Ind. J. Pharm. Edu. Res., 2026; 60(2):729-738.
https://www.ijper.org

Original Article

Sophoricoside Alleviates Oxidative Stress and Inflammation in Streptozotocin-Induced Diabetes Mellitus in Rats

Jie Yang[1,#], Lu Yan[2,#], Xinrong Zhang[3,*], Jiawei Zhang[4,*]

[1]Department of Infectious Diseases, Affiliated Hospital of Hebei University, Baoding, CHINA.
[2]Blood Collection Center, Affiliated Hospital of Hebei University, Baoding, CHINA.
[3]Joint Surgery, Affiliated Hospital of Hebei University, Baoding, CHINA.
[4]Special Ward of Geriatric Medicine, Affiliated Hospital of Hebei University, Baoding, CHINA.
#These authors contributed equally to the work.

ABSTRACT

Background: Diabetes mellitus, a chronic metabolic condition defined by chronic hyperglycemia, presents a major global health challenge with increasing prevalence and profound implications for individual's well-being and healthcare systems. **Objectives:** This work was aimed at studying the anti-diabetic properties of sophoricoside against Streptozotocin (STZ)-induced diabetes in rats. **Materials and Methods:** In this experimental model, diabetic condition was initiated in rats by injecting a single dosage of STZ (65 mg/kg). Following diabetes induction, the rats were treated orally with 50 mg/kg of sophoricoside for 8 weeks. After treatments, the effect of sophoricoside on the blood glucose and insulin level in the experimental rats was evaluated. The concentrations of creatinine, urea, lipid peroxidation and antioxidants, and inflammatory markers in the experimental rats were evaluated. Histological study was performed on the pancreas of experimental rats. **Results:** The findings of this work showed that sophoricoside considerably diminished blood glucose and augmented the insulin concentration in the diabetic rats. The sophoricoside also reduced the creatinine and urea concentrations in the diabetic rats. Additionally, the administration of sophoricoside effectively reduced inflammatory markers and alleviated oxidative stress by enhancing antioxidants. The findings of histological study of the pancreas further confirmed the salutary characteristics of sophoricoside. **Conclusion:** The findings of this work demonstrate that sophoricoside exerts beneficial activities in mitigating the diabetes in rats. These results recommend that sophoricoside may offer as a viable therapeutic option to treat diabetes.

Keywords: Hyperglycemia, Insulin, Sophoricoside, Pancreas, Streptozotocin, Oxidative stress.

Correspondence:
Dr. Jiawei Zhang
Special Ward of Geriatric Medicine, Affiliated Hospital of Hebei University, Baoding-071000, CHINA.
Email: 13315295181@163.com

Dr. Xinrong Zhang
Joint Surgery, Affiliated Hospital of Hebei University, Baoding-071000, CHINA.
Email: 15830288353@163.com

Received: 14-05-2025;
Revised: 03-07-2025;
Accepted: 29-09-2025.

INTRODUCTION

Diabetes mellitus is a common metabolic disorder characterized primarily by chronic hyperglycemia, stemming from lack of insulin production, insulin activity, or both. This intricate condition impacts a significant portion of the global population and is recognized as one of the four prioritized non-communicable diseases, owing to its increasing prevalence and the increasing number of affected individuals over recent decades. The pathophysiology of diabetes is complex, involving both genetic predispositions and environmental influences, ultimately leading to impaired glucose homeostasis and either a deficiency or complete absence of insulin secretion.[1] Clinically, diabetes manifests across a broad spectrum, ranging from asymptomatic states to severe conditions such as ketoacidosis or coma, contingent on the extent of the underlying metabolic derangement. The increasing rates of diabetes are alarming, with projections estimating that approximately 600 million individuals will be affected by 2035. The chronic hyperglycemia associated with diabetes instigates damage to various organs, tissues, and systems within the body, resulting in complications that impose significant economic and physical burdens on patients.[2]

Diabetes mellitus is clinically categorized into two distinct types, each characterized by unique etiologies and pathophysiological mechanisms. Type 1 diabetes mellitus is defined by autoimmune-mediated destruction of pancreatic β-cells, resulting in lack of insulin. Type 2 diabetes mellitus, accounts for the majority of diabetes incidences, is defined by insulin resistance and β-cell dysfunction, often connected with obesity,

DOI: 10.5530/ijper.20262129

physical inactivity, and genetic predisposition.[3] The onset of type 2 diabetes is complex, encompassing a genetic predisposition and environmental influences that lead to insulin resistance, impaired insulin secretion, and ultimately, hyperglycemia.[4] The complications connected with diabetes mellitus are multifaceted and can affect nearly every organ system in the body, leading to significant morbidity and mortality. Cardiovascular diseases is a major reason of mortality in individuals with diabetes, attributed to accelerated atherosclerosis and increased risk of thrombotic events.[5] Neuropathy, or nerve damage, is a primary issue of diabetes, affecting sensory, motor, and autonomic nerves, leading to pain, numbness, and loss of function, with diabetic neuropathy being a leading cause of foot ulcers and amputations. Nephropathy and retinopathy are the other 2 serious complications of diabetes, which affect most of the patients.[6]

Current therapeutic strategies mostly focus on managing blood glucose levels through a combination of lifestyle modifications, pharmacological interventions, and in some cases, insulin therapy.[7] Furthermore, many current therapies primarily target the symptoms of diabetes rather than addressing the underlying causes, such as insulin resistance or impaired insulin secretion. Many patients ultimately require insulin because traditional oral therapies are typically effective at lowering hyperglycemia at first but do not stop the disease from getting worse. Unfortunately, patients may not adhere to treatment recommendations because most antidiabetic therapies are linked to weight gain or hypoglycemia risk.[8]

The exploration of plant-derived bioactive compounds as alternative therapeutic candidates for diabetes mellitus has gained considerable attention in recent times, driven by their extensive biological effects.[9] Sophoricoside is a bioactive isoflavone glycoside compound, which is derived from the dried fruit of Sophora japonica (Leguminosae), a component of traditional Chinese medicine. Several previous studies are already reported the numerous biological activities of the sophoricoside, including anti-allergic inflammation, anti-hepatitis, anti-dermatitis, hepatoprotective, anti-arthritis, anti-asthma, and anti-sepsis activities.[10-16] Already been reported that sophoricoside has inhibited the lipogenesis and increased glucose uptake *in vitro*.[17] However, there are no much reports to claim the antidiabetic effects of sophoricoside on the animal models. Therefore, this study was designed at assessing the antidiabetic properties of sophoricoside against Streptozotocin (STZ)-induced diabetes in rats.

MATERIALS AND METHODS

Animals

Male Sprague-Dawley rats were utilized in the current work. The rats were caged in sterilized polypropylene confines inside controlled laboratory settings, sustaining a temperature of 22-26ºC and humidity of 50-60%. A 12-hr cycle of alternating light and dark was instituted. Throughout the entire study duration, all rats were granted unrestricted access to standard rodent diet and pure drinking water. Prior to the initiation of the experiments, all rats were allotted a 7-day acclimatization period in a laboratory setting.

