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Protective Effects of Combination Therapy with *Moringa oleifera* Leaf Extract and Sitagliptin against Streptozotocin-Induced Diabetic Nephropathy in Rats via Inhibition of Oxidative Stress

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Abstract

Diabetic nephropathy, a kidney complication of diabetes, is often associated with oxidative stress. This study was designed to evaluate the protective effects of *Moringa oleifera* leaf extract, alone and in combination with sitagliptin, at a comparatively lower dose against streptozotocin-induced diabetic nephropathy in rats via inhibition of oxidative stress. Thirty (30) Swiss Albino male rats were allocated into five groups. Except for the normal control group, diabetes was induced using a single dose of streptozotocin (STZ, 45 mg/kg, intraperitoneally). Over a 4-week experimental period, the effects of STG (Sitagliptin, 100 mg/70kg BW), MoLE (Moringa oleifera leaves extract, 200 mg/kg BW), and STG + MoLE (integrative therapy of Sitagliptin, 50 mg/70kg BW with ethanolic *M. oleifera* leaves extract, 100 mg/kg BW) were evaluated. The study assessed blood glucose, serum insulin and kidney function markers such as creatinine, urea, uric acid and calcium and protein level (albumin), as well as endogenous enzyme (SOD, CAT). The STG, MoLE, and STG + MoLE (combination therapy) groups showed a significant reduction ($p < 0.05$) in plasma glucose (5.98 ± 0.44, 6.10 ± 0.50 and 5.74 ± 0.53 mmol/L respectively) compared to diabetic control (13.76 ± 0.83 mmol/L) as well as significant increase insulin levels (2.62 ± 0.07, 2.06 ± 0.10 and 2.94 ± 0.12 ng/mL respectively) compared to diabetic control rats (1.18 ± 0.16 ng/mL) after 4 weeks of treatment. Diabetics rats treated with STG, MoLE, and STG + MoLE significantly attenuated the elevation of creatinine (2.02 ± 0.11 vs 0.92 ± 0.04, 0.88 ± 0.03

and 0.7 ± 0.02 mg/dL respectively; diabetics vs STG, MoLE, and STG + MoLE treated group), urea (181.60 ± 2.42, 88.20 ± 1.28, 67.40 ± 1.81 and 59.60 ± 2.32 mg/dL respectively), uric acid (10.34 ± 0.31, 6.3 ± 0.24, 5.52 ± 0.20, and 3.44 ± 0.24 mg/dL respectively), and calcium (3.47 ± 0.18, 2.36 ± 0.16, 2.23 ± 0.05, and 2.07 ± 0.08 mmol/L respectively). Albumin levels decreased in diabetic rats; after treatment, both were restored toward normal. Rats with diabetes had significantly lower levels of the endogenous antioxidant enzymes SOD and CAT. The treatment of STG, MoLE, and STG + MoLE significantly elevated these reduced enzyme levels. The study demonstrated that *Moringa oleifera* leaf extract and its combination with sitagliptin exhibited antidiabetic activity by decreasing blood glucose and increasing insulin levels, and nephroprotective effects by normalizing albumin and renal functional parameters by minimizing oxidative stress by increasing endogenous antioxidant enzyme.

Keywords

Moringa oleifera, Diabetic Nephropathy, Nephroprotective Effects, Streptozotocin, Oxidative Stress

1. Introduction

Diabetes mellitus is an endocrine disease of multiple aetiologies in insulin secretion. A deficiency in insulin results in hyperglycemia with metabolic disturbances of biomolecules [1]. Weight, obesity, and sedentary lifestyle are the emerging global epidemic of diabetes, and this is considered a degenerative disease of the blood glucose system, characterized by pancreatic beta cells' deficiency to produce insulin or sufficient insulin, resulting in chronic hyperglycemia, which is associated with long-term microvascular (retinopathy, nephropathy, and neuropathy) and macrovascular (cardiovascular) complications [2]. Individuals with diabetes have high levels of inflammatory cytokines, activation of leukocytes, and increased tissue fibrosis [3]. Oxidative stress is also a consequence of the imbalance between the oxidative and antioxidant systems that results in the overproduction of reactive oxygen species (ROS), which play a crucial role in the initiation and progression of diabetic nephropathy [4]. Accumulation of ROS leads to oxidative stress, which is associated with increased damage to β-cells and biomolecules [5]. Moreover, because of the relatively low expression of antioxidant enzymes such as catalase (CAT) and superoxide dismutase (SOD) in diabetes, pancreatic β-cells may be vulnerable to ROS attack when the system is under oxidative stress situations [6]. Similarly, elevated levels of free radicals, due to inefficiency of the antioxidant defense system, may lead to disruption of cellular function by enhancing the susceptibility of membranes to lipid peroxidation [7]. Due to this increasing prevalence of diabetes and the complications induced by this, in both developed and developing countries, scientists are facing challenges to further conduct research in sourcing potent therapeutic agents from natural sources for more efficient us-

age in the treatment and management of diabetes as well as the complications arising from diabetes [8]. So, the maximum therapeutic and minimum side effects of herbal remedies have been verified in numerous scientific investigations. Presently, plant materials play major roles in primary health care as therapeutic remedies in many developing countries [9]. This is the reason why plant materials are continuously being scrutinized and investigated for their potential use as hypoglycemic agents.

