech. Ageing Dev. 164, 61–66. https://doi.org/10.1016/j.mad.2017.04.004.

Pu, X., Luo, A., Su, H., Zhang, K., Tian, C., Chen, B., Chai, P., Xia, X., 2020. Optimization and mechanism of postponing aging of polysaccharides from Chinese herbal medicine formula. Toxicol. Res. 9, 239–248. https://doi.org/10.1093/toxres/tfaa020.

Puri, D., Wagner, W., 2023. Epigenetic rejuvenation by partial reprogramming. BioEssays News Rev. Mol. Cell. Dev. Biol. 45, e2200208. https://doi.org/10.1002/bies.202200208.

Qian, L., Du, M., Yang, X., Wang, Q., Huang, S., Ma, Y., Sun, Y., 2023. Microanalysis Characterization and Immunomodulatory Effect for Selenium-Enriched Polysaccharide from *Morchella esculenta* (L.) Pers. Mol. Basel Switz 28, 2885. https://doi.org/10.3390/molecules28072885.

Roy, Z., Bansal, R., Siddiqui, L., Chaudhary, N., 2023. Understanding the Role of Free Radicals and Antioxidant Enzymes in Human Diseases. Curr. Pharm. Biotechnol. 24, 1265–1276. https://doi.org/10.2174/1389201024666221121160822.

Saleh, E.A.M., Al-Dolaimy, F., Qasim Almajidi, Y., Baymakov, S., Kader M, M.A., Ullah, M.I., Abbas, A.H.R., Khlewee, I.H., Bisht, Y.S., Alsaalamy, A.H., 2023. Oxidative stress affects the beginning of the growth of cancer cells through a variety of routes. Pathol. Res. Pract. 249, 154664. https://doi.org/10.1016/j.prp.2023.154664.

Salminen, A., Ojala, J., Kaarniranta, K., 2011. Apoptosis and aging: increased resistance to apoptosis enhances the aging process. Cell. Mol. Life Sci. CMLS 68, 1021–1031. https://doi.org/10.1007/s00018-010-0597-y.

Sasako, T., Ueki, K., 2016. Insulin/IGF-1 signaling and aging]. Nihon Rinsho Jpn. J. Clin. Med. 74, 1435–1440.

Shi, Y., Ye, D., Cui, K., Bai, X., Fan, M., Feng, Y., Hu, C., Xu, Y., Huang, J., 2024. Melatonin ameliorates retinal ganglion cell senescence and apoptosis in a SIRT1-dependent manner in an optic nerve injury model. Biochim. Biophys. Acta Mol. Basis Dis. 1870, 167053. https://doi.org/10.1016/j.bbadis.2024.167053.

Song, G., Chen, F., Chen, S., Ye, S., 2021. Polysaccharides from *Premna microphylla* turcz ameliorate inflammation via the enhancement of intestinal resistance in host. J. Ethnopharmacol. 276, 114208. https://doi.org/10.1016/j.jep.2021.114208.

Sonnenburg, E.D., Sonnenburg, J.L., 2019. The ancestral and industrialized gut microbiota and implications for human health. Nat. Rev. Microbiol. 17, 383–390. https://doi.org/10.1038/s41579-019-0191-8.

Sudheesh, N.P., Ajith, T.A., Janardhanan, K.K., 2009. *Ganoderma lucidum* (Fr.) P. Karst enhances activities of heart mitochondrial enzymes and respiratory chain complexes in the aged rat. Biogerontology 10, 627–636. https://doi.org/10.1007/s10522-008-9208-9.

Takaya, K., Asou, T., Kishi, K., 2023. *Cistanche deserticola* Polysaccharide Reduces Inflammation and Aging Phenotypes in the Dermal Fibroblasts through the Activation of the NRF2/HO-1 Pathway. Int. J. Mol. Sci. 24, 15704. https://doi.org/10.3390/ijms242115704.

