Reishi Mushroom (*Ganoderma lucidum*) Extract Ameliorate Hyperglycemia and Liver/Kidney Functions in Streptozotocin-induced Type 2 Diabetic Rats

Samah A Elsemelawy[1], Mai A Gharib[2] and Yousif A Elhassaneen[2*]

[1]Department of Home Economics, Faculty of Specific Education, Tanta University, Tanta, Egypt.
[2]Department of Nutrition and Food Science, Faculty of Home Economics, Minoufiya University, Shebin El-Kom, Egypt

[*] Corresponding Author: yousif12@hotmail.com

ABSTRACT

Diabetes is a metabolic condition characterized by hyperglycemia and insufficient insulin production or activity. Since ancient times, the reishi mushroom (Ganoderma lucidum) has been utilized as a traditional herbal treatment. ***Aim of the study:*** *investigate the effectiveness of Ganoderma lucidum extract (GLE) to ameliorate hyperglycemia and liver/kidney functions in streptozotocin-induced type 2 diabetic rats. Six groups of adult male Sprague–Dawley rats were formed at random. Group 1: Normal rats with a normal diet. Group 2: Diabetic rats by injection Streptozotocin (STZ) and fed without intervention as a model control group, Groups 3-6: GLE, diabetic rats with intervention groups receiving GLE at doses of 200, 400, 600, and 800 mg/kg BW via oral gavage for 28 days. After GLE intervention, blood samples were tested for changes in hyperglycemia, glycosylated hemoglobin, insulin, liver, and kidney functioning.* ***Results:*** *Within the first two weeks of GLE intervention, blood glucose levels were reduced, and insulin levels in diabetic rats in the GLE group were considerably higher at four weeks than in the positive control group. Furthermore, it was discovered that GLE intervention significantly improved the liver and kidney functioning of diabetic rats.* ***Conclusion:*** *This research suggests that GLE consumption may help reduce blood glucose levels by boosting insulin production. Meanwhile, GLE therapy was linked to a reduction in diabetes problems in type 2 diabetic rats by improving their liver and renal functioning.*

Keywords: *Ganoderma lucidum, Weight, blood glucose, glycosylated hemoglobin, insulin.*

INTRODUCTION

Fasting and postprandial blood glucose levels rise because of his actions. Hyperglycemia develops if the unbalanced homeostasis does not return to normal and persists for an extended period of time, leading to diabetes mellitus (DM), **(WHO, 1999 and Tiwari and Madhusudana, 2002).**

Furthermore, people with diabetes have bodies that either do not produce enough insulin or cannot use the insulin they do produce as well as they should. When there Insulin is not enough or cells stop responding to it, blood sugar stays too much in your system. This can lead to serious health problems at the end. Such as reviewed by **WHO, (1999) and Yang et al., (2016),** the primary complications of DM due to damage in small blood vessels include damage to the eyes (Diabetic retinopathy), kidneys (diabetic nephropathy), and nerves (Diabetic neuropathy). DM is also a leading cause of blindness, kidney failure, heart attacks, strokes, and lower limb amputations, according to **Konstantinos *et al.*, (2018)**. This disease is divided into two types. Type 1 diabetes (T1D), also known as insulin-dependent diabetes (IDD), and Type 2 diabetes (T2D), also known as noninsulin-dependent diabetes, are two types of diabetes (NIDDM). T2D is the most common type of diabetes, accounting for more than 90% of all diabetes cases around the world (IDF, 2021). Hyperglycemia in T2D is caused by the body's cells' failure to respond adequately to insulin, a condition known as insulin resistance **(Stumvoll *et al.*, 2005).** Insulin resistance reduces the hormone's effectiveness, resulting in an increase in insulin production. Because of the pancreatic beta cells' inability to keep up with demand, insufficient insulin production might develop over time. According to the International Diabetes Federation (IDF), 537 million adults (20-79 years) would have diabetes by 2021, accounting for one out of every 10 persons. This number is predicted to rise to 643 million by 2030, and to 783 million by 2045. Diabetes will be the cause of 6.7 million deaths in 2021, or one every five seconds. Low- and middle-income countries have a higher prevalence of diabetes than high-income countries (**Tiwari**

and Madhusudana, 2002). In Egypt, People with diabetes (20-79 y) estimates 10.93 million in 2020 which predicted to rise to 13.74 million by 2030 and 19.98 million by 2045 **(IDF, 2021).**

Furthermore, the expense of administering contemporary anti-diabetic medications is out of reach for the majority of low-income people and those living in rural areas **(Jevas, 2011).** In this context, DM caused at least USD 966 billion dollars in health expenditure by 2021 – a 316% increase over the last 15 years. For all of these reasons, numerous traditional medicinal systems take a more holistic approach to healing. Modern techniques are still unable to describe the fundamental mechanics of these medical systems. Traditional remedies are made up of a number of plant components (vegetables, fruits, herbs, spices, algae, and so on) that are said to work on a variety of objectives through a variety of modes and methods **(Tiwari and Madhusudana , 2002; Elhassaneen *et al.*, 2016 and Matsui *et al.*, 2006).** As a result, there has been a surge in interest in plant-based medicines that can be used by the public but are difficult to maintain over term with the least number of side effects and the best preventive outcomes (**Matsui *et al.*, 2006**). The reishi mushroom (*Ganoderma lucidum*) is a wood-decaying fungus that belongs to the Polyporales family Ganoder-maceae and has hard fruiting bodies **(Leskosek *et al.*, 2010).** According to nutritional research, G. *lucidum* is primarily composed of protein, fat, carbohydrate, and fibre **(Stojkovi *et al.*, 2014).** *G. lucidum*'s fruiting body, mycelia, and spores contain roughly 400 distinct bioactive/ phytochemical chemicals, primarily triterpenoids, polysaccharides, nucleotides, ster-ols, steroids, fatty acids, proteins/peptides, and trace elements. *G. lucidum* has been reported to have immune-modulating, anti-inflammatory, analgesic, chemo-preventive, anti-tumor, radio protective, sleep promoting, antibacterial, antiviral (including anti-HIV), hypo-lipidemic, anti-fibrotic, hepato-protective, anti-oxidative and radical-scavenging, anti-aging, hypoglycemic, and anti-ulcer properties due to its unique content of bioactive compounds and their biological roles (reviewed in **Liu,**

1998; McKenna *et al.*, 2002 and Wasser, 2005). Although there have been few investigations on the association between *G. lucidum* nutrition and diabetes. As a result, the current work used a streptozotocin (STZ) -induced diabetic rat model to assess the efficiency of in regulating hyperglycemia. GLE's influence on liver and renal functions, as well as several biomarkers of hyperglycemic consequences were studied.

MATERIAL AND METHODS

Material

Reishi mushroom:

Dried fruits of reishi mushroom (*Ganoderma lucidum*) were purchased from ElMisryia Company for Trading Herbs and Medical Plants (Haraz), Bab ElKhalk, Cairo, Egypt. Taxo-nomic confirmation of *G. lucidum* was carried out by the Agricultural Plant Department, Faculty of Agriculture, Menoufia University, Shebin El-Kom, Egypt.

Chemicals:

Streptozotocin (STZ), which was utilized to induce DM in rats, was purchased from Sigma Chemical Co. in St. Louis, Missouri. Morgan Company for Chemicals provided casein as the primary protein source. Cairo is the capital of Egypt. El - Ghomhorya Company for Trading Drugs, Chemicals and Medical Instru-ments, Cairo, Egypt, provided analytical quality vitamins and salts mixes, organic solvents, and other chemicals.

Kit's: Kit's assays for serum glucose, alanine aminotransferase (ALT), aspartate aminotransferase (AST) and alkaline phosphatase (ALP) were purchased from BIODIAGNOSTIC, Dokki, Serum creatinine and urea from Biocon Company, Cairo, Egypt.

Machines:

All biochemical analyses were performed with a UV-visible -light spectrophotometer (UV-160A; Shimadzu Corporation, Kyoto, Japan).

Methods

Preparation of Ganoderma lucidum* ethanol extract *(GLE)

Dried fruits of *Ganoderma lucidum* samples were ground in high miller speed (Moulinex Egypt, Al-Araby Co., Egypt), reduced to powder (20 mesh), and mixed to obtain homogeneous samples. GLE was prepared such as mentioned in **Oludemi *et al.*,**

(2017). Five grams of *G. lucidum* dry powder were extracted in an 80 percent ethanol Soxhlet apparatus (Soxhelt Semiautomatic equipment Velp business, Italy) for 5-6 hours (25-5 minutes per cycle). To obtain the dried solvent extract, the solvent was evaporated under reduced pressure (rotary evaporator Büchi R-210, Switzerland) and stored at 4 0C before use. The total yield of GLE was 1.16% (w/w) in terms of the *G. lucidum* fruiting body.

Biological experimental

Ethical approval

The biological experiments for this study were approved by the Scientific Research Ethics Committee (Animal Care and Use), Faculty of Home Economics, Menoufia University, Shebin El-Kom, Egypt (Approval no. 05- SREC- 11-2020).

Animals

Adult male albino rats (130-140 g) were procured from Helwan Station, Ministry of Health and Population, Helwan, Cairo, Egypt, for this investigation.

