Food & Medicine Homology

ISSN 3006-6867 (print); 3006-4252 (online)
https://doi.org/10.26599/FMH.2025.9420046

Review Araicle

Hypoglycemic effects of edible fungus polysaccharides: A mini review

Yan-Long Cui[1, 2, 3], Bo Li[3] (✉)

[1] *Postdoctoral Innovation Practice Base, Henan Institute of Science and Technology, Xinxiang 453000, China*
[2] *Postdoctoral Research Center, Henan Bainong Seed Industry Co., Ltd. Xinxiang 453000, China*
[3] *College of Food Science, Henan Institute of Science and Technology, Xinxiang 453000, China*

Received: 28 June 2024 / **Revised:** 10 July 2024 / **Accepted:** 10 July 2024

Abstract: Diabetes mellitus (DM) is a chronic metabolic disorder with the feature of hyperglycemia, which has severely endangered human health. Edible fungus polysaccharides (EFP), which has great development potential, have attracted enormous attention since their natural and safe characteristics as well as obvious benefits against diabetes. This review summarized the hypoglycemic effect of EFP and the underlying mechanism against diabetes by inhibiting digestive enzyme activity, increasing insulin sensitivity and resistance, improving pancreatic function and lipid metabolism, alleviating oxidative stress and inflammation, regulating gut microbiota and signal transduction. In addition, the relationships between structure and hypoglycemic activity as well as future prospect of EFP were also discussed. This current review provides valuable insights for readers and healthcare professionals developing preventive and therapeutic of diabetes and development of functional products or foods of edible fungi in the future.

Keywords: edible fungus; polysaccharides; hypoglycemic effect; mechanisms

Citation: Cui Y. L., Li B. Hypoglycemic effects of edible fungus polysaccharides: A mini review. *Food & Medicine Homology*, 2025, 2: 9420046. https://doi.org/10.26599/FMH.2025.9420046

1 Introduction

Diabetes mellitus (DM) is a kind of chronic metabolic disorder characterized by chronic hyperglycemia, mainly owed to deficiency insulin output or impaired cellular response to insulin in the human body[1]. According to a survey conducted by International Diabetes Federation in 2021, 536.6 million (ages from 20 to 79) people suffering from diabetes mellitus around the world, and the number of people is expected to reach 783.2 million by 2045[2]. Clinical treatment of DM is generally applied via insulin injection or oral hypoglycemic medicaments, which mainly contains biguanide hypoglycemic agents[3], α-glucosidase inhibitors[4], thiazolidinediones[5], and sulfonylureas[6]. Nevertheless, oral chemical drugs or biological injections may lead to obvious side effects in gastrointestinal tract (such as vomiting, diarrhea and other adverse reactions) and tolerability issues[7]. Interestingly, it was found that various sources of natural products or extracts, including polysaccharides, polyphenols, alkaloids, flavonoids as well as others, displaying positive hypoglycemic capacities and minimal toxicity *in vivo* or *vitro* experiments[8]. Notably, natural polysaccharides are not only regarded as one base of tissue structure and body energy but also possess efficient hypoglycemic capacity, which is one of the hot topics in the research field of polysaccharide bioactivity over recent years[9].

Edible fungus, also widely called as mushrooms, are found approximately around 15 thousand species all over the world[10]. In recent years, edible fungus have attracted increasing attention attributed to nutritive and medicinal values and generous bioactive ingredient, including active polysaccharides[11], proteins[12], glycosides[13], polyphenols[14], terpenoids[15], and organic acids[16]. Polysaccharide is one of the major components in edible fungus and have various medicinal and health benefits. Various investigations have shown that EFP possess various medicinal effects, such as immunomodulatory, antioxidant, anti-inflammatory and hypoglycemic effect[17,18]. Moreover, many investigations revealed that EFP play a vital role in relieving oxidative stress and inflammation, promoting glucose and lipid metabolism, regulating signal transduction, and reshaping gut microbiota, which might be interrelated to the process of morbidity and development of diabetes, implying a prospective therapeutic agent of EFP on DM[19-25].

In this review, we provide an all-encompassing insight into the hypoglycemic properties, potential molecular mechanisms and examine structure-hypoglycemic activity relationship of EFP. This review will give readers a deep understanding of the hypoglycemic property of EFP. Moreover, we hope it can help to find more novel EFP with higher hypoglycemic activity and new hypoglycemic mechanisms, which is crucial for developing personalized dietary EFP and therapeutic strategies to prevent diabetes in the future.

Address correspondence to Bo Li, libo@hist.edu.cn

2 Hypoglycemic mechanisms of polysaccharides from edible fungus

Many pharmacological researches have proved that various sources of EFP could own hypoglycemic capabilities via multiple mechanisms, such as regulating enzymatic activity, regulating gut microbiota, repairing impaired islet β-cells, alleviating oxidative stress, and reducing inflammation. The latent hypoglycemic mechanisms of EFP in this study are showed in Fig. 1.

CAT (Catalase), SOD (Superoxide dismutase), ROS (Reactive oxygen species), GSH-Px (Glutathione peroxidase), MDA (Malondialdehyde), AGEs (Advanced glycation end products), PDX-1 (Pancreatic duodenal homeobox-1), iNOS (Inducible nitric oxide synthase), GP (Glycogen phosphorylase), Bcl-2 (B-cell lymphoma-2), GSK-3 (Glycogen synthase kinase 3), PEPCK (Phosphoenolpyruvate carboxykinase), PK (Pyruvate kinase), HK, Hexokinase), GS (Glutamine synthetase), GLUT4 (Glucose transporter 4).

2.1 Inhibition of digestive enzymes activities

It is well known that dietary polysaccharides possess inhibitory activity towards to α-amylase and α-glucosidase, which related to the digestion and absorption of digestible carbohydrate[26]. Inhibiting the activities of α-amylase and α-glucosidase presents the ability to block the hydrolysis of dietary starch into glucose and block glucose absorption in the human body, leading to goal of controlling postprandial hyperglycaemia. According to the reports, EFP form *Pleurotus eryngii* and *Hypsizygus marmoreus* also showed α-glucosidase inhibitory capacity with the IC_{50} values of 0.2971 mg/mL and 0.832 mg/mL, respectively[27,28]. *Lentinula edodes* polysaccharides (LEP) was treated by γ-irradiation, characterized its chemical composition, physicochemical features, and then measured its inhibitory capabilities to α-amylase and α-glucosidase *in vitro*. The experimental data also revealed that the molecular weight (*Mw*) of LEP was 301.0–691.2 kDa. In addition, the IC_{50} values range of LEP inhibitory activities towards to α-amylase and α-glucosidase were 1.22–2.40 mg/mL and 1.20–3.93 mg/mL[29]. A novel neutral exopolysaccharide from *Cordyceps militaris*, named EPS-III, was a homogeneous polysaccharide owned the average *Mw* of 1.56×10^3 kDa, which contained mannose (Man), glucose (Glc), and galactose (Gal) with the molar ratios of 1.68: 1: 1.83. EPS-III showed α-glucosidase inhibitory rate of 55.94% at 3 mg/mL. Moreover, EPS-III could dramatically relieve diabetes via relieving weight loss, reducing plasma glucose concentration, and increasing glucose tolerance in streptozotocin (STZ) induced diabetic mice experimental model[30]. Besides, a study found that *Cantharellus yunnanensis* polysaccharide (CY-2) inhibit α-glucosidase activity with the inhibitory rate of 79.24% at 1 mg/mL. When compared to metformin, CY-2 also owned a superior activity to increase blood glucose consumption and metabolism in HepG2 cells[31]. A novel *Tricholoma matsutake* polysaccharide (Tmp) contained arabinose (Ara), Man, Glc and Gal with the molar ratios of 1.9: 13.6: 42.7: 28.3, respectively, with an average *Mw* of 72.14 kDa. Tmp could inhibit α-amylase and α-glucosidase activities with the IC_{50} values of 0.10 mg/mL and 3.75 mg/mL[32]. In addition, there are other similar reports listed in Table 1. These above reported studies offer relevant insights into the potential of EFP to inhibit some key enzymes involved in glucose metabolism in human body, potentially being conducive to managing DM. Generally, it is clear that EFP could effectively inhibit α-amylase and α-glucosidase activities and reach the purpose of controlling blood sugar level. However, future research needs to be conducted to explore the prospective enzyme activities of EFP and their clinical implications.

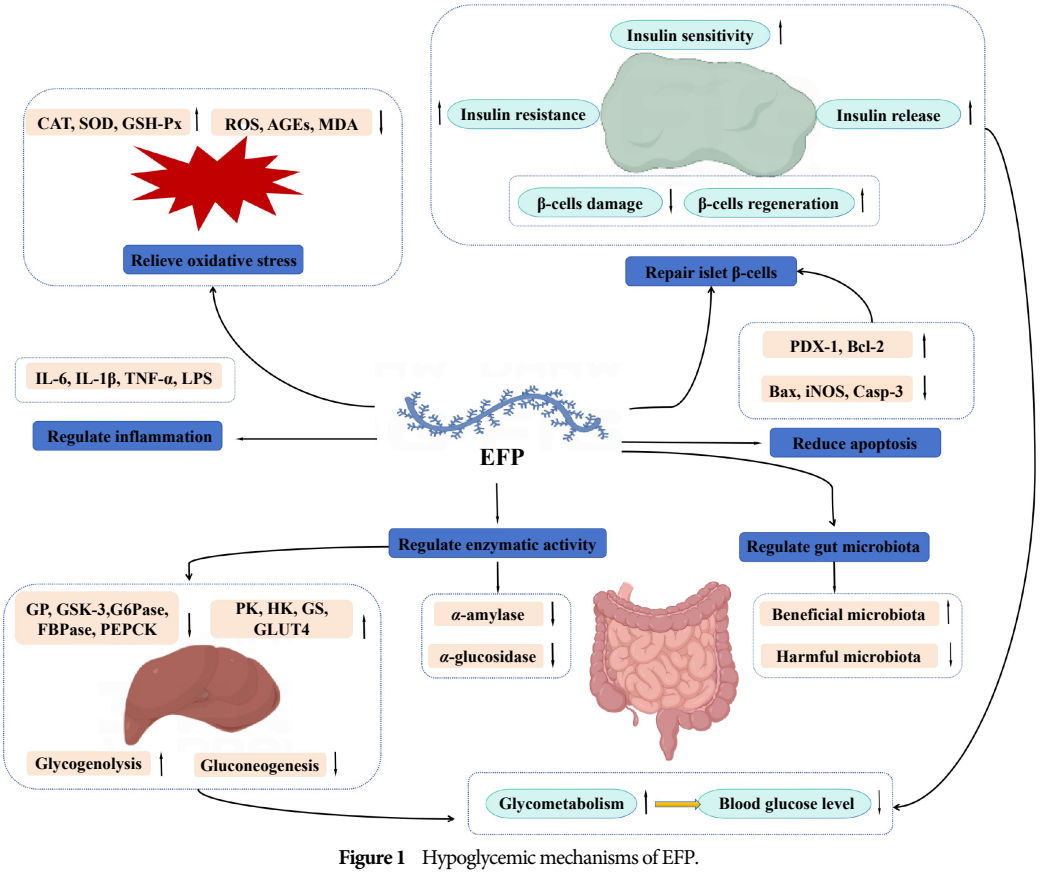

Figure 1 Hypoglycemic mechanisms of EFP.

