Pharmacological Importance of Medicinal Mushroom *Ganoderma* Specie for the Treatment of Diabetes

Sidra Altaf[1,*], Asmara[2], Arslan Iftikhar[3] and Humaira Muzaffar[3]

[1]Department of Pharmacy, University of Agriculture, Faisalabad, Pakistan
[2]Institute of Physiology and Pharmacology, University of Agriculture, Faisalabad, Pakistan
[3]Department of Physiology, Govt. College University Faisalabad, Pakistan
*Corresponding author: sidra.altaf@uaf.edu.pk

Abstract

Ganoderma mushrooms are a "fungi" family member and achieved international fame for their curative properties and availability. Pharmacotherapy with natural substances is today considered an emerging future alternative to the traditional treatment of diabetic mellitus. When the body cannot produce enough insulin or when the insulin it produces cannot be utilized appropriately. Regarding their antidiabetic activity, this chapter discusses the opinions, current trends, and key issues concerning the medicinal mushroom species of *Ganoderma*. The polysaccharides and triterpenoids, which include terpenoids and triterpenoids are the most active components in such mushrooms. There are quite several applications involving *Ganoderma* in folk and especially traditional Chinese medicine. Among its numerous qualifications which feature anti-cancer, antihepatotoxic, and immunomodulatory properties; they are used to deal with other various chronic diseases including diabetes, insomnia, nephritis, arthritis, hypertension, and asthma. The *Ganoderma* has many applications in traditional Chinese medicine. They are used to treat a wide range of chronic illnesses such as diabetes, insomnia, nephritis, arthritis, hypertension, and asthma, because of their anti-hepatotoxic, and immunomodulatory anti-cancer qualities. Thus, to close the study gap and utilize Magoderna medicinal mushrooms' clinical potential to prevent non-communicable diseases**.**

Keywords: *Ganoderma*; Antidiabetic; Polysaccharide; Triterpenoid; Tetraterpenoid

Cite this Article as: Altaf S, Asmara, Iftikhar A and Muzaffar H, 2025. Pharmacological importance of medicinal mushroom *Ganoderma* specie for the treatment of diabetes. In: Khan A, Hussain R, Tahir S and Ghafoor N (eds), Medicinal Plants and Aromatics: A Holistic Health Perspective. Unique Scientific Publishers, Faisalabad, Pakistan, pp: 9-14. https://doi.org/10.47278/book.HH/2025.423

A Publication of Unique Scientific Publishers

Chapter No: 25-002

Received: 19-Jan-2025
Revised: 21-Apr-2025
Accepted: 22-May-2025

Introduction

Diabetes is a metabolic condition characterized by hyperglycemia due to insulin deficiency and malfunction. Diabetes has become a severe disease. The disease is no longer thought to be constitutional. It affects the majority of the people in the world and become a topic of numerous discussions (Sen et al., 2016). International Diabetes Federation published data in eight editions of the global map of diabetes indicating that the number of individuals with diabetes (20-79 years old) worldwide surpassed 415 million in 2017 (Yang et al., 2024). In 2000 it was worth noting, that 151 million patients were there. Approximations propose that by 2045, the diabetic population could extent 629 million. Previously, diabetes was divided into two groups. The presence or absence of autoantibodies compared to pancreatic islet β-cell antigens differentiated these groups (types 1 and 2). The second criterion was the patient's age upon diagnosis. A third group consisted of old individuals with the latent autoimmune diabetes (LATA). Usually diabetes has been recognized through occurrence of glutamic acid decarboxylase antibodies (GADAs) (Davis et al., 2000).

There are five types of this disease. Initial kind is known as severe autoimmune diabetes (SAID).in young people this type of diabetes diagnosed with moderate BMI. This one is distinguished by disturbed metabolic regulation, insulin insufficiency, and the occurrence of GADA. The 2nd form is called immature diabetes, however it is destructive GADA (Sabbah, 2000). Kind, like type 1, is distinguished by a slow BMI, insufficient insulin secretion, and poor metabolic regulation. The diabetes of type 2nd is characterized by significant insulin deficiency. The 3rd form of diabetes linked to weight rather than age. The 3rd type is distinguished by resistance of insulin. This is referred to severe insulin resistant diabetes (SIRD). The 4th kind of Diabetes (Ahlqvist et al., 2022) is referred to as diabetes known as mild obesity-diabetes (MOD). The 5th form of diabetes affects the elderly and is slighter (only slight metabolic alterations are noted). Patients with this kind condition can be treated through medicine instead insulin injections. This form is referred to as mild age-related diabetes (MARD). Separation allows for better-quality tailoring of treatment strategy to specific occasion. There are several strategies to treat diabetes. The diabetes mellitus is currently treated using a variety of hypoglycemic medications that act through multiple pathways to achieve ant diabetic effects (Patel et al., 2012). Metformin, a biguanide, is the 1st best treatment for 2nd type of diabetes. This medicine is distinguished through its great efficacy, low price, and protection. In the treatment of non-insulin-dependent diabetic mellitus (NIDDM) caused by insulin disaster, intestinal carbohydrate digestion is inhibited or delayed. Sugars are the primary elements in our everyday diet. Inhibiting α-glucosidase activity is a potential treatment strategy (Tundis et al., 2010).

