RESEARCH ARTICLE

Comparative Effect of Oyster and Button Mushroom Loaded Phytosomes with Glibenclamide on Renal Function in STZ Induced Diabetic Rats

Chauhan Monika*, Dubey K Subodh

School of Pharmacy, ITM University, Gwalior Madhya Pradesh, India.

Received: 12nd February, 2024; Revised: 20th April, 2024; Accepted: 20th June, 2024; Available Online: 31st August, 2024

ABSTRACT

Diabetes is a chronic, life-threatening condition that can affect a vast variety of organ systems, including the kidney. The present study is based on the effect of phytosome-based mushroom extract of oyster and button mushroom on renal functioning factors such urea, uric acid, and creatine as well as the glucose level in streptozocin (STZ) -induced rats with diabetes. The results indicated the blood sugar level was found to decrease significantly in the groups treated with a combination of lactobacillus with phytosomes of oyster mushroom and button mushroom in contrast to a control group of diabetics ($p \leq 0.05$). Similarly, the phytosome of oyster mushroom with lactobacillus and phytosomes of button mushroom with lactobacillus treatment showed a substantial decline in the level of creatinine, uric acid, and urea ($p \leq 0.05$). Thus, these can be used as effective medication for the treatment of diabetes alternative to allopathic medication.

Keywords: Diabetes, Phytosome, Oyster & Button mushroom, Glibenclamide, Streptozocin.

International Journal of Pharmaceutical Quality Assurance (2024); DOI: 10.25258/ijpqa.15.3.40

How to cite this article: Monika C, Subodh DK. Comparative Effect of Oyster and Button Mushroom Loaded Phytosomes with Glibenclamide on Renal Function in STZ Induced Diabetic Rats. International Journal of Pharmaceutical Quality Assurance. 2024;15(3):1345-1348.

Source of support: Nil.

Conflict of interest: None

INTRODUCTION

A kind of metabolic disease called diabetes mellitus is one that is not communicable and are characterized by persistent hyperglycemia caused by abnormalities in insulin action, secretion, or both.[1] It is a persistent, potentially fatal illness that can result in heart attacks, strokes, and persistent problems with the eyes, feet and nerves. About one-third to half of those with diabetes go on to develop renal disease, making diabetes a significant risk factor for kidney disease.[2,3] High blood sugar levels have the potential to harm all of the body's blood vessels, including the kidneys. Gradually impairing renal function, the glomeruli-tiny blood arteries found within the kidneys can get thicker and damaged. This reduces their capacity to filter waste from the blood. Uncontrolled diabetes can cause hypertension, which can aggravate the kidneys' already damaged blood vessels and hasten the process of kidney destruction. The kidneys may experience oxidative damage and inflammation as a result of persistently elevated blood sugar levels. These conditions make it harder for the kidneys to perform at their best and cause cellular damage. Diabetic kidney disease can arise as a result of oxidative stress and the inflammatory response over time.

Diabetes is a disorder that is often managed with appropriate dietary practices. Currently, efforts are being made to identify and develop novel therapeutic alternatives that can stop the fast-increasing natural course of diabetic nephropathy. The negative effects of many synthetic hypoglycemia diabetic medications render them ineffective. Currently, scientists are concentrating on mushrooms because of their growing recognition as a food that is crucial for human health, nutrition, and disease. Many biologically active substances, such as proteins, peptides, terpenoids, polyphenols, polysaccharides, mineral elements, and vitamins, are present in them. As a result, they are said to have effects such as immunomodulatory, hypocholesterolemic, hypoglycemic, anti-inflammatory, and anti-cancer.[4] Moreover, the absence of effective and affordable treatments for both types of diabetes is expected to lead to a rise in global cases, significantly affecting populations in developing countries.[5] Natural medications with antidiabetic properties have not yet been developed into industrial drugs despite their recognition for therapeutic benefits in traditional medicine systems.[6]

In the current investigation, two significant therapeutic mushrooms viz. *Pleurotus ostreatus* (oyster mushroom) and *Agaricus bisporus,* or white button mushroom, were employed. One of the edible mushroom species that is edible is the white button mushroom, or *A. bisporus*. Most abundant worldwide because of its special chemical that has biological activity and medicinal qualities.[7] In a similar way, *Pleurotus ostreatus* mushrooms are highly nutritious and therapeutic, making them a special kind of delicacy. In diabetics, pleurotus mushrooms

*Author for Correspondence: chauhanmonika15@gmail.com

have a positive synergistic effect on the kidney and liver. Situations because of all these therapeutic characteristics.[8] In the current study, the impact of two medicinal mushrooms, *Agaricus bisporus* and *P. ostreatus* extract-based phytosomes on renal functioning factors such as urea, uric acid, and creatine as well as the glucose level in rats with diabetes produced by (STZ) determined.