Plants are well known in traditional medicine for their hypoglycaemic effects and available literature indicates that there are more than 800 plant species showing hypoglycaemic activities *in vivo* [10]. *Moringa oleifera* Lam. (Family: Moringaceae) (*M. oleifera*) is a medium-sized tree, growing in Asia, Africa and tropical areas of the world as a valuable food source. Various parts of *M. oleifera* tree have been studied for several pharmacological actions. Many reports have described its leaves as antifungal, antimicrobial, antiatherosclerotic, antifertility, relieving pain, central nervous system depressant, antiinflammatory, diuretic and regulating hyperthyroidism. Published research showed that *M. oleifera* seeds (MOS) have pharmacological activities such as blood glucose-lowering, anti-inflammatory, and antitumor effects and are also used to treat diabetic nephropathy [11]. Herbs are frequently used in conjunction with conventional medications to minimize adverse effects and boost effectiveness at lower dosages.

Diabetic nephropathy can be treated with a variety of oral antidiabetic medications, such as sitagliptin, which can be used alone or in combination for optimal results. It is still difficult to manage diabetes without experiencing any negative side effects because many of these oral antidiabetic medications have a number of major side effects [12]. Diabetic nephropathy was treated with sitagliptin (ST), a dipeptidyl peptidase-4 (DPP-4) inhibitor [13] [14]. However, the increasing resistance to these medications and their many adverse effects have increased the demand for alternative therapies with fewer or even no side effects for diabetics. In recent years, the use of herbal therapies to treat hyperglycemia and other diabetes-related issues has grown in popularity. A previous study assessed the hepatoprotective, hypolipidemic, and antidiabetic effects of Moringa oleifera leaves. In streptozotocin-induced diabetic rats, the current study aimed to evaluate the nephroprotective effects of extracts from Moringa oleifera leaves both individually and in combination with sitagliptin, albeit at a lower dose.

2. Materials and Methods

2.1. Collection of Leaves and Preparation of Extract

For extraction, the maceration technique was used with some modifications [15]. Fresh mature *Moringa oleifera* leaves were picked from the surrounding countryside, located at 24.2253˚N, 89.6687˚E in Bangladesh. Fresh leaves were collected, rinsed with tap water, and then distilled. For three days, the clean leaves were left to dry in the shade of the sun. An electronic grinder was used to crush the dried *Moringa oleifera* leaves. The fine powder was soaked at a 5:1 ratio in sealed glass

bottles (amber) with 95% ethanol [16]. It was subsequently left to stand at 25˚C - 30˚C for 10 - 12 days while being frequently shaken manually. After quickly passing through cotton, the extract was passed through filter papers (Whatman grade-1). The extract was then allowed to air dry at RT. The crude leaf extract was kept at 4˚C in a glass container that was tightly sealed.

2.2. Chemicals, Reagents and Drugs

For extraction, 95% ethanol from Merck KGaA, Darmstadt, Germany, was used. The active pharmaceutical ingredient Sitagliptin was generously provided by Square Pharmaceuticals PLC, Pabna, Bangladesh. Streptozotocin has been acquired from Sisco Research Laboratories Pvt. Ltd, Mumbai, India. All chemicals and reagents utilized were of analytical grade.

2.3. Experimental Animal

Thirty (30) Swiss Albino male rats, weighing 120.5 g (ranging from 110 g to 150 g) and aged 1.5 months, were procured from a commercial laboratory rat supplier in the Rajshahi district of Bangladesh. The rats were maintained in clear polypropylene cages under a 12-hour light/dark cycle at 24˚C - 26˚C and provided with a regular mouse chow and sterile tap water *ad libitum* during the study. Rats were utilized for experimentation following a ten-day acclimatization period. The Khwaja Yunus Ali University ethics committee in Bangladesh examined and authorized the animal experiment, with the ethical clearance certificate number KYAU/DEAN/EGC/2024/014. Experiments followed EU guidelines (Directive 2010/63/EU) for pharmacological analysis and experimental design, as well as the WMA statement on the use of animals in biomedical research [17].

2.4. Dose Selection

Dose selection study was performed previously and described clearly in other research work [17].

2.5. Experimental Design

A total of thirty (30) Swiss Albino male rats were utilized in the experiment and separated into five groups by simple randomization. Diabetes was produced in rats, excluding the normal control group, using a jab of streptozotocin (STZ, 45 mg/kg, I.P.), made in 0.1 M citrate buffer at pH 4.5 [17] [18]. The therapy duration was four weeks. At the conclusion of the testing session, rats were anaesthetized and euthanized.

Group Name	Treatment Features
NC	Nondiabetic rats received a balanced diet and tap water *ad libitum*.
DC	Diabetic rats received a balanced diet and tap water *ad libitum*.
STG	Diabetic rats received Sitagliptin (100 mg/70kg BW) orally.
MoLE	Diabetic rats received *M. oleifera* extract (200 mg/kg BW) orally.
STG + MoLE	Diabetic rats were received Sitagliptin (50 mg/70kg BW) + *M. oleifera* extract (100 mg/kg BW) orally.

