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Progress of *Ganoderma lucidum* in regulating aging-mediated disorders of glycolipid metabolism

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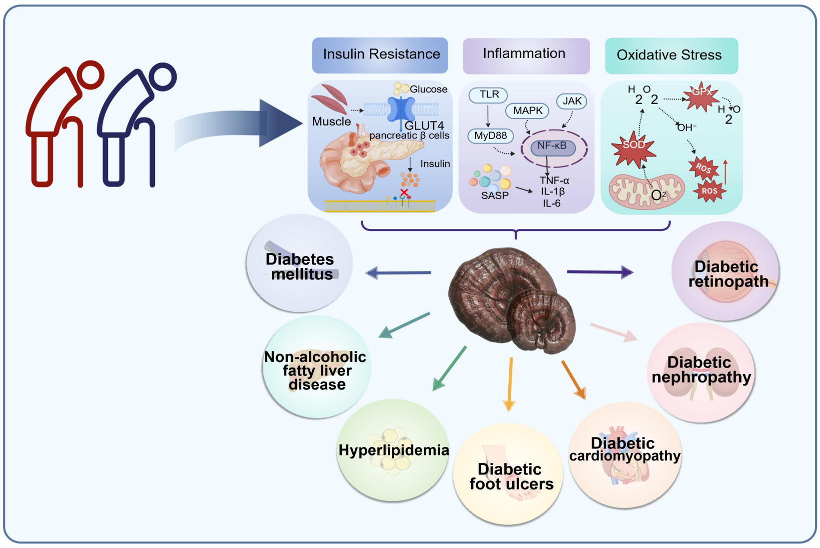
Abstract

As the aging population continues to grow, age-related health issues are becoming increasingly prominent, attracting widespread attention and concern from society. While research on the mechanisms of aging is relatively extensive, studies on the association between aging and related diseases remain limited. *G. lucidum*, a traditional medicinal fungus, has garnered significant attention due to its diverse bioactive properties. Recent studies have revealed that *G. lucidum* and its active components exhibit significant potential in anti-aging and regulating dysregulation of glucose and lipid metabolism. However, a comprehensive and detailed review of recent research findings has yet to be thoroughly explored. This paper summarizes and elucidates the latest advances in the pathological mechanisms of aging-related glucose and lipid metabolism disorders by retrieving data from databases such as X-mol and PubMed, provides a detailed account of the regulatory effects of *G. lucidum*'s primary active components on aging and lipid metabolism, and explores their potential mechanisms. Additionally, it discusses the application prospects of *G. lucidum* in the fields of anti-aging and metabolic regulation, aiming to provide a reference for research on aging-mediated lipid metabolism disorders and to lay a theoretical foundation for the further development and application of *G. lucidum*.

Keywords: aging; lipid metabolism; *G. lucidum*



Author contributions

Zhao XH was responsible for writing manuscripts, reviewing and editing. Dai XW and Pei HY participated in the manuscript revision. Du R was responsible for overseeing and writing-commenting. Wang W was involved in the conceptualization. He ZM was responsible for supervision and review. All authors contributed to the article and approved the final submitted version.

Competing interests

The authors declare no conflicts of interest.

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Abbreviations

Akt, protein kinase B; DAMPs, damage-associated molecular patterns; DM, diabetes mellitus; ER, endoplasmic reticulum; GLP, *G. lucidum* polysaccharides; GLPP, *G. lucidum* polysaccharide peptides; GLSO, *G. lucidum* spore oil; GLUT4, glucose transporter 4; HDL-C, high-density lipoprotein cholesterol; IL-1β, interleukin-1β; IL-6, interleukin-6; IR, insulin resistance; IRS, insulin receptor substrate; LDL-C, low-density lipoprotein cholesterol; MAPK, mitogen-activated protein kinase; NAFLD, non-alcoholic fatty liver disease; PI3K, phosphoinositide 3-kinase; PTP1B, protein tyrosine phosphatase 1B; ROS, reactive oxygen species; SASP, senescence-associated secretory phenotype; TC, total cholesterol; TG, triglyceride; TNF-α, tumor necrosis factor-alpha; VEGF, vascular endothelial growth factor.

Citation

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Highlights

1. Focusing on the mechanisms through which aging mediates disorders of glycolipid metabolism, particular attention is given to insulin resistance, inflammation, and oxidative stress.
2. The review examines the mechanisms by which the active components of *Ganoderma lucidum* improve insulin resistance, alleviate chronic inflammation, and reduce oxidative stress.
3. It summarizes the regulatory effects of the active components of *Ganoderma lucidum* on diseases associated with glycolipid metabolism disorders.

Medical history of objective

Ganoderma lucidum was first documented in *Shen Nong Ben Cao Jing* (compiled around 200–250 C.E.) as a superior medicinal herb, and later systematically described in *Compendium of Materia Medica* (compiled in 1578 C.E.) by Shizhen Li of the Ming Dynasty. It is recorded in the *Pharmacopoeia of the People's Republic of China* for its effects in replenishing Qi (to boost vitality), calming the mind (to ease anxiety), and relieving cough (to soothe respiratory discomfort). Modern studies have demonstrated that *Ganoderma lucidum* possesses a wide range of pharmacological activities, including immunomodulatory, antitumor, hepatoprotective, hypoglycemic, hypolipidemic, antioxidant, anti-inflammatory, and neuroprotective effects.

Introduction

Globally, the population aged 65 and above is projected to double from 700 million in 2019 to over 1.5 billion by 2050 [1]. The aging research report released by the World Health Organization predicts that by the middle of this century, the elderly population in many countries will exceed 30% of the total population, including China, South Korea, Europe, etc [2]. With the accelerated aging of the global population, aging-related diseases have become an important issue affecting human health and socio-economic development, so research on aging-related diseases is of great significance [3].

Aging is a complex and variable physiological process. It is an irreversible process of decline and death that occurs with increasing age, manifested by the gradual decline of bodily tissue and organ function, leading to the development of various degenerative diseases such as cancer, diabetes, Alzheimer's disease, and osteoporosis [4]. Its main characteristics include mitochondrial dysfunction, impaired immune function, reduced autophagy, epigenetic changes, telomere loss, altered nutrient sensing, and disrupted protein homeostasis. These changes not only accelerate the body's aging process but also serve as important risk factors for various age-related diseases. As research in the field of aging continues to deepen, numerous researchers have proposed various theories regarding aging, including the free radical oxidative stress theory, the telomere theory, and the inflammatory aging theory [5, 6]. Studies have shown that senescent cells remain metabolically active for a period of time and exhibit significant changes, with four typical characteristics: cell cycle arrest, senescence-associated secretory phenotype (SASP), macromolecular damage, and metabolic disorders [7].

Aging is a complex biological process and one of the main causes of metabolic diseases. Aging is closely related to lipid metabolism disorders, which are interdependent. Lipid metabolism disorders are common metabolic abnormalities in the aging process and are closely related to the onset and development of various chronic diseases. The causes of sugar and lipid metabolism disorders are complex and varied, mainly including aging, genetic factors, lifestyle, and the effects of drugs [8]. Abnormal sugar and lipid metabolism can lead to multiple organ dysfunction and has become the eighth leading cause of death [9]. Age-related disorders of glucose and lipid metabolism not only increase the risk of chronic diseases such as cardiovascular disease, diabetes, and metabolic syndrome, but also seriously endanger patients' health, affect their quality of life, and impose a heavy burden on families and society. Figure 1 illustrates several diseases associated with disorders of glucose and lipid metabolism. Therefore, it is of great significance to conduct in-depth research on age-related disorders of glucose and lipid metabolism.

