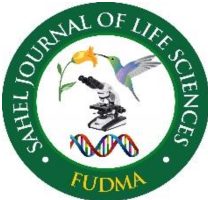

*Sahel Journal of Life Sciences FUDMA (SAJOLS)*
June 2024 Vol. 2(2):141-148
ISSN: 3027-0456 (Print)
ISSN: 1595-5915(Online)
DOI: https://doi.org/10.33003/sajols-2024-0202-19

*Research Article*

# Ameliorative Effect of *Justicia carnea* Methanol Leaf Extract against Nephrotoxicity in Streptozotocin-Induced Diabetic Wistar Rats

**Samuel I. Ojeaburu[1] and *Olusanya Olasehinde[1,2,3]**

**[1]Department of Biochemistry, Faculty of Life Sciences, University of Benin, Benin City, Nigeria**
**Laboratory of Protein and Peptide Pharmaceuticals and Proteomics Laboratory, Institute of Biophysics, Chinese [2]Academy of Sciences, Beijing 100101, China.**
**[3]University of Chinese Academy of Sciences, Beijing 100049, China**
***Corresponding Author's email**: olusanya.olasehinde@uniben.edu.ng/+2348032291658

**ABSTRACT**

This study investigated the antioxidant capabilities of methanol extract from *Justicia carnea* leaves in streptozotocin (STZ)-induced diabetic Wistar rats, emphasizing its nephroprotective potential. Thirty-six (36) Wistar albino rats were randomized into six (6) groups (n=6/group). Group 1 served as the normal control, while groups 2-6 were induced with diabetes using 50 mg/kg of STZ intraperitoneally. Group 2 remained untreated, group 3 received 50 mg/kg body weight of Metformin, and groups 4, 5, and 6 were administered 100, 200, and 500 mg/kg body weight of the methanol *Justicia carnea* extract, respectively. Parameters assessed included fasting blood glucose (FBG), body weight changes, acute toxicity, and oxidative stress markers. Acute toxicity testing indicated no deaths at 5000 mg/kg of the extract. The extract significantly lowered FBG levels in STZ-induced diabetic rats ($p < 0.05$). The control group exhibited the highest weight gain compared to the treated groups ($p < 0.05$). Treatment with the extract notably increased catalase (CAT), superoxide dismutase (SOD), and glutathione peroxidase (GPx) levels, while decreasing malondialdehyde (MDA) concentrations ($p < 0.05$) compared to diabetic controls. Overall, the methanol extract of *Justicia carnea* ameliorated oxidative stress in the kidneys of diabetic Wistar rats, suggesting its potential to mitigate nephrotoxicity associated with type I diabetes-induced kidney damage. These findings underscore its therapeutic promise in combating oxidative stress-related complications of diabetes.

**Keywords:** *Justicia carnea*, Nephrotoxicity, Antioxidants, Streptozotocin, Diabetes, Oxidative stress

**Citation:** Ojeaburu, S. I. and Olasehinde, O. (2024). Ameliorative Effect of *Justicia carnea* Methanol Leaf Extract against Nephrotoxicity in Streptozotocin-Induced Diabetic Wistar Rats. *Sahel Journal of Life Sciences FUDMA*, 2(2): 141-148. DOI: https://doi.org/10.33003/sajols-2024-0202-19

## INTRODUCTION

The therapeutic use of plants for maintaining good health has been extensively documented. Historically, plants and their derivatives have formed the basis of many pharmaceuticals that are employed in treating various ailments (Petrovska, 2012; Ochekwu *et al.*, 2015). It is estimated that about 80% of the world's population relies on plant-based alternative medicines for healthcare (WHO, 2001). Medicinal plants, which contain bioactive compounds that are used for therapeutic purposes or as precursors for vital drugs, become recognized as such when their biological activity is either ethnobotanically reported or scientifically established (Alamgir, 2017).Africa has more than 500 plant species with known medicinal value. Many of these plants are being evaluated for their phytochemical compositions, medicinal and therapeutic properties such as antioxidant, anti-ulcer, anti-cancer, anti-diabetic, anti-hypertensive, hepatoprotective and nephroprotective effects amongst others. The World Health Organization recognizes the importance of conducting scientific research on herbal medicine, as these natural products have the potential to make a significant contribution to healthcare (Ayoka *et al*., 2006).

Type I Diabetes is a common non-communicable metabolic condition characterized by long-term high blood sugar levels and disturbances in the metabolism of carbohydrates, lipids, and proteins. These disturbances are caused by a lack of insulin secretion and/or reduced effectiveness of insulin (WHO, 2001). Hyperglycemia, a characteristic feature of this condition, stimulates the generation of reactive oxygen species (ROS), which harm the membranes of beta cells in the pancreas and other organs (Rendra *et al.*, 2019). The major objective of diabetes treatment is to sustain glucose levels within acceptable parameters to minimize the likelihood of enduring problems (WHO, 2001).