Basal Diet

The basic diet for rats was made according to the following formula, as stated by **Reeves *et al.*, (1993) with some modified:** protein, 10%; corn oil, 10%; vitamin mixture, 1%; mineral combination, 4%; choline chloride 0.2 percent; methionine 0.3 percent; cellulose 5%; and corn starch, 69.5 percent. According to **AIN, (1993)** the vitamins and salts mixture components were formulated.

Induction of diabetes

In the trials, normal healthy rats were given a single intraperitoneal injection of STZ at a low dose (45 mg/kg body weight, dissolved in 0.05 M citrate buffer, pH 4.5, shortly before usage) to create a diabetic state, as described by **Ji et al., (2011).** After 72 h injection of STZ, fasting blood glucose (FBG) levels were determined from tail blood using a specific kit (Bio diagnostic, Dokki Cairo, Egypt). The rats with FBG levels were higher than 126 mg/dl demonstrating a successful induction of diabetes. (**Wang *et al.*, 2010**).

Experimental design

All biological studies were carried out the National Research Council's Institute of Laboratory Animal Resources, Commission on

Life Sciences rules **(NRC, 1996)**. Rats (n=36 rats), were housed individually in wire cages in a room maintained at 25 ± 2 ^{0}C and kept under normal healthy conditions. For acclimation, all rats were fed a basic diet for one week before beginning the experiment. The rats were divided into two groups after a one-week period for acclimation; all rats were fed a basic diet for one week before beginning the experiment. The rats were divided into two groups after a one-week period. The first group, normal control, group 1 (6 rats) still fed on basal/standard diet (SD). The other main group (30 rats) was used for diabetes induction and classified into five sub-groups as follow: group (2), model control, fed on standard diet only as a positive control (rats with diabetes) and groups (3-6) fed on BD and administered by oral gavages, using a feeding needle with 200, 400, 600, and 800 mg/kg BW GLE, respectively. GLE extract concentrations were selected for experiments based on many of the results of our previous studies **(Salman, 2016; Elhassaneen *et al.*, 2016, Sayed-Ahmed *et al.*, 2020).** For 28 days, each of the above groups was housed in a single cage. Rats were weighed at the start of the trial, then weekly, and finally at the completion of the experiment.

Biological evaluation

The diet consumed was recorded every day; body weight was every week during the experimental period (28 days). The following equations were used to compute the body weight gain (BWG, percent), food intake (FI), and food efficiency ratio (FER) according to **Chapman *et al.*, (1959)**: BWG (%) = (Final weight – Initial weight)/ Initial weight×100, FER = Grams gain in body weight (g/28 day)/ Grams feed intake (g/28 day)**.**

Blood sampling

At the end of the 28-day trial, blood samples were taken from the abdominal aorta after 12 hours of fasting, and rats were sacrificed under ether an aesthesia. For collecting plasma and serum, blood samples were deposited in clean, dry centrifuge tubes and allowed to clot at room temperature before being spun for 10 minutes at 3000 rpm to separate the serum, according to **Drury and Wallington (1980).** The serum was gently aspirated, transferred to

clean sterile tubes, and frozen until analysis at -20°C.

Hematological analysis

The following procedures were used to determine the various measured parameters in serum: aspartate aminotransferase (AST), alanine aminotransferase (ALT) and alkaline phosphatase (ALP) activities according to **Tietz, (1976),** and **Yound, (1975),** respectively. Colorimetric measurement of serum glucose was done using enzymes according to **Yound, (1975) and Tietz, (1976).** Insulin level was determined according to the method of **Held (2009).** Serum creatinine and urea concentrations were determined using the modified kinetic methods of **Fawcett and Soctt, (1960)**, Chaney **and Marbach (1962)**, respectively. Glycosylated hemo-globin was determined according to the improved colorimetric assay of ***Parker et al.*, (1981).**

Statistical Analysis

Student *t*-test and MINITAB 12 computer programme statistical software were used to evaluate the data (Minitab Inc., State College, PA). The results were presented as means ± a standard deviation (SD). Differences between treatments at $P \leq 0.05$ were considered significant **(Snedecor and Cochran, 1967).**

RESULTS AND DISCUSSION

Effect of GLP intervention on body weight gain (BWG), feed intake (FI) and feed efficiency ratio (FER) of diabetic rats

BWG, FI and FER of diabetic and intervention by *G. lucidum* ethanol extract (GLE) were shown in Table (1) and Figure (1). From such data it could be noticed that the STZ-treated rats exhibited significantly ($p \leq 0.05$) decreased in percent change of BWG (-38.82), FI (-31.72) and FER (-23.29) compared to the normal group. However, intervention with GLE (200 to 800 mg/kg BW) in feeding rats for 28 days significantly ($p \leq 0.05$) led to an increase the levels of BWG, FI and FER. The rate in those parameters exhibited a dose-dependent increase with GLE intervention. Such data are in agreement with that observed by many authors whither it is in *G. lucidum* or other genera of algae **(Salman, 2016; Elhssaneen *et al.*, 2019; Sayed-Ahmed *et al.*, 2020 and Essa, 2021)**. Such as reported by **Sayed-Ahmed et al., (2020)** the

decreasing in BWG, FI and FER as the result of *G. lucidum* consumption could be attributed to its bioactive compounds content and the consequences thereof biological effects. In the same context, **Tahoon, (2019),** and **Elhassaneen *et al.*, (2021)** reported that injection of rats by CCl_4 induced hepatotoxic and diabetic effects led to decrease in BWG, FI and FER. Consumption of plant components containing bioactive chemicals, like as those found in GLE, helped such illnesses. **Hamzawy *et al.*, (2013) and Abd El-Rahman (2021)** discovered that hepatic rat problems caused by diabetes result in a considerable reduction in BW and FI. Furthermore, multiple studies have shown that people with diabetes and liver problems are at risk of malnutrition. Poor eating habits, maldigestion, malabsorption, and anomalies in macro and micronutrient metabolism and storage are among them **(Morresion and Hark, 1999; Elhassaneen *et al.*, 2014; Sayed Ahmed *et al.*, 2016; Aly *et al.*, 2017; and Abd El-Rahman, 2021).**

The effect of GLE intervention on serum glucose and insulin of diabetic rats

Data in Table (2) and Figures (2-3) were shown the effect of GLE on serum glucose and insulin concentration of STZ-induced diabetic rats. Such data indicated that treatment of rats with STZ caused a significant increase ($P \leq 0.01$) in serum glucose concentration by percent change as 283.68% compared to normal controls. Intervention with GLE (200, 400, 600 to 800 mg/kg BW) in feeding rats for 28 days led to significantly ($P \leq 0.05$) decrease the levels of serum glucose, which recorded 256.07, 223.82, 158.94 and 141.13% change compared to the normal controls, respectively. The opposite direction was observed for insulin level. Treatment of rats with STZ caused a significant decreasing ($p \leq 0.01$) in serum insulin concentration by the ratio -49.75% change compared to normal controls. Intervention with GLE (200, 400, 600 to 800 mg/kg BW) in feeding rats for 28 days led to a significantly ($p \leq 0.05$) increase the levels of serum insulin which recorded -44.38, -41.09, -32.43, and 30.64% change versus the normal controls, respectively. The

rate of increase in serum glucose and insulin were exhibited a dose-dependent boost with GLE intervention. When comparing the diabetes (model) group to the control/normal group, serum insulin levels were found to be considerably lower in the diabetic (model) group. These findings are consistent with **Kocak *et al.*, (2000); Melhem *et al.*, (2002) and Kandeil *et al.*, (2007)**.

Streptozotocin is a commonly utilized DM inducer in laboratory animals. It can cause chronic or persistent diabetes in these animals by selectively destroying pancreatic islet cells **(Mathe, 1995; Elhassaneen *et al.*, 2021).** The results demonstrated that serum glucose concentrations in diabetic rats were substantially higher than in normal rats. As in the case of insulin-dependent diabetes mellitus IDDM, chronic hyperglycemia can be caused by a deficiency in insulin secretion **(Kandeil *et al.*, 2007).** STZ generates several types of reactive oxygen species/radicals (ROS) that attack DNA generating DNA-strand breaks in β-cell, as stated by **Lenzen, (2008)** in experimental diabetes that may represent a model of T2D. The breaks cause the poly adenosine diphosphate-ribose (ADP-ribose) polymerase (PARP) to be activated, which uses nicotinamide adenine dinucleotide^{+} NAD+ as a substrate to repair the DNA. As a result, NAD+ levels within cells decrease. NAD+ deficiency limits ATP synthesis and cellular processes, as well as insulin synthesis and secretion, and the β-cell eventually dies **(Pusztai *et al.*, 1996).** This would result in decreased glucose uptake by peripheral tissues such as muscles and adipose tissue, as well as increased glycogenolysis, gluco-neogenesis, and hepatic glucose synthesis. **(Gold, 1970; Caro, 1990; Raju *et al.*, 2001; Beck-Nielsen, 2002 and Jung *et al.*, 2011).** Perhaps this notion is supported by the current study's findings, which show that serum glucose levels in the diabetic group intervention GLE were much lower and serum insulin levels were significantly higher than in the diabetic/model group. The numerous bioactive components discovered in GLE may be responsible for its hypoglycemic impact in STZ-induced diabetic mice. **Skalicka-Wozniak *et al.*, (2012), Liu *et al.*, (2017), and Darija *et al.*, (2018)** discovered

that G. *lucidum* is a rich source of bioactive components such as phenolic, lycopene, Polysaccharides, terpenoids, flavonoids, triterpenoids, and vitamins (A, B, and E). Sterols, amino acids, soluble proteins, oleic acid, cyclooctasulfur, ergosterol peroxide, and cerebrosides are all found in Reishi (**Mizuno, 1995; McKenna *et al.*, 2002; Gao *et al.*, 2003**). These compounds are known for their antioxidant properties, lipid oxidation suppression, and free radical/ROS scavenging action, all of which aid type 2 diabetes patients with glycemic control, metabolic dysregulation of free fatty acids, and insulin resistance **(Elhassaneen *et al.*, 2012-2015; Aly *et al.*, 2017; Elbasouny *et al.*, 2019).**