2.6. Blood Collection and Kidney Homogenate Preparation

After the experiment, blood samples were taken straight from the heart, and the whole blood was centrifuged for 10 min at 1066 × g to separate the serum [19]. Immediately after sacrifice, both the kidneys were dissected; rinsed with isotonic saline. A homogenate was prepared with 10% (w/v) phosphate-buffered (0.1 M, pH 7.4) using a homogenizer. Homogenates were centrifuged at 15,000 rpm for 10 min at 4˚C and the supernatant was estimated for kidney antioxidant parameters.

2.7. Monitoring Plasma Glucose and Serum Insulin Level

The blood glucose levels of the rats were monitored prior to and following the experiment. Blood samples were drawn from the tail vein, and a glucometer (VivaChek Biotech (Hangzhou) Co., Ltd., China) was used to measure the glucose level. Serum insulin levels were measured using a commercial enzyme-linked immunosorbent assay kit according to the manufacturer's instruction.

2.8. Estimation of Biomarkers of Oxidative Stress

A portion of the supernatant from the centrifuged kidney homogenate was used to assess endogenous superoxide dismutase (SOD) and enzyme catalase (CAT) activities. Kidney catalase activity was assayed following the method of Kar and Mishra, 1976 [20]. And superoxide dismutase (SOD) activity was assayed according to the method of Marklund and Marklund [6] [21].

2.9. Biochemical Analyses

For determining serum uric acid, urea, creatinine, albumin and calcium, commercial kits (ACCUREX, Biomedical Pvt. Ltd.) were utilized. The biochemical analyses for each component were conducted according to the manufacturer protocols.

2.10. Statistical Analysis

The data were expressed using means ± SEM. For statistical comparisons, p values < 0.05 were deemed significant, and the one-way ANOVA and t-test were employed. For data analysis, GraphPad Prism 9.4.1 (USA) was used.

3. Results

3.1. Glucose and Insulin Level

Figure 1(A), **Figure 1(B)** demonstrate the outcome of *M. oleifera* extracts, sitagliptin, and their combination therapy on the plasma blood glucose (PBG) and insulin in STZ-induced DN rats. STZ-evoked DN rats exhibited a marked elevation in PBG and a concomitant decrease in serum insulin concentration compared to control rats, which confirms the progression of a diabetic state in the STZ-evoked DN rats ($p < 0.05$).

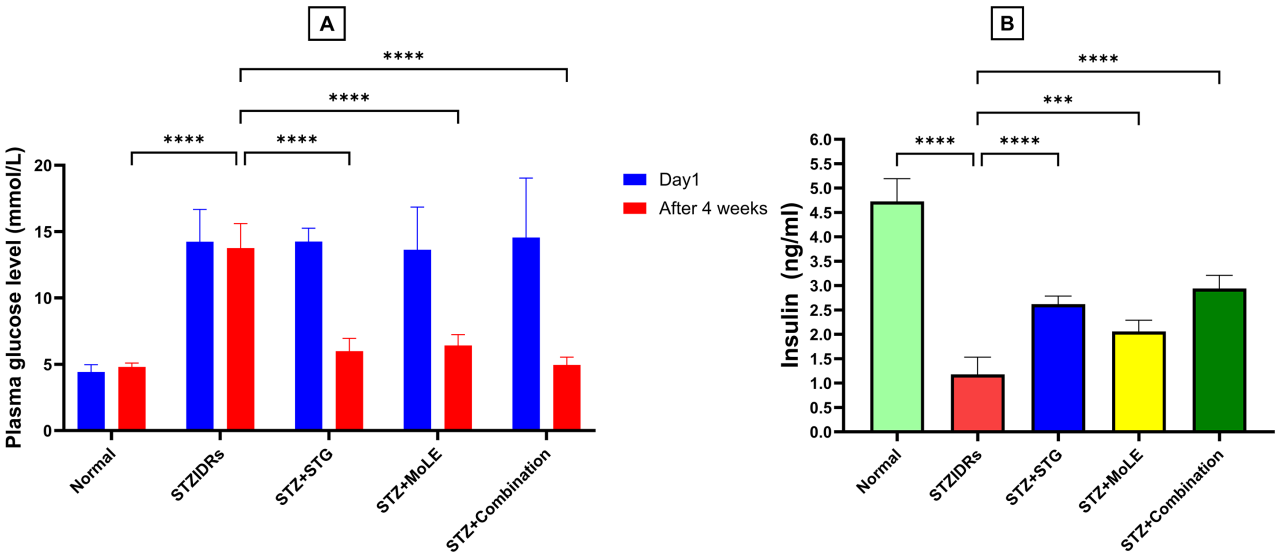
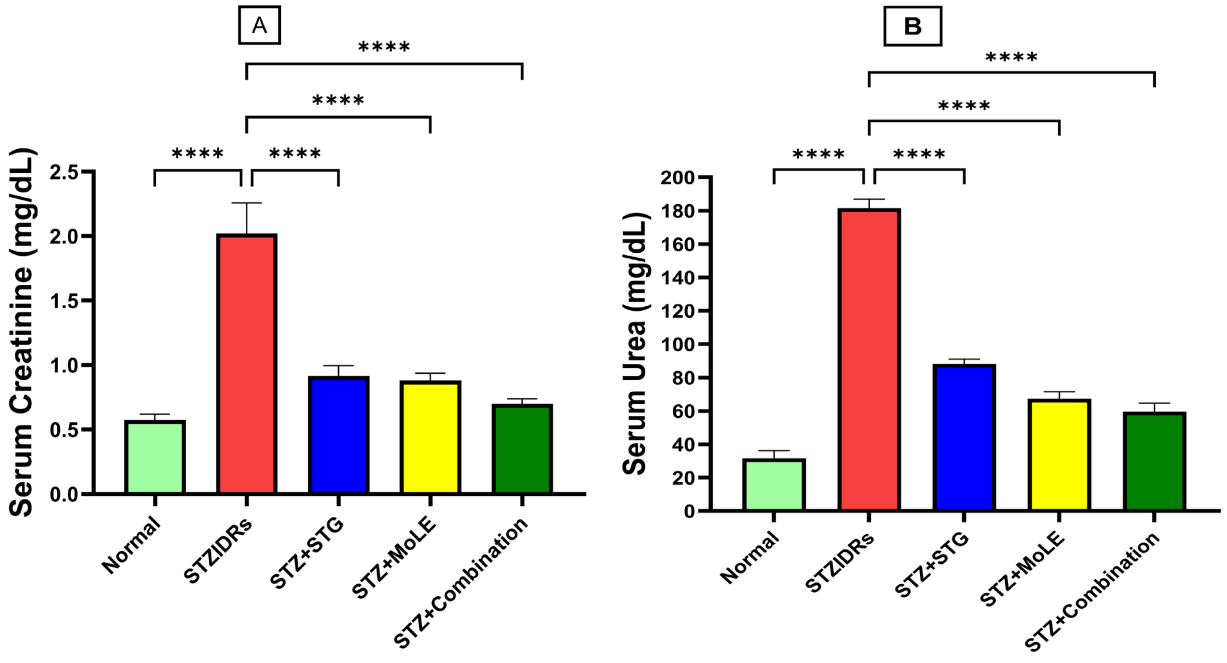