Acarbose and miglitol are two examples of ant diabetic medications that are often used in some Asian regions. The α-glucosidase is found in epithelium of small intestine and catalyzes conversion of oligosaccharide and disaccharides to glucose. Taking α-glucosidase inhibitors can end carbohydrate breakdown, reducing blood glucose levels after meals (AG, 1994) . Furthermore, acarbose reversibly prevents pancreatic α-amylase. The metformin, rises insulin sensitivity in tissues while decreasing glucose synthesis in the liver. However, extended usage of this medication increases the chance of developing lactic acidosis thiazolidinedione (TZD) like pioglitazone and rosiglitazone mostly used when metformin is contraindicated, however they have a long list of adverse effects. Increased the retention of fluid -reported in the patients who treated with thiazolidinedione may contribute to weight gain and heart failure (Bailey, 2005).

The sulfonylureas, like glyburide and glimepiride usually used to cope diabetes. They function by decreasing levels the sugar of blood, primarily through boosting secretions of insulin from the Langerhans islets. Weight gain is the side effect (Ampatzis, 2007). It is because of the increased hypoglycemia risk; sulfonylureas are not recommended as a first-line treatment for type 2 diabetes. Furthermore, they lose efficacy in around 44% of patients after six years of usage (Ryali, 2008). New anti-diabetic medications include DPP-4 inhibitors, prevent the breakdown of intestinal incretion hormones also they rise bioavailability and period. The FDA and EMA have authorized medications in this category, including linagliptin, sitagliptin, alogliptin vildagliptin, saxagliptin, linagliptin. They improved the secretion of insulin (Scheen, 2018). There are variety of limitations which are associated with the use of present artificial antidiabetic medications, these are actively considering for natural alternatives. One is, utilizing Ganoderma-derived drugs. The *Ganoderma* genus contains species may b 300, the majority of which grow natively in hot areas. Mushrooms of this family are often not usually declared as edible mushroom because fruiting bodies of the mushroom are marked by corkiness, width, extreme stiffness, and a deficiency of soft surface (Loyd et al., 2018).

Fungi, *Ganoderma* have a wide range of applications in the natural medicine, particularly traditional Chinese medication (Paterson, 2006). They are used to treat a variety of chronic disorders, including diabetes, insomnia nephritis, arthritis, hypertention and asthma, as well as, anti-hepatotoxic, immunomodulatory and anti-cancer, properties. The *G. lucidum* and *G. sinense* hubs are very common, while new species like *G. tsuage, G. capense, G. cochlear, G. capense*, and *G. tsuage* are as well utilized for therapy (sharif etal., 2025). Most extensively researched species of the genus *Ganoderma* is *G. lucidum*, also known as "Ling-Zhi" in Chinese, "Reishi" in Japanese, and "Yeongji" in Korean. Food foodstuffs containing this fungus are said to boost vitality and longevity (Loyd et al., 2018).

1. Diabetic Properties of Ganoderma Lucidum

Ganoderma lucidum, also known as the reishi fungus, is studied for its potential benefits in diabetes management. Here are some ways Ganoderma lucidum may be used in diabetes therapies.

2.1. Blood Sugar Regulation

Excepts of *Ganoderma lucidum* have been illustrated to have hypoglycemic properties, i.e., lowering the concentration of blood sugar. Most of this effect is tied to polysaccharides and triterpenes within the fungus (Ma et al., 2015).

2.2. Insulin Sensitivity

Research has shown that *Ganoderma lucidum* may enhance insulin sensitivity, which is beneficial to patients with type 2 diabetes. Enhanced insulin sensitivity increases the responsiveness of cells to insulin and the utilization of glucose (Wińska et al., 2019).

2.3. Anti-inflammatory Properties

Chronic infection is associated with insulin resistance and diabetes. The *Ganoderma lucidum* contains anti-inflammatory qualities that may help reduce infection signals within the body, hence improving overall metabolic health (Ekiz et al., 2023).