Table 1 The effects of EFP on digestive enzymes

Source	Name	Molecular weight (kDa)	Monosaccharide composition	Molar ratio	Experimental models	Hypoglycemic effects	Reference
Lentinula edodes	LEP4	492.4	Man, Rib, Rha, GlcA, Glc, Xyl, Ara and Fuc	1.00: 0.03: 0.03: 0.21: 0.55: 0.01: 0.18: 0.08	α-amylase and α-glucosidase inhibitory activity	1.25 and 2.91 ($IC_{50,}$ mg/mL)	[29]
	LEP8	472.1	Man, Rib, Rha, GlcA, Glc, Xyl, Ara and Fuc	1.00: 0.03: 0.07: 0.44: 1.15: 0.02: 0.14: 0.29	α-amylase and α-glucosidase inhibitory activity	1.64 and 3.93 ($IC_{50,}$ mg/mL)	
Schizophyllum commune	UE-SPGs	11.0 and 2.1	Man, Rib, Rha, GlcA, GalA and Glc	1: 0.09: 0.22: 0.26: 3.12: 0.17	α-amylase and α-glucosidase inhibitory activity	64.62% and 60.83% (10 mg/mL)	[85]
	ME-SPGs	16.6 and 1.0	Man, Rha, GlcA, GalA, Fuc and Glc	1: 0.23: 0.32: 5.35: 0.17: 0.09	α-amylase and α-glucosidase inhibitory activity	61.73% and 52.32% (10 mg/mL)	
	HWE-SPGs	527.2 and 1.9	Man, Rib, Rha, GlcA, GalA, Glc, Gal, Xyl, Ara and Fuc	(1: 0.08: 0.27: 0.15: 8.08: 0.41: 0.04: 0.02: 0.05: 0.02	α-amylase and α-glucosidase inhibitory activity	56.71% and 51.05% (10 mg/mL)	
	HPE-SPGs	15.9 and 2.3	Man, Rha, GlcA, GalA and Glc	1: 0.26: 0.29: 3.05: 0.18	α-amylase and α-glucosidase inhibitory activity	55.89% and 37.60% (10 mg/mL)	
Tremella fuciformis	UAP	-	-	-	α-amylase inhibitory activity	77.78% (5 mg/mL)	[86]
	EAP	-	-	-		71.08% (5 mg/mL)	
	EUP	-	-	-		77.99% (5 mg/mL)	
Cantharellus yunnanensis	CY-2	26.90	Glc and Man	33.5: 56.9	α-glucosidase inhibitory activity	79.24% (1 mg/mL)	[31]
Hypsizygus marmoreus	HMP-1	1.92×10^3	Man, Glc and Gal	1.15: 5.2826: 1.16	α-glucosidase inhibitory activity	0.832 ($IC_{50,}$ mg/mL)	[27]
Tricholoma matsutake	Tmp	72.14	Ara, Man, Glc and Gal	1.9: 13.6: 42.7: 28.3	α-glucosidase and α-amylase inhibitory activities	3.75 and 0.10 ($IC_{50,}$ mg/mL)	[32]

Note: -, Not detected. Ara (arabinose), Rib (ribose), Fuc (fucose), Man (mannose), Glc (glucose), Gal (galactose), Rha (rhamnose), GlcA (glucuronic acid), GalA (galacturonic acid), Xyl (xylose).

2.2 Improve insulin sensitivity and insulin resistance

During the past several decades, the antidiabetic medications have been developed by targeting insulin secretion and insulin sensitivity[33]. EFP can be considered as potential hypoglycemic healthy food owing to their abilities to lower blood sugar, increase insulin sensitivity and improve insulin resistance. For instance, in Hepa1-6 cells, the treatment of 0.1 mg/mL neutral alkali-soluble *Armillaria mellea* polysaccharide (AAMP-N) could stimulate insulin-mediated phosphorylation of insulin receptor (IR) as well as its downstream kinase of AKT. In addition, AAMP-N ameliorated damaged glucose tolerance in db/db mice in the 2 h period of glucose tolerance tests (GTT), with the hypoglycemic rate ratio of 30%. Thus, AAMP-N could show hypoglycemic effects via decreasing blood glucose and improving insulin sensitivity[34]. *Grifola frondosa* polysaccharide fraction (GF5,000), the *Mw* of which was greater than 5,000 Da, could improve insulin resistance via restoring the gut microbiota dysbiosis in diabetic rat[35]. Although the inflammation, serious renal injury and inferior insulin sensitivity were occurred in diabetic mice, the treatment of *Ganoderma lucidum* polysaccharide (F31) could relieve inflammatory factor release, ameliorate carbohydrate metabolism, and upgrade insulin sensitivity, resulting to the purpose of protecting the kidney function and inhibition of gluconeogenesis in diabetic mice[36]. Hence, the above reports demonstrated the role of EFP in the amelioration of insulin sensitivity and insulin resistance, and provided theoretical basis for the advancement of EFP as a kind of potential hypoglycemic healthy foods in the future.

2.3 Regulation of key enzymes expression in glycolysis and glucose metabolism

The liver is a meaningful organ which can regulate blood glucose levels in the human body. Glucose metabolism in liver cells mainly contain glycogenolysis and gluconeogenesis. Recent studies have shown that EFP can regulate blood sugar levels and glucose metabolism. For example, a polysaccharide from *Grifola frondosa* (GFP) was proved to have the ability to enhance the absorptive capacity of glucose in HepG2 cells with a dose-dependent behavior at 30 μg/mL during 24 h. The experimental data revealed that the treatment of GFP can activate insulin receptor protein (IRS) and increase the expression level of phosphorylated-AktSer473, which can restrain the activation of glycogen synthase kinase (GSK-3) and synthesis of intracellular glycogen[37]. In a mice study, the hepatic mRNA expression levels of glucose transporter 4 (GLUT4), glucose-6-phosphatase (G6Pase), fructose 1,6-bisphosphatase (FBPase) as well as phosphoenolpyruvate carboxykinase (PEPCK) were significantly increased in high-fat diet (HFD) and STZ-induced type 2 diabetes mellitus (T2DM) mice, while the situation was significantly revered after the treatment of GFP (900 mg/kg day) in T2DM mice. However, GFP could not significantly increase the expression levels of PI3K and Akt[38]. Moreover, in insulin-resistant-human hepatoma cell line (IR-HepG2) experiment, the treatment of *Tricholoma matsutake* polysaccharide (Tmp) could improve the glucose consumption and increase activities of hexokinase (HK) and pyruvate kinase (PK), resulting the increase of glycolysis and glucose metabolism[32]. In another study, *Ganoderma lucidum* polysaccharides (GLPs) was prepared and investigated the hypoglycemic effects and mechanisms of oral gavage of GLPs in experimental T2DM mice. The corresponding results showed that GLPs could decrease the epididymal fat/BW ratio and markedly decrease hepatic mRNA expression levels of PEPCK, glycogen phosphorylase (GP), FBPase, as well as G6Pase[39]. Based on the above analysis results, we found that EFP own the hypoglycemic capacities via regulating glycolysis and glucose metabolism.

2.4 Antioxidant and anti-inflammation activity

Excessive oxidative stress and inflammation in the body have been regarded as frequent risk factors involved to the pathogenesis of diabetes and related metabolic disorders, as the total antioxidant defense might be reduced because of dyslipidemia and hyperglycemia in prediabetes. It was reported that some EFP

exhibited hypoglycemic activity by protecting the body from oxidative stress (Table 2). For example, in STZ-induced diabetes mice, *Inonotus obliquus* polysaccharides (IOs) increased the expression levels of catalase (CAT), superoxide dismutase (SOD), and glutathione peroxidase (GSH-Px) and decreased the production of malondialdehyde (MDA) in serum[40]. *Auricularia polytricha* polysaccharide (APP) inhibited oxidative stress induced by STZ via decreasing the levels of AR, reactive oxygen species (ROS), MDA, advanced glycation end products (AGEs), as well as MG and improving the levels of SOD, CAT and glutathione S-transferase (GST) in liver tissue[41]. Besides, polysaccharides from *Catathelasma ventricosum*, *Grifola frondose*, *Catathelasma ventricosum* and *Cordyceps militaris* also showed hypoglycemic activity via improving antioxidant capacity[42-44].

Once the mice experimental diabetes model was constructed, the hepatic and intestinal tissue in diabetes mice were obviously damaged owing to the presence of serious inflammation and oxidative stress. However, polysaccharides from *Agrocybe cylindracea* residue (PACR) alleviated the inflammation via reducing the levels of IL-1β, IL-6, and lipopolysaccharide (LPS) in liver and colon[45]. Similarly, in STZ-induced diabetic mice experimental model, oral treatment of *Heimioporus retisporus* polysaccharide (HRP) for 4 weeks could significantly reduce blood glucose levels, and reduce the expression levels of IL-6 and TNF-α, resulting the decreasing of heart organ index[22]. Moreover, *Grifola frondose* polysaccharide named PGF could reverse the inflammation via reducing IL-6, IL-1β, TNF-α, TGF-β1 and FN in the renal tissue in STZ-induced diabetes mice[43]. Basing on the above reports, those investigations revealed that EFP possessed positive antioxidant activities， which might protect the severity of diabetes through improving the antioxidant enzymes expression activities, activating Nrf2 pathway and regulating inflammation in organisms.

