An Alternative Treatment of Diabetes with *Ganoderma lucidum*: A Case Report

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Abstract

Ganoderma lucidum (L) is considered an effective medicinal mushroom. The main goal of this research was to investigate whether the beneficial effects of *G. lucidum* found in various in vitro or animal studies can be translated to chronic metabolic diseases such as diabetes in humans. Here, we present a case study of a person with diabetes after treatment with *G. lucidum* and provide important information on fasting blood glucose (FG) levels, glycated hemoglobin (HbA1c), lipid profile, and various other blood parameters. After taking *G. lucidum* hot water extract for three months, FG levels decreased from 198 mg/dL to 177.3 mg/dL. HbA1c fell by 1.5%. Serum total cholesterol (TC) decreased from 210 to 170 mg/dL, and triglyceride (TG) levels decreased from 220 to 150 mg/dL, while serum high-density cholesterol (HDL-C) increased from 25 to 35 mg/dL. Low-density cholesterol (LDL-C) only decreased by 9 mg/dL. Serum creatinine, alkaline phosphatase (ALP), alanine aminotransferase (ALT), and total bilirubin levels were not changed. Therefore, it is concluded that *G. lucidum* hot water extract had antidiabetic and antidyslipidemic effects without affecting hepatorenal functions.

Keywords: Ganoderma lucidum, diabetes, glycemia, Ganotea, hypercholesterolemia, hypertriglyceridemia, dyslipidemia

Abbreviations: FG: fasting blood glucose, ALP: alkaline phosphatase, ALT: alanine aminotransferase, OSCC: oral squamous cell carcinoma, BMI: body mass index, CBC: complete blood count, Hb: hemoglobin, HbA1c: glycated hemoglobin, TG: triglyceride, TC: total cholesterol, HDL-C: high-density cholesterol, LDL-C: low-density cholesterol

1. Introduction

Diabetes represents a major public health burden worldwide, including in Bangladesh, where the prevalence of this disease is increasing every year [1]. All over the world, in addition to allopathic, alternative treatments are being considered to combat diabetes and its associated costs. This article examines a case report demonstrating an alternative treatment approach for diabetes using the *G. lucidum* mushroom. Due to its medicinal benefits, *G. lucidum* (L) has been the subject of hundreds of investigations worldwide in numerous areas, from cancer to inflammatory diseases, from metabolic to microbial diseases, but most of these have been in vitro or animal studies [2–4]. This fungus is relatively new to

Bangladesh and is said to have many beneficial effects on human diseases. Accordingly, G. lucidum (L) is capturing a lucrative share of the herbal medicine market in Bangladesh. However, many contemporary doctors, not only in Bangladesh but also in Western and European countries, believe that the claims made in the commercials about the potential effectiveness of G. lucidum products are fake or untrue. These Western medicine physicians even claim that the effect of G. lucidum is paradoxical or due to the placebo effect. This doubt is probably due to at least two facts: i) the lack of adequate clinical trials outside China, the country of origin of G. lucidum, where it has been found and used to treat various diseases for more than two millennia [5–7] and ii) the effectiveness of G. lucidum has remained largely untested and

unmonitored in areas outside China. The insufficient data on side effects, especially in Bangladesh, also contributes to physicians doubting the effectiveness of *G. lucidum*.

We previously reported that G. lucidum ethanol extract has potential utility in the palliative form of treatment of patients with oral squamous cell carcinoma (OSCC) [8]. Before reporting this effect in OSCC patients, we also previously reported that the ethanol extract of this mushroom protected against paracetamol-induced hepatotoxicity [9] and heavy metal-lead (Pb)-induced hemolytic toxicity [10] in rats and memory impairment in the amyloid beta peptide $(A\beta_{1-42})$ -infused Alzheimer's disease model rats [11, 12]. These results suggest that the beneficial effects of G. lucidum found in animal studies may potentially lead to beneficial effects in human diseases [8]. G. lucidum has also been shown to have antidiabetic effects in floxacin/streptozotocin-induced diabetes model animals [13–15], meaning that this fungus may have significant effects on diabetes in humans.