Several previous studies, along with others, have proven that bioactive compounds (Phe-nolic, flavonoids and lycopene) which was spotted in this study inside *G. lucidum* play an important vital role in preventing and/or treating many diseases including diabetes **(Elhassaneen *et al.*, 2014; 2016, Sayed Ahmed *et al.*, 2016; Aly *et al.*, 2017 and Abd El-Rahman, 2021).** In addition, **Tiwari and Madh-usudana (2002)** reviewed that bioactive compounds found in G. *lucidum*, such as polyphenolics, have been reported to inhibit alpha-amylase and sucrose, and have been shown to be the primary substance for suppressing postprandial hyperglycemia, in addition to their well-known antioxidant properties. Further more, **Wasser (2005)** demonstrated in experimental animals that the polysaccharide fractions of G. *lucidum* had potential hypoglycemic and hypolipidemic effects. In addition, a water extract of *G. lucidum* reduced the increase in blood glucose and blood insulin levels in rats (50 mg p.o.) following oral glucose test. Additionally, *G. lucidum* glycan's have shown significant hypoglycemic activity in mice.

Effect of GLE intervention on glycosylated hemoglobin (HbA_1c) level of diabetic rats

Data in Table (3) and Figures (4-5) were shown the effect of GLE on glycosylated hemoglobin (HbA_1c) level of STZ-induced diabetic rats. Such data indicated that treatment of rats with STZ caused a significant increased ($p \leq 0.01$) in HbA_1c concentration by the ratio 97.93% change

compared to normal controls. Intervention with GLE (200, 400, 600 to 800 mg/kg BW) in feeding rats for 28 days led to significantly ($p \leq 0.05$) decrease the levels of HbA_1c, which recorded 80.04, 62.15, 40.30 and 32.02%, change compared to the normal controls, respectively. The rate of increasing in HbA_1c was exhibited a dose-dependent boost with GLE intervention. The HbA1c measurement results show that diabetic rats treated with dose of 800 mg/kg BW GLE has the best outcome compared to the other treatments. HbA1c measurement may become a parameter for the capability of GLE in producing anti-diabetes effect on diabetic rats. This is fending in line with the results of plasma glucose and insulin level measurement. Some researches show close relationship between HbA1c concentration and mean blood glucose level **(Begley, 2012 and Nuniek et al., 2018).**

HbA1c is a form of hemoglobin (Hb) that is chemically linked to a sugar (all monosaccharides, including glucose, galactose and fructose). The formation of the sugar hemoglobin linkage indicates the presence of excessive sugar in the bloodstream, often indicative of diabetes **(Bunn and Higgins, 1981).** Because it is so easy to identify, A_1C is of particular interest. It is utilized to detect the three-month average blood glucose level and a DM diagnostic test as well as a glycemic management assessment test in persons with diabetes (WHO, 2011). As the average amount of plasma glucose increases, the fraction of glycated hemoglobin (HbA_1c) increases in a predictable way. The International Diabetes Federation (IDF) recommend HbA_{1c} values below 48 mmol/mol (6.5 DCCT % , Diabetes Control and Complications Trial,), while the American Diabetes Association (ADA) recommends HbA_{1c} be below 53 mmol/mol (7.0 DCCT %) for most patients **(Miedema, 2005).** Persistent elevations in HbA_{1c} increase the risk of long-term vascular complications of diabetes, such as coronary disease, heart attack, stroke, heart failure, kidney failure, blindness, erectile dysfunction, neuropathy etc. (**Shubrook and Shubrook, 2010; Saleh, 2015).** In the current study $HbA_{1c,}$ levels significantly decreased in diabetic group intervention GLE the

diabetic / model group. Such hypoglycemic (HbA_{1c}) effect of GLE in STZ-induced diabetic rats may be related to the diverse bioactive compounds found in GLE. **Gao et al., (2003)** found that treatment with Ganopoly (GL poly-saccharide extract) significantly decreased the mean HbA1c from 8.4% at baseline to 7.6% at 12 weeks.

Effect of GLE intervention on liver functions of diabetic rats

The effect of GLE intervention on serum liver functions enzymes activities AST, ALT and ALP of diabetic rats induced by STZ were shown in Table (4) and Figure (6-7). Such data indicated that STZ caused a significant ($p \leq 0.05$) increased in AST, ALT and ALT with 30.79, 29.85 and 45.68% change compared to normal control group, respectively. Intervention with GLE (200, 400, 600 to 800 mg/kg BW) in feeding rats for 28 days led to significantly ($p \leq 0.05$) decrease the levels of those enzymes activities, which recorded 21.87, 17.75, 11.35 and 10.53% (for AST), 28.62, 25.42, 18.94 and 12.44% (for ALT), and 39.74, 22.51, 16.02 and 14.14% (for ALP) compared to the normal controls, respectively. The rate of decreasing in serum liver enzymes activities were exhibited a dose- dependent increase with GLE intervention.

Intracellular enzymes include aminotransferases (ALT and AST) as well as ALP. As a result, high levels of aminotransferase (AST and ALT) and ALP in the blood indicate that cells that produce these enzymes have been damaged. Cell lysis in the liver and pancreas, for example, might result in the release of intracellular enzymes into the bloodstream **(Pagana and Pagana, 1997 and Sayed-Ahmed *et al.*, 2020).** *G. lucidum* has long been used to treat chronic hepatitis caused by a variety of reasons *G. lucidum* powder and extracts (primarily polysaccharides or triterpenoids) appear to protect against liver injury caused by toxic substances (e.g., CCl4), according to data from in vitro and animal experiments (**Sayd-Ahmed *et al.*, 2020**). The mechanisms underlying *G. lucidum*'s hepato-protective effects are unknown. Antioxidant and radical scavenging activities, modulation of hepatic Phase I and II meta-bolizing enzymes, inhibition of -glucuronidase, anti-fibrotic and antiviral activity,

modulation of NO production, maintenance of hepatocellular calcium homeo-stasis, and immunomodulatory effects are all possible mechanisms **(Gao *et al.*, 2003; Sayed-Ahmed *et al.*, 2020).** Also, *G. lucidum* are a rich source of different bioactive compounds including phenolic, lycopene, polysaccharides, terpenoids, flavonoids, triterpenoids and vitamins (A, B and **E) (Skalicka-Wo_zniak *et al.*, (2012), Liu *et al.* (2017)and Darija *et al.*, 2018).** Bioactive compounds could be lowered liver serum enzymes through many suggested effects including blocking the hepatocellular uptake of bile acids. Improving the antioxidant capacity of the liver. Diminishing the bilirubin concentration reducing the damage of hepatocytes. Scavengers of reactive oxygen species" **(Beattic *et al.*, 2005; El-Nashar, 2007; Aly *et al.*, 2017; Mahran *et al*., 2018 and Sayed-Ahmed *et al.*, 2020).**

Effect of GLE intervention on kidney functions of diabetic rats

The effect of GLE intervention on serum kidney functions parameters (urea and creatinine concentrations) of diabetic rats induced by STZ were shown in Table (5) and Figure (8-9). Such data indicated that STZ caused a significant ($p \leq 0.05$) increased with percent change in urea (65.37%) and creatinine (43.62%) parallel to normal controls, respectively. Presence of GLE (200, 400, 600 to 800 mg/kg BW) in feeding rats for 28 days led to a significantly ($p \leq 0.05$) decrease the levels of those parameters recorded 58.25, 47.57, 26.86 and 25.89% (for urea), and 35.77, 33.17, 27.25 and 16.48% (for creatinine), respectively. The rate of decrease in kidney functions parameters has exhibited a dose-dependent increase with GLE intervention.