2.4. Antioxidant Activity

Oxidative stress contributes to the development and progression of diabetes. The *Ganoderma lucidum* contains antioxidant components such as polysaccharides and triterpenes, which can help neutralize free radicals and prevent oxidative damage (Lin & Deng, 2019).

2.5. Liver Support

The liver plays a significant role in glucose metabolism and insulin regulation. The *Ganoderma lucidum* has been studied for its hepatoprotective properties, which may also help the liver and lead to improved glucose regulation (Lin & Deng, 2019).

2.6. Additional Benefits

Apart from regulating blood sugar levels, *Ganoderma lucidum* may offer other benefits that are of value to people with diabetes such as heart protection, immune support, and improvement in lifestyle satisfaction (Swallah et al., 2023).

It is essential to note that, despite the promising research on the potential benefits of *Ganoderma lucidum* in the control of diabetes, it is not necessary to update common medical treatments (El Sheikha, 2022). If you are considering using *Ganoderma lucidum* as a supplement to help you control your diabetes, you should consult a healthcare practitioner first, especially if you are already taking medicine for diabetes or another condition. They can give directed support according to your specific health requirements and help in showing whatever capacity interactions or results may be.

2. Compounds Present in *Ganoderma lucidium*

The *Ganoderma lucidum*, otherwise known as the reishi fungus, has a wide range of bioactive compounds that may help diabetics. Here are some of the major components that were discovered in *Ganoderma lucidum* and what they might have on diabetes.

3.1. Polysaccharides

The *Ganoderma lucidum* contains a few polysaccharides, which include beta-glucans. Such polysaccharides have been researched regarding their potential.

3.2. Lower Blood Glucose Levels

The polysaccharides can enhance insulin sensitivity and glucose uptake by activating cells, thereby altering blood glucose levels (Ganesan & Xu, 2019).

Stimulate Insulin Secretion: Some research suggests that polysaccharides extracted from *Ganoderma lucidum* can stimulate the secretion of insulin in the body by activating the pancreatic beta cells, which could be an advantage to the diabetic (Zheng et al., 2012). The *Ganoderma lucidum* also contains triterpenes as well as ganoderic acids (Liang et al., 2019). The following are the researched activities of these compounds on diabetes.

3.3. Improving Insulin Sensitivity

Triterpenes may enhance insulin sensitivity in tissues considering elevated glucose absorption and utilization (Teng et al., 2018). Triterpenes contain anti-inflammatory characteristics that might help reduce the inflammation linked with insulin resistance and diabetes.

Peptides derived from *Ganoderma lucidum* have been shown to potentially control blood glucose levels and increase insulin sensitivity (Teng et al., 2018). The *Ganoderma lucidum* has been known for its antioxidant activities, and such effects are due to polysaccharides and triterpenes. These antioxidants reduce free radicals and lessen oxidant hypertension, which are conducive to diabetic problems, including cardiovascular disease and nerve damage. Other bioactive compounds: This herb contains amino acids, nutrients, and minerals that may also help the overall fitness of an individual, no doubt to enhance metabolic health and diabetic management. While research into *Ganoderma lucidum's* specific benefits on diabetes is continuing and promising, it is critical to approach it as a supplement to standard medical therapy (Chang & Wasser, 2012). If you are contemplating introducing *Ganoderma lucidum* (Figure 1) into your diabetes management regimen, contact with a healthcare expert to confirm it is safe and appropriate for your specific fitness need.

Fig. 1: Structure of *Ganoderma lucidem*

4. Antidiabetic Effects of Ganoderma Extracts

The *G. lucidum* alcohol and aqueous extracts were investigated for blood sugar reduction in rats also with in wich te diabetes induced (Cheng et al., 2013). Employed diabetic rats, both normal and obese. Prior to plasma administration, 168.5 mg/dL, and was sugar level in plasma in rats in normal condition and 168.5mg/dl in obese. Capsule wich is made from extraction of water which contain 95% powder of sporocarb and of ganoderma specie and 5%.next 4 weeks when amisnistartion will be done.in both condition plasma glucose level be drop in norlmal condition it wil be drop 68.5mg/ld and on obese condition it will be drop 288.4mg/ld (Zheng et al., 2019). At the end test of hypoglycemic activity performed in normal and the in rats in which streptozotocin induced, gllucose level were measure in next 3 to 4 weeks. In normal condition glucose level is 90gm/ld and in obese condition it is 200gm/ld. Extract of ganoderma for normal condition rats is 100mg/dl and for obsese rats it wouild be 200mg/kg methanol and ethanol produced two different categories of extract of ganoderma (Soon & Tan, 2002). It is seen in research that rats in wich alloxan produced diabtes should be given with methanol extrat. The rats in which diabetes was induced through the streptozotocin should be treated with the alcoholic extract of ganoderma.