Diabetes is a serious health problem worldwide. Currently, 537 million adults aged 20 to 79 years are living with diabetes [16]. It is worth noting that many persons with diabetes would prefer to stop Western medication use. Others may be willing to switch from Western anti-diabetic medications to more natural remedies such as supplements. This is why we conducted this research. Like physicians, many consumers in Western countries are skeptical of fungal supplements that may cause side effects such as kidney failure and liver damage that are dangerous for consumers. This is partly because herbal and dietary supplements are not regulated like prescription medications in the United States, and there have been numerous reports of supporting concerns for contamination and fraudulent ingredients. However, the Eastern countries that have developed herbal medicines generally claim that they were designed and manufactured to maintain health and emphasize that they are naturally harmless because they contain no harmful chemicals. To eliminate this doubt, in this study, we did not use organic solvents such as ethanol or methanol to prepare G. lucidum extract, which may contain harmful chemical residues. Instead, G. lucidum powder, like tea prepared in water, was boiled in water for 30 minutes to make G. lucidum tea and taken twice a day for three months. Hereafter, the term 'hot water extract from G. lucidum' will be used synonymously as 'Ganotea' throughout the text, as it is now gradually becoming known by this name in Bangladesh. In contrast to the clear tea drink, the Ganotea appeared cloudy due to the insoluble particles and compounds in the woody pulp of G. lucidum. The extract is not filtered to remove its granular components. The extract had a bitter taste.

2. Case Presentation

2.1 Case report

A 54-year-old man had no family history of diabetes, obesity, or cardiovascular disease on either his mother's or paternal side. He experienced exhausting fatigue and suffered from excessive thirst and hunger. He also had to urinate more frequently, although the amount of water he normally drank did not change significantly. Then he called the doctor. The doctor advised him to have a blood test done first. He was then referred to a diagnostic clinic and asked for a routine health check-up. His systolic blood pressure was 115-122 mmHg, and his diastolic blood pressure was 76-82 mmHg. His body weight was 156.528 pounds, his height was 5 feet and 4 inches, and his body mass index (BMI) was 26.9. His laboratory tests included a complete blood count (CBC), fasting blood glucose (FG), hemoglobin (Hb), glycated hemoglobin (HbA1c), lipid profiles, and hepatorenal functional markers, including serum creatinine, total bilirubin, serum alkaline phosphatase (ALP), and alanine aminotransferase (ALT).

2.2 Diagnostic work-up

Laboratory findings (Table 1) showed that the patient's FG level was 198 mg/dL, and HbA1c was 9.9 (%). His total cholesterol (TC), low-density cholesterol (LDL-C), high-density cholesterol (HDL-C), and triglyceride (TG) levels were 210, 114, 25, and 220 mg/dL, respectively. His serum creatinine was 1.3, ALP 115, ALT 52, and his serum bilirubin was 1.0. A value of > 200 mg/dL TC is considered borderline high. LDL-C should be < 100 mg/dL, HDL-C should be > 40mg/dL, and TG should be 120 mg/dL. The physical appearance of a diabetes-prone patient has different characteristics, but risk factors such as obesity, especially in the abdominal area, and a sedentary lifestyle may be obvious and indicate a predisposition to diabetes. There are also skin problems such as dryness or slow wound healing, often accompanied by symptoms such as increased thirst and frequent urination. An individual is categorized as prediabetic if their HbA1c level falls within the range of 5.7% to 6.4%, whereas a diagnosis of diabetes is established when the HbA1c value is 6.5% or above [19, 20]. The patient was, therefore, diagnosed with diabetes and suffered from mild hypercholesterolemia and hypertriglyceridemia. In Bangladesh, recent estimates place the average BMI of the population between 19~20 kg/m² [21–23], lower than estimates in the USA (27 kg/m²) [24], Japan (23.5 kg/m²) [25], and India (21.7 kg/m²) [26]. The BMI of the person's family members was between 19 and 20 kg/m². These BMI values thus indicate that the person in our case was also more overweight. Therefore, his high BMI (26.9 kg/m²) suggested that heavy sitting during sedentary work made him an overweight person. Until then, the patient had neither vision problems nor cardiac complications (Figure 1).