The liver produces urea as a byproduct of protein metabolism. Protein is broken down into amino acids during digestion, which are catabolized, resulting in the formation of free ammonia. The ammonia are mixed to make urea (**Pagana and Pagana, 1997**). Ammonia is highly toxic, it is detoxified through conversion to urea, which is nontoxic and water-soluble and is excreted through urine by the kidneys. Hence, blood urea level can be considered a predictor of hepatic or renal

functional status (**Bennett *et al.*, 1995 and Pagana and Pagana, 1997**). Creatinine is a breakdown product of creatine phosphate in a muscle that the body produces at a relatively consistent pace (depending on muscle mass). It is an easily detectable by product of muscle metabolism that is eliminated unchanged by the kidneys. Serum creatinine (a blood measurement) is an essential indicator of renal health **(Pagana and Pagana, 1997)**. The decreasing in serum urea and creatinine as the result of GIE could be attributed to its high content of bioactive compounds such phenolics, lycopene, polysaccharides, terpenoids , flavonoids, triterpenoids and vitamins (A, B and **E) (Elhassaneen *et al.*, 2012, Skalicka – Wo _ zniak *et al.*, (2012), Liu *et al.* (2017) 2016b and Darija *et al.*, 2018).** Similar research **(Bedawy, 2008)** found that eating plant parts resulted in lower serum urea and creatinine levels due to their increased phenolic component content. Furthermore, **El-Sayed *et al.*, (2012)** discovered that increasing the amount of *henada*, lemon balm leaves, hawthorn leaves, rose of Jericho, and corn cob silk in the diet by 5 and 10% in the presence of CCl4 resulted in significant improvements in all kidney functions, including serum urea and creatinine levels. One or more of the following processes could explain the proposed mechanisms of kidney serum parameters reducing the investigated by-products. GLE polyphenols boosted the activity of superoxide dismutase in the kidney and improved kidney weight and serum levels of urea nitrogen, creatinine, and creatinine clearance (reviewed in **El-Nashar, 2007**). Flavonoids also reduced plasma creatinine and urea levels, indicating improved kidney function following surgery (**Van Hoorn *et al.*, 2006**).

Correlation studies

The correlation analysis revealed significant differences between biological (BW) and biochemical [serum glucose, serum insulin, HbA_1c, liver functions (AST, ALT and ALP) and kidney functions (urea and creatinine)] parameters in diabetic rats administrated GLE (Table 6). It was discovered from the data that BW and serum glucose had a negative significant ($p \leq 0.05$) association ($r^2 = -0.6331$) and

HbA1c (r^2 = - 0.5964) while the relevance was positive with serum insulin (r^2 = 0.6057). Also, high positive significant ($p \leq 0.05$) relation with recorded between serum glucose and HbA_1c (r^2 = 0.7796), serum creatinine (r^2 = 0.6117) and urea (r^2 = 0.5974) and negative with insulin (r^2 =- 0.7998). Furthermore, no significant rapport was observed between serum glucose and all liver functions parameters including AST, ALT and ALP. These findings corroborated our findings, which indicated a significant rise ($p \leq 0.05$) in mean BWG in diabetic rats given GLE compared to diabetic rats; although still lower than control rats. GLE is also an insulin sensitizer, according to **Wasser (2005),** since it can promote insulin-stimulated glucose absorption, improve insulin sensitivity, and hence increase BW. Furthermore, GLE is potential to improve insulin sensitivity and speed pancreatic- β-cells regeneration can nearly reverse metabolic changes associated with diabetes and boost BW. The HbA1c measurement results show that diabetic rats treated with dose of 800 mg/kg BW GLE have the best outcome compared to the other treatments. Thus, HbA1c measurement may become a parameter for the capability of GLE in producing an anti-diabetic effect on diabetic rats. This is in line with the results of serum glucose and insulin levels measurement. Such as shown in the present correlation analysis, some researches show close interrelation between HbA1c concentration and mean serum glucose level **(Sultanpur et al., 2010 and Begley, 2012).**

CONCLUSION

The results of this investigation show that the selected (*Ganoderma lucidum*) extract is effective to ameliorate hyperglycemia and its complications in diabetic rats. The mechanisms of the anti-diabetic effects of *G. lucidum* have been not fully understood. However, accumulating evidence by the present study suggests several possible mechanisms: accelerating recovery of pancreatic β-cells, i.e. increasing the insulin secretion / sensitivity, improving insulin stimulated glucose uptake, and reducing the damage of liver and kidney cells. Such strategies can almost completely reverse the metabolic changes caused by

diabetes. These findings provide the use of the *Ganoderma lucidum* extract for the protection and improvement of type 2 diabetes.

REFERENCES

Abd El-Rahman N (2021):
Potential effect of olive and mango leaves in diabetic rats induced by aloxane ". MSc. *Thesis in Nutrition and Food Science, Faculty of Home Economics, Minoufiya University,* Shebin El-Kom, Egypt.

Aly A; Elbassyouny GM and Elhassaneen YE (2017):
Studies on the antioxidant properties of vegetables processing by-products extract and their roles in the alleviation of health complications caused by diabetes in rats. Proceeding of the *1st International Conference of the Faculty of Specific Education, Kafrelsheikh University,* "Specific Sciences, their Developmental Role and Challenges of Labor Market" 24-27 October, 2017, PP 1-24, Sharm ElSheikh, Egypt.

Beattic J; Crozier A and Duthie G (2005):
Potential Health Benefits of berries. *Current Nutrition & Food Science*. 1: 71-86.

Bec-Nielsen H (2002):
Insulin resistance: organ manifestations and cellular mechanisms. *Ugeskr. Laeger*, 15; 164(16): 2130-5.

Bedawy O (2008):
Relationship between phyto -sulphur compounds and lipid of blood in experi-mental animals. M. Sc. *Thesis in Nutrition and Food Science, Faculty of Home Economics, Minoufiya University,* Egypt.

Begley J (2012):
HbA1c in Diabetes. Case Studies Using IFCC Units. *Ann. Clin. Biochem.,* 49(5), 512–512.

Bennett PH; Mogensen CE and Keane WF(1995):
Prevention of diabetic renal disease with special refe-rence to microalbuminuria. *Lancet,* 346:1080–4.

Bunn HF and Higgins PJ (1981):
"Reaction of monosaccharides with proteins: possible evolutionary significance". *Science,* 213 (4504): 222–24.

Caro JF (1990):
Effect of glyburide on carbohydrate metabolism and insulin action. *Am. J. Med*., 89 (20): 17S-24S.

Chaney AL and Marbach EP (1962):
Modified reagents for determination of urea and ammonia. *Clin Chem*; 8:130-132.

Chapman DG; Castilla R and Champbell JA (1959):
Evaluation of protein in food. I.A Method for the determination of protein efficiency ratio. Can. *J. Biochemistry on Liver Disorder Initiation* by carbon Tetra Chloride. M. Sc Thesis, Faculty of Home Physiology, 37: 679-686.

Darija C; Željko K and Maša K (2018):
Anti-tumor, Anti-microbial, Anti-oxidant and Anti-acetylcholinesterase Effect of *Ganoderma Lucidum* Terpenoids and Polysaccharides: A Review. *Molecules*. 13;23(3):649.

Drury RA and Wallington EA (1980):
Carlton's Histological Technique. Fifth Ed. Oxford Univ. Economics, Menoufia University, Shebin Elkom, Egypt.

Elbasouny G; Shehata N and Elhassaneen Y (2019):
Feeding of some selected food industries by-products induced changes in oxidants /antioxidant status, lipids profile, glucose and immunological parameters of blood obese rats. *The 6th Scientific and 4th International Conference* "The Future of Specific Education and people with Special Needs in Light of the Concept of Quality ", 24-26 February 2019, Faculty of Specific Education, Ain Sokhna University, El-Ain El-Soghna, Egypt.

Elhassaneen Y; Ragab S; Thoraya M; Azza E and Abeer A (2012):

Effect of Sweet Violet (Viola odorata L.) Blossoms Powder on Liver and Kidney Functions as well as Serum Lipid Peroxidation of Rats Treated with Carbon Tetrachloride. The Journal of American Science, 9 (5):88-95.

Elhassaneen Y; Samia G; Ryeaan S and Mayada Y (2016):

Onion, orange and prickly pear peel extracts mixed with beef meatballs ameliorates the effect of alloxan induced diabetic rats. *American Journal of Pharmacology and Phyto-therapy*, 1 (1): 15-24.

Elhassaneen Y; Mohamed M and Hassan H (2014):

The effect of some food products mixed with plant parts on blood sugar levels of rats. *3rd International-17 th Arab Conference of Home Economics* "Home Economics in the Service of Science, Industry and Society Issues" 9-11 September, 2014, Faculty of Home Economics. Minoufiya University, Egypt. *Journal of Home Economics* (Special issue), 24(4): 85-109.

Elhassaneen Y; Ragab S and Saleh A (2015):

Effect of selected plant parts extracts on liver injuries induced by CCl_4 *in vitro*. *Pyrex Journal of Medicinal Plant Research*, 2 (2): 8-20.

Elhassaneen Y; Sherif M; Seham K and Salman NM (2019):

Effect of Some Plant Parts Powder on Obesity Complications of Obese Rats. *Journal of Home Economics*

Elhassaneen Y; Ragab S; Abd El-Rahman A and Arafa S (2021):

Vinca (Catharanthus roseus) Extracts Attenuate Alloxan-Induced Hyperglycemia and Oxidative Stress in Rats. *American Journal of Food Science and Technology*, 9 (4): 161-172.

El-Nashar NG (2007):
Development of primary liver cell culture from fish as a valuable tool in nutrition and biotechnology research. Ph.D. *Thesis in Nutrition and Food Science, Faculty of Home Economics, Minoufiya University*, Egypt.