Figure 1. (A) Effect of *M. oleifera* extracts, Sitagliptin, and their combination therapy on plasma glucose. (B) Insulin level of Streptozotocin-Induced Diabetic Nephropathy in Rats.

The administration of *M. oleifera* extracts, sitagliptin, and their combination therapy demonstrated an appreciable reduction in the PBG level and restored the level of insulin. This finding demonstrated the potential effect of M. oleifera extracts, sitagliptin, and their combination therapy against STZ-induced DN rats.

3.2. Effects on Renal Function

Effects of *M. oleifera* extracts, sitagliptin, and their combination therapy on creatinine, **Figure 2(B)**: urea, uric acid, and calcium levels in STZ-induced diabetic rats as shown in **Figures 2(A)-(D)**.



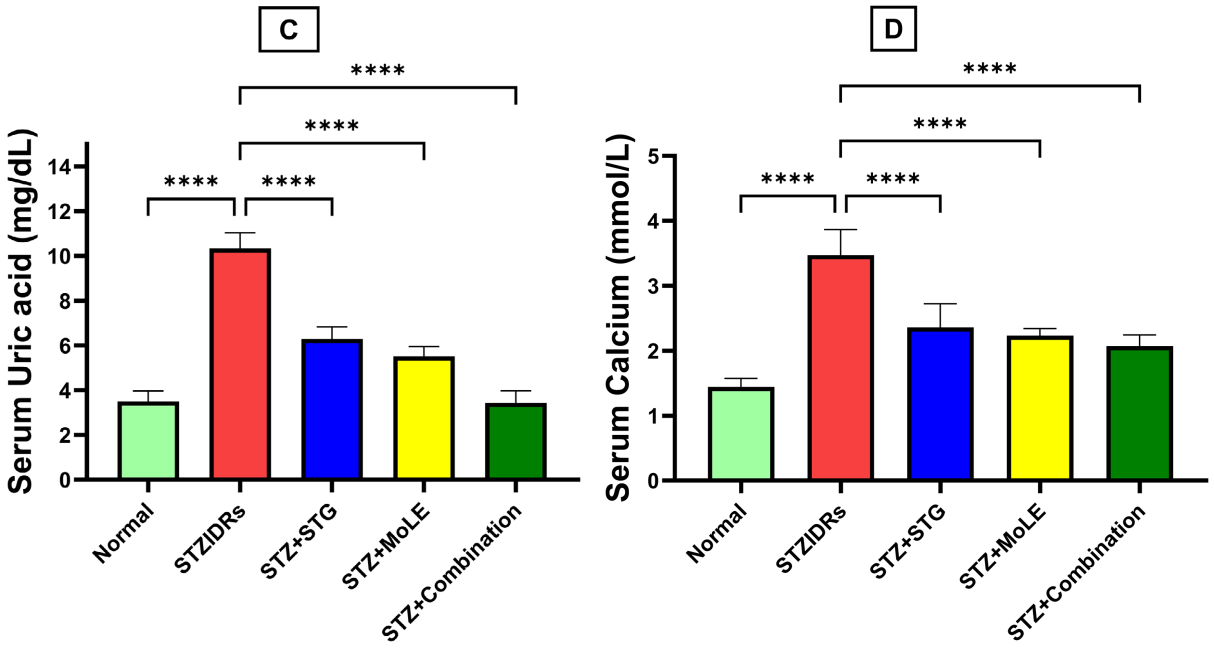


Figure 2. Effects of *M. oleifera* extracts, sitagliptin, and their combination therapy on (A): creatinine, (B): urea, (C): uric acid, and (D): calcium levels in STZ-induced diabetic rats.