5. Antidiabetic Activity

The long-term repercussions of diabetes indicate organ's malfunction and failure (Bombelli et al., 2011). Many studies demonstrated that rats in which diabetes was induced have greater levels of oxidative stress, and redox inequity, strongly linked to disease expansion (Delmastro & Piganelli, 2011). This organism has antioxidant system, which should stable ROS generation and free radical searching. Animal investigations uses streptozotocin-induced diabetes revealed that the antioxidant, nonenzymatic enzymatic systems were considerably compromised. This is about the actions of free radical searching and oxidative stress. The *G. lucidum* polysaccharides served as exogenous antioxidants, restoring endogenous redox equilibrium by lowering the level of malondialdehyde and increasing antioxidant enzyme appearance (Abo Nahas et al., 2021).

The majority of endogenous ROS originate in the mitochondria and contribute to insulin resistance indirectly. The natural extract of polysaccharide from *G. lucidum* compact insulin resistance and harm to pancreatic islet cells, effectively reversing the whole diabetes development progression, and had a long period of activity (Seweryn et al., 2021). The preceding results in future suggest that clinical prosecutions, which currently lost for *G. lucidum* polysaccharides, oxidative stress level, polysaccharide dose and the period of its action on the tissue should be measured. The oxidative stress plays an important role, especially in the initial stages and at level of physiological glucose levels. The non-enzymatic interactions between glucose and proteins or lipids result in the production of advanced glycation end products (AGE), which disrupt the organism's metabolic and physiological functioning (Khalid et al., 2022).

The current treatments have limited efficacy, tolerance, and serious adverse effects. As a result, people are becoming more interested in natural remedies. The most intriguing discovery was that *G. lucidum* polysaccharides are equally harmless and effective like antioxidants.

Another significant conclusion was polysaccharides have antihyperglycemic properties (AKANDA, 2013). To this goal, liquid extracts from *G. lucidum* was also examined, representing typical mushroom intake. It was discovered that giving water extracts to experimental the animal in wich diabetes is induced considerably lowered level of blood glucose. The polysaccharides' hypoglycemic effects broadly explored both *in-vitro* and *in-vivo* diabetes is influenced by genetics, the environment, and bacterial ecology. Diabetes mellitus and intestinal dysbiosis have a substantial association, according to the research (Dedrick et al., 2020). Recent research suggests that GLP has influence on duodenal dysbiosis, which two linked to type 2 diabete. The duodenal dysbiosis causes immunological diseases, long-lasting inflammation, and diabetes by producing aberrant metabolites. Management with polysaccharide from *G. lucidum* for 3 to 4 weeks improved the levels of favorable bacteria and relieved hyperglycemia and hyperlipidemia in 2nd type of diabetic mice (Zhang et al., 2022).

Further investigation is needed before the relationship between *G. lucidum* polysaccharides and intestinal dysbiosis can be fully appreciated. The bioactive polysaccharides represent novel therapy methods for metabolic illnesses. After all, probable pharmacological approaches to avoiding the harmful effects of oxidative stress by dropping endogenous and exogenous causes of free radicals, preventing the inflammation, and incorporating antioxidant polysaccharides from *G. lucidum* look extremely promising (Zhang et al., 2024).

6. Ganoderma's Method of Treatment

Diabetes mellitus is a multi-factorial metabolic illness caused by impaired or insufficient β-cells in the pancreas, reducing insulin production. It can deteriorate overall bodily functions. It compares physiological glucose concentrations, high levels of glucose have a larger detrimental impact on a wider range of tissue organs (Newsholme et al., 2019). Severe hyperglycemia causes glucose toxicity by reducing insulin secretion and increasing insulin resistance. Hyperglycemia elevates responsive oxygen and nitrogen species in β-cells, impairing cellular processes. The glucotoxicity thereby reduces the body's antioxidant defense system (Lenzen, 2017). The *G. lucidum* polysaccharides dramatically reduce the activity of enzymes, nitric oxide synthase manganese superoxide dismutase, and glutathione peroxidase. The following harmful process noticed during diabetes mellitus is apoptosis. The *G. lucidum* polysaccharides' hypoglycemic activity is linked to variable the appearance of numerous important enzymes of the metabolism pathway in hepatic glucose including glucokinase, glucose-6-phosphate dehydrogenase, phosphoenolpyruvate carboxykinase, phosphofructokinase, and glycogen synthase fructose-1,6-bisphosphatase, phosphofructokinase (Lenzen, 2017). The dietary carbohydrates are certainly transformed into monosaccharides like fructose and glucose, which are easily absorbed by the small intestine and transported to the bloodstream. The oligosaccharide acclimatization is linked to α-glucosidase activity in the small intestine (Zhang et al., 2015). Several triterpenoids from *Genoderma* significantly inhibit this enzyme. The *Ganoderma* was employed in clinical investigations for a variety of illnesses due to its positive effects and medical promise.