2.5 Improvement in pancreatic function

The islet of Langerhans consists of endocrine cells (including α-cells, β-cells, and δ-cells) in organism. It is clear that pancreatic β-cells are closely related to producing insulin, which has the ability of converting glucose into energy or glycogen[46]. Emerging evidence revealed that polysaccharides have capabilities to restore and regenerate impaired islet β-cells, consequently reducing blood glucose levels. The situation of underwent compensatory expansion and enlargement of islets was occurred in db/db mice, which might due to peripheral insulin resistance. However, the treatment of AAMP-N reduced blood glucose, modulated lipid metabolism and restored the size of islets, indicating that AAMP-N could protect pancreatic islets from compensatory enlargement[34]. Zhang *et al.*[47] studied the impact of *Ganoderma lucidum* polysaccharides (Gl-PS) on STZ-induced diabetic rats. Their corresponding experimental findings revealed that Gl-PS could alleviate apoptosis of pancreatic β-cells and promote the β-cells regeneration in pancreatic tissues via up-regulating PDX-1 and Bcl-2 mRNA expression levels and down-regulating the expression levels of Bax, iNOS and Casp-3 proteins[47]. In addition, *Cordyceps militaris* polysaccharide (AEPSa) intervention relieved the serious pancreatic damage with an unsharp boundary and atrophy and decreased the contents of serum glucose, total cholesterol (TC) as well as triglyceride (TG) in T2DM mice[48]. These investigations collectively provided robust evidence that EFP can repair islet β-cells and maintain β-cell proliferation,

Table 2 The hypoglycemic effects of EFP involved oxidative stress

Source	Name	Molecular weight (kDa)	Monosaccharide composition	Molar ratio	Experimental models	Mechanism	Reference
Inonotus obliquus	IO1	7,572–32,637	-	-	STZ-induced diabetes	Increased the SOD, CAT and GSH-Px and reduced MDA in serum	[40]
	IO2	2,229–8,564	-	-			
	IO3	245–4,578	-	-			
	IO4	55–3,234	-	-			
	IO5	46–41,508	-	-			
Lentinus edodes	LNT-1	6.41	Rha, Fuc, Ara, GlcA, Gal, Man and Glc	1.00: 6.13: 1.28: 1.79: 20.62: 4.74: 842.17	HFD and STZ induced T2DM	Increased the mRNA and protein expression of the Nrf2 and HO-1 in liver tissue	[64]
Grifola frondosa	GFPS2	2.43–9.62	-	-	STZ-induced diabetes	GFPS2 only enhanced the serum levels of GSH-Px and CAT GFPS3 and GFPS4 groups had strongly enhanced levels of SOD, GSH-Px, and CAT, and reduced levels of MDA and ROS	[23]
	GFPS3	0.85–4.69	-	-			
	GFPS4	0.05–3.35	-	-			
Auricularia polytricha	APP	1.66	Fuc, Glc, Xyl, Gal, Rha, Man and Uronic acid	0.93: 1.00: 2.63: 0.87: 0.90: 0.79: 15.58	STZ-induced diabetic mice	APP decreased the levels of ROS, AGEs, MDA, MG, AR and improved the levels of SOD, CAT and GST in liver sample	[41]
	AAP	15.1		0.49: 1.00: 2.23: 0.86: 0.88: 0.91: 23.76			
Catathelasma ventricosum	CVP-1S	15.00	Glc, Gal and Fuc	94.2: 3.51: 1.3; %	STZ-induced diabetic mice	CVP-1S increased the SOD, CAT and GSH-Px and reduced MDA in liver and kidney	[42]
Cordyceps militaris	AE-PS	-	Fuc, Rib, Ara, Xyl, Man, Gal, and Glc	1.23: 0.57: 0.29: 2.12: 2.73: 4.66: 88.4; %	HFD and STZ induced T2DM	AE-PS increased the SOD, CAT and GSH-Px and reduced MDA in kidney hepatic homogenates and renal homogenates	[44]

Note: Ara (arabinose), Rib (ribose), Fuc (fucose), Man (mannose), Glc (glucose), Gal (galactose), Rha (rhamnose), GlcA (glucuronic acid), Xyl (xylose), HFD (high-fat diet), STZ (streptozotocin), T2DM (type 2 diabetes mellitus), CAT (Catalase), MDA (Malondialdehyde), SOD (Superoxide dismutase), GSH-Px (Glutathione peroxidase), GST (Glutathione S-transferase), ROS (Reactive oxygen), AGEs (Advanced glycation end products), MG (Methylglyoxal), AR (Aldose reductase). -, Not detected.

ultimately reducing blood glucose levels in diabetes.

2.6 Improvement in lipid metabolism

Diabetes patients were characterized by the disorders of glucose and lipid metabolism[49]. *Cordyceps militaris* polysaccharides (CBPS-II), with the average *Mw* of 1.273×10^3 kDa, could decrease the blood glucose concentration, regulate the lipid metabolism and gut microbiota in diabetic mice induced by STZ, indicating that CBPS-II may have potential ability in the management of lipid metabolism[50]. In a present investigation, the treatment of F31 may be upregulate the CYP4A12A expression, showing the ability to participate in lipid metabolism and lower the blood glucose via activating toward GCK[51]. In addition, supplementation of GFP (900 mg/kg day) improved the lipid metabolism via increasing the expressions levels of LDLr, CYP7A1, Acox1 as well as BSEP inhibited the expressions levels of ACC, Cd36, SREBP-1C, and HMGCR in diabetic mice[38]. Therefore, several EFP decrease the blood glucose and regulate the lipid metabolism possibly via increasing the levels of hydroxylase and LDLr and decreasing the specific lipid metabolism related genes. These findings suggest that EFP can protect against diabetic lipid metabolism disorder.

2.7 Regulating signaling pathways

The hypoglycemic features of EFP are mediated by several signaling pathways related to oxidative stress, glucose metabolism, insulin resistance, insulin sensitivity and inflammation. This multidimensional correlation leads to different ranges of hypoglycemic effects, which is involved diverse pathways, observed with EFP. Some notable pathways involved in hypoglycemic effects of EFP including NF-κB, MAPK, AMPK, PI3K/Akt, Nrf2, and PPARs pathways, which are depicted in Fig. 2.

EFP (Edible fungus polysaccharides), ROS (Reactive oxygen species), IR (Insulin receptor), IRS1 (Insulin receptor substrate 1), PI3K (Phosphoinositide 3-Kinase), Akt (Protein kinase B), GLU4 (Glucose transporter 4), AMPK (Adenosine 5'-monophosphate (AMP)-activated protein kinase), GP (Glycogen phosphorylase), PEPCK (Phosphoenolpyruvate carboxykinase), MAPK (Mitogen-activated protein kinase), PPARs (Peroxisome proliferator-activated receptors), PPREs (Peroxisome proliferator response elements), Nrf2 (Nuclear factor erythroid2-related factor 2), Keap1 (Kelch-like ECH-associated protein-1), HO-1 (Heme oxygenase-1), NF-κB (Nuclear factor kappa-B).

2.7.1 *NF-κB signaling pathway*

NF-κB plays a considerable role in diverse bioprocess including inflammation and oxidative stress responses[52]. It is known that the action cytokine (such as TNF-α, IL-6 and IFN-γ) mediated inflammatory response in organism. Oxidative stress responses are characterized by the decrease in antioxidant enzyme levels (such as CAT, SOD, and GSH-Px) and the increase of oxidative stress products (such as ROS and MDA). Increasing evidence has revealed that EFP could regulate NF-κB signaling pathway, alleviate inflammation and oxidative stress responses, and promote insulin levels[40, 43, 48, 53]. Yang *et al.*[53] reported that *Termitornyces albuminosus* polysaccharides (PTA) mainly contained Glc, Gal, Man, Rha, and xylose (Xyl) and had the *Mw* of 11.65 kDa. The potential therapeutic effect of PTA on db/db mice was also evaluated. The results show that PTA could reduce plasma glucose levels and the low-density lipid cholesterol (LDL-C) level, as well as improve the levels of HDL-C. Besides, PTA treatment also regulated the expression levels of IFN-γ, TNF-α, and M-CSF proteins in renal tissue. Furthermore, PTA treatment could also show strong inhibitory activity to the κB alpha (IκBα), κB kinase alpha + beta (IKKα + β) as well as NF-κB p65 in the renal tissue of db/db mice, further indicating that PTA has positive

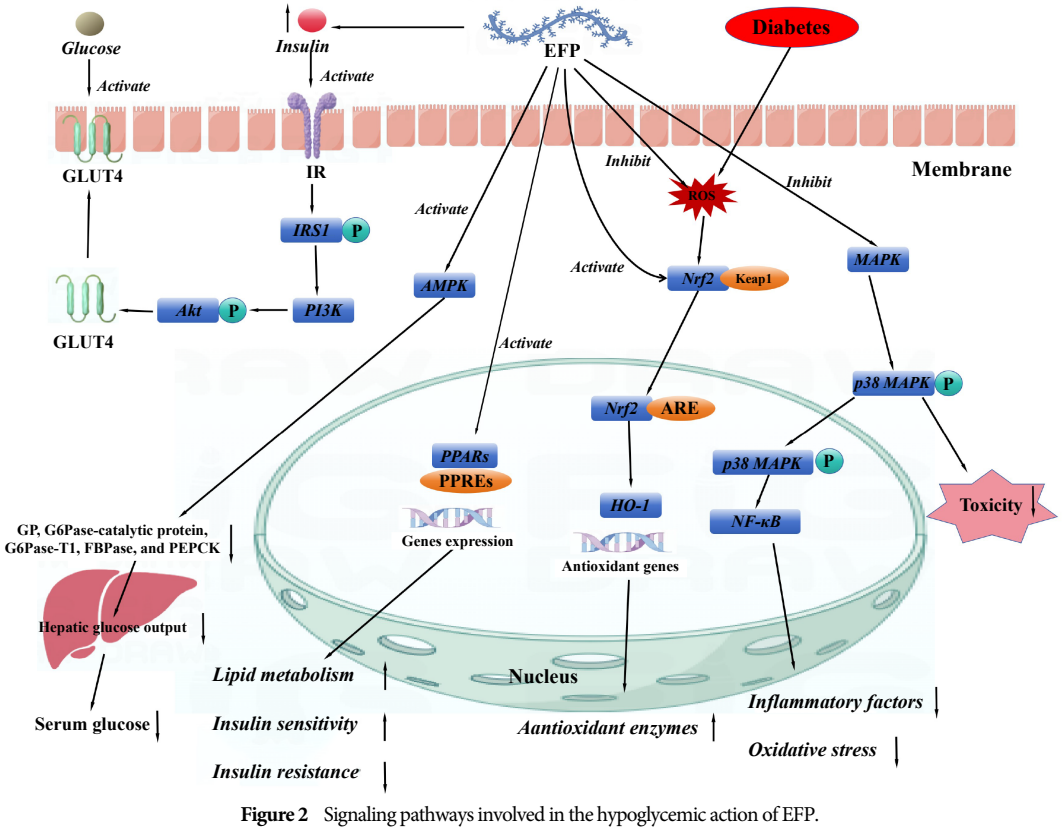

Figure 2 Signaling pathways involved in the hypoglycemic action of EFP.

hypoglycemic ability[53]. *Auricularia auricula* polysaccharides (AAP) could downregulate proinflammatory cytokines (IFN-γ, IL-6 and TNF-α), as well as the oxidative stress (AR, ROS, AGEs and MG), inhibit NF-κB and increase serum insulin in STZ-induced diabetic mice[41]. Moreover, the oral administration of *Cordyceps militaris* polysaccharide (AEPSa) to HFD/STZ-induced T2DM mice resulted in improved intestinal tight junction protein expression and serum lipid metabolism, decreased glucose level and inflammatory cytokines (IL-6, IL-1β, and TNF-α) in the serum, and inhibited TLR4/NF-κB pathway activation via decreasing the phosphorylation of NF-κB p65 and IκBα[48]. All those above researches proved that dietary EFP could alleviate inflammation and oxidative stress to regulate blood glucose and insulin levels via NF-κB signaling pathway.