Tan, Y., Yin, L., Sun, Z., Shao, S., Chen, W., Man, X., Du, Y., Chen, Y., 2020. Astragalus polysaccharide exerts anti-Parkinson via activating the PI3K/AKT/mTOR pathway to increase cellular autophagy level in vitro. Int. J. Biol. Macromol. 153, 349–356. https://doi.org/10.1016/j.ijbiomac.2020.02.282.

Tang, Cheng, L., Liu, Y., Wu, Z., Zhang, X., Luo, S., 2022a. Plant Polysaccharides Modulate Immune Function via the Gut Microbiome and May Have Potential in COVID-19 Therapy. Molecules 27, 2773. https://doi.org/10.3390/molecules27092773.

Tang, Y, L., K, L., L, X., P, Y., J, M., 2022b. Potential Applications of Lilium Plants in Cosmetics: A Comprehensive Review Based on Research Papers and Patents. Antioxid. Basel Switz. 11. https://doi.org/10.3390/antiox11081458.

Tang, Z., Huang, G., 2022. Extraction, structure, and activity of polysaccharide from Radix *astragali*. Biomed. Pharmacother. 150, 113015. https://doi.org/10.1016/j.biopha.2022.113015.

Tao, R., Lu, K., Zong, G., Xia, Y., Han, H., Zhao, Y., Wei, Z., Lu, Y., 2023. Ginseng polysaccharides: Potential antitumor agents. J. Ginseng Res. 47, 9–22. https://doi.org/10.1016/j.jgr.2022.07.002.

Thiab, N.R., King, N., Jones, G.L., 2015. Effect of ageing and oxidative stress on antioxidant enzyme activity in different regions of the rat kidney. Mol. Cell. Biochem. 408, 253–260. https://doi.org/10.1007/s11010-015-2503-2.

Tian, H., Ni, Z., Lam, S.M., Jiang, W., Li, F., Du, J., Wang, Y., Shui, G., 2022. Precise Metabolomics Reveals a Diversity of Aging-Associated Metabolic Features. Small Methods 6, e2200130. https://doi.org/10.1002/smtd.202200130.

Tian, L., Cai, Q., Wei, H., 1998. Alterations of antioxidant enzymes and oxidative damage to macromolecules in different organs of rats during aging. Free Radic. Biol. Med. 24, 1477–1484. https://doi.org/10.1016/s0891-5849(98)00025-2.

Tokita, Y., Nakajima, K., Mochida, H., Iha, M., Nagamine, T., 2010. Development of a Fucoidan-Specific Antibody and Measurement of Fucoidan in Serum and Urine by Sandwich ELISA. Biosci. Biotechnol. Biochem. 74, 350–357. https://doi.org/10.1271/bbb.90705.

Velarde, M.C., Flynn, J.M., Day, N.U., Melov, S., Campisi, J., 2012. Mitochondrial oxidative stress caused by Sod2 deficiency promotes cellular senescence and aging phenotypes in the skin. Aging 4, 3–12. https://doi.org/10.18632/aging.100423.

Wan, X., Yin, Y., Zhou, C., Hou, L., Cui, Q., Zhang, X., Cai, X., Wang, Y., Wang, L., Tian, J., 2022. Polysaccharides derived from Chinese medicinal herbs: A promising choice of vaccine adjuvants. Carbohydr. Polym. 276, 118739. https://doi.org/10.1016/j.carbpol.2021.118739.

Wang, Chen, X., Tang, Y., Wu, J.M., Qin, D.L., Yu, L., Yu, C.L., Zhou, X.G., Wu, A.G., 2022a. The Therapeutic Potential of Plant Polysaccharides in Metabolic Diseases. Pharm. Basel Switz. 15, 1329. https://doi.org/10.3390/ph15111329.