Diabetes can be created in experimental animals by using substances like alloxan or streptozotocin (STZ), which cause the destruction of pancreatic beta cells. This destruction leads to a decrease in the production and release of insulin. Diabetes is largely classified into Type 1 (T1DM) and Type 2 (T2DM). Type 1 diabetes mellitus (T1DM) is characterized by the immune system attacking and destroying the beta cells in the pancreas, resulting in a complete lack of insulin (Davis, 2006). Type 2 diabetes mellitus (T2DM), however, develops gradually as a result of an imbalance between insulin levels and sensitivity, which is commonly worsened by obesity and the aging process. Genetic factors play a crucial role in determining the likelihood of getting diabetes. Certain genetic regions, such as the major histocompatibility complex (MHC) and human leukocyte antigen (HLA) polymorphisms, are associated with an increased susceptibility to type 1 diabetes (T1DM) (Galicia-Garcia *et al*., 2020).

The availability of synthetic drugs used in the treatment of a specific disease is common but because of the high cost and side effects associated with their use (Chattopadhyay and Bandyopadhyay, 2005; Oze *et al.,* 2008), attention is currently being focused on the use of medicinal plant products in the prevention or management of various diseases or ailments.

The genus *Justicia* belongs to the large family of Acanthaceae consisting of about 600 species of herbs and shrubs native to the tropics and subtropics (Durkee, 1986; Corrêa and Alcântara, 2012). *Justicia carnea* is a flowering plant, widely distributed in various parts of Africa. In Nigeria, the shrubs of *J. carnea* are grown around homesteads and act as fences, which are easy to grow and propagate from stem cuttings by pushing the stems 1 to 2 inches into the soil (Mabberley, 1997). The deep purple colored juice from the leaves of this plant is extracted either by soaking or boiling in water, which can be drunk as tea. In some localities in Nigeria, the raw leaves are chewed and used as culinary vegetables to garnish yam porridge. Traditionally, several species of *Justicia* are used in the management of inflammation, gastrointestinal disorders, respiratory tract infection, fever, pain, diabetes, diarrhea, liver diseases, rheumatism and arthritis (Badami *et al.,* 2003; Corrêa and Alcântara, 2012). They also possess anti-inflammatory, anti-allergic, anti- tumoral, anti-viral and analgesic activities (Radhika *et al.,* 2013). Species of Justicia found in India, such as *Justicia traquebareinsis* and *Justicia wynaadensis,* have been reported to possess cardioprotective properties (Radhika *et al*., 2013) and antioxidant activity, respectively (Medapa *et al*., 2011).

The aim of this present study was to evaluate the ameliorative effects of *J. carnea* against nephrotoxicity produced by STZ in Wistar rats.

## MATERIALS AND METHODS

### Plant Sample Preparation

Fresh leaves of *J. carnea* were collected from Oke New Site, Owan West Local Government Area of Edo State and were authenticated by Dr Akinibosun of Plant and Biotechnology Department, University of Benin, Benin City, Nigeria. Fresh leaves of the *J. carnea* plant were thoroughly washed under running tap water. Following this, they were air-dried in a shaded area. The leaves were then crushed into a fine powder using a mechanical grinder. Methanol extraction was employed via a maceration process. Briefly, 1000 g of the powdered sample was soaked in 3000 mL of absolute methanol with constant stirring for 72 hours (3 days). The resulting dark purplish-red filtrate was then filtered using a double cheesecloth. Subsequently, the filtrate was concentrated under reduced pressure using a freeze dryer followed by further concentration in a water bath set at 40°C. This process yielded a dark purple, slurry-like extract termed *J. carnea* methanol extract (JCME). Using the formula below, we calculated the volume of stock to administer based on each animal's body weight:

$$V = \frac{D\,XP}{C}$$

Where: V=volume, D=dose to be administered, P=body weight of animal in kg, C=concentration of the stock

### Experimental Animals

A total of thirty-six (36) male Wistar rats were used in this study. These animals weighed between 150 and 200 g and were obtained from the animal house of the Department of Biochemistry at the University of Benin, Benin City, Edo State, Nigeria. The animals were randomly assigned to cages and allowed to

acclimatize for 2 weeks in a well-ventilated room with natural lighting. Throughout this period, the rats were provided with food daily and their cages were cleaned regularly. Additionally, their food and water containers were washed and rinsed with clean water at every feeding. All experimental procedures involving animal care adhered to the standard protocol outlined in the National Institutes of Health's "Guide for the Care and Use of Laboratory Animals" manual.