2.7.2 *MAPK and AMPK signaling pathway*

Mitogen-activated protein kinase (MAPK) is a prominent pathway for transmitting signals from the cell surface to the nucleus. MAPK has a regulatory effect on bioprocess such as cell proliferation, growth, differentiation, and apoptosis[54]. AMP-activated protein kinase (AMPK) is a metabolic regulatory factor that protects cellular metabolic balance by regulating intracellular metabolic processes such as glucose metabolism. Targeting the p38 MAPK and MAPK pathway has become a kind of prospective therapeutic strategies for managing diabetes and its associated complications through relieving oxidative stress, increasing insulin sensitivity, or regulating hepatic glucose regulatory enzymes. For example, *Agrocybe cylindracea* residue polyscaaharides (PACR) contained Man, ribose (Rib), Rha, GlcA, galacturonic acid (GalA), Glc, Gal, Xyl, Ara and fucose (Fuc) with the ratios 13.69: 4.23: 4.61: 6.31: 1.98: 17.33: 24.03: 8.78: 11.18: 7.86. PACR could relieve T2DM, decrease blood glucose, restore lipid levels, and relieve diabetes-oxidative stress and inflammatory response levels by inhibiting p38 MAPK signaling pathway in STZ-induced experimental diabetic mice[45]. Likewise, Cao *et al.* [55] revealed that a novel *Lentinus edodes* mycelia polysaccharide (LMP) could inhibit the activation of p38 MAPK, JNK, NF-κB signaling pathways as well as activating Nrf2 signaling pathway, resulting the protective effects on islet-β cells. Moreover, a novel *Ganoderma lucidum* polysaccharide fraction (F31) has the *Mw* of 15.90 kDa and contained Glc, Man, Xyl, Ara, Gal, Rib and Uronic acid (67.31: 17.79: 6.87: 3.16: 4.35: 0.52: 18.7; %, w/w). F31 could increase the mRNA levels of GLUT4, while decreasing the levels of fatty acid synthase (FAS), acetyl-CoA carboxylase (ACC1), and resisting in epididymal fat tissue in db/db mice. What's more, F31 activated AMPK pathway via up-regulated the ratio of (p-AMPK)/AMPK in hepatic tissue[56]. Taken together, these studies collectively reveal that EFP can exert hypoglycemic effects by regulating the MAPK and AMPK signaling pathway, activating hepatic glucose regulatory enzymes, reducing relieving oxidative stress, increasing insulin sensitivity, relieving diabetes-oxidative stress and inflammatory response levels in diabetic conditions.

2.7.3 *PI3K/Akt signaling pathway*

It is obvious that PI3K/Akt signaling pathway plays a notable role in regulating blood glucose levels and insulin signal transduction[57-59]. Increasing investigations have demonstrated that EFP can regulate PI3K/Akt signaling pathway, regulate blood glucose level, and increase insulin levels. *Lentinus edodes* polysaccharide (LNT) was extracted by ultrasound-assisted hot water method. The obtained LNT has the *Mw* of 395 kDa and mainly contained Glc, Gal, Man, and Ara with molar ratios of 10.20: 3.03: 1.15: 0.39. LNT could show the inhibitory activities to α-glucosidase and α-amylase and facilitate glucose consumption *in vivo*. Besides, LNT promoted the expression levels of PI3K and P-AKT in PI3K/AKTsignaling pathway, resulting the AKT phosphorylation[60]. Liu *et al.*[58] reported that dietary *ganoderma lucidum* polysaccharides (GLP) could dramatically improve the phosphorylation of Akt, and increase expression levels of glycogen synthase (GS), PI3K-p85, and GLUT4 proteins in HFD and STZ-induced experimental T2DM rats. *Hericium erinaceus* polysaccharides (HEP-C), which has the *Mw* of 263.6 kDa, contained Rha, Ara, Man, Glu, and Gal with the molar ratios of 9.0: 2.0: 1.0:4 0.7: 7.5. HEP-C could protect against hepatic lesions and improve the expression levels of Akt, p-Akt, PI3K-p110, and PI3K-p85 proteins in the livers tissue of STZ-induced experimental diabetic rats[61]. Another research revealed that *Pleurotus eryngii* polysaccharide (WPS) displayed α-glucosidase inhibitory effects with the IC_{50} of 0.4211 mg/mL. Meanwhile, WPS and *Grifola frondose* polysaccharide (GFP-W) promoted the expression levels of PI3K and Akt proteins, resulting to alleviating insulin resistance in IR-HepG2 Cells[28,59]. Basing on the above reports, these investigations revealed that dietary EFP possesses antioxidant abilities and can alleviate syndrome of diabetes via regulating PI3K/AKT pathway in organisms.

2.7.4 *Nrf2 signaling pathway*

The nuclear factor-erythroid 2-related factor 2 (Nrf2) signaling pathway involved in regulating oxidative stress level of the body. Under the hyperglycemia state, the high expression of Nrf2 can effectively decrease the generation of MDA and ROS through managing the expression levels of its downstream related proteins[62,63]. Gong *et al.*[64] reported that *Lentinus edodes* polysaccharide (LNT-1) contained Rha, Fuc, Ara, glucuronic acid (GlcA), Gal, Man and Glc with the molar ratios of 1.00: 6.13: 1.28: 1.79: 20.62: 4.74: 842.17, and owned the *Mw* of 6.41 kDa. The oral administration of LNT-1 evidently decreased the insulin resistance and MDA, promoted the expression of SOD and GSH, and improved the expression levels of the Nrf2/HO-1 mRNA and proteins in HFD and STZ induced experimental T2DM mice[64]. Similarly, *Paecilomyces hepiali* fermented mycelium polysaccharide (PHEA) mainly contained Rha, Gal, and Glc. The average *Mw* of PHEA was 3,011.47 kDa. In db/db mice, the treatment of PHEA markedly restrained the expression of ROS and MDA, and promoted the expression of CAT and SOD, and GSH-Px in serum and renal tissue via enhancing the expression of Nrf2 and HO-1[65]. Hence, EFP could regulate Nrf2 signaling pathway to achieve hypoglycemic activity. Those studies indicated the ability of EFP to regulate Nrf2 signaling pathway, reduce oxidative stress level, offering potential implications for the management of diabetes.

2.7.5 *PPARs signaling pathway*

Peroxisome proliferator-activated receptors (PPARs) are valuable nuclear transcription factors, which involved in maintaining homeostasis of lipid and blood glucose metabolism[66,67]. A previous study conducted by Huang *et al.*[68] explored the effect of *Pleurotus tuber-regium* extracellular polysaccharides (HP, MP and LP) on HFD and STZ induced experimental obese-diabetic mice. The corresponding results reveled that the treatment of extracellular polysaccharides increased fatty acid component n-6/n-3 ratio in serum and hepatic tissue, reduced ratios of MUFA/PUFA and MUFA/SFA. This hypolipidemic feature could be involved to increase expression of

PPAR-α at the levels of mRNA and protein in hepatic tissue ($P < 0.01$)[68]. PPAR-γ displays low expression in the hepatic tissue and skeletal muscles tissue and owns high expression level in the adipose tissue[69]. Through the activation of multiple genes occurred in the different tissues, PPAR-γ could activate multiple genes in the tissues, leading to the reduction of free fatty acid content, remission of insulin resistance, acceleration of glucose oxidation and uptaking of glucose and lipids[54]. *Tremella fuciformis* exopolysaccharides (Tf-EPS) and *Phellinus baumii* exopolysaccharides (Pb-EPS) have been shown to enhance adipose tissue PPAR-γ messenger RNA (mRNA) as well as the serum expression levels of PPAR-γ in ob/ob mice, ultimately leading to improvement of insulin sensitivity and indicating emergent potentiality in the management of lipid metabolism and hypoglycemic effect[70]. These findings collectively suggest that EFP can exert hypoglycemic effects by activating the PPAR-γ signaling pathway, enhancing glucose oxidation expression, accelerating lipids metabolism, and reducing insulin resistance in diabetic conditions.

2.8 Regulation of gut microbiota composition

Gut dysgenesis may play an a etiological role in obesity, diabetes, and cardiovascular disease [71]. Increasing investigations have affirmed the close interaction between dietary polysaccharides and gut microbiota[72]. Excessive intake of high sugar and high-fat diet may ruin the general gut microbiota, which might lead to T2DM or related complicating disease. There are several studies involved hypoglycemic effects of EFP by regulating gut microbiota listed in Table 3. For instance, in a HFD mice study, dietary *Tremella fuciformis* polysaccharides (TP) reduced the Firmicutes/Bacteroidetes ratio[73]. Guo *et al.*[38] reported that GFP extracted from *Grifola frondose* could reduce the relative abundance of *Enterococcus*, *Staphylococcus*, *Aerococcus*, and *Streptococcus*in in T2DM mice, while a polysaccharides fraction F31 from *Ganoderma lucidum* enriched the relative abundance of *Lactobacillus*, *Bacteroides* and *Ruminococcaceae*[74]. AEPSa obtained from *Cordyceps militaris* reshaped gut microbiota by increasing beneficial microbiota and decreasing *Ruminococcus*_torques_group and *Enterococcus*[48]. In addition, *Phellinus linteus* polysaccharides (PLPE) enhanced levels of *Anaerotruncus*, *Lachnospiraceae*-NK4A136, *Eubacterium_xylanophilum*, *Lachnospiraceae*-UCG-006, *Roseburia*, Prevotella 9, *Blautia*, Ruminiclostridium-9, and *Oscillibacter* in T2DM mice[72]. These above studies highlight the importance of gut microbiota homeostasis for the hypoglycemic effect of EFP.

Overall, these previous findings emphasize the need to further explore the hypoglycemic mechanisms of EFP on different signaling pathways, which is vital for developing personalized dietary and therapeutic strategies to prevent DM and its related diseases.

3 Structure-hypoglycemic activity relationship

Natural polysaccharides with virous structures may possess distinct biological activities. Interestingly, the structure of natural polysaccharides is closely related to their biological activity[75]. Since there are few studies on the structure-hypoglycemic biological activity of EFP, it is not easy to relate their hypoglycemic activity to their specific structure. However, some scientific inferences between hypoglycemic properties of dietary EFP and their individual structural features can be made from the published literature. The current studies about EFP mostly focused on individual bioactivity or their structural characteristics, While the relationships between structure and hypoglycemic activity of EFP were rarely reported. In this part, the hypoglycemic EFP with various structural features including *Mw*, monosaccharide composition, individual glycosides, and unique conformation were discussed, and their underlying relationships were deduced in Table 4.