The creatinine, urea, uric acid, and calcium levels were relatively higher in STZ-induced diabetic rats than in the control group. *M. oleifera* extracts, sitagliptin, and their combination therapy dramatically reduced the levels of creatinine, urea, uric acid, and calcium compared with those levels in the DM group, indicating that renal function improved after intervention.

The serum albumin levels were relatively lower and kidney-body weight ratio in STZ-induced diabetic rats than in the control group. *M. oleifera* extracts, sitagliptin, and their combination therapy significantly increased the levels of albumin and decreased kidney-body weight ratio compared with those levels in the DM group, as shown in Table 1, also indicating that renal function improved after intervention.

Table 1. Effect of *M. oleifera* extracts, sitagliptin, and their combination therapy on serum albumin and kidney, body weight ratio in control and experimental animals (Values are given as means ± SEM of five rats in each group. Same superscript letter indicating no significant difference).

Group	NC	DC	STG	MoLE	STG + MoLE
Albumin	29.66 ± 1.26	12.66 ± 1.13[a]	21.4 ± 0.88[b]	24.86 ± 1.06[b,c]	26.1 ± 0.79[c]
Kidney-Body Weight Ration	0.69 ± 0.02	1.03 ± 0.05[a]	0.78 ± 0.04[b]	0.80 ± 0.02[b]	0.72 ± 0.02[b]

3.3. Biomarkers of Oxidative Stress and Endogenous Antioxidants

The effect of *M. oleifera* extracts, sitagliptin, and their combination therapy on oxidative enzymes and oxidative stress markers is illustrated in Figure 3. Rats induced with STZ exhibited a marked reduction in SOD and CAT. DN rats treated with *M. oleifera* extracts, sitagliptin, and their combination therapy elevated the

level of SOD and CAT in serum. However, this result indicated that *M. oleifera* extracts, sitagliptin, and their combination therapy administration ameliorate oxidative stress and endogenous antioxidants in the DN rats.

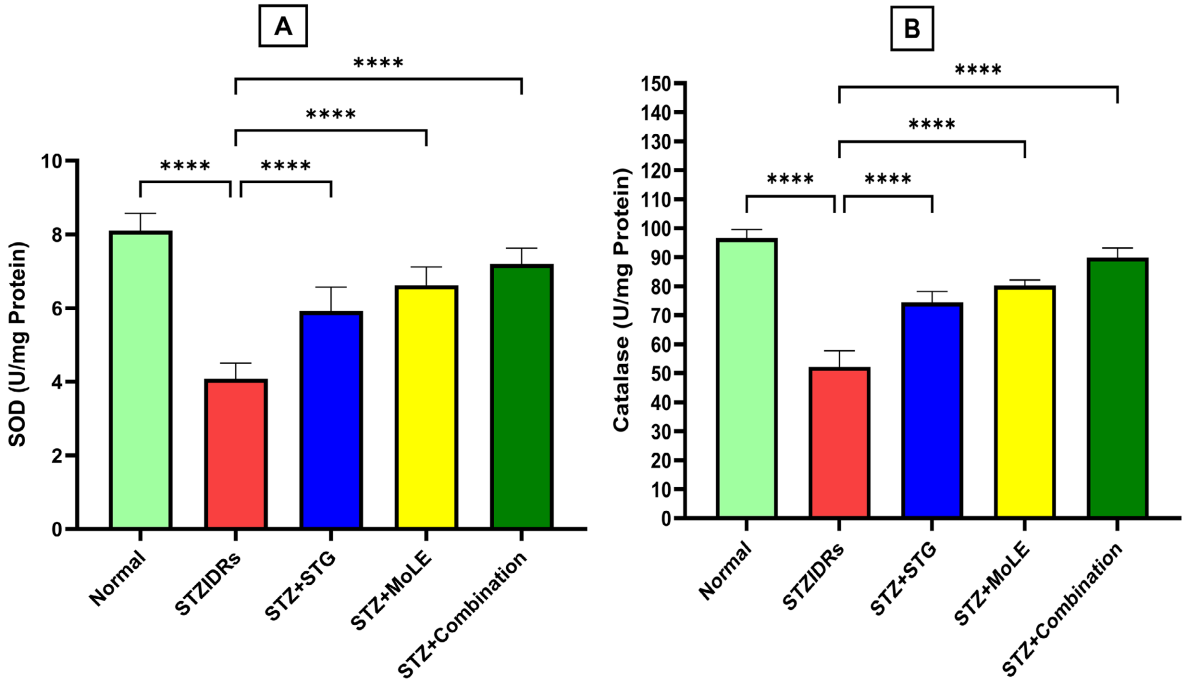


Figure 3. Effect of *M. oleifera* extracts, sitagliptin, and their combination therapy on oxidative stress biomarker. (A) Superoxidase (SOD), (B) Catalase (CAT).