**Toxicity Study**

An oral acute toxicity study was conducted on the JCME using the Lorke method. A total of twelve (12) albino rats were used in this two-phase study. In phase I, the rats were randomized into 3 groups of 3 animals each. Each group received a designated oral gavage dose of JCME (10, 100, or 1000 mg/kg body weight). The animals were initially observed for signs of toxicity 60 minutes after administration and were continuously monitored for 24 hours. The absence of mortality in phase I necessitated a second phase. In phase II, three rats were allocated to separate groups, with each group receiving a single, high-dose oral gavage of JCME (1500, 2900, or 5000 mg/kg body weight). These animals were observed for signs of toxicity within 24 hours, with extended monitoring for an additional 48 hours to assess for delayed mortality.

**Experimental Design**

Six (6) rats were randomly selected and assigned to separate cages labelled Group I to 6. Each animal was weighed individually, and the weights were recorded. Subsequently, all rats received an intraperitoneal injection of 50 mg/kg body weight of STZ dissolved in ice-cold normal saline. After 48 hours, blood glucose levels were measured again and documented as post-induction blood glucose levels. Animals exhibiting blood glucose levels exceeding 200 mg/dL were classified as diabetic. The following groups were established:

- Group 1: Normal control group (non-diabetic rats)
- Group 2: Diabetic rats untreated
- Group 3: Diabetic rats treated with standard anti-diabetic drug (metformin)
- Group 4: Diabetic rats + 100 mg/kg bwt of J. carnea methanol extract
- Group 5: Diabetic rats + 200 mg/kg bwt of J. carnea methanol extract
- Group 6: Diabetic rats + 500 mg/kg bwt of J. carnea methanol extract

**Body Weight Determination**

The body weights of the rats were monitored throughout the experiment. This included pre-induction weight measurements, weight measurements following diabetes induction, and weekly weight measurements throughout the treatment period. An electronic weighing balance was used for all weight measurements.

**Administration**

The *J. carnea* methanol extract and methformin were administered orally via gavage for 21 consecutive days.

**Animal Sacrifice and Tissue Collection**

Following 21 days of treatment, rats were fasted overnight and euthanized the following morning. Anesthesia was achieved by exposing the animals to a chamber saturated with chloroform vapors. To minimize pain and distress, euthanasia was performed according to established protocols for rodent Carbon Dioxide inhalation. Upon euthanasia, a laparotomy was performed to gain access to the abdominal cavity. Blood samples were collected via cardiac puncture using 5 mL syringes containing EDTA for hematological analysis. The kidneys were then carefully excised. Tissues were immediately rinsed in ice-cold saline (0.9% NaCl) to remove excess blood. Following rinsing, the organs were patted dry on pre-weighed Whatman filter paper before measurement of organ weights using a calibrated analytical balance.

**Homogenization**

Kidney tissues were individually homogenized in ice-cold saline (0.9% NaCl) using a mortar and pestle. The homogenate was then transferred to a sterile 5 mL centrifuge tube and labeled accordingly. Subsequently, the homogenate was centrifuged at a specified speed for a defined duration (e.g., 10,000 x g for 10 minutes) at 4°C. The supernatant was collected and preserved for further analysis.

**Determination of Superoxide Dismutase (SOD) activity**

The SOD activity was measured using the method described by Popov & Lewin (Popov & Lewin, 1999). This technique utilized xanthine oxidase as the substrate. The empty and sample tubes were assessed using distilled water as a point of comparison at a wavelength of 560 nm. The results were measured and expressed in units per liter (U/L).

**Formula for SOD Activity calculation:**

$$\text{SOD Activity } (U/L) = \left(\frac{\triangle A_{blank-} \triangle A_{sample}}{\triangle A_{blank}}\right) x\ Dilution\ factor\ x\ 100$$

**Where:**

**Δ Ablank:** Change in absorbance of the blank

**Δ Asample**: Change in absorbance of the sample

**Dilution Factor**: Factor by which the sample was diluted during preparation

**Determination of Catalase (CAT) activity**

The CAT enzyme's activity was evaluated using Aebi's technique, as outlined in Aebi's publication from Aebi (1984). The test quantifies the rate of decomposition of $H_2O_2$ at a specific wavelength of 240 nm. The findings were measured and documented in units per litre (U/L).

**Formula for CAT Activity Calculation:**

$$\text{CAT Activity } (U/L) = \left(\frac{\triangle_A}{\triangle_t}\right) X \left(\frac{V_t}{V_s}\right) X \left(\frac{1}{\varepsilon}\right)$$

**Where:**

ΔA: Change in absorbance at 240 nm

Δt: Change in time (in minutes)

Vt: Total volume of the reaction mixture (in litres)

Vs: Volume of the sample (in litres)

ε: Molar extinction coefficient of $H_2O_2$ (43.6 $M^{-1}$ $cm^{-1}$)

**Determination of Glutathione Peroxidase (GPX) activity (U/mg)**

Glutathione peroxidase activity was measured using the Beutler *et al*. (1963) technique. 200 µl of serum was supplemented with 800 µl of phosphate buffer. The initial absorbance (OD1) at a wavelength of 412 nm was measured. Subsequently, 100 µl of Ellman's reagent was introduced into the identical tube, and the second absorbance (OD2) was documented.