Treatment groups

Following a one-week acclimatization, rats were distributed into four groups (n=6). Group I rats are the control, receives standard rodent food, and is administered only a saline solution without any treatments. Group II rats received a single administration (i.p.) of STZ at a dosage of 65 mg/kg to initiate diabetes. Furthermore, rats were given glucose (0.5%) to prevent mortality resulting from abrupt hypoglycemia. After a three-day injection of STZ, we determined the blood glucose. Rats exhibiting FBG levels over 250 mg/dL was classified as diabetic and chosen for subsequent tests. Group III consisted of rats with diabetes that were subsequently administered the sophoricoside at a dosage of 50 mg/kg via oral route for 8 weeks. Group IV rats were induced with diabetes and administered a dosage of 5 mg/kg of glibenclamide for duration of 8 weeks.

Analysis of glucose and insulin levels

Before assessing the glucose levels, the experimental rats underwent an overnight fast. The blood was meticulously obtained from the orbital sinus and analyzed for glucose levels with a glucose assay kit (MyBioSource, USA). The insulin levels were assessed utilizing a commercial kit from CusaBio, USA.

Analysis of creatinine and urea levels

The serum levels of urea and creatinine were evaluated using commercial diagnostic kits sourced from Abcam, USA. The tests were performed in triplicate in accordance with the manufacturer's specified procedures.

Analysis of oxidative stress markers

The homogenates prepared from the pancreas and liver tissues of the experimental rats were utilized to evaluate the concentrations of lipid peroxidation marker and antioxidants. The Malondialdehyde (MDA), Superoxide Dismutase (SOD), Catalase (CAT), and Glutathione (GSH) was quantified utilizing kits procured from MyBioSource, USA. The tests were performed in triplicate following the manufacturer's indicated procedures.

Analysis of inflammatory cytokines

The Interleukin-6 (IL-6), IL-1β, and TNF-α concentration were determined in the serum of the experimental rats utilizing commercial diagnostic kits. The analysis was conducted using the procedures outlined by the manufacturer (Abcam, USA).

Histopathological analysis

The pancreas tissue samples were collected and treated with 10% neutral formalin to evaluate the histological changes. Subsequently, the pancreas were paraffinized, cut into a 5 µm diameter, and stained with eosin-hematoxylin. Finally, the pancreas tissues were assessed microscopically at 40× magnification to assess the histological alterations.

Statistical analysis

The data were evaluated utilizing GraphPad Prism, and the data are shown as the Mean±SD of triplicates. The data are studied using one-way ANOVA and Duncan's Multiple Range Test (DMRT), with a significance at $p<0.005$.

RESULTS

Effect of sophoricoside on glucose and insulin levels in experimental rats

The glucose and insulin concentrations in the experimental rats were evaluated, with results presented in Figures 1. The rats with STZ-induced diabetes exhibited markedly increased blood glucose and reduced insulin concentrations relative to the normal group. Fascinatingly, the treatment of sophoricoside at a dosage of 50 mg/kg notably diminished the blood glucose and increase in insulin concentrations in the STZ-induced rats. The standard drug glibenclamide also decreased the glucose and elevated insulin in the STZ-induced rats. These data indicate that sophoricoside significantly regulated glucose level via increasing insulin concentration in the diabetic rats.

Effect of sophoricoside on creatinine and urea levels in experimental rats

Figure 2 illustrates the impact of sophoricoside on the serum urea and creatinine levels in experimental rats. The STZ-induced diabetic rats demonstrated a considerable elevation in the serum levels of both urea and creatinine. Interestingly, the sophoricoside treatment at the 50 mg/kg concentration effectively reduced the urea and creatinine in the STZ-induced rats. These results also aligned with the outcomes of standard drug glibenclamide treatment.

Effect of sophoricoside on oxidative stress markers in experimental rats

Figure 3 displays the concentrations of oxidative stress markers, including MDA, SOD, CAT, and GSH in the liver and pancreas tissue homogenates of experimental rats. The diabetic rats demonstrated a drastic elevation in MDA and a reduction in SOD, CAT, and GSH levels in both liver and pancreas tissues. Captivatingly, the administration of 50 mg/kg of sophoricoside to the diabetic rats led to a diminution in MDA and an elevation in SOD, CAT, and GSH levels in both pancreas and liver tissues. The aforementioned results were similar to the results of glibenclamide, highlighting the antioxidant effects of sophoricoside.

Effect of sophoricoside on the inflammatory markers in experimental rats

The anti-inflammatory activity of sophoricoside in the diabetic rats was studied by measuring the serum levels of inflammatory cytokines (Figure 4). The STZ-induced diabetic rats exhibited considerable elevations in IL-1β, IL-6, and TNF-α level in their serum relative to the control. Remarkably, the sophoricoside treatment at 50 mg/kg dose notably reduced these pro-inflammatory cytokine levels in the serum of diabetic rats. The anti-inflammatory properties of sophoricoside further aligned with the outcomes of standard drug glibenclamide treatment.

Effect of sophoricoside on the pancreas tissue histopathology of experimental rats

Figure 5 illustrates the results of histopathological assessment of the pancreas tissue from the experimental rats. The pancreas from the normal control rats exhibited no signs of inflammation and revealed a normal cellular structure. Whereas, the pancreas of STZ-induced diabetic rats displayed increased inflammatory cell infiltrations, islet cell shrinkages and hypertrophy of adipose tissues in comparison to the normal control rats. Interestingly, these histological changes were successfully mitigated by the 50 mg/kg of sophoricoside treatment in the pancreas of diabetic rats, which is also reinforced by the findings of standard drug glibenclamide treatment.

DISCUSSION

Diabetes mellitus, a chronic metabolic condition defined by chronic hyperglycemia, presents a major global health challenge with escalating prevalence and profound implications for individual well-being and healthcare systems. The number of individuals affected by diabetes worldwide has reached epidemic rates, with projections indicating a continued surge in the coming decades. The multifaceted nature of diabetes extends beyond mere glucose dysregulation, encompassing a spectrum of microvascular and macrovascular complications that impair organ function and diminish the quality of life for affected individuals.[18] Microangiopathic complications, including nephropathy, retinopathy, and neuropathy, contribute to kidney failure, blindness, and nerve damage, respectively, while macroangiopathic complications, such as ischemic heart disease, stroke, and peripheral vascular disease, increase the risk of cardiovascular events and limb amputation. The economic ramifications of diabetes are staggering, with global health expenditures on diabetes and its complications reaching astronomical levels. Understanding the intricate pathogenesis of diabetes and its related problems is crucial to develop targeted

interventions to alleviate the disease's devastating impact on individuals and healthcare system.[19]