El-Sayed M; El- Sherif F; Elhassaneen Y and Abd El-Rahman A (2012):
Potential Therapeutic Effe-cts of some Egyptian Plant Parts on Hepatic Toxicity Induced by Carbon Tetrachloride in Rats. *Life Sci. J*., 9(4):3747-3755 [ISSN: 1097-8135]

Essa ME (2021):
Chemical and nutritional studies on extracts of food processing by-products and their effects on obesity complications in rats. MSc. *Thesis in Nutrition and Food Science, Faculty of Home Economics, Minou-fiya University, Shebin El-Kom*, Egypt.

Fawcett JK and Soctt JE (1960):
Determination of urea. *J. Clin. Path*., 13: 156-159.

Gao Y; Zhou SH; Huang M and Xu A (2003):
Antibacterial and antiviral value of the genus *Ganoderma P. Karst. Species*(Aphyllophoromycet ideae): a review.

Gold, A. H. (1970):
The effect of diabetes and insulin on liver glycogen synthetase activation. *J. Biol. Chem*., 245: 903-905.

Hamzawy MA; El-Denshary ES; Mannaa FA and Abdel Wahhab MA (2013):
Dietary supplementation of Calendula officinal is counteracts the oxidative stress and liver damage resulted from aflatoxin. *ISRN Nutrition*, 9 (10): 5402-538427.

Held, P. (2009):
Determination of Insulin Levels in Human Serum. BioTek Instruments, Inc., Winooski, Vermont, USA

IDF, (International Diabetes Federation) (2021):
IDF Diabetes Atlas, 10th edition, Brussels, Belgium.

Jevas O (2011):
Anti-diabetic effects of *Allium cepa* (onions) aqueous extracts on alloxan-induced diabetic *Rattus novergicus*. Journal of Medicinal Plants Research, 5(7): 1134-1139.

Ji Y; Jung Y; Min S; Ji Y and Oran K (2011):
Onion peel extracts ameliorate hyperglycemia and insulin resistance in high fat diet / streptozotocin-induced diabetic rats. *Nutrition & Metabolism*, 8:18: 1-8.

Jung Ji Y; Yeni L; Min S; Ji Y; Yeon K and Oran K (2011):
Onion peel extracts ameliorate hyperglycemia and insulin resistance in high fat diet / streptozotocin-induced diabetic rats, *Nutrition & Metabolism*, 8:18:2-8.

Kandeil MA; Amin KA; Hassanin KM; Ali KM and Mohamed ET (2007):
Serum levels of insulin and leptin in lipoic acid- treated and non-treated experiment-tally diabetic rats. *BS. VET. MED. J.*, 5TH scientific conference, PP. 87-95.

Kocak G; Aktan F; Canbolat O; Ozogul C; Elbeg S; Yildizoglu-Ari N and Karasu C (2000):
ADIC study group-antioxidants in diabetes-induced complications. Alph-alipoic acid treatment ameliorates metabolic para-meters, blood pressure, vascular reactivity and morphology of vessels already damaged by streptozotocin in diabetes. *Diabetes Nutr. Metab*., 13(6): 308-18.

Konstantinos P; Maciej B; Eleni B and Manfredi R (2018):
Complications of Diabetes 2017. *Journal of Diabetes Research* P.1-4.

Lenzen S (2008):
The mechanisms of alloxan- and streptozotocin-induced Diabetes. *Diabetologia.* 51: 216 –226.

Leskosek I; Sasa D; Lakic N and Niksic M (2010):
Ganoderma lucidum Medical mushroom as a raw material for beer with enhanced functional properties. *Food Research International* 43 (9) : 2262-2269.

Liu KC; Phounsavan SF; Huang RL; Liao C; Hsu SY and Wang KJ (1998):
Pharmacological and liver functional studies on mycelium of *Ganoderma lucidum. Chin Pharm J*.; 40: 21–9.

Liu Z; Xing J; Zheng S; Bo R; Luo L; Huang Y; Niu Y; Li Z; Wang D; Hu Y; Liu J and Wu Y (2017):
Ganoderma lucidum polysaccharides encapsulated in liposome as an adjuvant to promote Th1-bias immune response. *Carbohydr. Polym.* 142, 141e148.

Mahran MZ; Abd Elsabor RG and Elhassaneen YA (2018):
Effect of feeding some selected food-processing by-products on blood oxidant and antioxidant status of obese rats. Proceeding of the 1st Scientific *International Conference of the Faculty of Specific Education, Minia University*, "Specific Education, innovation and labor market" 16-17, 2018, Minia, Egypt.

Mathe, D. (1995):
Dyslipidemia and diabetes: animal models. *Diabetes. Metab*., 21(2): 106-111.

Matsui T; Ogunwande LA; Abesundara KJ and Matsumoto K (2006):
Anti-hyperglycemic potential of natural products. *Mini-Rev Med Chem.*, 6:109-120.

McKenna DJ; Jones K and Hughes K (2002):
Reishi Botanical Medicines. The Desk reference for Major Herbal Supplements, 2nd Ed.; *The Haworth Herbal Press: New York, London, Oxford.* P: 825–855.

Melhem MF; Craven PA; Liachenko J and DeRubertis FR (2002):
α-Lipoic acid attenuates hyperglycemia and prevents

glomerular mesangial matrix expansion in diabetes *J. Am. Soc. Nephrol.,* 13:108-116.

Miedema (2005):
Standardization of HbA1c and Optimal Range of Monitoring, Scandinavian. *Journal of Clinical and LaboratoryInvestigation, 65:s up240, 61-72.*

Mizuno T (1995):
Reishi, *Ganoderma lucidum* and *Ganoderma tsugae*: bioactive substances and medicinal effects. *Food Rev. Int.* 11 (1), 151–166.

Morresion G and Hark L (1999):
Medical Nutrition and Disease. *Second Edition. Black Whily, USA.*

NRC (National Research Council) (1996):
Guide for the Care and Use of Laboratory Animals Washin-gton: *National Academy Press.*

Nuniek I; Hernayanti1 S; Nuraeni E; Endang S and Dalia S (2018):
Effects of *Ganoderma lucidum* Extract on Diabetic Rats. *Biosaintifika* 10 (3): 642-647

Oludemi T; Heleno SA; Calhelha RC; Alves MJ; Barros L; González-Paramás AM; Barreiro MF and Ferreira I (2017).
The potential of *Ganoderma lucidum* extracts as bioactive ingredients in topical formul-ations, beyond its nutritional benefits. Food and chemical toxicology. *An international journal published for the British Industrial Biological Research Association.* 108 (Pt A), 139–147.

Pagana KD and Pagana TJ (1997):
Mosby's diagnostic and laboratory test references. *3 rd. ed., Mosby-year Book, Inc., New York.*

Parker KM; England JD; Da Costa J; Hess RL and Goldstein DE (1981):
Improved colorimetric assay for glycosylated hemoglobin. *Clin Chem*. 27(5):669-72.

Pusztai P; Prechl J; Somogy A; Szaleczky E and Feher J (1996):
Experimental models in research of the patho-mechanism of diabetes mellitus. *Orv. Hetil*., 137 (34):1865-1869.

Raju J; Gupta D; Rao AR; Yadava PK and Baquer NZ (2001):
Trigonellafoenum graecum (fenugreek) seed powder improves glucose homeostasis in alloxan diabetic rat tissues by reversing the altered glycolytic, gluconeogenic and lipogenic enzymes. *Mol. Cell. Biochem*., 224(1-2): 45-51.

Reeves PG; Rossow KL and Lindlauf J (1993):
Development and Testing of the AIN-93 Purified Diets for Rodents: Results on Growth, Kidney Calcification and Bone Mineralization in Rats and Mice. *Journal of Nutrition,* 123, 1923-1931.

Saleh J (2015):
Glycated hemoglobin and its spinoffs: Cardiovascular disease markers or risk factors? . *World Journal of Cardiology*. 7 (8): 449–53.

Salman MS (2016):
Immunomodulatory and mineral absorption improvement of some red mushroom. M.Sc. *Thesis in Nutrition and Food Science, Faculty of Home Economics, Minoufiya University, Egypt.*

Sayed Ahmed S; Elhassaneen Y; El-Waseef S and Fathy N (2016):
The effect of Plant by-products on liver functions and plasma glucose in rats fed a high fat diet induced obesity. *Port Saied Specific Education Journal* (PSSRJ), 19 (1): 649-659.

Sayed-Ahmed S; Shehata V and Elhassaneen Y (2020):
Potential Protective Effects of *Ganoderma lucidum* Powder against Carbon Tetrachloride Induced Liver Disorders in rats: Biological, Biochemical and Immunological Studies, Egypt. *Bulletin of the National Nutrition Institute of the Arab Republic of Egypt,* 56(2): 99-132.

Shubrook JH and Shubrook J (2010):
"Risks and benefits of attaining Hb A (1c) goals: Examining the evidence". The *Journal of the American Osteopathic Association. 110 (7 Supple*. 7): e7–e12.

Skalicka - Wo_zniak K; Szypowski J; Ło_SR; Siwulski M; Sobieralski K; Głowniak K and Malm A (2012):
Evaluation of polysaccharides content in fruit bodies and their antimicrobial activity of four *Ganoderma lucidum* (W Curt.: Fr.) P. Karst. Strains cultivated on different wood type substrates. *Acta Soc. Bot. Pol.*81, 17e21.