Ganoderma lucidum (Leyss. ex Fr.) Karst or *Ganoderma sinense* Zhao, Xu et Zhang is a traditional Chinese medicine with a wide variety of species and widespread distribution worldwide. *G. lucidum* has a long history and wide range of applications. According to classical medical texts such as *the Shen Nong Ben Cao Jing* and *Compendium of Materia Medica*, *G. lucidum* is classified into six categories based on color differences, as shown in Figure 2: red, green, yellow, purple, white and black. The characteristics and primary manifestations of the six distinct types of *G. lucidum* exhibit significant variability. *G. lucidum* is rich in various active ingredients, including polysaccharides, triterpenoids, nucleosides, sterols, proteins, and amino acids, which exert a variety of pharmacological effects, such as immune regulation, anti-aging, antioxidant, anti-inflammatory, liver protection, decrease blood glucose levels, and treatment of neurasthenia [10, 11]. In recent years, research has found that *G. lucidum* and its active ingredients have significant potential in regulating aging and related lipid metabolism disorders, attracting widespread attention. Compared with Western medicine, traditional Chinese medicine exhibits distinctive advantages due to its multi-component and multi-target characteristics. *G. lucidum*, in particular, demonstrates these properties through the synergistic actions of its unique bioactive compounds – such as polysaccharides, triterpenoids, and proteins – which together form a sophisticated regulatory network affecting multiple metabolic pathways.

This review retrieved literature from databases such as PubMed and X-mol using key search terms including "*G. lucidum*", "glucose metabolism", "lipid metabolism", "aging", "inflammation", "diabetes", and "disorders of glucose and lipid metabolism". By reviewing the titles and abstracts, studies that clearly did not meet the inclusion criteria were excluded, including duplicate publications, those with incomplete or irretrievable data, and those whose outcome measures substantially deviated from the target indicators. Figure 3 shows the literature screening process. The collected publications were comprehensively organized to provide a detailed discussion on the potential mechanisms by which *G. lucidum* ameliorates aging-mediated disorders of glucose and lipid metabolism. It lays a solid foundation for further research and development of this valuable medicinal herb, thereby better leveraging its potential in the medical field. Additionally, it offers new strategies for addressing age-related dysregulation of glucose and lipid metabolism, holding significant implications for future research.

Mechanisms of aging-related lipid metabolism disorders

Aging is an inevitable biological process, and disorders in glucose and lipid metabolism are one of the fundamental characteristics of aging. Glucose metabolism disorders primarily refer to abnormalities in the body's absorption, utilization, and storage of glucose, while lipid metabolism disorders refer to abnormalities in the body's synthesis, breakdown, transport, and storage of fats. These two processes are closely interrelated and mutually dependent [12]. During the aging process, the body's sensitivity to insulin decreases, leading to elevated blood sugar levels and increased insulin secretion, which can trigger insulin resistance and dysfunction of pancreatic beta cells. Imbalances in fat breakdown and synthesis result in fat accumulation and dyslipidemia. Current research primarily categorizes the mechanisms underlying age-related disturbances in glucose and lipid metabolism into several components: (1) Age-related reduction in pancreatic β-cell function and exacerbation of insulin resistance. (2) Age-related accelerated oxidative stress exacerbating glucose and lipid metabolism

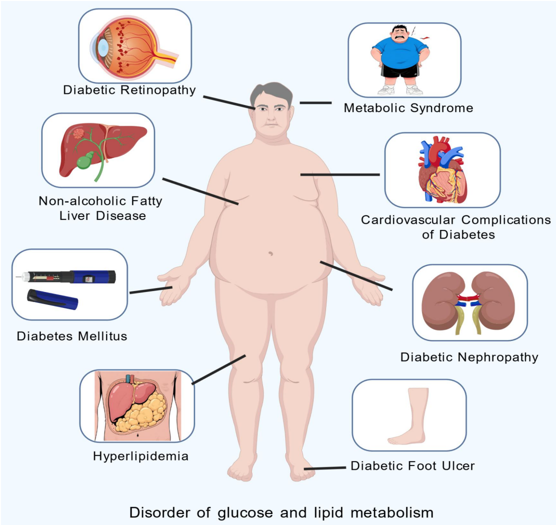

Figure 1 The harm caused by dyslipidemia to the body.
It increases the risk of chronic diseases such as diabetes, diabetic retinopathy, diabetic nephropathy, hyperlipidemia, cardiovascular disease, non-alcoholic fatty liver disease, and metabolic syndrome.

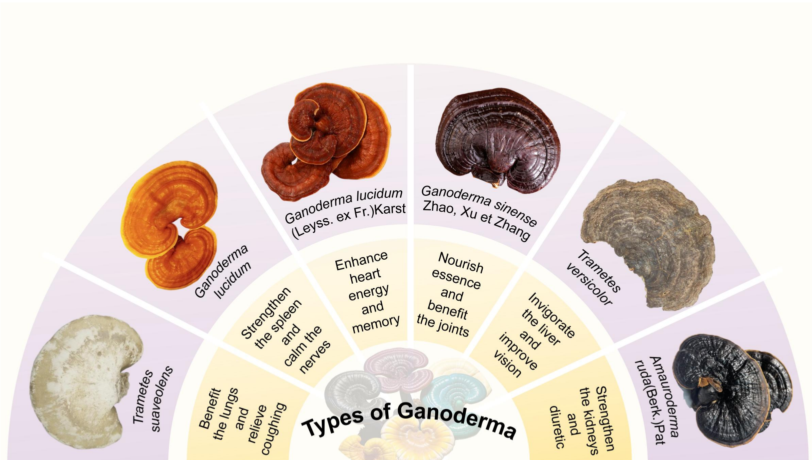

Figure 2 Classification and efficacy of *G. lucidum*

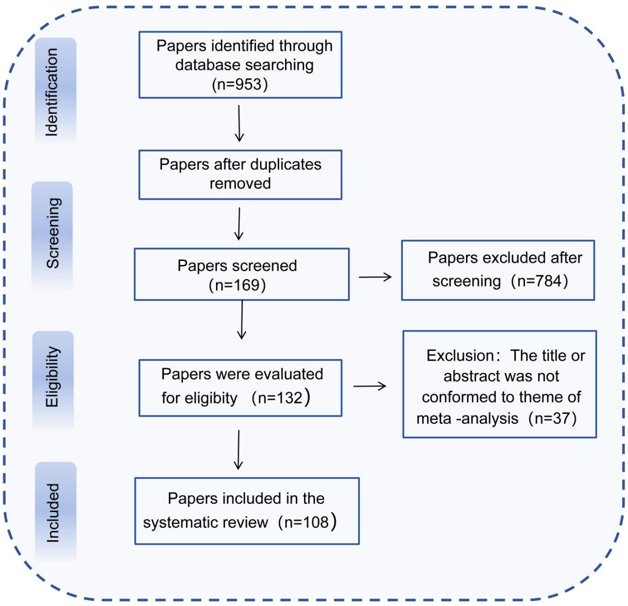

Figure 3 Literature search

disorders. (3) Age-related inflammatory metabolic dysfunction exacerbating glucose and lipid metabolism disorders (Figure 4).