The STZ-induced diabetic rat model has emerged as an useful tool for investigating the pathogenesis of diabetes and evaluating potential therapeutic interventions. STZ damages pancreatic-β cells, resulting in the lack of insulin and subsequent hyperglycemia, mirroring the pathophysiology of diabetes. This model allows researchers to examine the effects of prolonged hyperglycemia on various organs and tissues, providing insights into the onset of diabetic complications. By inducing a state of insulin deficiency, STZ administration results in pronounced hyperglycemia, which triggers a cascade of metabolic and biochemical abnormalities that mirror the pathophysiology of diabetes in humans.[20] Blood glucose levels serve as a direct indicator of glycemic control, reflecting the balance between glucose production, utilization, and excretion. Monitoring blood glucose fluctuations in STZ-induced diabetic rats allows researchers to assess the effectiveness of insulin analogs, oral hypoglycemic agents, and other experimental therapies in restoring normoglycemia.[21] Insulin, the primary hormone responsible for regulating glucose uptake and utilization, plays a central role in maintaining metabolic equilibrium. Measuring insulin concentrations in STZ-induced rats helps elucidate the

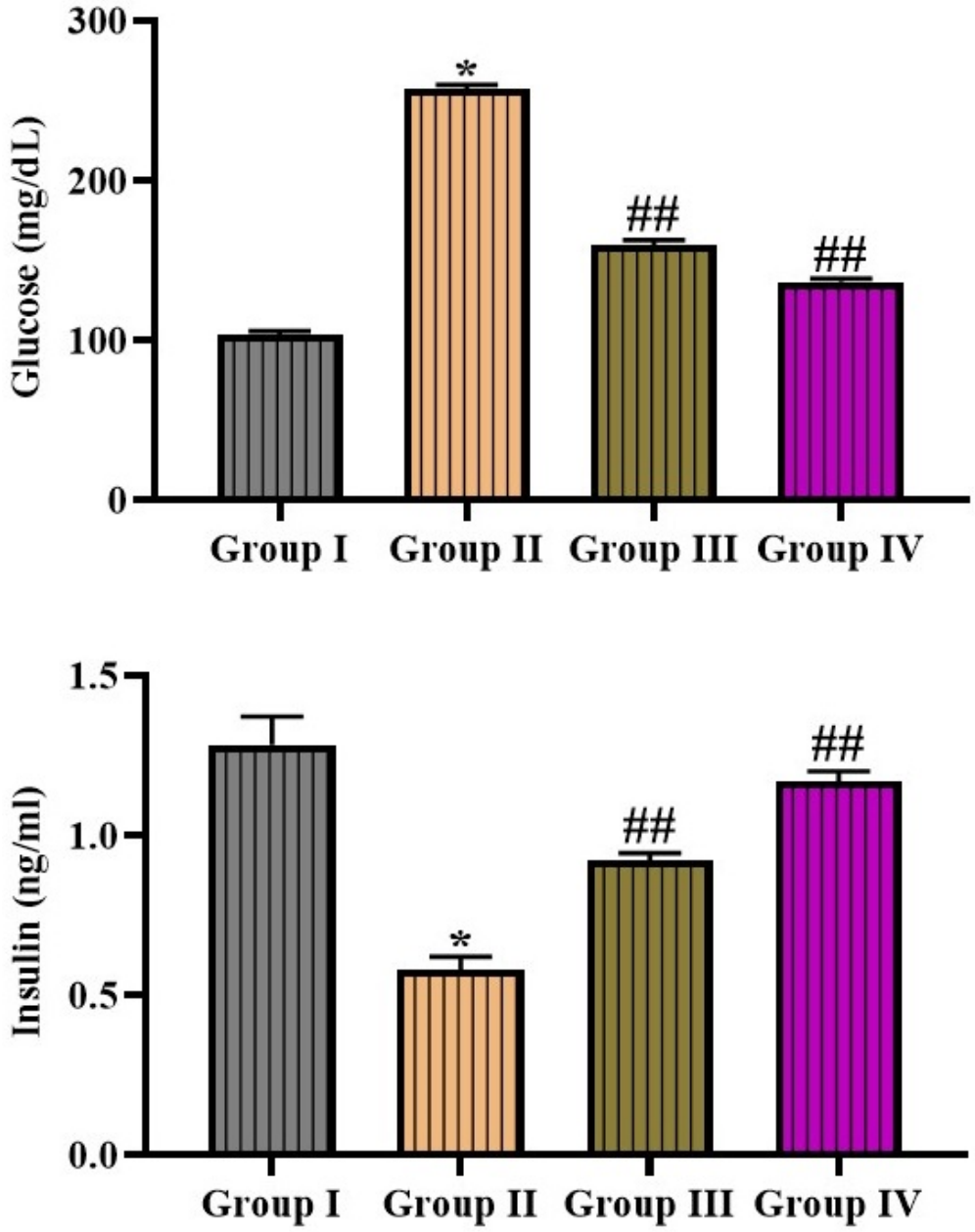

Figure 1: Effect of sophoricoside on the glucose and insulin levels in the experimental rats. The data were shown as the mean±SD of triplicates. The values are examined with one-way ANOVA and DMRT analyses. Note: '*' denotes statistical significance at $p<0.001$ relative to the control group; '##' denotes statistical significance at $p<0.005$ relative to the diabetes-induced group.