Snedecor GW and Cochran W G (1967):
Statistical Methods" 6th Ed. *Iowa State, USA.*

Stojkovic DS; Barros L; Calhelha RC; Glamoclija J; Ciric A; van Griensven, LJLD; Sokovic M and Ferreira, ICFR (2014):
A detailed comparative study between chemical and bioactive properties of *Ganoderma lucidum* from different origins. *Int. J. Food Sci. Nut*r., 65, 42e47.

Stumvoll M; Goldstein BJ and van Haeften TW (2005):
Type 2 diabetes: principles of pathogenesis and therapy. *Lancet*, 365:1333-1346.

Sultanpur CM; Deepa K and Kumar SV (2010):
Comprehensive Review on HbA1c in Diagnosis of Diabetes Mellitus. *Int J Pharm Sc Rev Resc*.;3:119-21.

Tahoon SR (2019):
Hepatoprotective effect of Apricot and Plum kernel on carbon tetrachloride induced hepatic rats ". M.Sc. *Thesis in Nutrition and Food Science, Faculty of Home Economics, Minoufiya Universit*y, Egypt.

Tietz NW (1976):
Fundamental of Clinical Chemistry. *Philadelphia, W.B. Saunders, P. 243.*

Tiwari A and Madhusudana J (2002):
Diabetes mellitus and multiple therapeutic appro-aches of

phytochemicals: Present status and future prospects. *Current Science*, 83 (1): 30-38.

Van Hoorn DE; Nijveldt RJ and Boelens PG (2006):
Effects of preoperative flavonoid supplementation on different organ functions in rats. *J Parenter Enteral Nutr.*, 30(4):302-8.

Wang Z; Yang Y; Xiang X; Zhu Y; Men J and He M (2010).
Estimation of the normal range of blood glucose in rats. Wei Sheng Yan Jiu. 39 (2): 133 - 137, *Chinese. PMID*: 20459020.

Wasser S (2005):
Reishi or Ling Zhi (*Ganoderma lucidum*). Encyclopedia of Dietary Supplements. Marcel Dekker Inc., *New York, NY,USA.pp. 603-622.*

WHO (1999):
Definition, diagnosis and classification of diabetes mellitus and its complications. World Health Organization Department of Non-ncomunicable Disease Surveillance. (http://whglibdoc.who.int/hg/1999/ WHO-NCD-NCS-99.2pdf). 60 p.

WHO (2011):
Use of glycated haemoglobin (HbA1c) in diagnosis of diabetes mellitus: abbreviated report of a WHO consultation (No. WHO / NMH / CHP/CPM/11.1)World Health Organization.

Yang Y; Hu X; Zhang Q and Zou R (2016):
"Diabetes mellitus and risk of falls in older adults: a systematic review and meta-analysis.". *Age and ageing.* **45** (6): 761–767.

Yound DS (1975):
Determination of GOT. *Clin. Chem.*, 22 (5): 21-27.

Table 1. Effect of GLE intervention on BWG, FI and FER of diabetic rats induced by STZ

Groups	BWG (%)	FI (g/day/rat)	FER
Normal control	0.85 ± 0.07^{a}	11.76 ± 0.86^{a}	0.073 ± 0.008^{a}
Model control	0.52 ± 0.03^{bcd}	8.03 ± 0.91^{c}	0.056 ± 0.010^{bc}
GLE intervention (200 mg/kg BW)	0.59 ± 0.06^{bc}	8.56 ± 0.53^{c}	0.058 ± 0.009^{b}
GLE intervention (400 mg/kg BW)	0.64 ± 0.05^{bc}	8.73 ± 0.55^{c}	0.059 ± 0.006^{b}
GLE intervention (600 mg/kg BW)	0.70 ± 0.02^{bc}	8.97 ± 0.69^{c}	0.062 ± 0.009^{b}
GLE intervention (800 mg/kg BW)	0.73 ± 0.04^{b}	9.35 ± 0.67^{b}	0.064 ± 0.007^{b}

Results are expressed as means ± SD (n = 6). Different superscript letters on the same column indicate significant difference (P ≤ 0.05). Normal control: healthy rats without intervention; Model control: STZ induced diabetic rats without intervention; GLE intervention: STZ induced diabetic rats with GLE intervention

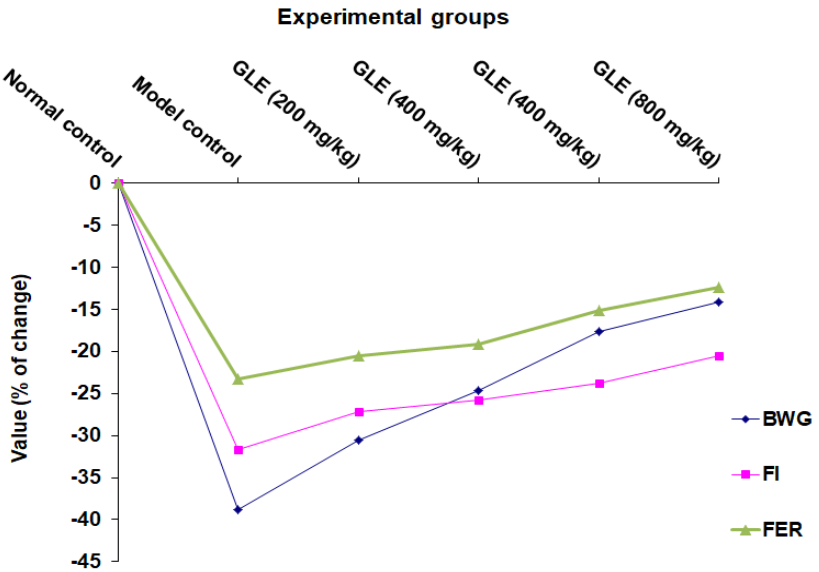

Figure 1. *Effect of GLE intervention on BWG, FI and FER (% of change) of diabetic rats induced by STZ*

Table 2. Effect of GLE intervention on serum glucose and insulin levels of diabetic rats induced by STZ

Groups	Serum glucose conc. (Mean ±SD, mg/dl)	Insulin level (Mean ±SD, µIU/mL)
Normal control	89.34 ± 10.25 ^{e}	13.97 ± 1.14 ^{a}
Model control	342.78 ± 21.23 ^{a}	7.02 ± 2.21 ^{bcd}
GLE intervention (200 mg/kg b w)	318.11 ± 15.78 ^{b}	7.77 ± 2.01 ^{bc}
GLE intervention (400 mg/kg b w)	289.30 ± 13.24 ^{c}	8.23 ± 0.99 ^{bc}
GLE intervention (600 mg/kg b w)	231.34 ± 22.23 ^{d}	9.44 ± 1.34 ^{b}
GLE intervention (800 mg/kg b w)	215.43 ± 9.4 ^{d}	9.69 ± 0.76 ^{b}

Results are expressed as means ± SD (n = 6, one-way ANOVA). Different superscript lowercase letters on the same column indicate significant difference (P ≤ 0.05). Normal control: healthy rats without intervention; Model control: STZ induced diabetic rats without intervention; GLE intervention: STZ induced diabetic rats with GLE intervention.

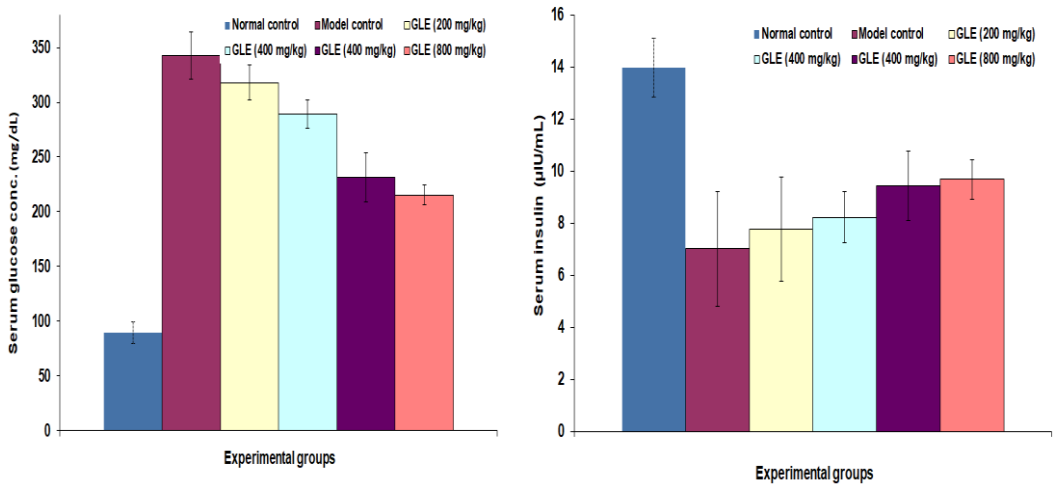

Figure 2. *Effect of GLE intervention on serum glucose and insulin level (values) of diabetic rats induced by STZ*