MATERIALS AND METHODS

Collection of Mushrooms

Edible mushroom *A. bisporus* (White button mushroom) was collected from the local market of Gwalior (India). *P. ostreatus* (Oyster mushroom) was grown on wheat and paddy straw.

Extraction of Mushroom

Fresh mushrooms were carefully rinsed in clean water. The mushroom's fruiting body was removed, dried for 48 hours at 60ºC in an oven, and then milled into a fine powder. Using a soxhlet apparatus, the hot percolation method was utilized to prepare the water extract. About 30 g of mushroom powder (i.e., 1:10, w/v) was utilized for 300ml of solvent (water) at a regulated temperature of 50ºC. In a rota evaporator, dry the extract. The extracts were stored at 4°C in a sterile, clean container for further use.[9]

Biosynthesis of Phytosomes of Mushroom

Solvent evaporation methods prepared phytosomes of oyster and button mushroom. Mushroom and soya lecithin were used to prepare phytosome. Separately, precisely weighed portions of mushrooms were dissolved in methanol and soy lecithin in dichloromethane. After being moved to a round-bottom flask, the two solutions were refluxed for two hours at 60°C. The solution was obtained at this point in a clear yellow color. After that, the mixture evaporated completely in a rotary evaporator at 60ºC, producing a thin film. After hydrating the thin film with phosphate buffer 7.4, the suspension was collected, filtered, vacuum-dried, and stored.[10]

Division and Distribution of Animal

36 Wistar rats were taken in the experiment and further divided in the following 6 groups: Group 1 consisted of diabetic Wistar rats that were induced with STZ and were not given any medication. Group 2 consisted of diabetic rats given an allopathic medication (Glibenclamide) at a dose of 40 mg per kg of body weight. Diabetic rats are treated with lactobacillus and oyster mushroom phytosomes at a dosage of 100 mg/kg body weight in group 3. Group 4 consists of lactobacillus-treated diabetic rats and white button mushroom phytosomes administered at a 100 mg/kg body weight dose. A diabetic rat treated with lactobacillus suspension (100 mg/kg body weight) is part of group 5. Group 6 consisted of Wistar rats that were not given STZ therapy, serving as a normal, healthy control group.

Test Design

Following the induction of diabetes, Groups 3, 4, and 5 of diabetic rats were treated with lactobacillus suspension, oyster mushroom phytosomes (100 mg/Kg of body weight), and white button mushroom phytosomes, respectively. There were 21 days in the test period. Following this time, blood samples were taken on day 21 in order to test creatinine, urea, uric acid, and glucose. Serums were separated and sent to a facility for the measurement of the previously stated parameters following a 15-minute centrifugation of blood at 3000 revolutions per minute.

Assessment of Biochemical Parameters

All biochemical parameters were tested using commercially available kits from Erba Diagnostic Kit Mannheim GmbH, Mallaustr, Germany, including creatinine, urea, and uric acid. Auto-analyzer Erba Chem-7.32 was utilized to ascertain the amounts of various biochemical parameters. An ACCU-CHEK sensor glucometer was used to measure the blood glucose levels.

Statistical Analysis

The mean ± SEM was examined using one-way ANOVA with descriptive statistics. A significance criterion of $p \leq 0.05$ was used in different groups. Data was analyzed using SPSS 17.

RESULTS

Urea levels of groups that were treated with a mix of lactobacillus and button and oyster mushroom phytosomes reduced substantially when contrasting with the diabetic control group. However, when compared to the group that was treated with an allopathic drug (Glibenclamide), there was no statistically significant difference ($p \leq 0.05$) (Table 1).

In comparison to diabetic control group and the group administered the allopathic medicine glibenclamide, groups treated with lactobacillus plus button and oyster mushroom phytosomes had substantially lower urinary acid levels ($p \leq 0.05$) (Table 1). A statistically significant ($p \leq 0.05$) reduction in creatinine levels was observed in the groups treated with a mixture of lactobacillus and button and oyster mushroom phytosomes compared to the diabetic control group; however, this reduction was not statistically significant compared to group treated by allopathic medicine (Glibenclamide) (Table 1). Diabetic control group had substantially higher blood glucose levels compared to the groups treated with a mix of lactobacillus and button and oyster mushroom phytosomes ($P \leq 0.05$) (Table 1).