3.1 Molecular weight

The *Mw* of a polysaccharide fragment is closely related to its bioactivity. Generally, polysaccharides with low *Mw* may exhibit more stronger hypoglycemic activity than polysaccharides with high *Mw*, which may be attributed to their higher surface area, better biocompatibility and solubility, easier membrane penetration, as well as effective interaction with receptors and

Table 3 The hypoglycemic effects of EFP involved regulating gut microbiota

Source	Name	Molecular weight (kDa)	Monosaccharide composition	Molar ratio/Percentage ratio (%)	Experimental models	Mechanism	Reference
Tremella fuciformis	TP	10.07 to 66.29	Man, Rha, GlcA, Glc, Gal, and Xyl	15.95: 0.31: 2.47: 1.20: 3.18: 1.72	HFD	TP reduced the Firmicutes/Bacteroidetes ratio	[73]
Grifola frondosa	GFP	18.2-15,850	Rha, Fuc, Man, Gal, GlcA, GalA and Glc	5.18: 9.92: 25.49: 15.02: 9.49: 7.30: 27.59; %	HFD and STZ induced T2DM	GFP reduced the relative abundance of *Streptococcus*, *Enterococcus*, *Staphylococcus* and *Aerococcus*	[38]
Ganoderma lucidum	F31	11.08	Ara, Gal, Glc, Xyl, Man, Rib and Rha	5.32: 5.47: 57.63: 0.84: 25.41: 1.95:3.38; %	HFD and STZ induced T2DM	F31 enriched *Lactobacillus*, *Bacteroides* and *Ruminococcaceae*,	[74]
Cordyceps militaris	AEPSa	87.80	Man, Gal and Glc	2.2: 15.1: 1	HFD and STZ induced T2DM	AEPSa reshaped gut microbiota by increasing Allobaculum, Alistipes, Lachnospiraceae_NK4A136_group and norank_f_Muribaculaceae and decreasing Enterococcus and Ruminococcus_torques_group	[48]
Phellinus linteus	PLPE	-	-	-	HFD and STZ induced T2DM	PLPE enhanced levels of Lachnospiraceae-NK4A136, Lachnospiraceae-UCG-006, Roseburia, Prevotella9, *Blautia*, *Ruminiclostridium-9*, *Eubacterium_xylanophilum*, *Anaerotruncus*, and *Oscillibacter*	[72]

Note: Ara (arabinose), Rib (ribose), Fuc (fucose), Man (mannose), Glc (glucose), Gal (galactose), Rha (rhamnose), GlcA (glucuronic acid), GalA (galacturonic acid), Xyl (xylose), HFD (high-fat diet), STZ (streptozotocin), T2DM (type 2 diabetes mellitus). -, Not detected.

Table 4 Structure-hypoglycemic activity relationship of EFP

Source	Name	Molecular weight (kDa)	Monosaccharide composition	Molar ratio	Experimental models	Dose / Duration	Hypoglycemic effects	Conformation	Reference
Lentinula edodes	LEP0	691.2	Man, Rib, Rha, GluA, Glu, Xyl, Ara and Fuc	1.00: 0.04: 0.03: 0.25: 0.29: 0.03: 0.26: 0.17	α-amylase and α-glucosidase inhibitory activity	0–10.0 mg/mL for 10 min	2.40 and 1.90 ($IC_{50,}$ mg/mL)	-	[29]
	LEP16	301.0		1.00: 0.03: 0.05: 0.42: 0.2: 0.02: 0.15: 0.43			1.22 and 1.20 ($IC_{50,}$ mg/mL)	-	
Grifola frondosa	GFP-W1	916.1	Ara, Fuc, Xyl, Man, Glc and Gal	1.95: 1: 1.49: 1.43: 20.94: 1.13,	Binding rates with sodium cholate and sodium glycocholate	Incubated for 60 min	30.32% and 25.08%	-	[76]
	GFP-W2	2.733×10^4		2.32: 1: 1.30: 1.67: 58.52: 2.65			37.41% and 33.68%	-	
	EP-X1	25.64		6.35: 1: 4.88: 1.41: 3.75: 5.45			47.62% and 38.70%	-	
Thelephora ganbajun	TZP1-1	2.07×10^3	Man, Rha, Gal, and Xyl	4: 1: 83.9: 7.5	α-amylase inhibitory activity	0–1 μg/mL for 10 min	23%	None	[77]
	TZP2-1	4.89	Man, Glc, Gal, and Xyl	5.4: 1: 79.0: 8.1			48.6%	Triple helix conformation	
Armillaria mellea	AAMP-A	-	Glc, Gal, Man, GlcA, and Fuc	9.0: 2.0: 1.0:4 0.7: 7.5	db/db mice	50 mg/kg/day	Reduced blood glucose, ALT and AST levels as well as increased insulin sensitivity	-	[34]
	AAMP-N	-	Glc, Gal and Man	49.8 :25.2 :18.2				-	
Pleurotus eryngii	WPS	450	Rha, Ara, Xyl, Man, Glc, and Gal	0.35: 0.24: 0.45: 0.24: 28.78: 1.10	α-glucosidase inhibitory activity	0–8 mg/mL for 15 min	0.4211 ($IC_{50,}$ mg/mL)	-	[28]
	P-1	22		0.95: 0.64: 0.66: 1.84: 60.69: 0.67			0.2971 ($IC_{50,}$ mg/mL)	-	
Cordyceps militaris	EPS-I	-	-	-	α-glucosidase inhibitory activity	0–3 mg/mL for 15 min	31.56 ± 0.78% (1.25 mg/mL)	None	[30]
	EPS-II	-	-	-			38.32 ± 0.69% (1.25 mg/mL)	None	
	EPS-III	1.56×10^3	Man, Glc, and Gal	1.68: 1: 1.83			44.18 ± 0.45% (1.25 mg/mL)	Triple helix structure	

Note: Ara (arabinose), Rib (ribose), Fuc (fucose), Man (mannose), Glc (glucose), Gal (galactose), Rha (rhamnose), GlcA (glucuronic acid), GalA (galacturonic acid), Xyl (xylose). -, Not detected.

enzymes[54]. For example, two intracellular *Grifola frondosa* polysaccharides (named GFP-W1 and GFP-W2) and a *Grifola frondosa* exopolysaccharide (EP-X1) were obtained and their hypolipidemic activity were investigated. The average *Mw* of GFP-W1, GFP-W2 and EP-X1 were 916.1 kDa, 2.733×10^4 kDa and 25.64 kDa, respectively. The experimental sodium cholate binding rates of GFP-W1, GFP-W2 as well as EP-X1 were showed as 30.32%, 37.41%, and 47.62%, respectively. In addition, the corresponding binding rates of them towards to sodium glycocholate were showed as 25.08%, 33.68%, and 38.70%, respectively. Thus, EP-X1 owned the strongest cholate-binding ability, which might be related to its lower *Mw* and more revealable hydroxyl groups[76]. In addition, two novel *Thelephora ganbajun* fruiting bodies polysaccharide components (named TZP1-1 and TZP2-1) were purified via DEAE-52 cellulose ion exchange column and Superdex 200 columns chromatography. The average *Mw* of TZP1-1 and TZP2-1 were showed as 2.07×10^3 kDa and 4.89 kDa, respectively. TZP2-1 (48.6%) displayed higher inhibitory activity on α-amylase than TZP1-1 (23%) in the concentration of 400 μg/mL, which might be related to its lower *Mw* of TZP2-1[77]. Based on above reported literatures, the *Mw* of EFP can affect their hypoglycemic activities to a certain degree. However, further comprehensive exploration is required to study the effect of EFP *Mw* on their hypoglycemic mechanisms.

3.2 Monosaccharide composition

Polysaccharides contained virous monosaccharides and molar ratios may show different hypoglycemic activity, often demonstrated through different monosaccharide composition ratios and the with or without of characteristic monosaccharides[54]. Natural polysaccharides exhibited hypoglycemic activities generally consist of Glc, Gal, Ara, or Xyl, with some of them also contain lesser quantities of galacturonic acid, fucose, or rhamnose[27,54,78]. For example, Gong *et al.*[77] conducted a study investigating the hypoglycemic abilities of two novel polysaccharide purified from *Thelephora ganbajun* mushroom. TZP1-1 contained Gal, Xyl, Man, and, Rha with the molar ratios of 83.9: 7.5: 4.0: 1.0, while TZP2-1 was composed of Gal, Xyl, Man, and Glc, with the molar ratios of 79.0: 8.1: 5.4: 1.0. Then, they also discovered that TZP2-1 exhibit better inhibitory abilities towards to α-amylase and α-glucosidase than TZP1-1, indicating that TZP2-1 possessing stronger hypoglycemic activity in contrast to TZP1-1. This diversity was owed to the deficiency of glucose in the monosaccharide composition of TZP1-1 compared to TZP2-1[77]. Yang *et al.*[34] obtained the neutral polysaccharide (AAMP-N) and acidic polysaccharide (AAMP-A) extracted from *Armillaria mellea*. The results revealed that AAMP-A contained Glc, Fuc, Gal, Man, and, GlcA, with molar ratios of 81.6: 3.1: 3.3: 3.5: 6.0, while AAMP-N contained Glc, Gal and Man with the molar ratios of 49.8: 25.2: 18.2. Interestingly, compared to AAMP-A, AAMP-N showed better hypoglycemic activity via reducing blood glucose, ALT and AST levels as well as increasing insulin sensitivity in db/db mice[34]. In addition, the molar ratio of monosaccharides inside natural polysaccharides similarly plays a significant role in their hypoglycemic effect. For example, a study explored two polysaccharide fractions derived from *Pleurotus eryngii*, namely WPS and P-1. The experimental result of gas chromatography (GC) revealed that they were contained Glc, Man, Rha, Ara, Xyl, and Gal, with the ratios of 60.69: 1.84: 0.95: 0.64: 0.66: 0.67 for P-1 and 28.78: 0.24: 0.35: 0.24: 0.45: 1.10 for

WPS. They also found that P-1 and WPS showed dose-dependent inhibitory effects towards to α-glucosidase, with the IC_{50} values of 0.2971 mg/mL and 0.4211 mg/mL, respectively. This diversity may be attributed to the difference of them in the monosaccharide composition ratios[28].