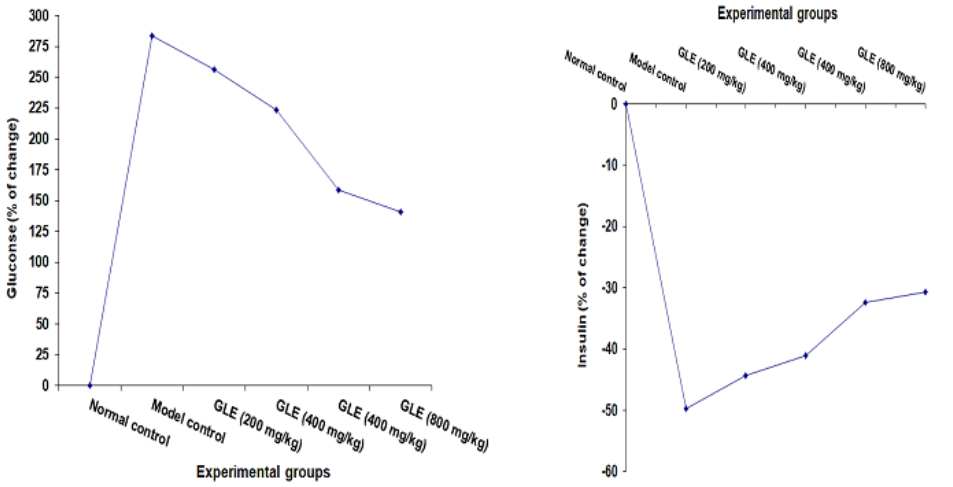

***Figure* 3.** *Effect of GLE intervention on serum glucose and insulin level (values) of diabetic rats induced by STZ*

Table 3. Effect of GLE intervention on Glycosylated hemoglobin (HbA_1c) level of diabetic rats induced by STZ

Group	HbA_1c (m mol/mol)	HbA_1c (%)
Normal control	34.64 ± 1.55 [f]	5.31 ± 0.25 [e]
Model control	91.48 ± 6.45 [a]	10.51 ± 1.04 [a]
GLE intervention (200 mg/kg BW)	81.09 ± 5.27 [b]	9.56 ± 0.85 [b]
GLE intervention (400 mg/kg BW)	70.71 ± 2.91 [c]	8.61 ± 0.47 [c]
GLE intervention (600 mg/kg BW)	58.03± 3.22 [d]	7.45 ± 0.52 [cd]
GLE intervention (800 mg/kg BW)	53.22± 3.04 [e]	7.01 ± 0.49 [d]

Results are expressed as means ± SD (n= 6). Different superscript letters on the same column indicate significant difference (P ≤ 0.05). Normal control: healthy rats without intervention; Model control: STZ induced diabetic rats without intervention; GLE intervention: STZ induced diabetic rats with GLE intervention.

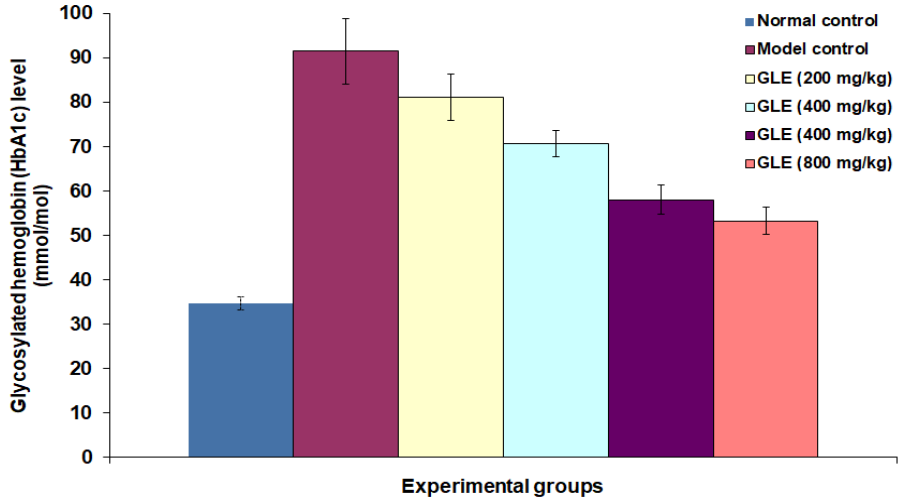

Figure 4. *Effect of GLE intervention on Glycosylated hemoglobin (HbA_1c, mmol/mol) level of diabetic rats induced by STZ*

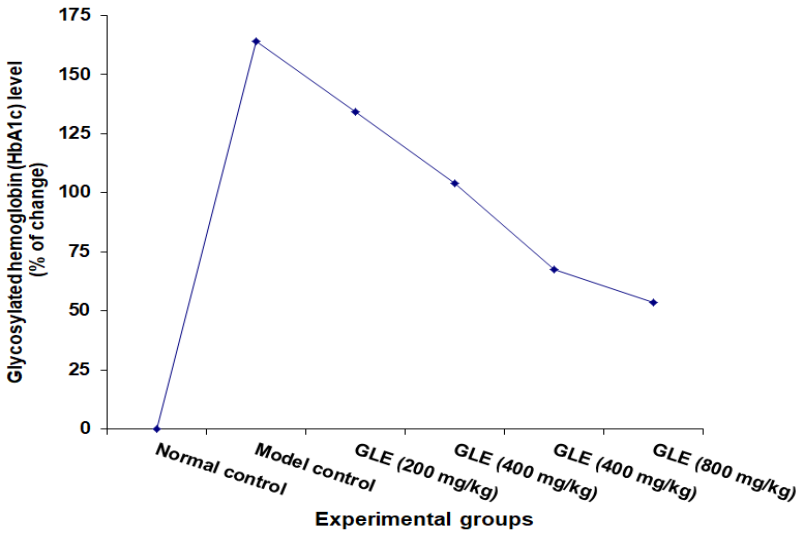

Figure 5. *Effect of GLE intervention on Glycosylated hemoglobin (HbA_1c, % of change) level of diabetic rats induced by STZ*

Table 4. Effect of GLE intervention on liver functions of diabetic rats induced by STZ

Group	AST (IU/L)	ALT (IU/L)	ALP (IU/L)
Normal control	68.56 ± 3.77 [ab]	29.51 ± 2.17 [b]	104.65 ± 9.11 [d]
Model control	89.67 ± 5.87 [a]	38.32 ± 4.31 [a]	152.45 ± 21.20 [a]
GLE intervention (200 mg/kg BW)	83.56 ± 4.63	37.95 ± 3.46 [a]	146.24 ± 14.12 [a]
GLE intervention (400 mg/kg BW)	80.73 ± 5.18 [a]	37.01 ± 1.98 [a]	128.21 ± 12.20 [b]
GLE intervention (600 mg/kg BW)	76.34 ± 5.5 [ab]	35.10 ± 2.90 [ab]	121.42 ± 16.57 [bc]
GLE intervention (800 mg/kg BW)	75.78 ± 4.53 [ab]	33.18 ± 3.11 [b]	119.45 ± 11.20 [bc]

Results are expressed as means ± SD (n = 6). Different superscript letters on the same column indicate significant difference (P ≤ 0.05). Normal control: healthy rats without intervention; Model control: STZ induced diabetic rats without intervention; GLE intervention: STZ induced diabetic rats with GLE intervention. AST, aspartate aminotransferase; ALT, alanine aminotransferase; ALP, alkaline phosphatase.

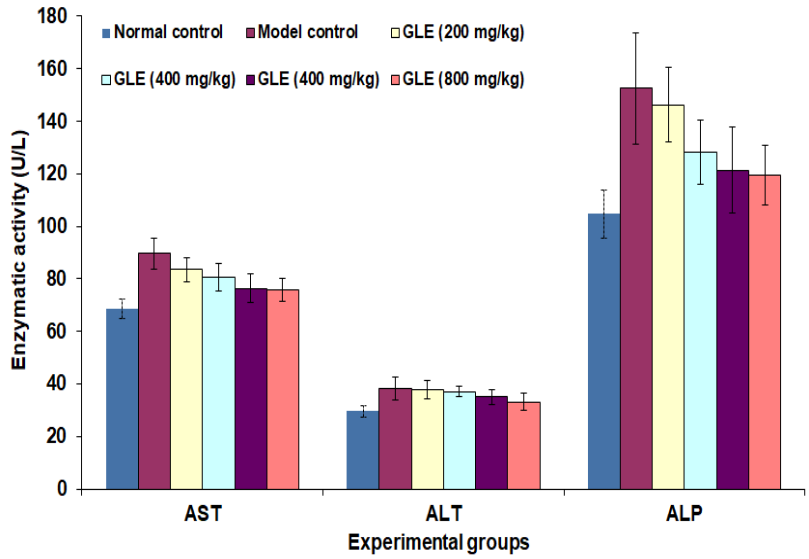

Figure 6. *Effect of GLE intervention on liver functions (IU/L) of diabetic rats induced by STZ*