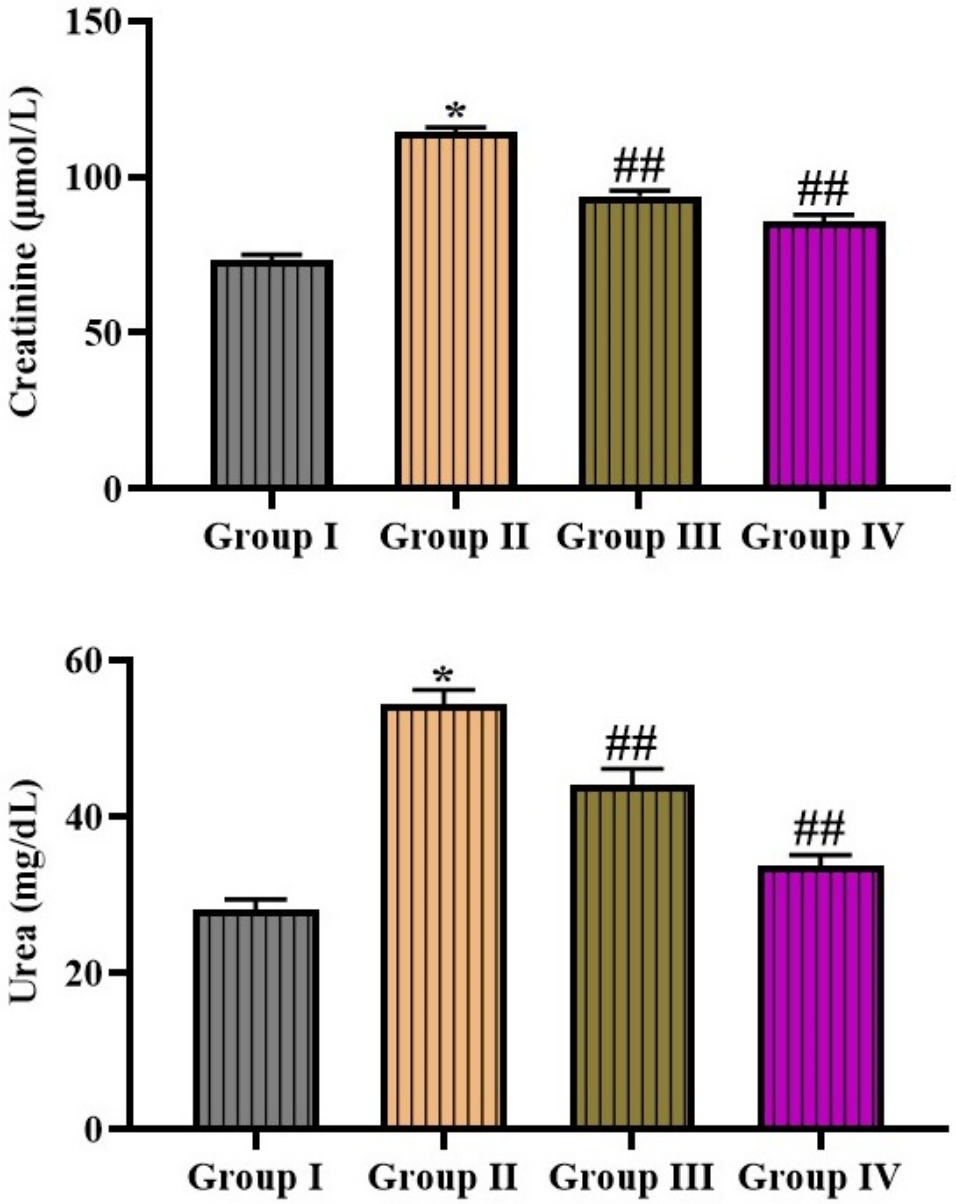

Figure 2: Effect of sophoricoside on the urea and creatinine levels in the experimental rats. The data were shown as the mean±SD of triplicates. The values are examined with one-way ANOVA and DMRT analyses. Note: '*' denotes statistical significance at $p<0.001$ relative to the control group; '##' denotes statistical significance at $p<0.005$ relative to the diabetes-induced group.

extent of beta-cell dysfunction and the impact of therapeutic interventions on insulin secretion. Changes in glucose and insulin levels can reveal the impact of interventions on insulin sensitivity, glucose effectiveness, and overall metabolic function.[22] In the current work, the STZ-induced rats demonstrated increased blood glucose and diminished insulin level than the control group. Interestingly, the sophoricoside treatment significantly diminished the glucose and elevated the insulin concentration in the STZ-induced rats. These findings highlighted that sophoricoside can regulate the glucose level via increasing insulin in the STZ-induced rats.

The onset of diabetic nephropathy is a multifaceted process, characterized by structural and functional derangements within the kidney. These changes encompass glomerular hyperfiltration, thickening of the glomerular membrane, mesangial expansion, and ultimately, glomerulosclerosis and tubulointerstitial fibrosis, all of which contribute to the decrease in renal function.[23] Creatinine, a byproduct of muscle metabolism, is freely filtered by the glomeruli and excreted in urine, with minimal tubular reabsorption; thus, its serum concentration serves as a reliable indicator of glomerular filtration rate. As renal function deteriorates, the excretion of creatinine diminishes, leading to an elevation in serum creatinine levels, indicative of impaired glomerular filtration. Serum creatinine was used to assess the presence and progress of diabetic nephropathy.[24] Urea, synthesized in the liver as the end product of protein metabolism,

is also filtered by the glomeruli, but unlike creatinine, a portion of it is reabsorbed by the tubules, with its reabsorption rate varying depending on hydration status and urine flow rate. In diabetic nephropathy, the increased protein catabolism and altered tubular handling of urea can lead to elevated serum urea levels.[25]

The measurement of serum creatinine and urea concentrations in STZ-induced rats holds immense significance in evaluating the onset of diabetic nephropathy and assessing the efficacy of therapeutic interventions. Elevated serum creatinine and urea concentrations in diabetic rats serve as indicators of impaired renal function, reflecting the extent of glomerular and tubular damage. Furthermore, the analysis of serum creatinine and urea levels enables the evaluation of potential renoprotective effects of novel therapeutic agents, providing a means to assess their ability to preserve renal function and mitigate the advancement of nephropathy.[26] The present work demonstrated the elevated serum concentrations of creatinine and urea in the diabetic rats. Whereas, the sophoricoside considerably diminished the creatinine and urea concentrations in the serum of diabetic rats. These results suggest that sophoricoside may exert renoprotective effects and maintain renal function in diabetic condition.

Oxidative stress, arising from an imbalance between ROS generation and the body's antioxidant mechanisms, is known as a crucial factor in the advancement of diabetic complications. The pathogenesis of diabetes and its complications is greatly influenced by oxidative stress, which is triggered by an increase in the generation of free radicals. Furthermore, hyperglycemia diminishes antioxidant defense mechanisms by glycosylating scavenging enzymes. In diabetes, oxidative stress is involved in the damage to various tissues and organs, including the pancreas and liver, which play crucial roles in glucose homeostasis and overall metabolic regulation.[27] The liver, as a central metabolic hub, is especially susceptible to oxidative stress. In diabetic conditions, the liver experiences heightened oxidative stress due to increased glucose flux and altered lipid metabolism, this can impair its normal function. The liver's role in detoxification and its exposure to high glucose levels make it susceptible to oxidative damage. Oxidative stress can compromise cell membrane integrity and trigger apoptosis, microvascular injury, and barrier disruption, ultimately resulting in the onset of diabetes symptoms.[28]

The pancreas, specifically the pancreatic-β cells responsible for insulin secretion, is also vulnerable to oxidative stress in the diabetic milieu. High glucose levels cause increased production of ROS, while antioxidant mechanisms are weakened by the glycation of scavenging enzymes. Oxidative stress can directly impair beta-cell function and contribute to their eventual destruction. Elevated amounts of ROS in the pancreas, along with diminished antioxidant defenses, may result in heightened oxidative damage, subsequently impairing insulin secretion. This oxidative damage disrupts insulin synthesis and secretion, leading to further elevation of blood glucose concentration and exacerbating the diabetic state. Therefore, strategies focused at decreasing oxidative stress in the pancreas have the potential to preserve beta-cell activity and improve glucose control in diabetic patients.[29]

The key biomarkers utilized to assess the degree of oxidative stress in biological tissues are MDA, SOD, CAT, and GSH. MDA is a final product of lipid peroxidation and offers as a biomarker of oxidative stress to cell membranes. SOD, CAT, and GSH are primary antioxidants that counteract the damaging effects of ROS. SOD is an enzyme that facilitates the conversion of superoxide radicals into H_2O_2 and O_2, representing a crucial first line of defense against oxidative stress.[30] CAT facilitates the breakdown of H_2O_2 into H_2O and O_2, preventing the buildup of