7. Isolated Polysaccharides from *Ganoderma* Species

Polysaccharides are lengthy chains of monosaccharide units joined together through glycosidic linkages that, when hydrolyzed, yield monosaccharides or oligosaccharides (Chaudhary et al., 2022). They have a direct to heavily branching form. Polysaccharides take the generic formula CX (H_2O) Y, wherever X and Y are often big numbers ranging from 200 to 2500. The scientists discovered that polysaccharides and glycoconjugates are not singly used as energy possessions and component elements in living organisms, but they also occur in the entire structures of cell membranes and exhibit significant physiological activity.

8. Isolated Terpenoids from the *Ganoderma* Species

Terpenes are the biggest class of secondary metabolites, with a wide range of biological features. They are made up of isoprene units that are joined in a variety of ways. Terpenes are hydrocarbons. Terpenoids, on the other hand, are compounds that include functional groups. The amount of isoprene units distinguishes, sesquiterpenes, triterpenes, tetraterpenes, monoterpenes, and diterpenes, sesterpenes politerpenes (Aramabašić Jovanović et al., 2021). The triterpenoids' anti-diabetic activities have been linked to enzyme inhibition, including aldose reductase, α-glucosidase, and HMG-CoA reductase (HMGR). Previous studies have identified more than 140 triterpenoids in mushrooms belonging to the genus *Ganoderma*. Remarkably, a single species, *G. lucidum*, can contain up to 15 different triterpenoids (Galappaththi et al., 2022). Triterpenes have six isoprene units in their structure. They belong to the primary class of secondary metabolites. They originate in the squalene biosynthetic pathway. The triterpenoids are structurally similar to steroid hormones; hence it is thought that their mode of action is linked to glucocorticoid-responsive elements (GRE). The binding to GRE inhibits the expression of pro-inflammatory proteins while increasing the appearance of anti-inflammatory proteins. The lipophilic triterpenes are which means triterpenes attached to the cell membranes and change their flexibility, potentially limiting their bioavailability though, it experimentally proved that triterpenoids enter both cell membranes. In addition, triterpenoids inhibit aldose reductase and α-glucosidase, which participate actively in the metabolism of glucose.

Enzyme in the polyol glass is aldose reductase. It turns glucose to sorbitol. The increase of sorbitol levels in body causes diabetes problems like, cataracts, neuropathy and retinopathy cataracts. The *G. lucidum* methanol extracts were reported the strongest inhibitory impact on aldose reductase (Tasleem et al., 2025, Wińska et al., 2019) among 17 different different eatable fungi used medicinally (Wińska et al., 2019). It was also discovered that ethanol extract of *G. lucidum* lowers the level of galactocitol in galactose-fed animal rats. The chloroform extract yielded three compounds: ganoderic acid C_2 (1), ganoderic acid Df A (2), and ganoderic acid Df ganoderenic acid A (3) (Wińska et al., 2019).

9. Meroterpenoids Isolated from *Ganoderma* Species

Eight different monoterpenes isolated from *G. leucocontextum* fruiting bodies were tested for their inhibitory effects on HMG-CoA reductase and α-glucosidase. Ganomycin, and emonstrated greater inhibitory action against HMG-CoA reductase than principles (Chen et al., 2017). The study's progressive control is atorvastatin The meroterpenes effectively inhibited α-glucosidase activity in yeast and animal used rat small intestine mucosa. The ganomycin is always the strongest inhibitor of both α-glucosidase and HMG-CoA reductase. The pharmacological

studies demonstrated that ganomycin I had powerful effective hypoglycemic, hypolipidemic, and insulin-sensitizing actions in KK-Ay rat or mice (Wang et al., 2017).