Wang, H., Zhu, W., Hong, Y., Wei, W., Zheng, N., He, X., Bao, Y., Gao, X., Huang, W., Sheng, L., Li, M., Li, H., 2024. Astragalus polysaccharides attenuate chemotherapy-induced immune injury by modulating gut microbiota and polyunsaturated fatty acid metabolism. Phytomedicine Int. J. Phytother. Phytopharm. 128, 155492. https://doi.org/10.1016/j.phymed.2024.155492.

Wang, J., Jiang, Y., Hou, X., Raza, T., He, Y., Liu, X., Xing, D., Wei, L., 2025. AMP1-1 derived from *Atractylodes macrocephala Koidz* prevents bone aging triggered by lead and cadmium. Comp. Biochem. Physiol. Toxicol. Pharmacol. CBP 294, 110189. https://doi.org/10.1016/j.cbpc.2025.110189.

Wang, J., Liang, Q., Zhao, Q., Tang, Q., Ahmed, A.F., Zhang, Y., Kang, W., 2021. The effect of microbial composition and proteomic on improvement of functional constipation by *Chrysanthemum morifolium* polysaccharide. Food Chem. Toxicol. Int. J. Publ. Br. Ind. Biol. Res. Assoc. 153, 112305. https://doi.org/10.1016/j.fct.2021.112305.

Wang, J.L., Xu, C.J., 2020. Astrocytes autophagy in aging and neurodegenerative disorders. Biomed. Pharmacother. Biomedecine Pharmacother. 122, 109691. https://doi.org/10.1016/j.biopha.2019.109691.

Wang, Sušac, L., Feigon, J., 2019a. Structural Biology of Telomerase. Cold Spring Harb. Perspect. Biol. 11, a032383. https://doi.org/10.1101/cshperspect.a032383.

Wang, Xu, X., Mao, G., Guo, Y., Wang, G., Sun, X., Xu, N., Zhang, Z., 2022b. Structural Characterization of *Gracilariopsis lemaneiformis* Polysaccharide and Its Property in Delaying Cellular Senescence. Front. Nutr. 9, 876992. https://doi.org/10.3389/fnut.2022.876992.

Wang, Z., Zhang, H., Shen, Y., Zhao, X., Wang, X., Wang, J., Fan, K., Zhan, X., 2018. Characterization of a novel polysaccharide from *Ganoderma lucidum* and its absorption mechanism in Caco-2 cells and mice model. Int. J. Biol. Macromol. 118, 320–326. https://doi.org/10.1016/j.ijbiomac.2018.06.078.

Wang, Zhang, Z., Zhou, H., Sun, X., Chen, X., Xu, N., 2019b. The anti-aging effects of *Gracilaria lemaneiformis* polysaccharide in Caenorhabditis elegans. Int. J. Biol. Macromol. 140, 600–604. https://doi.org/10.1016/j.ijbiomac.2019.08.186.

Webb, C.J., Zakian, V.A., 2016. Telomerase RNA is more than a DNA template. RNA Biol 13, 683–689. https://doi.org/10.1080/15476286.2016.1191725.

Wei, J.J., Li, X.J., Liu, W., Chai, X.J., Zhu, X.Y., Sun, P.H., Liu, F., Zhao, Y.K., Huang, J.L., Liu, Y.F., Zhao, S.T., 2023. Eucommia Polysaccharides Ameliorate Aging-Associated Gut Dysbiosis: A Potential Mechanism for Life Extension in Drosophila. Int. J. Mol. Sci. 24, 5881. https://doi.org/10.3390/ijms24065881.

Xia, G., Xin, N., Liu, W., Yao, H., Hou, Y., Qi, J., 2014. Inhibitory effect of *Lycium barbarum* polysaccharides on cell apoptosis and senescence is potentially mediated by the p53 signaling pathway. Mol. Med. Rep. 9, 1237–1241. https://doi.org/10.3892/mmr.2014.1964.