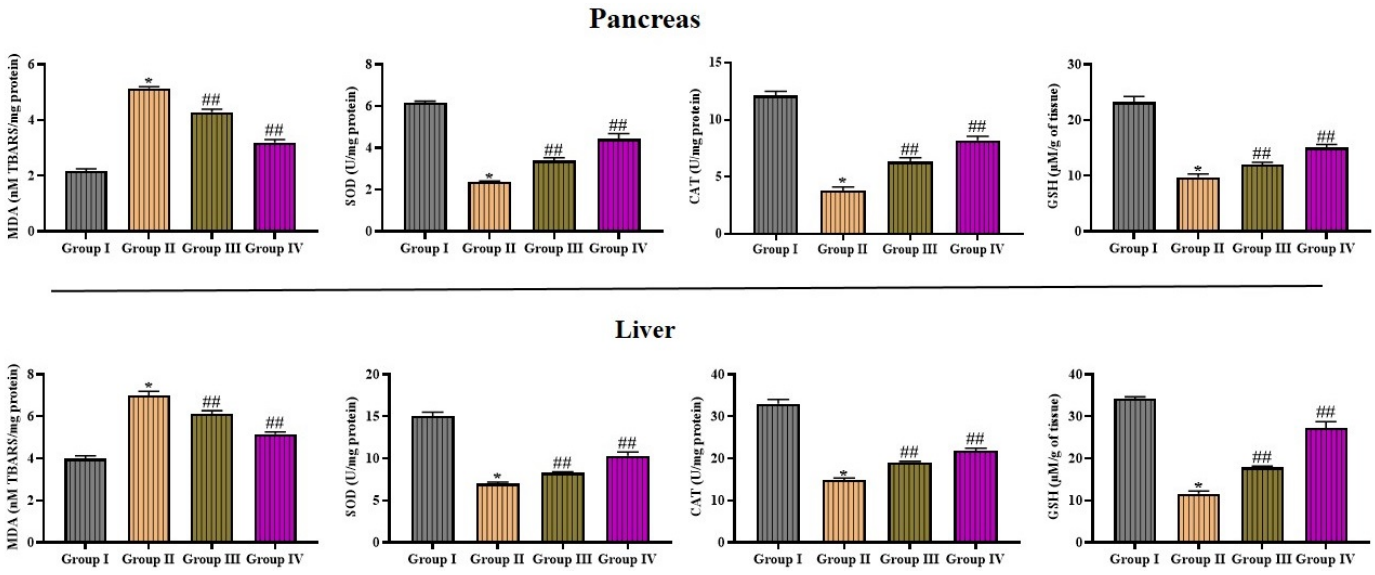

Figure 3: Effect of sophoricoside on the oxidative stress markers in the experimental rats. The data were shown as the mean±SD of triplicates. The values are examined with one-way ANOVA and DMRT analyses. Note: '*' denotes statistical significance at $p<0.001$ relative to the control group; '##' denotes statistical significance at $p<0.005$ relative to the diabetes-induced group.

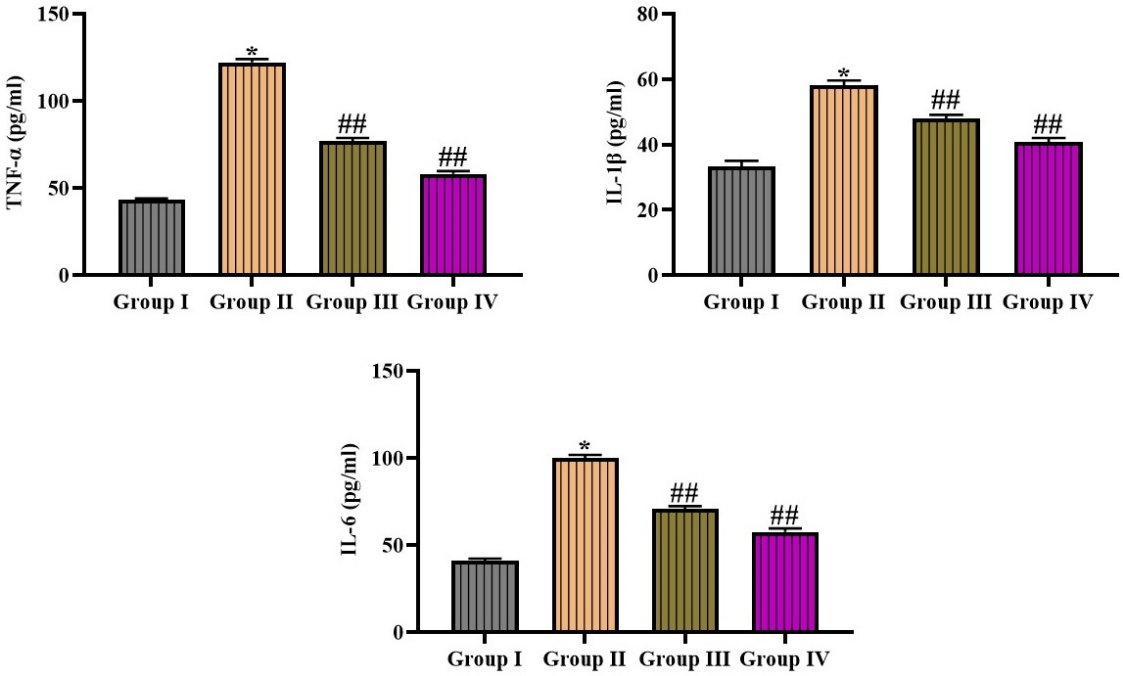

Figure 4: Effect of sophoricoside on the inflammatory cytokines in the experimental rats. The data were shown as the mean±SD of triplicates. The values are examined with one-way ANOVA and DMRT analyses. Note: '*' denotes statistical significance at $p<0.001$ relative to the control group; '##' denotes statistical significance at $p<0.005$ relative to the diabetes-induced group.

this potentially harmful molecule. GSH is an essential antioxidant that directly scavenges free radicals and serves as a cofactor for antioxidant enzymes, playing a crucial role in maintaining redox balance.[31] Analyzing the concentrations of these biomarkers in the pancreas and liver of STZ-induced rats offers valuable insights into the extent of oxidative stress and the effectiveness of antioxidant defenses in these crucial organs. In STZ-induced rats, increased MDA in the pancreas and liver would indicate elevated lipid peroxidation and oxidative damage, while decreased antioxidant levels would suggest impaired antioxidant capacity.[32] The present findings witnessed the increased MDA and decreased SOD, CAT, and GSH levels in both pancreas and liver tissues of the STZ-induced rats. Interestingly, the sophoricoside treatment successfully diminished the MDA and elevated the antioxidants in both liver and pancreas tissues of the diabetic rats, which suggests its antioxidant activities.