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Parameters	Before Ganotea	After Ganotea			
	Day 0	Day 45	Day 90	$\Delta^{\mathrm{Day45-0}}$	$\Delta^{ m Day 90-0}$
Fasting blood glucose (FG) (mg/dL)	198	180	177	-18	-21
*HbA1c (%)	9.9 (8.5)	8.5(7.9)	8.4 (7.8)	-1.4 (-0.6)	-1.5 (-0.7)
Hemoglobin (Hb) (g/dL)	14.0	14.4	15.5	0.4	1.5
Total cholesterol (TC) (mg/dL)	210	180	170	-30	-40
Low-density cholesterol (LDL-C)	114	110	108	-4	-6
High-density cholesterol (HDL-C)	25	27	35	2	10
Triglyceride (TG)	220	215	150	-5	-60
Serum creatinine	1.30	1.02	0.57	-0.28	-0.73
Serum alkaline phosphatase (ALP)	115	111	107	-4	-8
Serum alanine aminotransferase (ALT)	52	58	55	6	3
Serum total bilirubin	1.0	ND	1.04	-	0.04

Table 1: Effect of *Ganoderma lucidum* therapy on FG, lipid profile, ALP, ALT, and bilirubin levels of the diabetic patient. Results are the mean of quadruplicate determinations. At each clinic visit, fasting blood was collected twice (at 8 am and 9 am) by venipuncture, centrifuged at 2000 X g and 4°C, and subjected to analysis. Determination was performed in duplicate for each sample. As a result, the above table shows the average of four determinations. Day 0 is defined as the date of the first day the patient donated blood to test the parameters before starting to drink Ganotea. Likewise, day 45 means blood was drawn after drinking Ganotea for 90 days. $\Delta^{Day45\cdot0}$, the difference in values between day 0 and day 45. $\Delta^{Day90\cdot0}$, the difference in the value between day 0 and day 90. *HbA1c values given in brackets were determined according to the mathematical equation between HbA1c and FG value [17, 18].

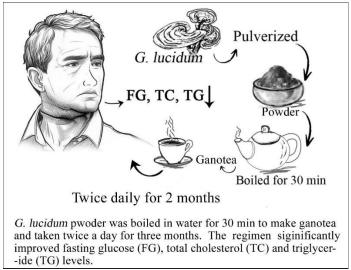


Figure 1: Depicts making Ganotea and its drinking regimen.

2.3 Treatment and follow up

However, the patient was very resistant to taking any Western medications for diabetes and dyslipidemia and preferred to 'wait and see.' He was also unable to reduce his sedentary time due to his occupational requirements. Regardless of the severity of the disease, the patient initially preferred herbal treatment and was accordingly prescribed *G. lucidum* powder as a drinking tea. The patient was informed that his FG and other blood parameters would be monitored. A blood test for diabetes was performed 45 days after the patient drank the *G. lucidum* tea twice a day. Again, the patient returned to the clinic 90 days later to be reassessed for diabetes and dyslipidemia for the third time.

2.4 Outcome

The results of the treatment of *G. lucidum* hot water extract are also shown in the table **(Table 1)**. 45 days later, the patient's FG levels decreased from 198 to 180 mg/dL. After 90 days, the FG level dropped to 177 mg/dL. HbA1c levels also decreased, but at the same time, Hb levels increased after both 45 and 90 days of Ganotea consumption **(Table 1)**. After 45 and 90 days of drinking Ganotea, TC levels decreased from an initial value of 210 mg/dL to 180 and 170 mg/dL, respectively. After the prescribed treatment, his TG levels dropped significantly from 220 to 150 mg/dL after drinking Ganotea for 90 days. LDL-C decreased by 6 mg/dL after 3 months, while HDL-C increased from an initial 25 to 35 mg/dL. Hepatorenal functional markers, including creatinine, ALP, ALT, and total bilirubin, were not significantly changed **(Table 1)**. The CBC was also not significantly changed (data not shown).

3. Discussion

The results of the current case report indicate that the patient was type 2 diabetic and suffered from mild hypercholesterolemia and hypertriglyceridemia. Drinking G. lucidum (~4 g/day) hot water extract, Ganotea, for three months, resulted in reductions in FG, TC, and TG levels as well as better HDL-C levels (Table 1). In addition, serum creatinine, ALT, ALP, bilirubin, and CBC were not changed, suggesting that drinking G. lucidum had no adverse effects on liver and kidney function. There were also no discernible corrosive effects on tooth enamel. The patient made no changes to his diet or lifestyle during the three months of taking G. lucidum. After drinking the G. lucidum hot water extract for three consecutive months, our patients' FG levels decreased from 198 mg/dL to 177 mg/dL, suggesting that the extract had a positive effect on lowering blood sugar levels. Because there is limited human research outside of China, the results of this case show that consumption of G. lucidum hot water extract had beneficial effects in this patient with a sedentary lifestyle, obesity, type 2 diabetes, and dyslipidemia. This provides clinical support for further research into the real-world effects of this supplement. Measurements of hemoglobin A1C (HbA1c) are considered to be far more meaningful data for diabetic prognosis than a single FG. It is the percentage of glycated hemoglobin in total Hb [27]. The population with lower Hb may have higher HbA1c [28] and vice versa, supporting the idea that HbA1c may be associated with Hb levels independently of glycemia. It can also vary by race [28] and gender [29]. Our patients' Hb levels increased after consuming Ganotea, resulting in a decrease in FG and HbA1c. Therefore, the exact mechanisms still need to be delineated.