3.3 Glycosidic bond

Edible fungus contains high content of β-*D*-glucans, especially β-glucan, a type of physiologically active dietary fiber which displayed positive impact in fighting against T2DM[79]. For instance, Gong *et al.*[28] revealed that WPS mainly contained α-glycosidic bonds and β-glycosidic bonds, while P-1 was only dominated by α-glycosidic bonds. They also found that WPS displayed dose-dependent inhibitory manner towards to cellular insulin resistance in IR-HepG2 Cells, but not P-1. This above difference may be attributed to the difference of them in the glycosidic bonds[28]. It was also reported that the 1,3-linked glycosidic bond of polysaccharides were closely related to their hypoglycemic effect[80,81]. For example, *Lentinula edodes* polysaccharides (LNT) can display the inhibitory rates towards to α-glucosidase and α-amylase, achieving 53.92% and 94.85% of the acarbose and relieve insulin resistance via regulating PI3K/AKT pathway in HepG2 cells, which may be related to the high level of 1,3-linked β-glycosidic bond in LNT[60]. Meanwhile, the dominant structure with high content of β-glycosidic bond mostly display high bioactivities in many EFP. Neutral *Hohenbuehelia serotina* polysaccharides (NHSPs) contained mainly 1,4-linked β-*D*-glucose, 1,6-linked α-*D*-mannose, and 1,6-linked β-D-galactose, 1,3-linked β-*D*-glucose, and 1,6-linked β-*D*-mannose and notably reduced the blood glucose level in type 2 diabetic mice[82]. In a word, it is easily revealed that virous glycosidic bonds could partly influence the hypoglycemic effects of EFP.

3.4 Conformation

In most cases, polysaccharides with the triple helix structure may enhance their hypoglycemic activity[83,84]. For example, two novel polysaccharides (TZP1-1 and TZP2-1) were purified from *Thelephora ganbajun*. Interestingly, TZP2-1 displayed better inhibitory activities on α-amylase and α-glucosidase than TZP1-1, which might be related to its triple helix conformation in TZP2-1[77]. Interestingly, three *Cordyceps militaris* polysaccharide fragments named EPS-I, EPS-II, and EPS-III and their inhibitory rates to α-glucosidase were showed as 31.56 ± 0.78%, 38.32 ± 0.69%, and 44.18 ± 0.45% with the concentration of 1.25 mg/mL, respectively. However, only EPS-III owned triple helix structure in NaOH solution, rather than EPS-II and EPS-III[30]. These above studies indicated that EFP with the triple helix structure may have better hypoglycemic effects.

Overall, the hypoglycemic effects of dietary EFP are affected by many factors, including *Mw*, monosaccharide composition, individual glycosides, and unique conformation. Moreover, changes in hypoglycemic bioactivity of EFP may be related to an improved solubility because of the introduced moiety. Future research should pay close attention to the intricate crosstalk between hypoglycemic effects and structure of EFP, which is crucial for developing personalized dietary EFP and therapeutic strategies to prevent diabetes.

4 Conclusion and future prospect

In summary, this current study reveals that EFP' hypoglycemic effects involve inhibiting digestive enzyme activity, increasing insulin sensitivity and resistance, improving pancreatic function and lipid metabolism, alleviating excessive oxidative stress and inflammation, and regulating gut microbiota. In addition, signaling pathways like NF-κB, MAPK, AMPK, PI3K/Akt, Nrf2 and PPARs mediate hypoglycemic effects of EFP. Characteristics of EFP such as *Mw*, monosaccharide composition and its ratio, glycosidic bond types, and triple helix structure affect their hypoglycemic activity. Obtaining EFP with hypoglycemic effects from natural and safe edible fungus and studying their regulatory mechanisms on the body can offer a theoretical basis for the development of new hypoglycemic agent. EFP with hypoglycemic effects have broad application prospects in the fields of functional foods and pharmaceuticals.

However, owing to the wide variety of edible fungus and the complex composition of EFP, there are still certain limitations in the current research on the hypoglycemic effect and prospective mechanism of action of EFP. Meanwhile, we should pay attention to that most reported studies were conducted *in vitro* or in animals, which cannot totally represent the actual effects in human body. Thus, the clinical investigations are needed to study the practical hypoglycemic application of EFP in human. Moreover, as the limitation of research methods and complexity of intracellular process, the hypoglycemic mechanism of EFP is still not fully revealed and needs in-depth investigation in the future. More uncovered targets and signaling pathways related with the hypoglycemic effect of EFP may be revealed in the future.

Regarding to probable future research directions and trends of EFP involved hypoglycemic effects. There are still many issues to be resolved in the future, such as: 1) There are numerous investigations on the hypoglycemic mechanism of EFP, which focus on some specific genes, proteins, and key known metabolic pathways. However, research on the overall metabolic changes that occur in the body under the intervention of EFP is relatively limited; 2) The structure of EFP is complex, and the hypoglycemic effect and prospective mechanism of action of a single component of EFP are relatively limited; 3) Although there are more investigations on the hypoglycemic activity and mechanism of action of EFP at the cellular and animal levels, and there is a lack of clinical trials. Further clinical trial research is needed in human body; 4) The investigation on the hypoglycemic effect of EFP lacks the understanding and treatment of the complications of diabetes. Therefore, it is necessary to deeply study the effect of EFP on the complications of diabetes; 5) The structure-hypoglycemic activity relationship of EFP is still relatively lacking and further in-depth research is needed to achieve the preparation of functional EFP fragments; 6) The development of metabolomics in food nutrition and drug development is not yet fully mature. It is necessary to further combine proteomics and transcriptomics to conduct a joint analysis of multiple genomics and further elaborate scientific issues, to sufficiently comprehend the preventive and therapeutic effects of EFP towards to diabetes.

Conflicts of interest

The authors declare that there are no conflicts of interest in this work.

Acknowledgements

The work was financially supported by Henan institute of science and technology (No. 103020224001/110).

References

[1] Pruhova, S., Dusatkova, P. Monogenic diabetes mellitus hidden in autoantibody-negative diabetes mellitus. *Nature Reviews Endocrinology*, **2023**, 19: 132–133. https://doi.org/10.1038/s41574-022-00800-5

[2] Ogurtsova, K., Guariguata, L., Barengo, N. C. W., et al. IDF diabetes atlas: global estimates of undiagnosed diabetes in adults. *Diabetes Research and Clinical Practice*, **2022**, 183: 109118. https://doi.org/10.1016/j.diabres.2021.109118

[3] Jones, V. C., Dietze, E. C., Jovanovic Talisman, T., et al. Metformin and chemoprevention: Potential for heart-healthy targeting of biologically aggressive breast cancer. *Frontiers in Public Health*, **2020**, 8: 509714. https://doi.org/10.3389/fpubh.2020.509714

[4] Dhameja, M., Gupta, P. Synthetic heterocyclic candidates as promising α-glucosidase inhibitors: An overview. *European Journal of Medicinal Chemistry*, **2019**, 176: 343–377. https://doi.org/10.1016/j.ejmech.2019.04.025

[5] Arnold, S. V., Inzucchi, S. E., Echouffo-Tcheugui, J. B., et al. Understanding contemporary use of thiazolidinediones an analysis from the diabetes collaborative registry. *Circulation-Heart Failure*, **2019**, 12: e005855. https://doi.org/10.1161/circheartfailure.118.005855

[6] Liaw, J., Harhay, M., Setoguchi, S., et al. Trends in prescribing preferences for antidiabetic medications among patients with type 2 diabetes in the UK with and without chronic kidney disease, 2006-2020. *Diabetes Care*, **2022**, 45: 2316–2325. https://doi.org/10.2337/dc22-0224

[7] Zhu, J., Liu, W., Yu, J., et al. Characterization and hypoglycemic effect of a polysaccharide extracted from the fruit of *Lycium barbarum* L. *Carbohydrate Polymers*, **2013**, 98: 8–16. https://doi.org/10.1016/j.carbpol.2013.04.057

[8] Ma, W., Xiao, L., Liu, H., et al. Hypoglycemic natural products with *in vivo* activities and their mechanisms: A review. *Food Science and Human Wellness*, **2022**, 11: 1087–1100. https://doi.org/10.1016/j.fshw.2022.04.001

[9] Xue, H., Hao, Z., Gao, Y., et al. Research progress on the hypoglycemic activity and mechanisms of natural polysaccharides. *International Journal of Biological Macromolecules*, **2023**, 252: 126199. https://doi.org/10.1016/j.ijbiomac.2023.126199

[10] Muszynska, B., Grzywacz-Kisielewska, A., Kala, K., et al. Anti-inflammatory properties of edible mushrooms: A review. *Food Chemistry*, **2018**, 243: 373–381. https://doi.org/10.1016/j.foodchem.2017.09.149

[11] Leong, Y. K., Yang, F. C. and Chang, J. S. Extraction of polysaccharides from edible mushrooms: emerging technologies and recent advances. *Carbohydrate Polymers*, **2021**, 251: 117006. https://doi.org/10.1016/j.carbpol.2020.117006

[12] Zhang, Y., Wang, D., Chen, Y., et al. Healthy function and high valued utilization of edible fungi. *Food Science and Human Wellness*, **2021**, 10: 408–420. https://doi.org/10.1016/j.fshw.2021.04.003

[13] Kang, J. Y., Lee, B., Kim, C. H., et al. Enhancing the prebiotic and antioxidant effects of exopolysaccharides derived from *Cordyceps militaris* by enzyme-digestion. *Lwt-Food Science and Technology*, **2022**, 167: 113830. https://doi.org/10.1016/j.lwt.2022.113830

[14] Zawadzka, A., Janczewska, A., Kobus-Cisowska, J., et al. The effect of light conditions on the content of selected active ingredients in anatomical parts of the oyster mushroom (*Pleurotus ostreatus L.*). *Plos One*, **2022**, 17: 0262279. https://doi.org/10.1371/journal.pone.0262279

[15] Chen, H. Y., Lei, J. Y., Li, S. L., et al. Progress in biological activities and biosynthesis of edible fungi terpenoids. *Critical Reviews In Food Science And Nutrition*, **2023**, 63: 7288–7310. https://doi.org/10.1080/10408398.2022.2045559

[16] Magdziak, Z., Siwulski, M. and Mleczek, M. Characteristics of organic acid profiles in 16 species of wild growing edible mushrooms. *Journal of Environmental Science and Health Part B-Pesticides Food Contaminants and Agricultural Wastes*, **2017**, 52: 784–789. https://doi.org/10.1080/03601234.2017.1356676

[17] Yin, Z. H., Liang, Z. H., Li, C. Q., et al. Immunomodulatory effects of polysaccharides from edible fungus: A review. *Food Science and Human Wellness*, **2021**, 10: 393–400. https://doi.org/10.1016/j.fshw.2021.04.001

[18] Guo, Q., Liang, S., Ge, C., et al. Research progress on extraction technology and biological activity of polysaccharides from edible Fungi: A review. *Food Reviews International*, **2023**, 39: 4909–4940. https://doi.org/10.1080/87559129.2022.2039182