The intricate interaction between inflammation and diabetes has gained substantial interest, as the inflammation is a crucial player in the pathogenesis of diabetes mellitus. Low-grade inflammation and the activation of the innate immune system can specifically result in β cell failure.[33] Comprehending the inflammatory mechanisms in diabetes facilitates treatment approaches, such as anti-inflammatory methods, to address and alleviate the disease's consequences.[34] Elevated circulating inflammatory markers are observed systemically and within the affected tissues, reflecting the systemic nature of inflammation in metabolic disorders. The measurement of serum inflammatory cytokines, like IL-1β, IL-6, and TNF-α, offers useful insights into the inflammatory status of an organism, especially in the context of diabetes.[35]

IL-1β is a key inflammatory cytokine, inhibits insulin signaling in liver, adipose, and muscle tissues, leading to insulin resistance. This cytokine is a key mediator of inflammation, orchestrating a cascade of events that promote immune cell recruitment, activation, and the release of other pro-inflammatory markers.[36] TNF-α, another crucial pro-inflammatory cytokine, plays a crucial role in the inflammatory processes related with diabetes. TNF-α exacerbates insulin resistance by disrupting insulin signaling pathways and enhancing lipolysis in adipocytes. In the context of diabetes, TNF-α contributes to pancreatic β-cell dysfunction and apoptosis, further exacerbating hyperglycemia.[37] Elevated serum levels of pro-inflammatory markers, such as IL-6, were linked to the onset of impaired glucose tolerance and type 2 diabetes. IL-6 plays a role in the proliferation and development of certain immunocompetent cells. It regulates adipocyte differentiation, body weight, and glucose homeostasis.[38] Understanding the involvement of cytokines like IL-1β, IL-6, and TNF-α, in the inflammatory processes associated with diabetes is critical for advancing targeted therapies. In this work, the findings illustrated the elevated IL-1β, IL-6, and TNF-α concentrations in the STZ-induced rats. Fascinatingly, the sophoricoside treatment successfully diminished these pro-inflammatory cytokine concentrations in the serum of diabetic rats, which highlights its anti-inflammatory activities. Whereas, the pancreas of STZ-induced diabetic rats displayed increased inflammatory cell infiltrations, islet cell shrinkages and hypertrophy of adipose

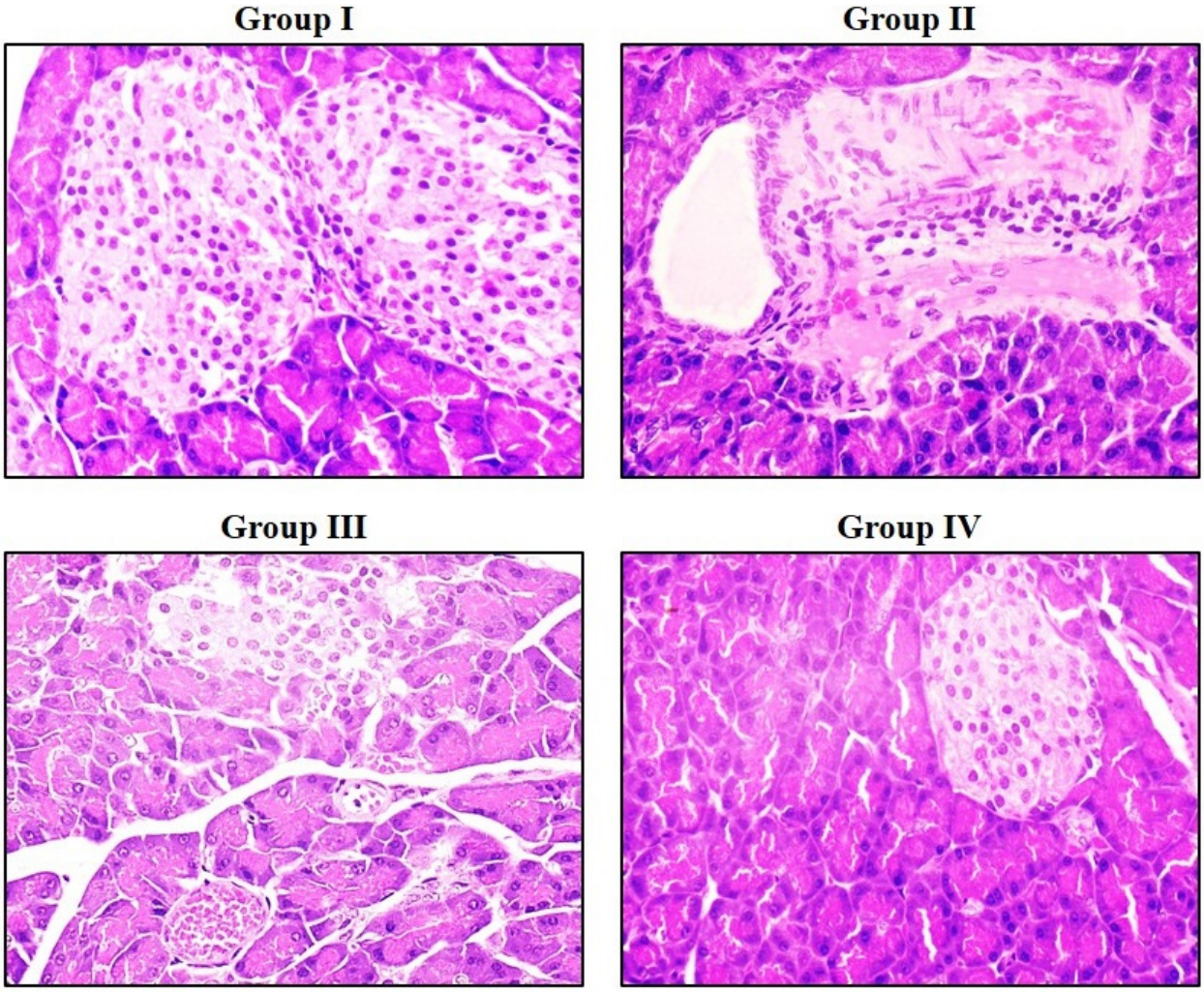

Figure 5: Effect of sophoricoside on the pancreas tissue histopathology of experimental rats.The pancreatic tissues from the normal control rats exhibited a normal cellular structure (Group I). The pancreas of STZ-induced diabetic rats displayed increased inflammatory cell infiltrations, shrinkage of islet cells, and hypertrophy of adipose tissues (Group II). The histological changes in the pancreas tissues of diabetic rats were successfully mitigated by the sophoricoside (50 mg/kg) and standard drug glibenclamide treatments (Groups III and IV, respective).

tissues in comparison to the normal control rats. Interestingly, these histological changes were successfully mitigated by the 50 mg/kg of sophoricoside treatment in the pancreas of diabetic rats, which is also reinforced by the findings of standard drug glibenclamide treatment.

CONCLUSION

The results of this work demonstrate that sophoricoside exerts beneficial activities on mitigating diabetes and its related complications in STZ-induced rats. Treatment with sophoricoside significantly reduced blood glucose, creatinine, and urea concentrations, while increasing insulin levels in diabetic rats. Furthermore, sophoricoside alleviated oxidative stress and inflammation by enhancing antioxidant levels and decreasing inflammatory cytokines in diabetic rats. These findings highlight that sophoricoside may be a viable therapeutic option to treat diabetes. However, additional studies are necessary to achieve a comprehensive understanding of its therapeutic benefits in managing diabetes.

ABBREVIATIONS

STZ: Streptozotocin; **FBG:** Fasting blood glucose; **GSH:** Glutathione; **SOD:** Superoxide dismutase; **MDA:** Malondialdehyde; **CAT:** Catalase; **IL-6:** Interleukin-6; **IL-1β:** Interleukin-1 beta; **TNF-α:** Tumor necrosis factor; **ROS:** Reactive oxygen species.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

ETHICAL APPROVAL

This research was approved by Affiliated Hospital of Hebei University, Baoding 071000, CHINA. Approved No. GWLCZXEC-SOP-K-2025-16.