In our previous research, *G. lucidum* has shown tremendous potential benefit in the palliative form of treatment of patients with OSCC. OSCC patients who received *G. lucidum* had increased appetite, increased tolerance to radiotherapy, better Karnofsky score, improved serum creatinine, ALP, AST, and Hb levels, and decreased serum TNFa and lipid peroxide (LPO) levels, showing that *G. lucidum* has potential benefits in the palliative form of treatment for patients with OSCC [8]. Similar beneficial effects of *G. lucidum* were observed in our previous animal and in vitro studies [8–12] with respect to hepatotoxicity, hemolysis, Pb toxicity, and impairments in memory-related brain cognition.

These references emphasize that *G. lucidum* also has obvious beneficial effects on human diseases and that the effects are not as controversial and/or imaginary as assumed by many modern physicians in various parts of the world but rather beneficial. Here too, the effect is a fact as the results of this case report provide clear evidence that the positive results of numerous previous in vitro and/or animal studies can also be translated into positive effects in human diseases. Although our data provide clear evidence for the antihyperglycemic effects of *G. lucidum* powder, we are unclear about the mechanisms associated with these beneficial effects.

Several molecular mechanisms by which G. lucidum improves diabetic status have been proposed. For example, polysaccharides from G. lucidum promote the regeneration of partially destroyed beta cells and stimulate insulin secretion [30], improve insulin resistance [31], inhibit postprandial intestinal absorption of glucose [32], increase glycolytic enzymes and/or inhibit gluconeogenesis [33, 34or glycogenolysis [34] and interfere with carbohydrate digestion by inhibiting glucosidase [35], which overall benefits diabetic. Whatever the mechanism, our case report supports that G. lucidum ameliorates diabetes in humans, and our results were qualitatively consistent with numerous other animal studies [13– 15, 30–33] reporting its antidiabetic effects.

Type 2 diabetes is associated with dyslipidemia, suggesting that elevated TC, TG, and LDL-C levels, while low HDL-C levels contribute to secondary complications of diabetes [36]. Our diabetic patient showed a significant decrease in TC and TG after drinking Ganotea, suggesting that our patients' cardiovascular risk factors improved. The antilipidemic effects were consistent with other studies [30]. It is generally accepted that the reduction in TC is due to decreased activity of the rate-limiting HMG-CoA enzyme reductase (hydroxymethylglutaryl-CoA reductase) or to inhibition of intestinal absorption of dietary cholesterol/or increased cholesterol secretion in the bile, thereby increased excretion of cholesterol through the feces. We do not know which of the above mechanisms contributed more to lowering blood cholesterol levels in our patient or if they all worked together, but these mechanisms may have contributed to the patient's cholesterol lowering.

In addition, other components found in G. lucidum, including glucans, lectins, triterpenes, ergostane, and lanosterol derivatives, can inhibit HMG-CoA reductase, in particular, ß-glucans are the fibrous components of *G. lucidum* that can interact with lipids and bile salts and thus influence cholesterol absorption and thereby lowering blood cholesterol levels [37, 38]. Currently, there is no clear consensus on how G. lucidum affects TG levels, although G. lucidum has been reported to reduce hypertriglyceridemia [39], probably by increasing beta-oxidation and directing TG into fecal excretion.

4. Conclusion

Finally, taking Ganotea for three months resulted in significant improvement in diabetes and diabetesrelated dyslipidemia. Based on this case report and review of current literature, Ganotea may be a useful approach for patients with type 2 diabetes and dyslipidemia who are unwilling to take Western medicines for diabetes. However, further studies on a large population with *G. lucidum* tea are essential to determine whether it has antihyperglycemic and antidyslipidemic effects. If so, this would be of great benefit to the treatment of diabetics in Bangladesh in the fight against the increasing prevalence and morbidity of diabetes.

Consent

Written informed consent was obtained from the patient for the publication of this case report.

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Conflicts of Interest

There are none.

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