Aging leads to increased insulin resistance and decreased pancreatic beta cell function

Insulin resistance (IR) is common during the aging process and is one of the core mechanisms underlying age-related glucose metabolism disorders. It is also the root cause of many chronic non-communicable diseases that develop with advancing age [13]. Insulin resistance leads to reduced responsiveness of insulin to blood glucose regulation, thereby decreasing the body's absorption and utilization of glucose, and disrupting blood glucose levels through weakened insulin action [14]. When the body is in an IR state, pancreatic beta cells compensate by secreting more insulin to balance and suppress hyperglycemia. This state has a negative impact on the beta cells themselves, leading to dysfunction. Research has shown that arachidonic acid (AA), an unsaturated fatty acid, is a basic metabolite that increases with age and is a factor contributing to excessive insulin secretion in mice. This leads to hepatic insulin resistance and β-cell exhaustion, triggering the onset of age-related diabetes in mice. Inhibiting AA production by suppressing phospholipase A2 (PLA2) activity can alleviate age-related glycometabolic disorders [15]. With aging, the body's sensitivity to insulin decreases, leading to elevated blood glucose levels and increased insulin secretion. Studies have shown that due to age-related differences in insulin resistance, insulin metabolism is significantly reduced in the elderly compared to the young.

As we age, the proliferation and regenerative capacity of pancreatic beta cells significantly decline. Young beta cells possess a certain degree of regenerative capacity when damaged, but this ability is markedly reduced in aged beta cells. Research has shown that the expression of cell cycle activators decreases in aged beta cells, while the expression of cell cycle inhibitors such as p16INK4a increases. p16INK4a inhibits the binding of Cyclin D to CDK4/CDK6, thereby preventing the phosphorylation of the retinoblastoma protein, leading to cell cycle arrest and cellular senescence. The increased apoptosis rate and reduced proliferation rate in aged β cells result in a decrease in the number of pancreatic β cells [16].

Aging β-cells exhibit reduced responsiveness to glucose stimulation, resulting in impaired insulin secretion capacity under glucose stimulation. Some studies have found that the expression of genes related to insulin synthesis in aging β-cells may be impaired, leading to reduced insulin synthesis. Additionally, during aging, impaired autophagy leads to the accumulation of misfolded protein aggregates, resulting in disrupted protein homeostasis [17], activation of endoplasmic reticulum (ER) stress and autophagy pathways, and increased risk of β-cell dysfunction. Elevated ER stress and inflammasome activity during aging also play a significant role in insulin resistance [18]. In summary, aging is an important factor in the development of insulin resistance and pancreatic β-cell damage.

Aging is one of the primary risk factors for muscle mass reduction, and persistent loss of appetite is a hallmark of aging that may increase the risk of developing sarcopenia [19]. Extensive epidemiological evidence indicates a significant association between muscle loss and insulin resistance. As individuals age, body fat undergoes proliferation, hypertrophy, and redistribution, with substantial fat infiltration occurring in skeletal muscle, leading to myosteatosis. Muscle cell lipids play a crucial role in inducing insulin resistance, with many lipid intermediates affecting insulin signaling. Lipid infiltration into muscle cells leads to the production of excessive reactive oxygen species, inducing mitochondrial dysfunction and increased levels of apoptosis, which are directly associated with the development of insulin resistance [20]. Muscle is one of the primary target tissues for insulin action. Muscle tissue sensitivity to insulin is positively correlated with muscle mass; a reduction in muscle mass implies a decrease in target tissues for insulin action, exacerbating insulin resistance. This is primarily because skeletal muscle is rich in glucose transporters 4 (GLUT4), which are responsible for glucose uptake, making it an important organ for glucose clearance. As age increases, GLUT4 levels decline, leading to reduced glucose utilization. Phenolic compounds produced by microorganisms upregulate GLUT4 and PI3K, increasing glucose uptake in muscle fibers and inducing anabolic responses that promote muscle mass synthesis. However, aging disrupts the gut microbiota, leading to insulin resistance. Aging also promotes the transformation of muscle fibers from type II to type I, thereby affecting glucose metabolism and

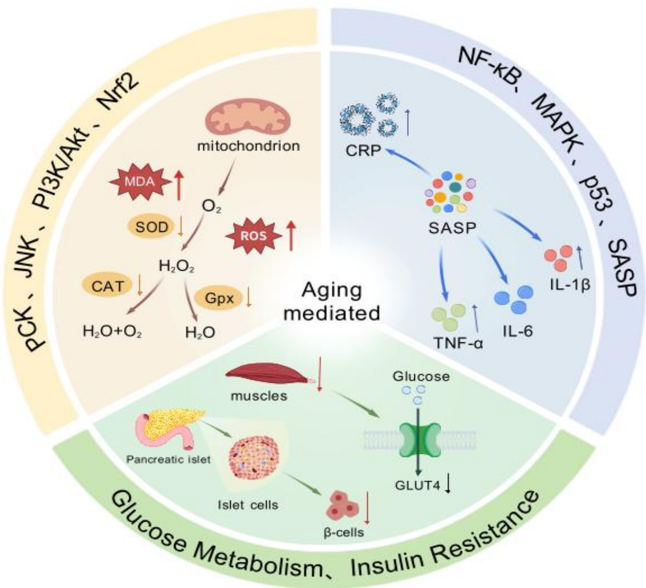

Figure 4 Aging mediates oxidative stress, inflammation, insulin resistance, and related pathways.

Aging leads to increased ROS and MDA, decreased SOD, CAT, and Gpx, and increased oxidative stress. Aging causes SASP to secrete proinflammatory factors, resulting in chronic inflammation. Aging leads to a decrease in the regenerative capacity of pancreatic β cells, muscle loss, and a decrease in GLUT4 in muscles, causing insulin resistance. JNK, c-jun n-terminal kinase; PCK, phosphoenolpyruvate carboxykinase; PI3K/Akt, phosphatidylinositol 3-kinase/protein kinase B signaling pathway; Nrf2, nuclear factor erythroid 2-related factor 2; MAPK, mitogen-activated protein kinase; p53, protein 53; CRP, c-reactive protein; SASP, senescence-associated secretory phenotype; GLUT4, glucose transporter type 4.

exacerbating insulin resistance [21].

Aging leads to a reduction in the number of muscle mitochondria and a decline in their function. Mitochondria are central to cellular energy metabolism, and mitochondrial dysfunction is one of the key causes of pancreatic β-cell apoptosis and impaired insulin secretion. Additionally, increased reactive oxygen species (ROS) production by mitochondria leads to oxidative stress, which may damage β-cells, reduce insulin secretion, impair muscle glucose oxidation and utilization, and decrease muscle insulin responsiveness, thereby exacerbating insulin resistance. Mitochondrial dysfunction may also impair muscle metabolic functions, such as glucose uptake and utilization, which may further exacerbate insulin resistance and β-cell damage [22]. Mitochondrial dysfunction leads to lipid accumulation within muscle cells, contributing to IR. Under conditions of unchanged energy demand, excessive fuel within mitochondria stimulates the production and release of oxidative stressors, ultimately leading to the development of IR [23]. Additionally, oxidative stress and antioxidant status may be associated with sarcopenia in elderly individuals with diabetes.

Oxidative stress caused by aging accelerates sugar and lipid metabolism disorders

During the aging process, mitochondrial dysfunction and the degradation of the antioxidant system induce the production of ROS. When ROS exceed the antioxidant capacity, oxidative stress and cellular dysfunction are induced, which are directly related to the development of many diseases that limit healthy aging. Aging-induced reductions in mitochondrial efficiency lead to increased ROS production in order to maintain sufficient ATP production. The increase in oxidative stress mediated by aging and the bidirectional promotion between oxidative stress and glucose and lipid metabolism disorders form a vicious cycle, significantly exacerbating the progression of metabolic diseases [24].