10. Future Prospects

Numerous investigations have highlighted the diverse biological activities of mushrooms used in traditional Chinese medicine. Among them, *Ganoderma lucidum* is a particularly well-known medicinal fungus, especially in Asian countries. A substantial body of pharmacological research has demonstrated its therapeutic efficacy, with many studies reporting minimal or no adverse effects, supporting its favorable safety profile. Despite considerable progress in recent years regarding the study of triterpenoids from *Ganoderma* species and their antidiabetic properties, significant research gaps remain before these compounds can be practically implemented as therapeutic agents. Future research should focus on standardizing *Ganoderma* species and their bioactive components, clarifying the relationship between the structure and function of individual triterpenoids and polysaccharides, and exploring the synergistic effects of active ingredients with dietary components. Additionally, there is a need to develop more efficient and cost-effective methods for isolating and modifying the most potent compounds, as well as establishing reliable techniques for determining the structures of polysaccharides. Based on these considerations, although various preclinical and clinical studies have investigated the antidiabetic potential of triterpenoids and polysaccharides from *Ganoderma* species, further clinical research is essential to confirm their efficacy and support their safe integration into therapeutic use (Zhang et al., 2015).

Conclusion

The current pharmacological findings demonstrated the antidiabetic effects of *Ganoderma* mushroom, effects that are corroborated and demonstrated by computational analyses. This might be because this mushroom contains a variety of active ingredient kinds. The polysaccharides, terpenoids and tetraterpenoids found in the mushroom are most likely the bioactive substances in charge of those actions. Therefore, using *Ganoderma* mushrooms as an extract or as veggies will help with diabetes management.

References

Abo Nahas, H. H., Darwish, A. M. G., Abo Nahas, Y. H., Elsayed, M. A., Abdel-Azeem, M. A., & Abdel-Azeem, A. M. (2021). Fungi as a gold mine of antioxidants. *Industrially Important Fungi for Sustainable Development: Volume 2: Bioprospecting for Biomolecules*, 73–113.

AG, H. B. B. (1994). Pharmacology of α-glucosidase inhibition. *European Journal of Clinical Investigation*, *24*(S3), 3–10.

Ahlqvist, E., Prasad, R. B., & Groop, L. (2022). 100 YEARS OF INSULIN: Towards improved precision and a new classification of diabetes mellitus. *Journal of Endocrinology*, *252*(3), R59–R70.

AKANDA, M. D. (2013). *Phytochemical and Pharmacological Investigations of Genoderma Lucidum*. East West University, Pp (1-99).

Ampatzis, K. (2007). *Pharmacology of the 2nd type of diabetes mellitus-a review*. http://hdl.handle.net/20.500.11956/12091

Aramabašić Jovanović, J., Mihailović, M., Uskoković, A., Grdović, N., Dinić, S., & Vidaković, M. (2021). The effects of major mushroom bioactive compounds on mechanisms that control blood glucose level. *Journal of Fungi*, *7*(1), 58.

Bailey, C. J. (2005). Treating insulin resistance in type 2 diabetes with metformin and thiazolidinediones. *Diabetes, Obesity and Metabolism*, *7*(6), 675–691.

Bombelli, M., Facchetti, R., Sega, R., Carugo, S., Fodri, D., Brambilla, G., Giannattasio, C., Grassi, G., & Mancia, G. (2011). Impact of body mass index and waist circumference on the long-term risk of diabetes mellitus, hypertension, and cardiac organ damage. *Hypertension*, *58*(6), 1029–1035.

Chang, S.-T., & Wasser, S. P. (2012). The role of culinary-medicinal mushrooms on human welfare with a pyramid model for human health. *International Journal of Medicinal Mushrooms*, *14*(2), 95-134..

Chaudhary, S., Jain, V. P., & Jaiswar, G. (2022). The composition of polysaccharides: monosaccharides and binding, group decorating, polysaccharides chains. In *Innovation in nano-polysaccharides for eco-sustainability* (pp. 83–118). Elsevier.

Chen, B., Tian, J., Zhang, J., Wang, K., Liu, L., Yang, B., Bao, L., & Liu, H. (2017). Triterpenes and meroterpenes from Ganoderma lucidum with inhibitory activity against HMGs reductase, aldose reductase and α-glucosidase. *Fitoterapia*, *120*, 6–16.

Cheng, P. G., Phan, C. W., Sabaratnam, V., Abdullah, N., Abdulla, M. A., & Kuppusamy, U. R. (2013). Polysaccharides-Rich Extract of Ganoderma lucidum (M.A. Curtis:Fr.) P. Karst Accelerates Wound Healing in Streptozotocin-Induced Diabetic Rats. *Evidence-based complementary and alternative medicine : eCAM*, *2013*, 671252. https://doi.org/10.1155/2013/671252

Davis, T. M. E., Zimmet, P., Davis, W. A., Bruce, D. G., Fida, S., & Mackay, I. R. (2000). Autoantibodies to glutamic acid decarboxylase in diabetic patients from a multi-ethnic Australian community: the Fremantle Diabetes Study. *Diabetic Medicine*, *17*(9), 667–674.