Xiang, Q., Zhou, W.Y., Hu, W.X., Wen, Z., He, D., Wu, X.M., Wei, H.P., Wang, W.D., Hu, G.Z., 2015. Neuroprotective effects of *Rhizoma Dioscoreae* polysaccharides against neuronal apoptosis induced by in vitro hypoxia. Exp. Ther. Med. 10, 2063–2070. https://doi.org/10.3892/etm.2015.2819.

Xu, S., Sun, X., Zhu, Z., Xin, Y., Chen, C., Luo, J., 2024. The extract of buds of *Chrysanthemum morifolium* ramat alleviated UVB-induced skin photoaging by regulating MAPK and Nrf2/ARE pathways. J. Ethnopharmacol. 332, 118352. https://doi.org/10.1016/j.jep.2024.118352.

Xu, Wang, S., Jiang, Y., Wu, J., Chen, L., Ding, Y., Zhou, Y., Deng, L., Chen, X., 2023a. *Poria cocos* Polysaccharide Ameliorated Antibiotic-Associated Diarrhea in Mice via Regulating the Homeostasis of the Gut Microbiota and Intestinal Mucosal Barrier. Int. J. Mol. Sci. 24, 1423. https://doi.org/10.3390/ijms24021423.

Xu, Zeng, X., Liu, Y., Wu, Z., Zheng, X., Zhang, X., 2023b. Inhibitory effect of *Dendrobium officinale* polysaccharide on oxidative damage of glial cells in aging mice by regulating gut microbiota. Int. J. Biol. Macromol. 247, 125787. https://doi.org/10.1016/j.ijbiomac.2023.125787.

Xu, Z.H., Su, X., Yang, G., Qin, T., Liu, Y., 2022. *Ganoderma lucidum* polysaccharides protect against sepsis-induced cardiac dysfunction by activating SIRT1. J. Pharm. Pharmacol. 74, 124–130. https://doi.org/10.1093/jpp/rgab142.

Xue, H., Liang, B., Wang, Y., Gao, H., Fang, S., Xie, K., Tan, J., 2024. The regulatory effect of polysaccharides on the gut microbiota and their effect on human health: A review. Int. J. Biol. Macromol. 270, 132170. https://doi.org/10.1016/j.ijbiomac.2024.132170.

Yan, Y., Wang, M., Chen, N., Wang, X., Fu, C., Li, Y., Gan, X., Lv, P., Zhang, Y., 2022. Isolation, structures, bioactivities, application and future prospective for polysaccharides from Tremella aurantialba: A review. Front. Immunol. 13, 1091210. https://doi.org/10.3389/fimmu.2022.1091210.

Yao, Chen, J.M., Shen, L.E., Yu, Y.S., Tang, Z.H., Zang, G.Q., Zhang, Y., Chen, X.H., 2022a. Astragalus polysaccharide alleviated hepatocyte senescence via autophagy pathway. Kaohsiung J. Med. Sci. 38, 457–468. https://doi.org/10.1002/kjm2.12495.

Yao, Liu, H., Ma, C., Pu, L., Yang, W., Lei, Z., 2022b. A Review on the Extraction, Bioactivity, and Application of Tea Polysaccharides. Mol. Basel Switz. 27, 4679. https://doi.org/10.3390/molecules27154679.

Ye, Y.X., Pan, J.C., Wang, H.C., Zhang, X.T., Zhu, H.L., Liu, X.H., 2024. Advances in small-molecule fluorescent probes for the study of apoptosis. Chem. Soc. Rev. 53, 9133–9189. https://doi.org/10.1039/d4cs00502c.

Yin, M., Zhang, Y., Li, H., 2019. Advances in Research on Immunoregulation of Macrophages by Plant Polysaccharides. Front. Immunol. 10, 145. https://doi.org/10.3389/fimmu.2019.00145.

Yu, M., Xiao, B., Hao, X., Tan, J., Gu, J., Wang, G., Wang, W., Zhang, Y., 2019. Pumpkin polysaccharide preparation, simulated gastrointestinal digestion, and *in vivo* biodistribution. Int. J. Biol. Macromol. 141, 1293–1303. https://doi.org/10.1016/j.ijbiomac.2019.09.037.