4. Discussion

Diabetic nephropathy, a kidney complication of diabetes, is often associated with oxidative stress. In this investigation, the effect of *M. oleifera* and sitagliptin combination treatment was observed in different parameters related to oxidative stress and renal function measurement of streptozotocin induced diabetic rats. In our investigation, diabetes was produced in rats using streptozotocin (STZ, 45 mg/kg, I.P. injection). Our findings demonstrate that the treatment of STZ-induced diabetic rats with *Moringa oleifera* leaves extract (MoLE) alone and combination therapy with sitagliptin (STG + MoLE) significantly reduced blood glucose levels and insulin compared to untreated diabetic rats as shown in **Figure 1** demonstrating a definite antidiabetic effect.

The increased the levels of creatinine, urea, uric acid, calcium, and kidney-body weight ratio decreased the albumin compared to non-diabetic control rats are major sign of diabetic nephropathy [22]. The results in **Figure 2** and **Table 1** show significant ($p < 0.05$) increase in the level of serum creatinine, urea, uric acid, calcium and decrease in plasma albumin in the diabetic rats when compared with respective control rats, while, after the treatment of STZ diabetic rats with *M. oleifera* extracts (MoLE), sitagliptin (STG), and a combination of sitagliptin (50 mg/70kg BW) and the ethanolic leaves extract of *M. oleifera* (100 mg/kg BW)

(STG + MoLE) the levels of creatinine, urea, uric acid, calcium and kidney-body weight ratio were significantly ($p < 0.05$) decreased and albumin level was increased. These results are in agreement with other previous studies on the *Moringa oleifera* Lam. seed extract [11] and leaves extracts [23] on diabetic nephropathy in streptozotocin-induced diabetic rats.

As illustrated in **Table 1**, a marked ($p < 0.05$) reduction in plasma albumin level was observed in diabetic rats and this is consistent with the results obtained by Annamalai Prakasam *et al*. [24]. The decrease in albumin may be due to albuminuria, which are important clinical markers of diabetic nephropathy, and/or may be due to increased protein catabolism [24]. The results of the present study demonstrated that the treatment of diabetic rats with the *M. oleifera* extracts, sitagliptin, and their combination therapy caused a noticeable elevation in the albumin levels as compared with their normal levels. Such improvement of serum albumin was previously observed after the oral administration of *Moringa oleifera* Lam. seeds on streptozotocin induced diabetes and diabetic nephropathy in male rats [25].

Moringa oleifera (MO) has rich antioxidant content and diverse therapeutic abilities. Previous investigation identified MO with the ability to prevent the occurrence and complications of diabetic-induced kidney injury through its protective effect on the oxidative status and inflammatory cytokines in the kidneys of diabetic rats. Whereas, an experimental study showed that sitagliptin can restore the GLP-1 by restoring the DPP4 protein in the kidney of diabetic rat [26]. Hyperglycemia-induced oxidative stress has been shown to be actively involved in the onset and progression of diabetes, leading to various complications such as cardiovascular diseases, nephropathy, amputation of limbs and blindness [27]. ROS cause lipid peroxidation, and when this happens, the lipids of the cell membrane undergo catabolism, leading to damage of tissues. CAT and SOD like antioxidant enzymes delay ROS induced oxidative stress, where SOD is responsible for the conversion of superoxide free radical to water and CAT eliminates the synthesizing of hydrogen peroxide and hydroxyl radical [28] [29]. There is also evidence that sitagliptin can significantly diminish the increased ROS generation and restore the antioxidant defense by decreasing the oxidative stress in the kidney of diabetic rats [25] [30]. In this study, rats induced with STZ exhibited a marked reduction in SOD and CAT. DN rats treated with *M. oleifera* extracts, sitagliptin, and their combination therapy elevated the level of SOD and CAT in serum significantly. Thus, this result indicated that *M. oleifera* extracts, sitagliptin, and their combination therapy administration ameliorate oxidative stress and endogenous antioxidants in the DN rats.

5. Conclusion

Diabetic nephropathy, a kidney complication of diabetes, is often associated with oxidative stress. The study demonstrated that *Moringa oleifera* leaf extract and its combination with sitagliptin exhibited antidiabetic activity by decreasing blood

glucose and increasing insulin levels, and nephroprotective effects by normalizing albumin and renal functional parameters by minimizing oxidative stress by increasing endogenous antioxidant enzyme. This result suggested protective effects of combination therapy with *Moringa oleifera* leaf extract and sitagliptin at a lower dose against streptozotocin-induced diabetic nephropathy in rats via inhibition of oxidative stress.