ROS can directly damage the DNA, proteins, and organelles such as mitochondria of pancreatic beta cells, leading to apoptosis or dysfunction of these cells. This reduces insulin synthesis and secretion, further exacerbating hyperglycemia. Increased ROS levels can also cause abnormalities in glucose metabolism pathways. Under hyperglycemic conditions, glucose can generate ROS through multiple metabolic pathways, such as the polyol pathway, hexosamine pathway, and protein kinase C pathway. The activation of these pathways not only increases ROS production but also further disrupts normal glucose metabolism, creating a vicious cycle [25]. Additionally, as the body ages, antioxidant enzyme activity decreases, antioxidant capacity declines, leading to weakened free radical scavenging ability and elevated free radical levels. Similar to ROS, free radicals also cause oxidative stress, and the activity of free radical scavenging enzymes weakens with age, contributing to the adverse effects of oxidative stress on age-related diseases. Free radicals can directly damage pancreatic β-cells or indirectly cause β-cell dysfunction by affecting insulin synthesis and secretion-related signaling pathways, leading to glucose metabolism disorders [26]. Oxidative stress can damage intracellular insulin signaling pathway-related proteins, impairing insulin signal transmission and reducing insulin sensitivity. Studies have shown that oxidative stress can activate multiple signaling pathways, such as the protein kinase C pathway and the JNK pathway [27]. The activation of these pathways interferes with insulin signaling, leading to insulin resistance. For example, protein kinase C activation increases serine phosphorylation of insulin receptor substrate (IRS), inhibits tyrosine phosphorylation of IRS, thereby reducing phosphorylation of protein kinase B (Akt) and GLUT4 to the cell membrane, thereby impairing glucose uptake and utilization. Age-related oxidative stress accelerates the progression of glucose metabolism disorders through the above mechanisms [28].

Oxidative stress-induced impairment of glucose metabolism similarly extends to lipid metabolism, with both processes being intimately intertwined at the molecular level. In lipid metabolism, oxidative stress can affect the function of adipocytes, promoting lipid synthesis and inhibiting lipid breakdown. On one hand, oxidative stress can activate certain transcription factors, such as peroxisome proliferator-activated receptor gamma, thereby promoting lipid synthesis; on the other hand, oxidative stress can inhibit the activity of enzymes involved in lipid breakdown, such as hormone-sensitive lipase, leading to reduced lipid breakdown [29]. Oxidative stress can lead to the oxidative modification of low-density lipoprotein cholesterol (LDL-C), forming oxidized LDL-C. Oxidized LDL-C is more easily taken up by macrophages, forming foam cells, which in turn promote the development of atherosclerosis. Additionally, oxidative stress can affect hepatic lipid metabolism, leading to increased triglyceride (TG) synthesis and reduced high-density lipoprotein cholesterol (HDL-C) levels [30]. Oxidative stress can induce the production of inflammatory factors in adipose tissue, such as tumor necrosis factor-alpha (TNF-α) and interleukin-6 (IL-6). These inflammatory factors not only exacerbate oxidative stress but also disrupt lipid metabolism, leading to dyslipidemia and insulin resistance. In summary, oxidative stress disrupts glucose and lipid metabolism through multiple mechanisms, creating a vicious cycle that further exacerbates the onset and progression of metabolic diseases. Therefore, antioxidant therapy may be of significant importance in improving glucose and lipid metabolism disorders.

Inflammatory metabolic disorders caused by aging exacerbate sugar and lipid metabolism disorders

There is also a close relationship between aging and inflammatory metabolic dysfunction . With advancing age, significant remodeling of the immune system, systemic inflammation, and metabolic changes such as insulin resistance, hypertension, and dyslipidemia increase [31]. Senescent cells possess a pro-inflammatory secretome, contributing to a pro-inflammatory environment and reduced ability to respond to infectious challenges. Additionally, the accumulation of age-related damage-associated molecular patterns (DAMPs) is an important trigger for inflammation and is considered a potential driver of inflammation. DAMPs can initiate inflammatory responses by binding to cell surface receptors on innate immune cells. Age-related increases in oxidative stress, mTOR signaling, and cellular senescence make cells or tissues in aged animals more susceptible to necrotic apoptosis, leading to the release of DAMPs, which contribute to chronic inflammation with advancing age [32]. Studies have shown that elevated endoplasmic reticulum stress responses during aging also lead to greater inflammatory responses, partly due to impaired autophagy activity in aged adipose tissue [33, 34]. Aging promotes the accumulation of senescence-associated cell load in VAT, which also contributes to inflammation [35]. Aging-related chronic low-grade inflammation is closely associated with adipose tissue dysfunction, which in turn serves as a central node in the pathogenesis of metabolic disorders. Research indicates that during aging, preadipocyte function undergoes changes including reduced preadipocyte replication, decreased adipogenesis, increased lipid toxicity, elevated pro-inflammatory cytokines, chemokines, extracellular matrix modifying proteases, and stress response elements, leading to adipose tissue dysfunction and ultimately chronic inflammation [36]. Aging is often accompanied by a chronic low-grade inflammatory state, with increased secretion of inflammatory factors such as TNF-α and IL-6. These inflammatory factors can interfere with insulin signaling pathways, inhibit the phosphorylation of insulin receptor substrates, and reduce insulin sensitivity. Anti-inflammatory cytokines have potential therapeutic effects in treating aging-mediated insulin resistance. Lipid metabolism and lipid signaling participate in regulating aging and longevity, and conversely, aging and longevity signals also regulate lipid metabolism. Inflammation in adipose tissue is widely recognized as a major factor in age-related metabolic dysfunction and disease. Studies have shown that chronic low-grade inflammation in adipose tissue contributes to the development of metabolic diseases, including insulin resistance in aging, and that reducing adipose tissue inflammation can improve glucose tolerance [37]. Additionally, long-term excessive dietary intake and metabolic excess can stimulate an immune response in the body, which in turn activates inflammatory pathways, elevates inflammatory factors, and ultimately induces pancreatic inflammation, causing damage to pancreatic β-cell function, and even leading to pancreatic β-cell apoptosis, resulting in disrupted glucose and lipid metabolism [38].

Aging is a process characterized by the progressive loss of tissue and organ function, with senescent cells acquiring an irreversible SASP [39]. NF-κB signaling is the primary pathway for SASP production during aging [40]. SASP includes cytokines, chemokines, growth factors, proteases, and extracellular matrix components, which can influence the surrounding tissue microenvironment and regulate various biological processes, including inflammation, immunity, tissue remodeling, and tumorigenesis. Increasing evidence suggests that lipid metabolism and SASP are interconnected at multiple levels. For example, certain lipids (such as ceramides, S1P, and prostaglandins) can regulate the expression or activity of key SASP regulatory factors, including p53, NF-κB, p38 MAPK, JNK, mTOR, IL-1α/β, and STAT3 [41, 42]. Conversely, some SASP factors, such as IL-1β, IL-6, IL-8, and TNF-α, can influence lipid metabolism by altering the expression or activity of lipogenic enzymes, lipolytic enzymes, lipid transporters, fatty acid oxidases, and PPARs that regulate lipid metabolism [43, 44]. SASP factors can also regulate lipids by affecting key signaling pathways such as the phosphoinositide 3-kinase (PI3K)/Akt/mTOR and sphingosine kinase 1/S1P pathways. SASP can regulate glucose metabolism activity by altering the expression and activity of key metabolic enzymes and transcription factors such as AMPK. SASP can also impair glucose uptake and utilization in these tissues by interfering with insulin signaling and inducing insulin resistance, leading to dysregulation of glucose and lipid metabolism [45]. Figure 5 shows the interaction mechanisms among pathways involved in glucose and lipid metabolism disorders.