Yuan, Y., Kang, N., Li, Q., Zhang, Y., Liu, Y., Tan, P., 2019. Study of the Effect of Neutral Polysaccharides from *Rehmannia glutinosa* on Lifespan of Caenorhabditis elegans. Mol. Basel Switz. 24, 4592. https://doi.org/10.3390/molecules24244592.

Zeng, P., Li, J., Chen, Y., Zhang, L., 2019. The structures and biological functions of polysaccharides from traditional Chinese herbs. Prog. Mol. Biol. Transl. Sci. 163, 423–444. https://doi.org/10.1016/bs.pmbts.2019.03.003.

Zeng, X., Tang, S., Dong, X., Dong, M., Shao, R., Liu, R., Li, T., Zhang, X., Wong, Y.H., Xie, Q., 2024. Analysis of metagenome and metabolome disclosed the mechanisms of *Dendrobium officinale* polysaccharide on DSS-induced ulcerative colitis-affected mice. Int. J. Biol. Macromol. 277, 134229. https://doi.org/10.1016/j.ijbiomac.2024.134229.

Zhang, L., Pitcher, L.E., Yousefzadeh, M.J., Niedernhofer, L.J., Robbins, P.D., Zhu, Y., 2022. Cellular senescence: a key therapeutic target in aging and diseases. J. Clin. Invest. 132, e158450. https://doi.org/10.1172/JCI158450.

Zhang, Wang, S., Fan, Y., Liu, W., Zheng, Y., Wang, Z., Ren, S., Li, W., 2023a. Preparation of a new resource food-arabinogalactan and its protective effect against enterotoxicity in IEC-6 cells by inhibiting endoplasmic reticulum stress. Int. J. Biol. Macromol. 249, 126124. https://doi.org/10.1016/j.ijbiomac.2023.126124.

Zhang, Yang, H., Wang, Y., Zhang, J., Zhang, H., Cao, X., Hu, T., Lin, J., Tang, X., Yan, X., Zhuang, H., Chen, X., Liang, Y., Luo, P., Shen, L., 2023b. Proteomic Study on the Mechanism of Arsenic Neurotoxicity in the Rat Cerebral Cortex and the Protective Mechanism of Dictyophora Polysaccharides against Arsenic Neurotoxicity. ACS Chem. Neurosci. 14, 2302–2319. https://doi.org/10.1021/acschemneuro.3c00009.

Zhang, Zhang, M., Li, W., Ma, L., Liu, X., Ding, Q., Yu, W., Yu, T., Ding, C., Liu, W., 2023c. Research progress of natural plant polysaccharides inhibiting inflammatory signaling pathways and regulating intestinal flora and metabolism to protect inflammatory bowel disease. Int. J. Biol. Macromol. 253, 126799. https://doi.org/10.1016/j.ijbiomac.2023.126799.

Zhao, R.H., Yang, F.X., Bai, Y.C., Zhao, J.Y., Hu, M., Zhang, X.Y., Dou, T.F., Jia, J.J., 2023. Research progress on the mechanisms underlying poultry immune regulation by plant polysaccharides. Front. Vet. Sci. 10, 1175848. https://doi.org/10.3389/fvets.2023.1175848.

Zhao, Y., Yan, B., Wang, Z., Li, M., Zhao, W., 2020. Natural Polysaccharides with Immunomodulatory Activities. Mini Rev. Med. Chem. 20, 96–106. https://doi.org/10.2174/1389557519666190913151632.

Zhao, Y, Z., W, L., C, D., 2021. *Aronia melanocarpa* polysaccharide ameliorates inflammation and aging in mice by modulating the AMPK/SIRT1/NF-κB signaling pathway and gut microbiota. Sci. Rep. 11. https://doi.org/10.1038/s41598-021-00071-6.