DISCUSSION

The result showed a significant hypoglycemic effect of the phytosome including button mushroom and oyster extract at dose of 100 mg/kg of body weight. Numerous researches demonstrated that mushrooms particularly *Pleurotus* species.[11] Significantly reduce blood glucose levels. *Agaricus bisporus,*[12] which postpone glucose absorption and cure hyperglycemia.[13] Additionally, research has demonstrated that β-cell proliferation is maintained and mushroom extracts from Boletus, Agaricus bisporus and *Pleurotus* spp[14] significantly impact β-cell functionality. Another study in which mice with diabetes brought on by alloxan, *P. ostreatus* intake significantly

Table 1: Effects of an oyster and button mushroom phytosome-based extract on kidney function enzyme levels (urea, uric acid, and creatinine) and blood glucose levels in STZ-induced diabetic rats were compared to an allopathic medication (Glibenclamide)

Parameters \ Groups	Diabetic Control	Glibenclamide	lactobacillus + oyster based phytosomes	lactobacillus + button based phytosomes	Lactobacillus suspension	Normal healthy control
Blood glucose	284.93 ± 12.65	157.83 ± 12.54	171.76 ± 12.81	177.73 ± 12.28	191.93 ± 12.65	90.92 ± 9.55
Urea	54.31 ± 3.25	38.40 ± 3.50	40.46 ± 3.54	40.80 ± 3.21	49.96 ± 3.35	32.55 ± 5.20
Uric acid	7.78 ± 0.77	4.85 ± 0.05	5.90 ± 1.05	5.90 ± 1.05	6.36 ± 0.42	4.65 ± 0.05
Creatinine	1.63 ± 0.38	0.88 ± 0.30	0.98 ± 0.13	1.16 ± 0.30	1.36 ± 0.22	0.71 ± 0.47

Note: The data are presented as follows: Mean ± SD, N = 6, $p < 0.05$,

reduced blood sugar levels and improved hyperlipidemia and reduced kidney function.

The current study's findings indicated a considerable drop in both the groups' serum levels of creatinine and urea viz. treated with a combination of lactobacillus with phytosome of oyster mushroom, lactobacillus with phytosome of button mushroom and allopathic drug Glibenclamide when compared with diabetic control group in STZ induced Wistar rats.

Diabetes poses a global health risk that needs to be treated with inexpensive, non-toxic medication. Many synthetic hypoglycemia diabetes medicines are ineffective due to side effects. Scientists are currently focusing on mushrooms since they are known to have naturally occurring bioactive components that may have antidiabetic properties. Biological properties of mushroom polyphenols including anti-inflammatory, anti-cancer, anti-tyrosine, antihyperglycemic, and antioxidant properties that are advantageous to human health and medicine. High concentrations of dietary fiber, antioxidants, beta glycans, folate, ergothioneine, and polyphenols have been found in white mushrooms,[15,16] indicating that the mushrooms may have hypoglycemic properties and be useful for those with diabetes mellitus It has been demonstrated that *A. bisporus* drops blood glucose levels in diabetic rats administered STZ.[17] It has been shown that eating mushrooms and the active ingredients they contain can help lower blood sugar and cholesterol levels.[18] White button mushrooms are rich in antioxidants, dietary fibre, and acidic polysaccharides. They also include polyphenol, ergothioneine, folate, and the vitamins C, B12, and D. have been linked to possible anti-inflammatory, hypoglycemic, and hypocholesterolemic effects.[19] A significant fraction of phytocompounds with bioactive properties are polar and water-soluble, hence phytocompounds are poorly absorbed in phospholipid structures. In order to address these issues, scientists have created phytosomes, which increase the water-soluble BPCs' (bioactive phytocompounds') bioavailability.[20,21]

Glibenclamide is a sulfonylurea of the second generation that functions by stimulating the pancreatic beta cells to produce insulin. Its action lasts for a long time, and metabolites with hypoglycemic activity raise the possibility of chronic hypoglycemia.[22] The difficulties and limitations caused by the widely used synthetic pharmaceuticals force researchers to look for antidiabetic therapies derived from plants that have better safety and efficacy profiles. Because of their remarkable success, plant-based medications have long been used to treat diabetes mellitus, much like they do for many other disorders, with reduced toxicity and side effects, affordability, and accessibility.[23] A variety of scientific data have demonstrated that those phytochemicals have the potential to be antihyperglycemic and can be utilized for treating diabetes and other metabolic disorders. The current study's findings showed that mushroom extract-loaded phytosomes at levels that were efficient are of beneficial effects on kidney functions and blood glucose level. Thus, these can be used as effective medication for the treatment of diabetes.[24-26]