G. lucidum regulates aging-related lipid metabolism disorders

In recent years, significant progress has been made in research on the regulation of age-related lipid and glucose metabolism disorders by *G. lucidum*. Multiple studies have shown that *G. lucidum* and its active components can improve lipid and glucose metabolism disorders during the aging process through various mechanisms. *G. lucidum*, also known as "Reishi mushroom", was first recorded in *the Shen Nong Ben Cao Jing* and classified as a superior herb, with a long history and widespread application. As a traditional Chinese herbal medicine, its use in traditional medicine can be traced back thousands of years. Reishi mushroom is rich in various active components, including polysaccharides, triterpenoids, nucleosides, sterols, proteins, and amino acids, which exert multiple pharmacological effects such as immune regulation, anti-aging, antioxidant, anti-inflammatory, liver protection, blood sugar reduction, and treatment of neurasthenia [46]. *G. lucidum* and its active components hold significant potential in regulating aging and related lipid and glucose metabolic disorders, *G. lucidum* polysaccharides demonstrate more prominent efficacy in improving glucose metabolism and enhancing insulin sensitivity, whereas Ganoderma triterpenoids exhibit superior advantages in modulating lipid metabolism and exerting anti-inflammatory effects. These two major bioactive components act synergistically to collectively address disorders of glucose and lipid metabolism. Figure 6 illustrates the diverse mechanistic pathways through which the bioactive components in *Ganoderma lucidum* improve glucose metabolism.

G. lucidum improves sugar metabolism

Diabetes mellitus. Diabetes mellitus (DM) is a metabolic disorder characterized by chronic inflammation, β-cell dysfunction, and insulin resistance, resulting in elevated blood glucose levels and a range of associated symptoms. Research indicates that impaired glucose and lipid metabolism is a key factor in the onset and progression of type 2 diabetes mellitus (T2DM) [47]. Current therapeutic mechanisms for T2DM primarily include improving IR, addressing insufficient insulin secretion, inhibiting hepatic gluconeogenesis, exerting anti-inflammatory effects, reducing oxidative stress, and modulating gut microbiota. Numerous studies have demonstrated that *G. lucidum* exhibits significant therapeutic effects on diabetes [48]. *G. lucidum* polysaccharides (GLP) and triterpenoid compounds have been shown to exert their effects through distinct mechanisms, such as improving glucose metabolism, regulating the mitogen-activated protein kinase (MAPK) system, inhibiting the NF-κB pathway, and protecting pancreatic β-cells [49]. *G. lucidum* polysaccharides can influence biological pathways and processes such as carbohydrate metabolism, fatty acid biosynthesis, glycolysis and gluconeogenesis, lipid and lipoprotein metabolism, etc. They exert hypoglycemic effects through multiple mechanisms, including regulating hepatic glucose metabolism enzymes, improving glucose metabolism disorders, and protecting pancreatic islet cells, thereby improving diabetes [50]. *G. lucidum* polysaccharides can regulate insulin secretion, improve insulin resistance, and thereby lower blood glucose levels. *G. lucidum* polysaccharide F31 can repair pancreatic damage, increase insulin secretion, and alleviate insulin resistance by reducing intestinal endotoxin release, modulating gut microbiota structure, and promoting the generation of antioxidant enzymes [51]. Ganoderma polysaccharides improve diabetes by preventing pancreatic β-cell apoptosis and enhancing β-cell regeneration. Protein tyrosine phosphatase 1B (PTP1B)-mediated dephosphorylation of IRS leads to dysfunction of insulin signaling pathways such as PI3K/Akt, resulting in negative regulation of both PI3K/Akt and MAPK pathways. AMPK can activate Akt and promote GLUT4 translocation, synergizing with the PI3K/Akt pathway to enhance glucose uptake and improve insulin sensitivity. Water-soluble high-molecular-weight polysaccharides extracted from *G. lucidum* fruiting bodies inhibit PTP1B activity, enhance insulin receptor activity, improve insulin resistance through GLUT4, increase insulin sensitivity, and thereby lower blood glucose levels [52]. Additionally, triterpenoids derived from *G. lucidum* exhibit significant hypoglycemic effects. Ganoderma acids have been shown to possess a range of bioactive properties beneficial for improving diabetes. Ganoderma acids inhibit α-amylase and α-glucosidase, which can lower blood glucose and insulin levels, while also reducing free fatty acids in the liver and adipose tissue [53]. Ganoderol B regulates glucose metabolism by influencing key enzymes and pathways involved in glucose regulation. As an α-glucosidase inhibitor, it promotes glucose uptake by fat cells and muscle cells, thereby controlling blood glucose levels [54]. Furthermore, several other bioactive constituents present in *G. lucidum* also demonstrate antidiabetic properties. Treatment of STZ-induced type 1 diabetic rats with a *G. lucidum* water-ethanol extract containing β-glucan, protein, and phenolic compounds demonstrated that the extract possesses hypoglycemic and hypolipidemic properties, as well as the ability to repair diabetes-induced pancreatic damage [55]. Recombinant LZ-8 (an analog of the immune-modulating protein Ganoderma-8) induces pancreatic organ protection, promotes insulin secretion, lowers blood glucose and HbA1c levels, and inhibits TNF-α and IL-1β, primarily through its anti-inflammatory and T-cell-modulating effects [56]. Additionally, antioxidant activity is an important therapeutic approach for protecting pancreatic β-cell function, making *G. lucidum*'s antioxidant activity one of its key mechanisms for improving diabetes. Meanwhile, antioxidant intervention serves as a crucial therapeutic approach for protecting pancreatic β-cell function. Consequently, the antioxidant activity of *G. lucidum* represents one of its key mechanisms in ameliorating diabetes. *G. lucidum* polysaccharides and triterpenoids reduce oxidative stress, protect pancreatic cells from oxidative damage, and maintain normal insulin secretion function [57]. *G. lucidum* polysaccharide FYGL exhibits antioxidant activity by scavenging free radicals [58]. Studies indicate that FYGL demonstrates significant efficacy in inhibiting pancreatic β-cell damage associated with reduced ROS and NO levels [59]. Furthermore, FYGL can inhibit PTP1B activity while activating PI3K/Akt, ultimately restoring insulin-mediated glucose synthesis in HepG2 cells [60]. Furthermore, treatment of L6 myoblasts with FYGL leads to AMPK activation and increased GLUT4 expression, promoting