Conflicts of Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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References

[1] Omodanisi, E., Aboua, Y. and Oguntibeju, O. (2017) Assessment of the Anti-Hyperglycaemic, Anti-Inflammatory and Antioxidant Activities of the Methanol Extract of *Moringa oleifera* in Diabetes-Induced Nephrotoxic Male Wistar Rats. *Molecules*, **22**, Article 439. https://doi.org/10.3390/molecules22040439

[2] Forbes, J.M. and Cooper, M.E. (2013) Mechanisms of Diabetic Complications. *Physiological Reviews*, **93**, 137-188. https://doi.org/10.1152/physrev.00045.2011

[3] Donath, M.Y. and Shoelson, S.E. (2011) Type 2 Diabetes as an Inflammatory Disease. *Nature Reviews Immunology*, **11**, 98-107. https://doi.org/10.1038/nri2925

[4] Chang, T., Chen, Y., Li, S. and Chen, J. (2021) NRF-2 Mediated Heme Oxygenase-1 Activation Contributes to the Anti-Inflammatory and Renal Protective Effects of *Ginkgo biloba* Extract in Diabetic Nephropathy. *Journal of Ethnopharmacology*, **266**, Article ID: 113474. https://doi.org/10.1016/j.jep.2020.113474

[5] Jaiswal, D., Rai, P.K., Mehta, S., Chatterji, S., Shukla, S., Rai, D.K., *et al.* (2013) Role of *Moringa oleifera* in Regulation of Diabetes-Induced Oxidative Stress. *Asian Pacific Journal of Tropical Medicine*, **6**, 426-432. https://doi.org/10.1016/s1995-7645(13)60068-1

[6] Sohag, M.S.U., Paul, M., Al-Bari, M.A.A., Wahed, M.I.I. and Khan, M.R.I. (2019) Potential Antidiabetic Activities of Probiotic Strains, *L. acidophilus* and *L. bulgaricus* against Fructose-Fed Hyperglycemic Rats. *Food and Nutrition Sciences*, **10**, 1419-1432. https://doi.org/10.4236/fns.2019.1012101

[7] Haidara, M., Yassin, H., Rateb, M., Ammar, H. and Zorkani, M. (2006) Role of Oxidative Stress in Development of Cardiovascular Complications in Diabetes Mellitus. *Current Vascular Pharmacology*, **4**, 215-227. https://doi.org/10.2174/157016106777698469

[8] Gupta, R., Mathur, M., Bajaj, V.K., Katariya, P., Yadav, S., Kamal, R., *et al.* (2012) Evaluation of Antidiabetic and Antioxidant Activity of *Moringa oleifera* in Experi-

mental Diabetes. *Journal of Diabetes*, **4**, 164-171. https://doi.org/10.1111/j.1753-0407.2011.00173.x

[9] Gagliano, N., Grizzi, F. and Annoni, G. (2007) Mechanisms of Aging and Liver Functions. *Digestive Diseases*, **25**, 118-123. https://doi.org/10.1159/000099475

[10] Maton, A. (1997) Human Biology and Health. Prentice Hall.

[11] Wen, Y., Liu, Y., Huang, Q., Liu, R., Liu, J., Zhang, F., *et al.* (2022) *Moringa oleifera* Lam. Seed Extract Protects Kidney Function in Rats with Diabetic Nephropathy by Increasing GSK-3β Activity and Activating the Nrf2/HO-1 Pathway. *Phytomedicine*, **95**, Article ID: 153856. https://doi.org/10.1016/j.phymed.2021.153856

[12] Wild, S., Roglic, G., Green, A., Sicree, R. and King, H. (2004) Global Prevalence of Diabetes: Estimates for the Year 2000 and Projections for 2030. *Diabetes Care*, **27**, 1047-1053. https://doi.org/10.2337/diacare.27.5.1047

[13] Mega, C., Teixeira de Lemos, E., Vala, H., Fernandes, R., Oliveira, J., Mascarenhas-Melo, F., *et al.* (2011) Diabetic Nephropathy Amelioration by a Low-Dose Sitagliptin in an Animal Model of Type 2 Diabetes (Zucker Diabetic Fatty Rat). *Experimental Diabetes Research*, **2011**, Article ID: 162092. https://doi.org/10.1155/2011/162092

[14] Ashraf, A., Akhtar, T., Shabbir, A., Aftab, U. and Shahzad, M. (2023) Sitagliptin Ameliorates Diabetic Nephropathy by Upregulating Renal Nephrin and Podocin Expression through Modulation of Adipokines Levels. *Fundamental & Clinical Pharmacology*, **37**, 549-555. https://doi.org/10.1111/fcp.12864

[15] Sohag, M.S.U., Al-Monsur, M., Rahman, M.M., Amin Sarker, M.A., Dutta, S. and Ahmed, F.R.S. (2024) Antioxidant Activities of Seeds and Sprouts of *Momordica charantia* and Their Antibacterial Efficacies against Pathogenic Bacteria Isolated from Hospitalized Patients. *Journal of King Saud University—Science*, **36**, Article ID: 103580. https://doi.org/10.1016/j.jksus.2024.103580

[16] Sohag, M.S.U., Bari, Q.I., Sultana, A., *et al.* (2022) Preliminary Qualitative Analysis, Total Phenolic, Flavonoid Contents, and Antioxidant Activities of Ethanolic Extract of Young and Mature Stems of *Piper chaba* Hunter: A Comparative Study. *Khwaja Yunus Ali University Journal*, 5, 52-57. https://journal.kyau.edu.bd/articlesDetail/109

[17] Shahria, N., Saifullah, M.K., Talukder, M.S., Sohag, M.S.U., Sohag, S.M., Khatun, M.F., *et al.* (2025) Integrative Therapy with *Moringa oleifera* Leaf Extract and Sitagliptin Potentiates Antidiabetic, Antidyslipidemic, and Hepatoprotective Effects in Streptozotocin-Induced Diabetic Rats. *Pharmacology & Pharmacy*, **16**, 150-163. https://doi.org/10.4236/pp.2025.165010