[19] Hwang, H. S., Yun, J. W. Hypoglycemic effect of polysaccharides produced by submerged mycelial culture of *Laetiporus sulphureus* on streptozotocin-induced diabetic rats. *Biotechnology and Bioprocess Engineering*, **2010**, 15: 173–181. https://doi.org/10.1007/s12257-009-0160-6

[20] Li, Y. M., Zhong, R. F., Chen, J., et al. Structural characterization, anticancer, hypoglycemia and immune activities of polysaccharides from *Russula virescens*. *International Journal of Biological Macromolecules*, **2021**, 184: 380–392. https://doi.org/10.1016/j.ijbiomac.2021.06.026

[21] Yang, S., Qu, Y., Zhang, H., et al. Hypoglycemic effects of polysaccharides from *Gomphidiaceae rutilus* fruiting bodies and their mechanisms. *Food & Function*, **2020**, 11: 424–434. https://doi.org/10.1039/c9fo02283j

[22] Feng, X. B., Wang, P., Lu, Y. X., et al. A novel polysaccharide from *Heimioporus retisporus* displays hypoglycemic Activity in a diabetic mouse model. *Frontiers in Nutrition*, **2022**, 9: 964948. https://doi.org/10.3389/fnut.2022.964948

[23] Kou, L., Du, M., Liu, P., et al. Anti-diabetic and anti-nephritic activities of *Grifola frondosa* mycelium polysaccharides in diet-streptozotocin-induced diabetic rats via modulation on oxidative stress. *Applied Biochemistry and Biotechnology*, **2018**, 184: 310–322. https://doi.org/10.1007/s12010-018-2803-6

[24] Chen, Y., Liu, D., Wang, D., et al. Hypoglycemic activity and gut microbiota regulation of a novel polysaccharide from *Grifola frondosa* in type 2 diabetic mice. *Food and Chemical Toxicology*, **2019**, 126: 295–302. https://doi.org/10.1016/j.fct.2019.02.034

[25] Liu, N., Chen, X., Song, J., et al. Hypoglycemic effects of *Auricularia auricula* polysaccharides on high fat diet and streptozotocin-induced diabetic mice using metabolomics analysis. *Food & Function*, **2021**, 12: 9994–10007. https://doi.org/10.1039/d1fo02022f

[26] Cao, H., Ma, S., Guo, H., et al. Comparative study on the monosaccharide compositions, antioxidant and hypoglycemic activities *in vitro* of intracellular and extracellular polysaccharides of liquid fermented *Coprinus comatus*. *International Journal of Biological Macromolecules*, **2019**, 139: 543–549. https://doi.org/10.1016/j.ijbiomac.2019.08.017

[27] Song, Q., Teng, A. G., Zhu, Z. Chemical structure and inhibition on α-glucosidase of a novel polysaccharide from *Hypsizygus marmoreus*. *Journal of Molecular Structure*, **2020**, 1211: 128110. https://doi.org/10.1016/j.molstruc.2020.128110

[28] Gong, P., Long, H., Guo, Y., et al. Isolation, structural characterization, and hypoglycemic activities *in vitro* of polysaccharides from *Pleurotus eryngii*. *Molecules*, **2022**, 27: 7140. https://doi.org/10.3390/molecules27207140

[29] Yin, C., Li, C., Ma, K., et al. The physicochemical, antioxidant, hypoglycemic and prebiotic properties of γ-irradiated polysaccharides extracted from *Lentinula edodes*. *Food Science and Biotechnology*, **2023**, 32: 987–996. https://doi.org/10.1007/s10068-022-01234-5

[30] Sun, H., Yu, X., Li, T., et al. Structure and hypoglycemic activity of a novel exopolysaccharide of *Cordyceps militaris*. *International Journal of Biological Macromolecules*, **2020**, 166: 496–508. https://doi.org/10.1016/j.ijbiomac.2020.10.207

[31] Tian, R., Zhang, Y. Z., Cheng, X., et al. Structural characterization, and *in vitro* hypoglycemic activity of a polysaccharide from the mushroom *Cantharellus yunnanensis*. *International Journal of*

Biological Macromolecules, **2023**, 235: 127200. https://doi.org/10.1016/j.ijbiomac.2023.127200

[32] Yang, H. R., Chen, L. H., Zeng, Y. J. Structure, antioxidant activity and *in vitro* hypoglycemic activity of a polysaccharide purified from *Tricholoma matsutake*. *Foods*, **2021**, 10: 2184. https://doi.org/10.3390/foods10092184

[33] Yang, W., Jiang, W., Liao, W., et al. An estrogen receptor *α*-derived peptide improves glucose homeostasis during obesity. *Nature Communications*, **2024**, 15: 3410. https://doi.org/10.1038/s41467-024-47687-6

[34] Yang, S., Yan, J., Yang, L., et al. Alkali-soluble polysaccharides from mushroom fruiting bodies improve insulin resistance. *International Journal of Biological Macromolecules*, **2018**, 126: 466–474. https://doi.org/10.1016/j.ijbiomac.2018.12.251

[35] Xiao, C., Jiao, C., Xie, Y., et al. *Grifola frondosa* GF5000 improves insulin resistance by modulation the composition of gut microbiota in diabetic rats. *Journal of Functional Foods*, **2021**, 77: 104313. https://doi.org/10.1016/j.jff.2020.104313

[36] Jiao, J., Yong, T., Huang, L., et al. A *Ganoderma lucidum* polysaccharide F31 alleviates hyperglycemia through kidney protection and adipocyte apoptosis. *International Journal of Biological Macromolecules*, **2022**, 226: 1178–1191. https://doi.org/10.1016/j.ijbiomac.2022.11.231

[37] Ma, X., Zhou, F., Chen, Y., et al. A polysaccharide from *Grifola frondosa* relieves insulin resistance of HepG2 cell by Akt-GSK-3 pathway. *Glycoconjugate Journal*, **2014**, 31: 355–363. https://doi.org/10.1007/s10719-014-9526-x

[38] Guo, W. L., Deng, J. C., Pan, Y. Y., et al. Hypoglycemic and hypolipidemic activities of Grifola frondosa polysaccharides and their relationships with the modulation of intestinal microflora in diabetic mice induced by high-fat diet and streptozotocin. *International Journal of Biological Macromolecules*, **2019**, 153: 1231–1240. https://doi.org/10.1016/j.ijbiomac.2019.10.253

[39] Xiao, C., Wu, Q. P., Cai, W., et al. Hypoglycemic effects of *Ganoderma lucidum* polysaccharides in type 2 diabetic mice. *Archives of Pharmacal Research*, **2012**, 35: 1793–1801. https://doi.org/10.1007/s12272-012-1012-z

[40] Wang, J., Hu, W., Li, L., et al. Antidiabetic activities of polysaccharides separated from Inonotus obliquus via the modulation of oxidative stress in mice with streptozotocin-induced diabetes. *Plos One*, **2017**, 12: 0180476. https://doi.org/10.1371/journal.pone.0180476

[41] Xiang, H., Sun-Waterhouse, D. , Cui, C. Hypoglycemic polysaccharides from *Auricularia auricula* and *Auricularia polytricha* inhibit oxidative stress, NF-κB signaling and proinflammatory cytokine production in streptozotocin-induced diabetic mice. *Food Science and Human Wellness*, **2021**, 10: 87–93. https://doi.org/10.1016/j.fshw.2020.06.001

[42] Liu, Y., Chen, D., You, Y., et al. Structural characterization and antidiabetic activity of a glucopyranose-rich heteropolysaccharide from *Catathelasma ventricosum*. *Carbohydrate Polymers*, **2016**, 149: 399–407. https://doi.org/10.1016/j.carbpol.2016.04.106

[43] Jiang, T., Wang, L., Ma, A., et al. The hypoglycemic and renal protective effects of *Grifola frondosa* polysaccharides in early diabetic nephropathy. *Journal of Food Biochemistry*, **2020**, 44: 13515. https://doi.org/10.1111/jfbc.13515

[44] Zhao, H., Lai, Q., Zhang, J., et al. Antioxidant and hypoglycemic effects of acidic-extractable polysaccharides from *Cordyceps militaris* on type 2 diabetes mice. *Oxidative Medicine and Cellular Longevity*, **2018**, 2018: 9150807. https://doi.org/10.1155/2018/9150807

[45] Sun, W., Zhang, Y. and Jia, L. Polysaccharides from *Agrocybe cylindracea* residue alleviate type 2-diabetes-induced liver and colon injuries by p38 MAPK signaling pathway. *Food Bioscience*, **2022**, 47: 101690. https://doi.org/10.1016/j.fbio.2022.101690

[46] Ashcroft, F. M., Rohm, M., Clark, A., et al. Is type 2 diabetes a glycogen storage disease of pancreatic β cells? *Cell Metabolism*, **2017**, 26: 17-23. https://doi.org/10.1016/j.cmet.2017.05.014

[47] Zheng, J., Yang, B., Yu, Y., et al. *Ganoderma lucidum* polysaccharides exert anti-hyperglycemic effect on streptozotocin-induced diabetic rats through affecting β-cells. *Combinatorial Chemistry & High Throughput Screening*, **2012**, 15: 542–550. https://doi.org/10.2174/138620712801619168

[48] Zhao, H., Li, M., Liu, L., et al. *Cordyceps militaris* polysaccharide alleviates diabetic symptoms by regulating gut microbiota against TLR4/NF-κB pathway. *International Journal of Biological Macromolecules*, **2023**, 230: 123241. https://doi.org/10.1016/j.ijbiomac.2023.123241

[49] Anders, H.-J., Huber, T. B., Isermann, B., et al. CKD in diabetes: diabetic kidney disease versus nondiabetic kidney disease. *Nature Reviews Nephrology*, **2018**, 14: 361–377. https://doi.org/10.1038/s41581-018-0001-y

[50] Shang, X. L., Pan, L. C., Tang, Y., et al. ^{1}H NMR-based metabonomics of the hypoglycemic effect of polysaccharides from *Cordyceps militaris* on streptozotocin-induced diabetes in mice. *Natural Product Research*, **2018**, 34: 1366–1372. https://doi.org/10.1080/14786419.2018.1516216

[51] Xiao, C., Wu, Q., Xie, Y., et al. Hypoglycemic mechanisms of *Ganoderma lucidum* polysaccharides F31 in db/db mice via RNA-seq and iTRAQ. *Food & Function*, **2018**, 9: 6496–6508. https://doi.org/10.1039/c8fo01656a

[52] Capece, D., Verzella, D., Flati, I., et al. NF-κB: blending metabolism, immunity, and inflammation. *Trends in Immunology*, **2022**, 43: 757–775. https://doi.org/10.1016/j.it.2022.07.004