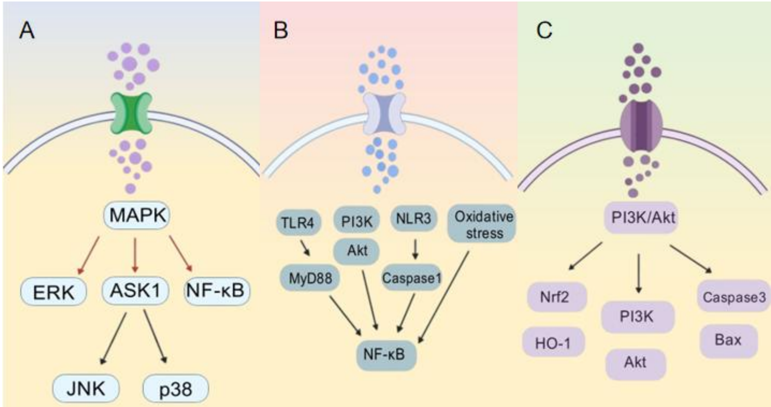

Figure 5 Mechanisms of action between pathways involved in glycolipid metabolism disorders.
MAPK, mitogen-activated protein kinase; ERK, extracellular signal-regulated kinase; ASK1, apoptosis signal-regulating kinase 1; JNK, c-jun n-terminal kinase; p38, p38 mitogen-activated protein kinase; TLR4, toll-like receptor 4; NLR3, nacht, lrr and pyd domains-containing protein 3; PI3K, phosphatidylinositol 3-kinase; Akt, protein kinase B; MyD88, myeloid differentiation primary response 88; caspase1, cysteine-dependent aspartate-specific protease 1; BAX, bcl-2-associated x protein; Caspase3, cysteine-aspartate protease 3; HO-1, heme oxygenase-1.

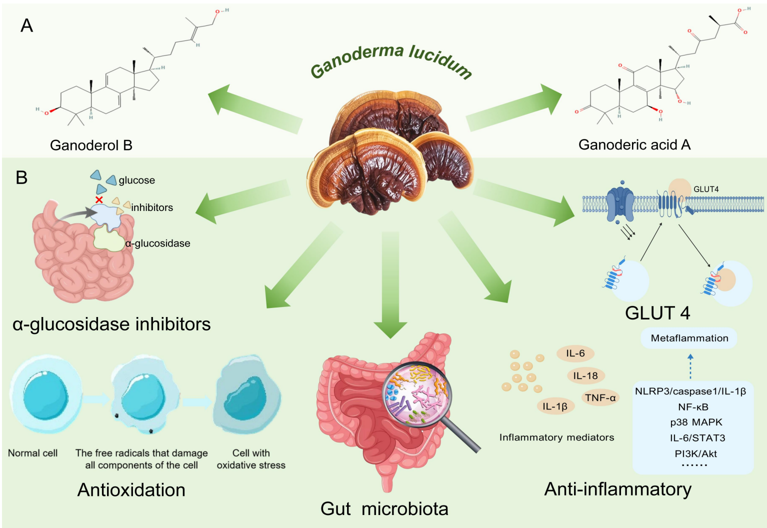

Figure 6 Mechanism of action of active ingredients in *G. lucidum* in improving glucose metabolism

glucose uptake [61]. It is noteworthy that a well-established association exists between the gut microbiota and diabetes, with mechanisms involving energy metabolism, the immune system, changes in intestinal permeability, and alterations in low-grade systemic inflammatory states [62]. Polysaccharides derived from *G. lucidum* have been shown to increase the abundance of beneficial gut bacteria, improve the gut microecological environment, and modulate host metabolic products. By regulating the composition of the gut microbiota and enhancing intestinal barrier function, they ameliorate disorders of glucose and lipid metabolism. Specifically, compared to healthy individuals, type 2 diabetic patients exhibit a higher Firmicutes/Bacteroidetes ratio. Treatment with GLP leads to an increased abundance of *Adlercreutzia* and *Rothia*, which are known to modulate intestinal disorders, enhance host immune function, and attenuate inflammatory responses. Furthermore, GLP significantly elevates the levels of *Lactococcus* – a beneficial bacterium critically involved in the treatment of metabolic diseases [63].

Complications of diabetes. Diabetes complications are one of the main health threats faced by diabetes patients, including diabetic nephropathy, diabetic cardiovascular disease, and diabetic neuropathy [64]. These complications severely affect patients' quality of life, increase the risk of death, and place a heavy burden on families and society. Research has shown that *G. lucidum* also shows potential in improving these complications.

Diabetic nephropathy. Dysregulation of glucose and lipid metabolism is one of the primary causes of diabetic nephropathy. With the increasing number of newly diagnosed cases and a five-year survival rate of approximately 20%, diabetic nephropathy has garnered significant attention [65]. GLP exhibit renal protective effects. GLP exerts significant protective effects in diabetic nephropathy by reducing renal pathological damage, lowering blood glucose and glycated hemoglobin levels, and improving renal function through reduced serum creatinine, blood urea nitrogen, and 24-hour urine protein levels, as well as renal α. GLP inhibits the PI3K/Akt/mTOR signaling pathway and suppresses apoptosis markers such as caspase-3 and caspase-9 expression. These effects may be mediated by stimulating beclin-1, activating autophagy through LC3-II/LC-I, and reducing p62 expression. These findings may help explain the molecular mechanisms underlying GLP's ability to alleviate renal tissue fibrosis, suggesting its potential application in the treatment of diabetic nephropathy [66]. *G. lucidum* polysaccharides can protect kidney tissue by inhibiting inflammatory responses and oxidative stress. For example, *G. lucidum* water extracts can reverse albumin-induced tubulointerstitial injury and reduce intracellular ROS production.

Diabetic cardiomyopathy. Cardiovascular disease is one of the major complications of diabetes. Hyperglycemia leads to increased production of reactive oxygen species and promotes the secretion of pro-inflammatory cytokines, which subsequently cause oxidative stress and inflammation, thereby triggering cardiovascular disease.

Certain active components of *G. lucidum* can prevent the progression of cardiovascular disease in diabetes [67]. Diabetic cardiomyopathy is the leading cause of death among diabetes complications. This is a diabetes-induced pathophysiological condition independent of hypertension-related heart disease, coronary artery atherosclerotic heart disease, valvular heart disease, and other heart diseases. *G. lucidum* polysaccharides alleviate diabetic cardiomyopathy by activating the Nrf2 antioxidant pathway, controlling inflammation through the NLRP3/Caspase-1/IL-1β signaling pathway, and utilizing gut microbiota metabolites [68]. *G. lucidum* polysaccharides can improve cardiac function in rats with heart failure, inhibit myocardial fibrosis, improve myocardial energy metabolism, and reduce p38/MAPK signal activation levels. *G. lucidum* polysaccharides can inhibit the production of inflammatory factors such as TNF-α and IL-6, increase the production of anti-inflammatory factors, and protect myocardial cells. Studies have shown that diabetes is associated with atherosclerosis through mechanisms such as inflammation and oxidative stress [69]. *G. lucidum* prevents and treats atherosclerosis through mechanisms such as antioxidant effects, repairing damaged endothelial cells by increasing the number of endothelial progenitor cells, exerting anti-inflammatory effects during macrophage phenotype conversion, and regulating intestinal microbiota by influencing short-chain fatty acid levels [70]. *G. lucidum* spore ethanol extract exerts lipid-lowering and anti-atherosclerotic effects by upregulating the expression of liver X receptor and downstream genes associated with reverse cholesterol transport and metabolism, providing new strategies and directions for atherosclerosis prevention [71]. *G. lucidum* polysaccharide peptides exhibit significant anti-inflammatory, antioxidant, and anti-lipid metabolism disorder effects in the treatment of diabetic cardiomyopathy, effectively improving the condition of patients with diabetic cardiomyopathy. They hold promise as an adjunctive therapy for coronary artery disease caused by atherosclerosis [72].