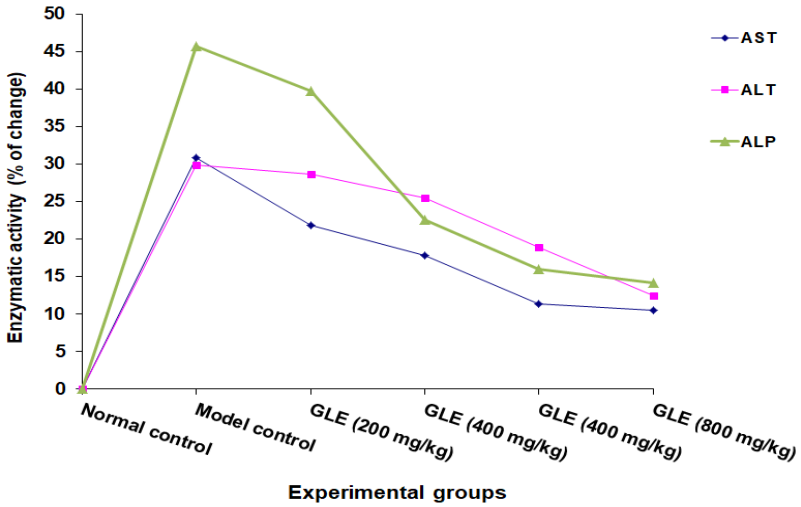

Figure 7. *Effect of GLE intervention on liver functions (% of change) of diabetic rats induced by STZ*

Table 5. Effect of GLE intervention on kidney functions of diabetic rats induced by STZ

Groups	Serum creatinine conc. (µmol/L)	Serum urea concentration (mmol/L)
Normal control	43.56 ± 4.76 ^{d}	3.09 ± 0.82 ^{d}
Model control	62.56 ± 7.43 ^{a}	5.11 ± 1.02 ^{a}
GLE intervention (200 mg/kg BW)	59.14 ± 3.95 ^{a}	4.89 ± 1.08 ^{a}
GLE intervention (400 mg/kg BW)	58.01 ± 5.01 ^{ab}	4.56 ± 0.98 ^{b}
GLE intervention (600 mg/kg BW)	55.43 ± 7.22 ^{b}	3.92 ± 0.57 ^{bc}
GLE intervention (800 mg/kg BW)	50.74 ± 6.43 ^{c}	3.89 ± 0.61 ^{bc}

Results are expressed as means ± SD (n= 6). Different superscript letters on the same column indicate significant difference (P ≤ 0.05). Normal control: healthy rats without intervention;

Model control: STZ induced diabetic rats without intervention; GLE intervention: STZ induced diabetic rats with GLE intervention.

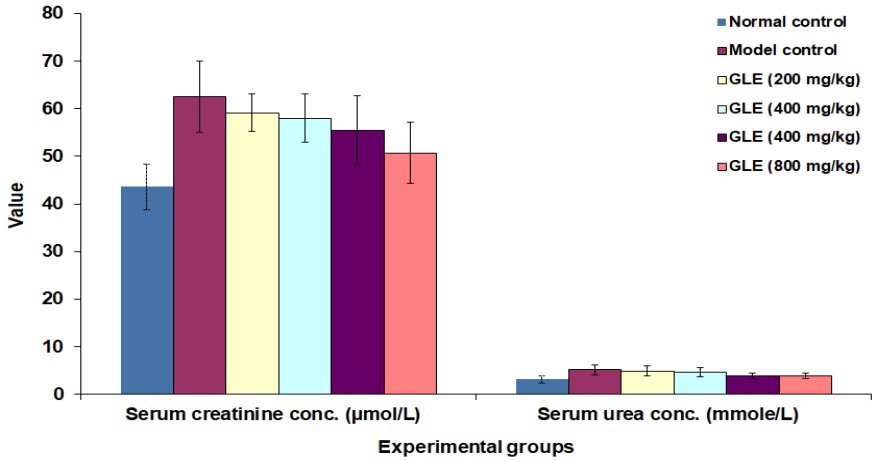

Figure 8. *Effect of GLE intervention on kidney functions (Value) of diabetic rats induced by STZ*

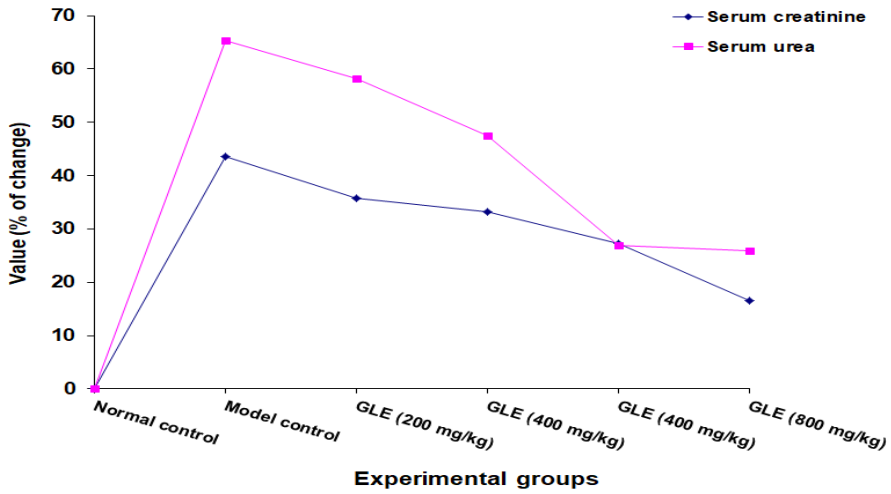

Figure 9. *Effect of GLE intervention on kidney functions (% of change) of diabetic rats induced by STZ*

Table 6. Correlation studies between biological and biochemical parameters in diabetes rats administrated with GLE*+

Parameters	r^{2*}	Parameters	r^{2*}
BW/Serum glucose	- 0.6331	Serum glucose/AST	0.4945
BW/ Serum insulin	0.6057	Serum glucose/ALT	0.4734
BW/ HbA_1c	- 0.5964	Serum glucose/ALP	0.4821
Serum glucose /Insulin	- 0.7998	Serum glucose/Urea	0.5974
Serum glucose / HbA_1c	0.7796	Serum glucose/Creatinine	0.6117

** $P \leq 0.05$*

مستخلص الفطر الريشي (جانوديرما لوسيدوم) يحسن فرط سكر الدم ووظائف الكبد والكلى في الجرذان المصابة بمرض السكري من النوع-٢ المستحث بالاستربتوزوتوسين

سماح عبدالله السملاوى[١] ، مى عبد الخالق غريب[٢]، يوسف عبد العزيز الحسانين[٢]

[١] قسم الاقتصاد المنزلى- كلية التربية النوعية - جامعة طنطا - طنطا - مصر
[٢] قسم التغذية وعلوم الأطعمة- كلية الاقتصاد المنزلى - جامعة المنوفية - شبين الكوم – مصر

الملخص العربي

يُعرَّف مرض السكري بأنه اضطراب استقلابي يتميز بارتفاع السكر في الدم وعدم كفاية إفراز أو عمل هرمون الأنسولين الداخلي .الفطر الريشي (جانوديرما لوسيدوم) تم استخدامة كدواء عشبي تقليدي منذ العصور القديمة. ***هدف الدراسة:*** *التحقق من فعالية مستخلص الجانوديرما لوسيدوم (GLE) لتحسين ارتفاع السكر في الدم ووظائف الكبد والكلى في الجرذان المصابة بمرض السكري من النوع الثانى المستحث بالإستربتوزوتوسين. تم تقسيم ذكور الجرذان البالغة بشكل عشوائي إلى ست مجموعات (ن = ٦ لكل مجموعة). المجموعة ١: الضابطة الطبيعية،جرذان طبيعية تم تغذيتها على الوجبات القياسية ؛ المجموعة ٢: الضابطة الموجبة، ائجرذان المصابة بداء السكري التى تم تغذيتها على الوجبات القياسية دون تدخل ؛ المجموعات ٣-٦ (المعاملة بـ GLE) ، وهى الجرذان المصابة بداء السكري المتناولة الوجبات القياسية مع GLE بتركيزات ٢٠٠، ، ٤٠٠ ، ٦٠٠ ، ٨٠٠ ملجم/كجم من وزن الجسم عن طريق الحقن الفموي لمدة ٢٨ يومًا. تم تحليل التغيرات لمستويات الجلوكوز ، والهيموجلوبين المرتبط بالسكر، والأنسولين ، ووظائف الكبد والكلى في عينات الدم لكل المجاميع.* ***النتائج:*** *حدث انخفاض مستوى الجلوكوزخلال الأسبوعين الأولين ، وزاد مستوى الأنسولين في الجرذان المصابة بالسكري مع GLE بشكل ملحوظ في نهاية التجربة (٤ أسابيع) مقارنة بالمجموعة الضابطة الموجبة. علاوة على ذلك ، وجد أن التدخل بالـ GLE قد أدى إلى تحسن كبير في وظائف الكبد والكلى في الجرذان المصابة بمرض السكري.* ***الخلاصة:*** *قد تشير هذه الدراسة إلى أن استهلاك الـ GLE يمكن أن يوفر تأثيرًا مفيدًا من حيث خفض مستويات السكر في الدم من خلال تعزيز تخليق الأنسولين. كما ارتبط علاج الـ GLE أيضًا بتحسين مضاعفات مرض السكري من خلال تحسين وظائف الكبد والكلى في الجرذان المصابة بمرض السكري من النوع الثانى.*

الكلمات المفتاحية: *غانوديرما لوسيدوم، الوزن ، جلوكوز الدم، الهيموجلوبين المرتبط بالسكر، الأنسولين.*