[53] Yang, C., Feng, Q., Liao, H., et al. Anti-diabetic nephropathy activities of polysaccharides obtained from *Termitornyces albuminosus* via regulation of NF-κB signaling in db/db Mice. *International Journal of Molecular Sciences*, **2019**, 20: 5205. https://doi.org/10.3390/ijms20205205

[54] Zhang, Y., Lu, J., Li, H., et al. Advances in dietary polysaccharides as hypoglycemic agents: Mechanisms, structural characteristics, and innovative applications. *Critical Reviews In Food Science And Nutrition*, **2023**, 2293254: 1–21. https://doi.org/10.1080/10408398.2023.2293254

[55] Cao, X. Y., Liu, D., Bi, R. C., et al. The protective effects of a novel polysaccharide from *Lentinus edodes* mycelia on islet β (INS-1) cells damaged by glucose and its transportation mechanism with human serum albumin. *International Journal of Biological Macromolecules*, **2019**, 134: 344–353. https://doi.org/10.1016/j.ijbiomac.2019.05.033

[56] Xiao, C., Wu, Q. P., Zhang, J. M., et al. Antidiabetic activity of *Ganoderma lucidum* polysaccharides F31 down-regulated hepatic glucose regulatory enzymes in diabetic mice. *Journal of Ethnopharmacology*, **2017**, 196: 47–57. https://doi.org/10.1016/j.jep.2016.11.044

[57] Niu, B., Feng, S., Xuan, S., et al. Moisture and caking resistant *Tremella fuciformis* polysaccharides microcapsules with hypoglycemic activity. *Food Research International*, **2021**, 146: 110420. https://doi.org/10.1016/j.foodres.2021.110420

[58] Liu, Y., Li, Y., Zhang, W., et al. Hypoglycemic effect of inulin combined with *Ganoderma lucidum* polysaccharides in T2DM rats. *Journal of Functional Foods*, **2019**, 55: 381–390. https://doi.org/10.1016/j.jff.2019.02.036

[59] Chen, Y., Liu, Y., Sarker, M. M. R., et al. Structural characterization and antidiabetic potential of a novel heteropolysaccharide from *Grifola frondosa* via IRS1/PI3K-JNK signaling pathways. *Carbohydrate Polymers*, **2018**, 198: 452–461. https://doi.org/10.1016/j.carbpol.2018.06.077

[60] Xia, F., Cao S. L., Wang, M. W., et al. Optimizing extraction, structural characterization, and *in vitro* hypoglycemic activity of a novel polysaccharide component from *Lentinus edodes*. *Food Bioscience*, **2023**, 55: 103007 . https://doi.org/10.1016/j.fbio.2023.103007

[61] Cai, W. D., Ding, Z. C., Wang, Y. Y., et al. Hypoglycemic benefit and potential mechanism of a polysaccharide from *Hericium erinaceus* in streptozotoxin-induced diabetic rats. *Process Biochemistry*, **2020**, 88: 180–188. https://doi.org/10.1016/j.procbio.

2019.09.035
[62] Zuo, C., Cao, H., Song, Y., et al. Nrf2: An all-rounder in depression. *Redox Biology*, **2022**, 58: 102522. https://doi.org/10.1016/j.redox.2022.102522
[63] Rotimi, D. E., Ojo, O. A., Olaolu, T. D., et al. Exploring Nrf2 as a therapeutic target in testicular dysfunction. *Cell and Tissue Research*, **2022**, 390: 23–33. https://doi.org/10.1007/s00441-022-03664-3
[64] Gong, P., Wang, X., Liu, M., et al. Hypoglycemic effect of a novel polysaccharide from *Lentinus edodes* on STZ-induced diabetic mice via metabolomics study and Nrf2/HO-1 pathway. *Food & Function*, **2022**, 13: 3036–3049. https://doi.org/10.1039/d1fo03487a
[65] Hu, W., Wang, J., Guo, W., et al. Studies on characteristics and anti-diabetic and -nephritic effects of polysaccharides isolated from *Paecilomyces hepiali* fermentation mycelium in db/db mice. *Carbohydrate Polymers*, **2020**, 232: 115766. https://doi.org/10.1016/j.carbpol.2019.115766
[66] Defour, M., van Weeghel, M., Hermans, J., et al. Hepatic ADTRP overexpression does not influence lipid and glucose metabolism. *American Journal of Physiology-Cell Physiology*, **2021**, 321: C585–C595. https://doi.org/10.1152/ajpcell.00185.2021
[67] Gross, B., Pawlak, M., Lefebvre, P., et al. PPARs in obesity-induced T2DM, dyslipidaemia and NAFLD. *Nature Reviews Endocrinology*, **2017**, 13: 36–49. https://doi.org/10.1038/nrendo.2016.135
[68] Huang, H. Y., Korivi, M., Yang, H. T., et al. Effect of *Pleurotus tuber-regium* polysaccharides supplementation on the progression of diabetes complications in obese-diabetic rats. *The Chinese Journal of Physiology*, **2014**, 57: 198–208. https://doi.org/10.4077/cjp.2014.bac245
[69] Hu, T., Lin, Q., Guo, T., et al. Polysaccharide isolated from *Phellinus linteus* mycelia exerts anti-inflammatory effects via MAPK and PPAR signaling pathways. *Carbohydrate Polymers*, **2018**, 200: 487–497. https://doi.org/10.1016/j.carbpol.2018.08.021
[70] Cho, E. J., Hwang, H. J., Kim, S. W., et al. Hypoglycemic effects of exopolysaccharides produced by mycelial cultures of two different mushrooms *Tremella fuciformis* and *Phellinus baumii* in ob/ob mice. *Applied Microbiology and Biotechnology*, **2007**, 75: 1257–65. https://doi.org/10.1007/s00253-007-0972-2
[71] Dong, Y. H., Wang, Z. X., Chen, C., et al. A review on the hypoglycemic effect, mechanism and application development of natural dietary polysaccharides. *International Journal of Biological Macromolecules*, **2023**, 253: 127267. https://doi.org/10.1016/j.ijbiomac.2023.127267
[72] Liu, Y., Wang, C., Li, J., et al. *Phellinus linteus* polysaccharide extract improves insulin resistance by regulating gut microbiota composition. *The FASEB Journal*, **2019**, 34: 1065–1078. https://doi.org/10.1096/fj.201901943rr
[73] He, G., Chen, T., Huang, L., et al. *Tremella fuciformis* polysaccharide reduces obesity in high-fat diet-fed mice by modulation of gut microbiota. *Frontiers in Microbiology*, **2022**, 13: 1073350. https://doi.org/10.3389/fmicb.2022.1073350
[74] Shao, W., Xiao, C., Yong, T., et al. A polysaccharide isolated from *Ganoderma lucidum* ameliorates hyperglycemia through modulating gut microbiota in type 2 diabetic mice. *International Journal of Biological Macromolecules*, **2021**, 197: 23–38. https://doi.org/10.1016/j.ijbiomac.2021.12.034
[75] Zhan, K., Ji, X., Luo, L. Recent progress in research on *Momordica charantia* polysaccharides: extraction, purification, structural characteristics and bioactivities. *Chemical and Biological Technologies in Agriculture*, **2023**, 10: 58. https://doi.org/10.1186/s40538-023-00433-4
[76] Yang, W., Wu, J., Liu, W., et al. Structural characterization, antioxidant and hypolipidemic activity of *Grifola frondosa* polysaccharides in novel submerged cultivation. *Food Bioscience*, **2021**, 42: 101187. https://doi.org/10.1016/j.fbio.2021.101187
[77] Gong, L. L., Meng, F. J., Hou, Y. C., et al. Purification, characterization, and bioactivity of two new polysaccharide fractions from *Thelephora ganbajun* mushroom. *Journal of Food Biochemistry*, **2020**, 44: 13092. https://doi.org/10.1111/jfbc.13092
[78] Chen, J., Zhang, X., Huo, D., et al. Preliminary characterization, antioxidant and α-glucosidase inhibitory activities of polysaccharides from *Mallotus furetianus*. *Carbohydrate Polymers*, **2019**, 215: 307–315. https://doi.org/10.1016/j.carbpol.2019.03.099
[79] Dubey, S. K., Chaturvedi, V. K., Mishra, D., et al. Role of edible mushroom as a potent therapeutics for the diabetes and obesity. *3 Biotech*, **2019**, 9: 450. https://doi.org/10.1007/s13205-019-1982-3
[80] Hao, Y., Sun, H., Zhang, X., et al. A novel polysaccharide from *Pleurotus citrinopileatus* mycelia: Structural characterization, hypoglycemic activity and mechanism. *Food Bioscience*, **2020**, 37: 100735. https://doi.org/10.1016/j.fbio.2020.100735
[81] Ru, Y., Chen, X., Wang, J., et al. Structural characterization, hypoglycemic effects and mechanism of a novel polysaccharide from *Tetrastigma hemsleyanum Diels et Gilg*. *International Journal of Biological Macromolecules*, **2019**, 123: 775–783. https://doi.org/10.1016/j.ijbiomac.2018.11.085
[82] Liu, Q., Wu, J., Wang, P., et al. Neutral polysaccharides from *Hohenbuehelia serotina* with hypoglycemic effects in a type 2 diabetic mouse model. *Frontiers in Pharmacology*, **2022**, 13: 883653. https://doi.org/10.3389/fphar.2022.883653
[83] Cao, C., Huang, Q., Zhang, B., et al. Physicochemical characterization and *in vitro* hypoglycemic activities of polysaccharides from *Sargassum pallidum* by microwave-assisted aqueous two-phase extraction. *International Journal of Biological Macromolecules*, **2018**, 109: 357–368. https://doi.org/10.1016/j.ijbiomac.2017.12.096
[84] Feng, S., Luan, D., Ning, K., et al. Ultrafiltration isolation, hypoglycemic activity analysis and structural characterization of polysaccharides from *Brasenia schreberi*. *International Journal of Biological Macromolecules*, **2019**, 135: 141–151. https://doi.org/10.1016/j.ijbiomac.2019.05.129
[85] Chen, Z., Yin, C., Fan, X., et al. Characterization of physicochemical and biological properties of *Schizophyllum commune* polysaccharide extracted with different methods. *International Journal of Biological Macromolecules*, **2019**, 156: 1425–1434. https://doi.org/10.1016/j.ijbiomac.2019.11.183
[86] Li, Y., He, Y., Zhang, H., et al. Effects of ultrasonic-enzymatic-assisted ethanol precipitation method on the physicochemical characteristics, antioxidant and hypoglycemic activities of *Tremella fuciformis* polysaccharides. *Ultrasonics Sonochemistry*, **2023**, 101: 106682. https://doi.org/10.1016/j.ultsonch.2023.106682