Diabetic retinopath. Diabetic retinopathy is the most common microvascular complication of diabetes and one of the leading causes of blindness [73]. Vascular endothelial growth factor (VEGF) is upregulated in diabetic eyes and has been identified as a key driver of DR pathogenesis. Chronic hyperglycemia induces inflammation, leading to leukocyte stasis and capillary nonperfusion, resulting in hypoxia, which stimulates VEGF expression [74]. Studies have shown that the active components of *G. lucidum* can inhibit VEGF production, thereby improving diabetic retinopathy. GLP achieves this by directly inhibiting vascular endothelial cell proliferation and inducing cell death, as well as indirectly suppressing VEGF production within cells [75]. *G. lucidum* polysaccharides and methanol extracts can inhibit VEGF production in tumors, with the methanol extract acting through the Erk and Akt pathways [76].

Diabetic foot ulcers. Diabetic foot ulcers are the most common lower limb complication in diabetic patients, with the primary causes primarily attributed to diabetic peripheral vascular disease, neuropathy, and wound infection [77]. Hyperglycemia slows healing, and non-healing ulcers may lead to amputation of the toes, part of the foot, or the lower leg, posing serious risks to patients [78]. The mechanisms of action of *G. lucidum*'s active components in the treatment of diabetic foot ulcers are complex, involving immune regulation, antioxidant effects, anti-inflammatory properties, and improved microcirculation. These mechanisms work together to create favorable conditions for the healing of diabetic foot ulcers. Extracts from *G. lucidum* fruiting bodies have a significant impact on wound healing in mouse skin and the acceleration of human fibroblasts. Studies have shown that *G. lucidum* water extracts can significantly accelerate wound healing and improve wound healing rates by promoting THP-1 cell proliferation and enhancing the migratory capacity of NIH/3T3 cells. Additionally, during treatment, *G. lucidum* extracts enhance antioxidant capacity in rats and reduce oxidative damage. This suggests that *G. lucidum* extracts may have a positive effect on diabetic foot ulcers through antioxidant and wound-healing mechanisms [79]. *G. lucidum* polysaccharides may promote wound healing by activating the Wnt/β-catenin signaling pathway and upregulating TGF-β1, which may be a promising source for skin wound healing [80]. *G. lucidum* polysaccharides accelerate the healing of refractory wounds in diabetic patients by inhibiting mitochondrial oxidative stress [81]. *G. lucidum* spore oil (GLSO) can regulate the skin microbiome to accelerate skin wound healing and downregulate inflammation. GLSO significantly accelerated the skin wound healing process and regulated the levels of Gram-negative and Gram-positive bacteria. Additionally, GLSO reduced the levels of LPS, TLR4, and other related inflammatory cytokines [82]. In the field of diabetic wound healing, the application of novel materials has become an important research direction. *G. lucidum* polysaccharide-carboxymethyl chitosan hydrogel (G-GLP) accelerates the healing of full-thickness wound models by reducing inflammation, promoting vascular repair, and enhancing collagen deposition [83]. These results indicate that G-GLP has the potential to serve as an effective wound repair dressing. The discovery of these potential therapeutic applications for accelerating skin healing provides scientific evidence for the use of *G. lucidum* in the treatment of diabetic foot ulcers.

G. lucidum improves lipid metabolism

Hyperlipidemia. Hyperlipidemia is a common metabolic disorder characterized by abnormally elevated blood lipid levels, and it is an important risk factor for cardiovascular diseases such as atherosclerosis and coronary heart disease. With the deepening of research into natural medicines, *G. lucidum*, a traditional medicinal fungus, has increasingly drawn attention for its potential value in treating hyperlipidemia. Studies have shown that *G. lucidum* polysaccharides have a positive impact on lipid levels. Research indicates that *G. lucidum* polysaccharides can activate the Nrf2/HO-1 pathway and inhibit oxidative stress reactions, thereby reducing lipid levels and improving hyperlipidemia [84]. *G. lucidum* polysaccharides exert their lipid-lowering effects by reducing the levels of malondialdehyde in serum and the small intestine, enhancing the antioxidant enzyme system, and inhibiting lipid peroxidation reactions and cell apoptosis [85]. The activation of the NF-κB inflammatory signaling pathway promotes ROS release and oxidative stress, making it one of the key factors in lipid abnormalities. The Nrf2 transcription factor activates downstream antioxidant gene transcription by degrading Keap1. *G. lucidum* mycelium polysaccharides can activate the Nrf2-Keap1 pathway, inhibit the NF-κB signaling pathway, improve oxidative stress and inflammatory responses, alleviate abnormal expression of SREBP1C and PPARα, positively regulate lipid metabolism-related proteins, and simultaneously promote cholesterol transport from peripheral tissues to the liver via the ABCA1/ABCG1 signaling pathway, thereby lowering serum cholesterol levels and exerting a lipid-lowering effect. This has a significant role in improving lipid metabolism disorders in the liver and reducing excessive lipid accumulation. *G. lucidum* polysaccharide F31 promotes AMPK phosphorylation and reduces the level of hepatic glucose-regulating enzyme mRNA in liver tissue, increases GLUT4 levels, and reduces body weight [86].

Studies have shown that in a mouse model of hyperlipidemia, Ganoderic acid A significantly reduces serum total cholesterol (TC), TG, and LDL-C levels while increasing HDL-C levels. Additionally, Ganoderic Acid A can improve intestinal microbiota composition by regulating the composition of gut microbiota, the relative abundances of *Prevotella*, *Blautia*, *Ruminococcus*, and *Isobaculum* were increased, while those of *Turicibacter*, *Clostridium* XIII, *Clostridium* XIVa, *Romboutsia*, and *Roseburia* were decreased. This shift was associated with elevated short-chain fatty acid levels and an improved gut microecological environment, ultimately influencing host lipid metabolism. These findings provide new evidence that Ganoderic acid A alleviates disorders of lipid metabolism and ameliorates gut microbiota dysbiosis [87, 88]. *G. lucidum* spores *G. lucidum* spore polysaccharides can inhibit obesity and hyperlipidemia induced by a high-fat diet in C57BL/6J mice. The mechanism may be related to regulating the intestinal microbiota, maintaining intestinal barrier function, increasing short-chain fatty acid production, influencing

GPR43 expression, and inhibiting the TLR4/Myd88/NF-κB signaling pathway [89]. *G. lucidum* polysaccharide peptides (GLPP) improve hyperlipidemia caused by lipid metabolism disorders by regulating intestinal microbiota structure and modulating genes involved in liver lipid and cholesterol metabolism. Oral administration of GLPP significantly alleviates dyslipidemia by reducing TG, TC, free fatty acids, and LDL-C, and significantly inhibits liver lipid accumulation and steatosis, thereby exerting a hypolipidemic effect. Additionally, GLPP treatment can regulate the mRNA expression of genes involved in hepatic lipid metabolism and promote the excretion of total bile acids in feces [90]. *G. lucidum* holds great potential as a dietary supplement or adjunctive therapy for hyperlipidemia [91].