CONCLUSION

For people with diabetes, it is essential to comprehend the complex connection between kidney health and the disease. One major diabetes complication that requires careful monitoring and effective treatment is diabetic kidney damage. People can drastically lower their risk of kidney injury or halt its progression by following a healthy lifestyle, maintaining blood pressure, and regularly monitoring their blood sugar and blood pressure. This study shows that giving oyster and button mushroom extract-based phytosomes to rats that were experimentally treated with STZ leads to significant improvements in blood glucose, urea, uric acid, and creatinine levels in their serum. More research is necessary to determine and evaluate the appropriate molecular pathways of the pharmacological effects shown by the described antidiabetic phytochemicals. Even though plants and/or dietary plant components are thought to be safe to eat, potential antidiabetic phytochemicals should still be assessed for toxicity tests in order to create safe and effective phytomedicines.

REFERENCES

1. Kharroubi AT, Darwish HM. Diabetes mellitus: The epidemic of the century. World Journal of Diabetes. 2015 25;6(6):850-67. doi: 10.4239/wjd.v6.i6.850.
2. Bakris GL. Recognition, pathogenesis, and treatment of different stages of nephropathy in patients with type 2 diabetes mellitus. InMayo Clinic Proceedings. 2011;86(5):444-56. doi: 10.4065/mcp.2010.0713.
3. Harjutsalo V, Groop PH. Epidemiology and risk factors for diabetic kidney disease. Advances in chronic kidney disease. 2014;21(3):260-6. doi: 10.1053/j.ackd.2014.03.009.