SUMMARY

The present work focuses on assessing the studying the anti-diabetic properties of sophoricoside against STZ-induced diabetes in rats. In this experimental model, diabetic condition was initiated in rats by injecting a single dosage of STZ (65 mg/kg) and diabetes induction; the rats were treated with 50 mg/kg of sophoricoside. After treatments, the effect of sophoricoside on the blood glucose and insulin level in the experimental rats was evaluated. The concentrations of creatinine, urea, lipid peroxidation and antioxidants, and inflammatory markers in the experimental rats were evaluated. Histological study was performed on the pancreas of experimental rats. The findings of this work showed that sophoricoside considerably diminished blood glucose and augmented the insulin concentration in the diabetic rats. The sophoricoside also reduced the creatinine and urea concentrations in the diabetic rats. Additionally, the administration of sophoricoside effectively reduced inflammatory markers and alleviated oxidative stress by enhancing antioxidants. The findings of histological study of the pancreas further confirmed the salutary characteristics of sophoricoside. These findings highlight that sophoricoside may be a viable therapeutic option to treat diabetes.

REFERENCES

1. Ong KL, Stafford LK, McLaughlin SA, Boyko EJ, Vollset SE, Smith AE, *et al.* Global, regional, and national burden of diabetes from 1990 to 2021, with projections of prevalence to 2050: a systematic analysis for the Global Burden of Disease Study 2021. Lancet. 2023; 402(10397): 203-34. doi: 10.1016/S0140-6736(23)01301-6, PMID 37356446.
2. Sun H, Saeedi P, Karuranga S, Pinkepank M, Ogurtsova K, Duncan BB, *et al.* IDF Diabetes Atlas: global, regional and country-level diabetes prevalence estimates for 2021 and projections for 2045. Diabetes Res Clin Pract. 2022; 183: 109119. doi: 10.1016/j.diabres.2021.109119, PMID 34879977.
3. Sanches JM, Zhao LN, Salehi A, Wollheim CB, Kaldis P. Pathophysiology of type 2 diabetes and the impact of altered metabolic interorgan crosstalk. FEBS Journal. 2023; 290(3): 620-48. doi: 10.1111/febs.16306, PMID 34847289.
4. Młynarska E, Czarnik W, Dzieża N, Jędraszak W, Majchrowicz G, Prusinowski F, *et al.* Type 2 diabetes mellitus: new pathogenetic mechanisms, treatment and the most important complications. Int J Mol Sci. 2025; 26(3): 1094. doi: 10.3390/ijms26031094, PMID 39940862.
5. Blaibel D, Fernandez CJ, Pappachan JM. Acute worsening of microvascular complications of diabetes mellitus during rapid glycemic control: the pathobiology and therapeutic implications. World J Diabetes. 2024; 15(3): 311-7. doi: 10.4239/wjd.v15.i3.311, PMID 38591086.
6. Raut SS, Acharya S, Deolikar V, Mahajan S. Navigating the frontier: emerging techniques for detecting microvascular complications in type 2 diabetes mellitus: a comprehensive review. Cureus. 2024; 16(1): e53279. doi: 10.7759/cureus.53279, PMID 38435878.
7. Su J, Luo Y, Hu S, Tang L, Ouyang S. Advances in research on type 2 diabetes mellitus targets and therapeutic agents. Int J Mol Sci. 2023; 24(17): 13381. doi: 10.3390/ijms241713381, PMID 37686185.
8. Aloke C, Egwu CO, Aja PM, Obasi NA, Chukwu J, Akumadu BO, *et al.* Current advances in the management of diabetes mellitus. Biomedicines. 2022; 10(10): 2436. doi: 10.3390/biomedicines10102436, PMID 36289697.
9. Singh S, Bansal A, Singh V, Chopra T, Poddar J. Flavonoids, alkaloids and terpenoids: a new hope for the treatment of diabetes mellitus. J Diabetes Metab Disord. 2022; 21(1): 941-50. doi: 10.1007/s40200-021-00943-8, PMID 35673446.
10. Kim SJ, Lee GY, Jung JW, Oh SR, Ahn EM, Kim SH, *et al.* The ameliorative effect of sophoricoside on mast cell-mediated allergic inflammation *in vivo* and *in vitro*. Molecules. 2013; 18(5): 6113-27. doi: 10.3390/molecules18056113, PMID 23698058.
11. Chen Y, Lei Y, Wang H, Wang L, Xu J, Wang S, *et al.* Sophoricoside attenuates autoimmune-mediated liver injury through the regulation of oxidative stress and the NF-κB signaling pathway. Int J Mol Med. 2023; 52(3): 78. doi: 10.3892/ijmm.2023.5281, PMID 37477163.
12. Lee HK, Kim HS, Kim YJ, Kim JS, Park YS, Kang JS, *et al.* Sophoricoside isolated from *Sophora japonica* ameliorates contact dermatitis by inhibiting NF-κB signaling in B cells. Int Immunopharmacol. 2013; 15(3): 467-73. doi: 10.1016/j.intimp.2013.01.025, PMID 23415872.
13. Li W, Lu Y. Hepatoprotective effects of sophoricoside against fructose-induced liver injury via regulating lipid metabolism, oxidation, and inflammation in mice. J Food Sci. 2018; 83(2): 552-8. doi: 10.1111/1750-3841.14047, PMID 29350757.
14. Liu Y, Zhao Y, Guo Q, Wang P, Li P, Du Q, *et al.* Sophoricoside reduces inflammation in type II collagen-induced arthritis by downregulating NLRP3 signaling. Biochem Biophys Rep. 2024; 40: 101867. doi: 10.1016/j.bbrep.2024.101867, PMID 39610833.
15. Kim BH, Lee S. Sophoricoside from Sophora japonica ameliorates allergic asthma by preventing mast cell activation and CD4+ T cell differentiation in ovalbumin-induced mice. Biomed Pharmacother. 2021; 133: 111029. doi: 10.1016/j.biopha.2020.111029, PMID 33254020.
16. Wu YX, Zeng S, Wan BB, Wang YY, Sun HX, Liu G, *et al.* Sophoricoside attenuates lipopolysaccharide-induced acute lung injury by activating the AMPK/Nrf2 signaling axis. Int Immunopharmacol. 2021; 90: 107187. doi: 10.1016/j.intimp.2020.107187, PMID 33249045.
17. Wu C, Luan H, Wang S, Zhang X, Wang R, Jin L, *et al.* Modulation of lipogenesis and glucose consumption in HepG2 cells and C2C12 myotubes by sophoricoside. Molecules. 2013; 18(12): 15624-35. doi: 10.3390/molecules181215624, PMID 24352018.
18. Yapanis M, James S, Craig ME, O'Neal D, Ekinci EI. Complications of diabetes and metrics of glycemic management derived from continuous glucose monitoring. J Clin Endocrinol Metab. 2022; 107(6): e2221-36. doi: 10.1210/clinem/dgac034, PMID 35094087.
19. Bjornstad P, Chao LC, Cree-Green M, Dart AB, King M, Looker HC, *et al.* Youth-onset type 2 diabetes mellitus: an urgent challenge. Nat Rev Nephrol. 2023; 19(3): 168-84. doi: 10.1038/s41581-022-00645-1, PMID 36316388.
20. Goyal SN, Reddy NM, Patil KR, Nakhate KT, Ojha S, Patil CR, *et al.* Challenges and issues with streptozotocin-induced diabetes–a clinically relevant animal model to understand the diabetes pathogenesis and evaluate therapeutics. Chem Biol Interact. 2016; 244: 49-63. doi: 10.1016/j.cbi.2015.11.032, PMID 26656244.
21. Baylan U, Korn A, Emmens RW, Schalkwijk CG, Niessen HW, Krijnen PA, *et al.* Liraglutide treatment attenuates inflammation markers in the cardiac, cerebral and renal microvasculature in streptozotocin-induced diabetic rats. Eur J Clin Investig. 2022; 52(9): e13807. doi: 10.1111/eci.13807, PMID 35488737.
22. Damasceno DC, Netto AO, Iessi IL, Gallego FQ, Corvino SB, Dallaqua B, *et al.* Streptozotocin-induced diabetes models: pathophysiological mechanisms and fetal outcomes. BioMed Res Int. 2014; 2014(1): 819065. doi: 10.1155/2014/819065, PMID 24977161.
23. Giglio RV, Patti AM, Rizvi AA, Stoian AP, Ciaccio M, Papanas N, *et al.* Advances in the pharmacological management of diabetic nephropathy: a 2022 international update. Biomedicines. 2023; 11(2): 291. doi: 10.3390/biomedicines11020291, PMID 36830828.
24. Patel SS, Molnar MZ, Tayek JA, Ix JH, Noori N, Benner D, *et al.* Serum creatinine as a marker of muscle mass in chronic kidney disease: results of a cross-sectional study and review of literature. J Cachexia Sarcopenia Muscle. 2013; 4(1): 19-29. doi: 10.1007/s13539-012-0079-1, PMID 22777757.
25. Hang T, Huang J, He G, Li J, Tao T. Blood urea nitrogen to serum albumin ratio as a new prognostic indicator in critically ill patients with diabetic ketoacidosis: a retrospective cohort study. Exp Clin Endocrinol Diabetes. 2024; 132(5): 249-59. doi: 10.1055/a-2274-0389, PMID 38387890.
26. Al-Qabbaa SM, Qaboli SI, Alshammari TK, Alamin MA, Alrajeh HM, Almuthnabi LA, *et al.* Sitagliptin mitigates diabetic nephropathy in a rat model of streptozotocin-induced type 2 diabetes: possible role of PTP1B/JAK-STAT pathway. Int J Mol Sci. 2023; 24(7): 6532. doi: 10.3390/ijms24076532, PMID 37047505.
27. Darenskaya MA, Kolesnikova LI, Kolesnikov SI. Oxidative stress: pathogenetic role in diabetes mellitus and its complications and therapeutic approaches to correction. Bull Exp Biol Med. 2021; 171(2): 179-89. doi: 10.1007/s10517-021-05191-7, PMID 34173093.
28. Bae CS, Lee Y, Ahn T. Therapeutic treatments for diabetes mellitus-induced liver injury by regulating oxidative stress and inflammation. Appl Microsc. 2023; 53(1): 4. doi: 10.1186/s42649-023-00089-2, PMID 37428327.
29. Dinić S, Arambašić Jovanović J, Uskoković A, Mihailović M, Grdović N, Tolić A, *et al.* Oxidative stress-mediated beta cell death and dysfunction as a target for diabetes management. Front Endocrinol. 2022; 13: 1006376. doi: 10.3389/fendo.2022.1006376, PMID 36246880.
30. Dilworth L, Stennett D, Facey A, Omoruyi F, Mohansingh S, Omoruyi FO. Diabetes and the associated complications: the role of antioxidants in diabetes therapy and care. Biomed Pharmacother. 2024; 181: 117641. doi: 10.1016/j.biopha.2024.117641, PMID 39541789.
31. Arabshomali A, Bazzazzadehgan S, Mahdi F, Shariat-Madar Z. Potential benefits of antioxidant phytochemicals in type 2 diabetes. Molecules. 2023; 28(20): 7209. doi: 10.3390/molecules28207209, PMID 37894687.
32. Jamal Gilani S, Nasser Bin-Jumah M, Al-Abbasi FA, Shahid Nadeem M, Afzal M, Sayyed N, *et al.* Fustin ameliorates hyperglycemia in streptozotocin induced type-2 diabetes via modulating glutathione/superoxide dismutase/catalase expressions, suppress lipid peroxidation and regulates histopathological changes. Saudi J Biol Sci. 2021; 28(12): 6963-71. doi: 10.1016/j.sjbs.2021.07.070, PMID 34866996.