Zheng, X., Wang, J., Bi, F., Li, Yilu, Xiao, J., Chai, Z., Li, Yunhong, Miao, Z., Wang, Y., 2021. Protective effects of *Lycium barbarum* polysaccharide on ovariectomy-induced cognition reduction in aging mice. Int. J. Mol. Med. 48, 121. https://doi.org/10.3892/ijmm.2021.4954.

Zheng, Y., Xie, Q., Wang, H., Hu, Y., Ren, B., Li, X., 2020. Recent advances in plant polysaccharide-mediated nano drug delivery systems. Int. J. Biol. Macromol. 165, 2668–2683. https://doi.org/10.1016/j.ijbiomac.2020.10.173.

Zheng, Z., Pan, X., Luo, L., Zhang, Q., Huang, X., Liu, Y., Wang, K., Zhang, Y., 2022. Advances in oral absorption of polysaccharides: Mechanism, affecting factors, and improvement strategies. Carbohydr. Polym. 282, 119110. https://doi.org/10.1016/j.carbpol.2022.119110.

Zhou, S., Wang, J., Ren, J., Xu, M., Jiang, Z., Zhang, X., Li, B., Yuan, L., Jiao, L., 2023. A neutral heteropolysaccharide from *Halenia elliptica* D. Don: Extraction, structural characterization, antioxidant and antiaging activities. Carbohydr. Polym. 322, 121330. https://doi.org/10.1016/j.carbpol.2023.121330.

Zhou, Y., Zhu, L., Li, H., Xie, W., Liu, J., Zhang, Y., Li, Y., Wang, C., 2022. In vivo and in vitro neuroprotective effects of *maca* polysaccharide. Front. Biosci. Landmark Ed. 27, 8. https://doi.org/10.31083/j.fbl2701008.

Zhu, K., Du, D., Shi, Y., Hu, F., Zhang, W., Ni, H., Hafeez, E., Chen, D., 2025. *Poria cocos* Polysaccharide Delays Aging by Enhancing the Antioxidant Ability and Suppressing the Expression of the Branched-Chain Amino Acid Transferase-Encoding Gene in *Drosophila melanogaster*. J. Agric. Food Chem. 73, 9033–9046. https://doi.org/10.1021/acs.jafc.4c12889.

Zhu, X., Li, B., Lou, P., Dai, T., Chen, Y., Zhuge, A., Yuan, Y., Li, L., 2021. The Relationship Between the Gut Microbiome and Neurodegenerative Diseases. Neurosci. Bull. 37, 1510–1522. https://doi.org/10.1007/s12264-021-00730-8.

Zia, A., Sahebdel, F., Farkhondeh, T., Ashrafizadeh, M., Zarrabi, A., Hushmandi, K., Samarghandian, S., 2021. A review study on the modulation of SIRT1 expression by miRNAs in aging and age-associated diseases. Int. J. Biol. Macromol. 188, 52–61. https://doi.org/10.1016/j.ijbiomac.2021.08.013.

Zinatizadeh, M.R., Schock, B., Chalbatani, G.M., Zarandi, P.K., Jalali, S.A., Miri, S.R., 2021. The Nuclear Factor Kappa B (NF-kB) signaling in cancer development and immune diseases. Genes Dis 8, 287–297. https://doi.org/10.1016/j.gendis.2020.06.005.

Zou, Y.F., JiZe, X.P., Li, C.Y., Zhang, C.W., Fu, Y.P., Yin, Z.Q., Li, Y.P., Song, X., Li, L.X., Zhao, X.H., Feng, B., Huang, C., Ye, G., Tang, H.Q., Li, N.Y., Chen, J., Chen, X.F., Tian, M.L., 2023. Polysaccharide from aerial part of *Chuanminshen violaceum* alleviates oxidative stress and inflammatory response in aging mice through modulating intestinal microbiota. Front. Immunol. 14, 1159291. https://doi.org/10.3389/fimmu.2023.1159291.