Dedrick, S., Sundaresh, B., Huang, Q., Brady, C., Yoo, T., Cronin, C., Rudnicki, C., Flood, M., Momeni, B., & Ludvigsson, J. (2020). The role of gut microbiota and environmental factors in type 1 diabetes pathogenesis. *Frontiers in Endocrinology*, *11*, 78.

Delmastro, M. M., & Piganelli, J. D. (2011). Oxidative stress and redox modulation potential in type 1 diabetes. *Journal of Immunology Research*, *2011*(1), 593863.

Ekiz, E., Oz, E., Abd El-Aty, A. M., Proestos, C., Brennan, C., Zeng, M., Tomasevic, I., Elobeid, T., Çadırcı, K., & Bayrak, M. (2023). Exploring the potential medicinal benefits of Ganoderma lucidum: From metabolic disorders to coronavirus infections. *Foods*, *12*(7), 1512.

El Sheikha, A. F. (2022). Nutritional profile and health benefits of Ganoderma lucidum "Lingzhi, Reishi, or Mannentake" as functional foods: Current scenario and future perspectives. *Foods*, *11*(7), 1030.

Galappaththi, M. C. A., Patabendige, N. M., Premarathne, B. M., Hapuarachchi, K. K., Tibpromma, S., Dai, D.-Q., Suwannarach, N., Rapior, S., & Karunarathna, S. C. (2022). A review of Ganoderma triterpenoids and their bioactivities. *Biomolecules*, *13*(1), 24.

Ganesan, K., & Xu, B. (2019). Anti-diabetic effects and mechanisms of dietary polysaccharides. *Molecules*, *24*(14), 2556.

Khalid, M., Petroianu, G., & Adem, A. (2022). Advanced glycation end products and diabetes mellitus: mechanisms and perspectives.