Non-alcoholic fatty liver disease. Non-alcoholic fatty liver disease (NAFLD) has a global prevalence of up to 25%, and its high prevalence makes it the fastest-growing cause of liver-related deaths worldwide, becoming the primary cause of chronic liver disease globally and attracting widespread attention. It begins as simple fatty degeneration (non-alcoholic fatty liver) and can progress to more severe non-alcoholic steatohepatitis (NASH). Notably, NASH often progresses to end-stage liver diseases such as liver fibrosis, cirrhosis, and hepatocellular carcinoma. Therefore, there is an urgent need to develop effective therapies to halt or reverse this progression [92]. Disruptions in glucose and lipid metabolism induce the onset and progression of NAFLD through multiple mechanisms, which interact to form a complex pathophysiological network [93]. *G. lucidum*, with its multiple bioactive components and hepatoprotective effects, has been proposed as a potential therapeutic option for non-alcoholic fatty liver disease. In mice with type 2 diabetes, GLP regulates lipid metabolism by activating the FAM3C-HSF1-CaM signaling pathway, thereby reducing hepatic fat accumulation [94]. *G. lucidum* polysaccharides can also improve insulin sensitivity by inducing white adipose tissue browning and promoting brown adipose tissue differentiation, thereby reducing hepatic lipid accumulation. GLPP improve NAFLD steatosis by regulating bile acid metabolism and inhibiting fatty acid synthesis [95]. Ganoderma triterpenes are one of the main chemical components of *G. lucidum*, most of which have a bitter taste and exhibit pharmacological effects such as hepatoprotection, antitumor activity, and antioxidant properties. Ganoderma triterpenoid compounds promote hepatocyte regeneration, inhibit hepatocyte apoptosis, thereby alleviating liver damage and exerting hepatoprotective effects. A study showed that Ganoderma triterpenes significantly reduced serum triglyceride, total cholesterol, and low-density lipoprotein levels, while significantly increasing high-density lipoprotein levels. Superoxide dismutase and total antioxidant capacity were also significantly higher than in the model group. This suggests that Ganoderma triterpenes have preventive and therapeutic effects on fatty liver in high-fat rats, with the mechanism potentially related to their inhibition of oxidative stress [96].

Discussion

Age-related dysregulation of glycometabolism and lipid metabolism is associated with increased susceptibility to various diseases. As individuals age, changes occur in glycometabolism and lipid metabolism, which may lead to conditions such as diabetes, cardiovascular disease, and non-alcoholic fatty liver disease, posing significant risks to overall health. Aging is a plastic process characterized by the accumulation of damage and the dynamic balance between repair mechanisms, exhibiting both intra-individual and inter-individual heterogeneity. It is intertwined with various biological processes. Therefore, reducing the risk of many chronic diseases associated with aging can be achieved by improving the aging process [97].

G. lucidum, also known as "the auspicious herb", is a traditional Chinese medicine with a long history. With ongoing research advances, over 300 compounds have been isolated from the fruiting bodies, mycelia, and spores of *G. lucidum*. Among these, the bioactive constituents of *G. lucidum* demonstrate significant potential in regulating aging-related disorders of glucose and lipid metabolism, along with broad prospects for clinical application. Numerous preclinical studies have explored the effects of *G. lucidum* on blood glucose control, insulin sensitivity, and complications associated with diabetes. The numerous active components of *G. lucidum* can improve glycometabolic disorders through multi-targeted, multi-pathway mechanisms, including enhancing insulin sensitivity [98], improving insulin resistance [99], regulating lipid synthesis and degradation [100], alleviating metabolic inflammation [101], and reducing oxidative stress [102]. These effects are of great significance for delaying the decline in metabolic function associated with aging.

Clinical application is a crucial basis for evaluating the efficacy and safety of drugs. As research on *G. lucidum* continues to deepen, its clinical applications are also gradually expanding. Pharmaceuticals and health supplements primarily composed of *G. lucidum* have widespread applications in regulating glucose and lipid metabolism. Wu Ling capsules demonstrate good therapeutic efficacy in the clinical treatment of chronic hepatitis B and liver damage. Studies have shown that WL significantly reduces serum ALT and AST levels in rats and improves hepatic pathological abnormalities, primarily by inhibiting the activation of the TLR4-NF-κB signaling pathway to regulate macrophage polarization in liver fibrosis [103]. WL influences hepatic inflammation by regulating the HIF-1α signaling pathway, thereby protecting liver function and treating NAFLD [104]. Additionally, studies have shown that WL has blood sugar-regulating functions and can improve pancreatic function to some extent [105]. Based on the medicinal properties of *G. lucidum*, such as liver protection and blood sugar reduction, researchers have developed various *G. lucidum*-based pharmaceuticals and health supplements, as shown in the figure below. Studies have shown that the mechanisms of action of drugs that improve glucose metabolism include α-glucosidase inhibition, increasing glucose uptake through GLUT4 translocation to improve insulin resistance, improving the PI3K/Akt insulin signaling pathway, improving the expression of glucose and lipid genes, anti-inflammatory effects, and antioxidant effect [106]. The mechanisms of action for improving liver function include regulating fat synthesis and degradation, maintaining calcium homeostasis in hepatocytes, anti-inflammatory effects, antioxidant effects, and improving the TLR4-MyD88/NF-κB signaling pathway [107].

However, the clinical application of *G. lucidum* in improving lipid metabolism disorders still faces challenges. Although *G. lucidum* shows significant potential in improving age-related lipid metabolism disorders, its mechanism of action requires further investigation. Secondly, current clinical studies on *G. lucidum* in the treatment of glucose and lipid metabolism disorders are relatively scarce, and most are small-scale, short-term studies. Therefore, more large-scale, randomized controlled clinical trials are needed to validate the long-term efficacy and safety of *G. lucidum* in improving glucose and lipid metabolism disorders. Additionally, an increasing number of studies have highlighted the limitations of monotherapy and suggested the development of combination therapies. Combination therapies not only enhance treatment efficacy but may also reduce drug doses and minimize adverse reactions. Therefore, the synergistic effects of *G. lucidum* with other medications warrant further investigation.

As *G. lucidum* has been classified under the category of "medicinal and edible substances", its applications have become increasingly widespread. Its active components and health benefits have been extensively validated, driving the development and application of related functional foods. *G. lucidum* spore powder is rich in triterpenoids and polysaccharides, typically formulated into capsules, tablets, or powder packets, and is primarily used to enhance immune function. *G. lucidum* fruiting bodies are primarily used in decoctions, reishi tea, and reishi concentrate to regulate lipid and glucose metabolism. *G. lucidum* mycelium is produced through liquid fermentation technology and is widely used in functional beverages, nutritional supplements, and food additives [108]. However, its limitations have gradually become apparent, primarily due to the wide variety of active components in *G. lucidum*, but in small quantities, making it difficult to prepare single compounds. Products derived from different sources and extraction methods may exhibit significant differences in composition and activity, making standardization and quality control critical issues in the development of *G. lucidum* products. Therefore, enhancing the stability and bioavailability of key active components and establishing stringent quality control standards are of utmost importance. Despite its widespread application, the therapeutic mechanisms of *G. lucidum* for various diseases remain unclear, and there is a lack of comprehensive and systematic in-depth research on the pharmacological mechanisms of its active components. Clinical studies also lack long-term follow-up, and as a popular traditional Chinese medicine, its clinical research urgently needs to be strengthened. Future research should focus on the mechanisms of action of *G. lucidum*'s active components, study on the synergistic effects of *G. lucidum* with other drugs, the development of standardized products, and the conduct of large-scale clinical trials to promote the advancement of *G. lucidum* products in the fields of health and functional foods. In conclusion, as a traditional medicinal fungus, *G. lucidum* demonstrates promising potential in regulating age-related disorders of glucose and lipid metabolism.

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