[18] Mestry, S.N., Dhodi, J.B., Kumbhar, S.B. and Juvekar, A.R. (2017) Attenuation of Diabetic Nephropathy in Streptozotocin-Induced Diabetic Rats by *Punica granatum* Linn. Leaves Extract. *Journal of Traditional and Complementary Medicine*, **7**, 273-280. https://doi.org/10.1016/j.jtcme.2016.06.008

[19] Boniamin, M., Sohag, M.S.U., Ahmad, M.S., Hasan, M.R., Sumi, S.Y., Bari, Q.I., *et al.* (2024) Protective Effects of Nutrients and Antioxidant-Rich Seed Oil and Sprouted Seed Oil of *Benincasa hispida* against Formaldehyde-Induced Hepatic and Renal Damage. *Pharmacological Research—Modern Chinese Medicine*, **13**, Article ID: 100555. https://doi.org/10.1016/j.prmcm.2024.100555

[20] Kar, M. and Mishra, D. (1976) Catalase, Peroxidase, and Polyphenoloxidase Activities during Rice Leaf Senescence. *Plant Physiology*, **57**, 315-319. https://doi.org/10.1104/pp.57.2.315

[21] Marklund, S. and Marklund, G. (1974) Involvement of the Superoxide Anion Radical in the Autoxidation of Pyrogallol and a Convenient Assay for Superoxide Dismutase.

European Journal of Biochemistry, **47**, 469-474. https://doi.org/10.1111/j.1432-1033.1974.tb03714.x

[22] Laaroussi, H., Bakour, M., Ousaaid, D., Aboulghazi, A., Ferreira-Santos, P., Genisheva, Z., *et al.* (2020) Effect of Antioxidant-Rich Propolis and Bee Pollen Extracts against D-Glucose Induced Type 2 Diabetes in Rats. *Food Research International*, **138**, Article ID: 109802. https://doi.org/10.1016/j.foodres.2020.109802

[23] Thongrung, R., Pannangpetch, P., Senggunprai, L., Sangkhamanon, S., Boonloh, K. and Tangsucharit, P. (2023) *Moringa oleifera* Leaf Extract Ameliorates Early Stages of Diabetic Nephropathy in Streptozotocin-Induced Diabetic Rats. *Journal of Applied Pharmaceutical Science*, **13**, 158-166. https://doi.org/10.7324/japs.2023.89429

[24] Prakasam, A., Sethupathy, S. and Pugalendi, K.V. (2004) Influence of *Casearia esculenta* Root Extract on Protein Metabolism and Marker Enzymes in Streptozotocin-induced Diabetic Rats. *Polish Journal of Pharmacology*, **56**, 587-593.

[25] Al-Malki, A.L. and El Rabey, H.A. (2015) The Antidiabetic Effect of Low Doses of *Moringa oleifera* Lam. Seeds on Streptozotocin Induced Diabetes and Diabetic Nephropathy in Male Rats. *BioMed Research International*, **2015**, Article ID: 381040. https://doi.org/10.1155/2015/381040

[26] Marques, C., Gonçalves, A., Pereira, P.M.R., Almeida, D., Martins, B., Fontes-Ribeiro, C., *et al.* (2019) The Dipeptidyl Peptidase 4 Inhibitor Sitagliptin Improves Oxidative Stress and Ameliorates Glomerular Lesions in a Rat Model of Type 1 Diabetes. *Life Sciences*, **234**, Article ID: 116738. https://doi.org/10.1016/j.lfs.2019.116738

[27] Mbikay, M. (2012) Therapeutic Potential of *Moringa oleifera* Leaves in Chronic Hyperglycemia and Dyslipidemia: A Review. *Frontiers in Pharmacology*, **3**, Article 24. https://doi.org/10.3389/fphar.2012.00024

[28] McCune, L.M. and Johns, T. (2002) Antioxidant Activity in Medicinal Plants Associated with the Symptoms of Diabetes Mellitus Used by the Indigenous Peoples of the North American Boreal Forest. *Journal of Ethnopharmacology*, **82**, 197-205. https://doi.org/10.1016/s0378-8741(02)00180-0

[29] Anjaneyulu, M. and Chopra, K. (2004) Quercetin, an Anti-Oxidant Bioflavonoid, Attenuates Diabetic Nephropathy in Rats. *Clinical and Experimental Pharmacology and Physiology*, **31**, 244-248. https://doi.org/10.1111/j.1440-1681.2004.03982.x

[30] Civantos, E., Bosch, E., Ramírez Bustillo, E., Zhenyukh, O., Egido, J., Lorenzo, O., *et al.* (2017) Sitagliptin Ameliorates Oxidative Stress in Experimental Diabetic Nephropathy by Diminishing the miR-200a/Keap-1/Nrf2 Antioxidant Pathway. *Diabetes, Metabolic Syndrome and Obesity: Targets and Therapy*, **10**, 207-222. https://doi.org/10.2147/dmso.s132537

Abbreviations

STZ	Streptozotocin
MoLE	*Moringa oleifera* Leaves Extract
STG	Sitagliptin
STG + MoLE	Sitagliptin + *Moringa oleifera* Leaves Extract