Biomolecules, *12*(4), 542.
Lenzen, S. (2017). Chemistry and biology of reactive species with special reference to the antioxidative defence status in pancreatic β-cells. *Biochimica et Biophysica Acta (BBA)-General Subjects*, *1861*(8), 1929–1942.
Liang, C., Tian, D., Liu, Y., Li, H., Zhu, J., Li, M., Xin, M., & Xia, J. (2019). Review of the molecular mechanisms of Ganoderma lucidum triterpenoids: Ganoderic acids A, C2, D, F, DM, X and Y. *European Journal of Medicinal Chemistry*, *174*, 130–141.
Lin, Z., & Deng, A. (2019). Antioxidative and free radical scavenging activity of Ganoderma (Lingzhi). *Ganoderma and Health: Pharmacology and Clinical Application*, 271–297.
Loyd, A. L., Richter, B. S., Jusino, M. A., Truong, C., Smith, M. E., Blanchette, R. A., & Smith, J. A. (2018). Identifying the "mushroom of immortality": assessing the Ganoderma species composition in commercial Reishi products. *Frontiers in Microbiology*, *9*, 1557.
Ma, H.-T., Hsieh, J.-F., & Chen, S.-T. (2015). Anti-diabetic effects of Ganoderma lucidum. *Phytochemistry*, *114*, 109–113.
Newsholme, P., Keane, K. N., Carlessi, R., & Cruzat, V. (2019). Oxidative stress pathways in pancreatic β-cells and insulin-sensitive cells and tissues: importance to cell metabolism, function, and dysfunction. *American Journal of Physiology-Cell Physiology*, *317*(3), C420–C433.
Patel, D. K., Kumar, R., Laloo, D., & Hemalatha, S. (2012). Diabetes mellitus: an overview on its pharmacological aspects and reported medicinal plants having antidiabetic activity. *Asian Pacific Journal of Tropical Biomedicine*, *2*(5), 411–420.
Paterson, R. R. M. (2006). Ganoderma–a therapeutic fungal biofactory. *Phytochemistry*, *67*(18), 1985–2001.
Ryali, V. (2008). From Journal to Journal-A Continuing Learning Experience. In *Journal of Marine Medical Society* (Vol. 10, Issue 1, pp. 1–63). Medknow.
Sabbah, E. (2000). *Role of antibodies to glutamic acid decarboxylase in type 1 diabetes: relation to other autoantibodies, HLA risk markers and clinical characteristics*. Pp 85. URL: http://herkules.oulu.fi/issn03553221/
Scheen, A. J. (2018). The safety of gliptins: updated data in 2018. *Expert Opinion on Drug Safety*, *17*(4), 387–405.
Sen, S., Chakraborty, R., & De, B. (2016). *Diabetes mellitus in 21st century*. Pp 13-22. Springer.
Seweryn, E., Ziała, A., & Gamian, A. (2021). Health-promoting of polysaccharides extracted from Ganoderma lucidum. *Nutrients*, *13*(8), 2725.
Sharif, M. N., Hina, A., Gull, D., Tariq, M., Khaliq, H., Mahmood, W., Zakir, A., Ul Hassan, W., Altaf, S., & Sajjad, A. (2025). Eco-friendly biosynthesis of iron oxide nanoparticles for targeted cancer imaging and therapy. *Journal of Medical & Health Sciences Review*, 2(2), 4407-4418.
Soon, Y. Y., & Tan, B. K. H. (2002). Evaluation of the hypoglycemic and anti-oxidant activities of Morinda officinalis in streptozotocin-induced diabetic rats. *Singapore Medical Journal*, *43*(2), 77–85.
Swallah, M. S., Bondzie-Quaye, P., Wu, Y., Acheampong, A., Sossah, F. L., Elsherbiny, S. M., & Huang, Q. (2023). Therapeutic potential and nutritional significance of Ganoderma lucidum–a comprehensive review from 2010 to 2022. *Food & Function*, *14*(4), 1812–1838.
Tasleem, F., Shahzadi, S., Bassey, O. B., Shuja, A. A., Ali, M., Bibi, S., Ahmed, T., Hameed, M. K., & Altaf, S. (2025). 6-Amino flavone attenuates cadmium-induced memory impairment and neuroinflammation through p-JNK/NF-κB pathway inhibition in mice. *Journal of Medical & Health Sciences Review*, 2(2), 3615–3633.
Teng, H., Yuan, B., Gothai, S., Arulselvan, P., Song, X., & Chen, L. (2018). Dietary triterpenes in the treatment of type 2 diabetes: To date. *Trends in Food Science & Technology*, *72*, 34–44.
Tundis, R., Loizzo, M. R., & Menichini, F. (2010). Natural products as α-amylase and α-glucosidase inhibitors and their hypoglycaemic potential in the treatment of diabetes: an update. *Mini Reviews in Medicinal Chemistry*, *10*(4), 315–331.
Wang, K., Bao, L., Ma, K., Zhang, J., Chen, B., Han, J., Ren, J., Luo, H., & Liu, H. (2017). A novel class of α-glucosidase and HMG-CoA reductase inhibitors from Ganoderma leucocontextum and the anti-diabetic properties of ganomycin I in KK-Ay mice. *European Journal of Medicinal Chemistry*, *127*, 1035–1046.
Wińska, K., Mączka, W., Gabryelska, K., & Grabarczyk, M. (2019). Mushrooms of the genus Ganoderma used to treat diabetes and insulin resistance. *Molecules*, *24*(22), 4075.
Yang, K., Yang, X., Jin, C., Ding, S., Liu, T., Ma, B., Sun, H., Zhang, J., & Li, Y. (2024). Global burden of type 1 diabetes in adults aged 65 years and older, 1990-2019: population based study. *Bmj*, *385,* e078432.
Zhang, G., Hasek, L. Y., Lee, B.-H., & Hamaker, B. R. (2015). Gut feedback mechanisms and food intake: a physiological approach to slow carbohydrate bioavailability. *Food & Function*, *6*(4), 1072–1089.
Zhang, H., Li, Y., Fu, Y., Jiao, H., Wang, X., Wang, Q., Zhou, M., Yong, Y., & Liu, J. (2024). A structure-functionality insight into the bioactivity of microbial polysaccharides toward biomedical applications: A review. *Carbohydrate Polymers*, 122078.
Zhang, S., Lin, L. E. I., Yun, Z., Ye, F.-Y., & Zhao, G.-H. (2022). Roles of mushroom polysaccharides in chronic disease management. *Journal of Integrative Agriculture*, *21*(7), 1839–1866.
Zheng, J., Yang, B., Yu, Y., Chen, Q., Huang, T., & Li, D. (2012). Ganoderma lucidum polysaccharides exert anti-hyperglycemic effect on streptozotocin-induced diabetic rats through affecting β-cells. *Combinatorial Chemistry & High Throughput Screening*, *15*(7), 542–550.
Zheng, Y., Bai, L., Zhou, Y., Tong, R., Zeng, M., Li, X., & Shi, J. (2019). Polysaccharides from Chinese herbal medicine for anti-diabetes recent advances. *International Journal of Biological Macromolecules*, *121*, 1240–1253.