4. Elkhateeb WA, Daba GM. Medicinal mushroom what should we know. International Journal of Pharmaceutical Chemistry and Analysis. 2022;9(1):1-9 doi:10.18231/j.ijpca.2022.001.
5. Nikumbh KK, Patil RA, Upasani CD. Pre-clinical Study of Marketed Polyherbal Formulations on Blood Glucose Level and Associated Parameters in Streptozotocin-induced Diabetes. International Journal of Pharmaceutical Quality Assurance. 2023;14(4):847-852. https://doi.org/10.25258/ijpqa.14.4.03.
6. Pulipaka S, Suttee A, Kumar MR, Sriram P. Effective use of Phytotherapy in the Management of Diabetes by Plant-based Medicine: A Review. International Journal of Pharmaceutical Quality Assurance. 2022;13(3):337-346. doi:10.25258/ijpqa.13.3.20
7. Krishnamoorthi R, Srinivash M, Mahalingam PU, Malaikozhundan B. Dietary nutrients in edible mushroom, Agaricus bisporus and their radical scavenging, antibacterial, and antifungal effects. Process Biochemistry. 2022;121:10-17. doi:10.1016/j.procbio.2022.06.021.
8. Ng SH, Mohd Zain MS, Zakaria F, Wan Ishak WR, Wan Ahmad WA. Hypoglycemic and Antidiabetic Effect of Pleurotus sajor-caju Aqueous Extract in Normal and Streptozotocin-Induced Diabetic Rats. BioMed research international. 2015;2015(1):214918. doi: 10.1155/2015/214918.
9. Dubey S, Yadav C, Bajpeyee A, Singh MP. Effect of Pleurotus fossulatus aqueous extract on biochemical properties of liver and kidney in streptozotocin-induced diabetic rat. Diabetes, Metabolic Syndrome and Obesity. 2020:3035-3046. doi: 10.2147/DMSO.S265798. PMID: 32904440; PMCID: PMC7455752.
10. Das MK, Kalita B. Design and evaluation of phyto-phospholipid complexes (phytosomes) of rutin for transdermal application. Journal of applied pharmaceutical science. 2014;4(10):051-057. doi:10.7324/JAPS.2014.401010.
11. Asrafuzzaman M, Rahman MM, Mandal M, Marjuque M, Bhowmik A, Rokeya B, Hassan Z, Faruque MO. Oyster mushroom functions as an anti-hyperglycaemic through phosphorylation of AMPK and increased expression of GLUT4 in type 2 diabetic model rats. Journal of Taibah University medical sciences. 2018;13(5):465-71. doi: 10.1016/j.jtumed.2018.02.009.
12. Ekowati N, Yuniati NI, Hernayanti H, Ratnaningtyas NI. Antidiabetic potentials of button mushroom (Agaricus bisporus) on alloxan-induced diabetic rats. Biosaintifika: Journal of Biology & Biology Education. 2018;10(3):655-62. doi:10.15294/biosaintifika.v10i3.17126.
13. Aramabašić Jovanović J, Mihailović M, Uskoković A, Grdović N, Dinić S, Vidaković M. The effects of major mushroom bioactive compounds on mechanisms that control blood glucose level. Journal of Fungi. 2021;7(1):58. doi: 10.3390/jof7010058.
14. Zhang C, Li J, Hu C, Wang J, Zhang J, Ren Z, Song X, Jia L. Antihyperglycaemic and organic protective effects on pancreas, liver and kidney by polysaccharides from Hericium erinaceus SG-02 in streptozotocin-induced diabetic mice. Scientific Reports. 2017;7(1):10847. DOI: 10.1038/s41598-017-11457-w.
15. Koyyalamudi SR, Jeong SC, Song CH, Cho KY, Pang G. Vitamin D2 formation and bioavailability from Agaricus bisporus button mushrooms treated with ultraviolet irradiation. Journal of agricultural and food chemistry. 2009;57(8):3351-3355. doi: 10.1021/jf803908q.
16. Mattila P, Könkö K, Eurola M, Pihlava JM, Astola J, Vahteristo L, Hietaniemi V, Kumpulainen J, Valtonen M, Piironen V. Contents of vitamins, mineral elements, and some phenolic compounds in cultivated mushrooms. Journal of agricultural and food chemistry. 2001;49(5):2343-2348. doi: 10.1021/jf001525d.
17. Jeong SC, Jeong YT, Yang BK, Islam R, Koyyalamudi SR, Pang G, Cho KY, Song CH. White button mushroom (Agaricus bisporus) lowers blood glucose and cholesterol levels in diabetic and hypercholesterolemic rats. Nutrition research. 2010;30(1):49-56. doi: 10.1016/j.nutres.2009.12.003.
18. Yao HT, Lin P, Chang YW, Chen CT, Chiang MT, Chang L, Kuo YC, Tsai HT, Yeh TK. Effect of taurine supplementation on cytochrome P450 2E1 and oxidative stress in the liver and kidneys of rats with streptozotocin-induced diabetes. Food and chemical toxicology. 2009;47(7):1703-1709. doi: 10.1016/j.fct.2009.04.030.
19. Tourlouki E, Matalas AL, Panagiotakos DB. Dietary habits and cardiovascular disease risk in middle-aged and elderly populations: a review of evidence. Clinical interventions in aging. 2009;319-330. doi: 10.2147/cia.s5697.
20. Khan J, Alexander A, Saraf S, Saraf S. Luteolin–phospholipid complex: preparation, characterization and biological evaluation. Journal of Pharmacy and Pharmacology. 2014;66(10):1451-1462. doi: 10.1111/jphp.12280.
21. Khan J, Alexander A, Saraf S, Saraf S. Recent advances and future prospects of phyto-phospholipid complexation technique for improving pharmacokinetic profile of plant actives. Journal of controlled release. 2013;168(1):50-60. doi: 10.1016/j.jconrel.2013.02.025.
22. Rydberg T, Jönsson A, Karlsson MO, Melander A. Concentration-effect relations of glibenclamide and its active metabolites in man: modelling of Pharmacokinetics and Pharmacodynamics. British journal of clinical pharmacology. 1997;43(4):373-381. doi: 10.1046/j.1365-2125.1997.00571. x.
23. Lote S, Agrawal S, Ghune S, Gurjar P. Validated HPTLC Analysis for Estimation of Quercetin in Seeds of Anethum graveolens. International Journal of Pharmaceutical Quality Assurance. 2023;14(2):274-278. doi:10.25258/ijpqa.14.2.05.
24. Narwade VL, Singh N. Preparation, Optimization, Compatibility Study of Captopril Proniosome, and In-vitro, In-vivo Evaluation of Release Study. International Journal of Pharmaceutical Quality Assurance. 2023;14(2):323-329. doi:10.25258/ijpqa.14.2.14.
25. Dhakar S, Tare H. Profiling Potent Medicinal Plants: Allium sativum, Azadirachta indica, and Annona squamosa in Diabetes Management. International Journal of Drug Delivery Technology. 2024;14(1):581-588. DOI: 10.25258/ijddt.14.1.79.
26. Bhavani MS, Saravanan R. Beyond Syringes and Pills: Advances in Drug Delivery Systems for. Diabetes. International Journal of Drug Delivery Technology. 2023;13(3):1069-1077. DOI: 10.25258/ijddt.13.3.48.