33. Kovoor E, Chauhan SK, Hajrasouliha A. Role of inflammatory cells in pathophysiology and management of diabetic retinopathy. Surv Ophthalmol. 2022; 67(6): 1563-73. doi: 10.1016/j.survophthal.2022.07.008, PMID 35914582.
34. Rohm TV, Meier DT, Olefsky JM, Donath MY. Inflammation in obesity, diabetes, and related disorders. Immunity. 2022; 55(1): 31-55. doi: 10.1016/j.immuni.2021.12.013 , PMID 35021057.
35. Qian J, Huang Y. Expression of TNF-α and IL-1β in peripheral blood of patients with T2DM retinopathy. Comp Math Methods Med. 2022; 2022(1): 9073372. doi: 10.1155/2022/9073372, PMID 35979044.
36. Cano-Cano F, Gómez-Jaramillo L, Ramos-García P, Arroba AI, Aguilar-Diosdado M. IL-1β implications in type 1 diabetes mellitus progression: systematic review and meta-analysis. J Clin Med. 2022; 11(5): 1303. doi: 10.3390/jcm11051303, PMID 35268394.
37. dos Santos Haber JF, Barbalho SM, Sgarbi JA, de Argollo Haber RS, de Labio RW, Laurindo LF, *et al.* The relationship between type 1 diabetes mellitus, TNF-α, and IL-10 gene expression. Biomedicines. 2023; 11(4): 1120. doi: 10.3390/biomedicines11041120, PMID 37189738.
38. Kreiner FF, Kraaijenhof JM, von Herrath M, Hovingh GK, von Scholten BJ. Interleukin 6 in diabetes, chronic kidney disease, and cardiovascular disease: mechanisms and therapeutic perspectives. Expert Rev Clin Immunol. 2022; 18(4): 377-89. doi: 10.1080/1744666X.2022.2045952, PMID 35212585.

Cite this article: Yang J, Yan L, Zhang X, Zhang J. Sophoricoside Alleviates Oxidative Stress and Inflammation in Streptozotocin-Induced Diabetes Mellitus in Rats. Indian J of Pharmaceutical Education and Research. 2026;60(2):729-38.