**The Formula for GPX Activity Calculation:**

$$\text{GPX Activity } (U/mg) = \left(\frac{\triangle_{OD}}{\triangle_t}\right) X \left(\frac{V_t}{V_s}\right) X \left(\frac{1}{\varepsilon}\right) X \left(\frac{1}{\text{protein concentration}}\right)$$

**Where:**

- ΔOD: Change in absorbance (OD2−OD1)
- Δt: Change in time (typically in minutes)
- Vt: Total volume of the reaction mixture (in litres)
- Vs: Volume of the sample (in litres)
- ε: Molar extinction coefficient of the chromophore (typically 13,600 $M^{-1}$ $cm^{-1}$ for the DTNB-glutathione conjugate)
- Protein concentration: Concentration of protein in the sample (mg/ml)

**Determination of Malondialdehyde (MDA) level**

The MDA level was evaluated using the approach outlined by Gutteridge (1981). The absorbance measurements were obtained using a UV/VIS spectrophotometer at a specific wavelength of 532 nm.

**Formula for MDA Level Calculation:**

$$\text{MDA level } (nmol/ml) = \left(\frac{Absorbance\ at\ 532\ nm}{\varepsilon}\right) X \left(\frac{V_t}{V_s}\right)$$

**Where:**

Absorbance at 532 nm: Measured absorbance of the MDA-TBA adduct at 532 nm.

ε: Molar extinction coefficient of the MDA-TBA adduct (typically 1.56 \times 10^5 $M^{-1}$ $cm^{-1}$).

Vt: Total volume of the reaction mixture (in ml).

Vs: Volume of the sample (in ml).

**Data Analysis**

Data are presented as mean ± standard error of the mean (SEM). Statistical analysis was performed using a commercially available software package (e.g., GraphPad Prism, IBM SPSS Statistics). Normality of the data was assessed using appropriate tests (e.g., Shapiro-Wilk test). For normally distributed data, one-way analysis of variance (ANOVA) followed by post-hoc tests (e.g., Tukey's multiple comparison test) were used to compare group means. For non-normally distributed data, non-parametric tests (e.g., Kruskal-Wallis test with Dunn's multiple comparison test) were employed. P-values less than 0.05 were considered statistically significant.

## RESULTS

**Acute Toxicity Studies of Methanol Extract of *Justicia carnea* Leaves**

At the highest dose of 5000 mg/kg bwt, methanol extract of *J. carnea* did not produce any mortality in the rats (Table 1).

**Effect of *J. carnea* on Glucose Concentration of Streptozotocin Induced Diabetic Rats**

Graded doses of methanol extract of *J. carnea* leaves significantly reduced the blood glucose concentration of streptozotocin-induced diabetic rats ($p < 0.05$) (Table 2).

**Effect of *J. carnea* on Body Weight of Streptozotocin-Induced Diabetic Rats**

The greatest weight increase was observed in the control group when compared to the other groups ($p <$ 0.05)

**Effect of *J. carnea* Extract on Antioxidant Status in Streptozotocin-Induced Diabetic Rat**

The plant extract significantly increased the activities of CAT, SOD, and GPx, but it reduced the concentration of MDA significantly when compared with the diabetic control group ($p < 0.05$) (Table 4).

**Table 1:** Phase 1 Acute toxicity study

| Dose(mg/kg) | Mortality |
|---|---|
| **10** | 0/3 |
| **100** | 0/3 |
| **1000** | 0/3 |

**Table 2:** Phase 2 Acute toxicity study

| Dose(mg/kg) | Mortality |
|---|---|
| **1600** | 0/3 |
| **2900** | 0/3 |
| **5000** | 0/3 |

**Table 3:** Blood Glucose (mg/dl) Concentration of Diabetic Rats

| Group | Week | | | | |
|---|---|---|---|---|---|
| | **Initial** | **1** | **2** | **3** | **4** |
| **1** | 76.00±4.15[a] | _ | 103.67±2.53[a] | 92.33±2.37[a] | 65.5±3.42[a] |
| **2** | 94.67±14.45[a] | 305.00±27.40[a] | 475.00±41.02[b] | 368.00±54.08[b] | 369.33±28.01[b] |
| **3** | 62.20±3.88[a] | 310.80±56.81[a] | 286.40±55.00[c] | 204.60±51.17[c] | 168.00±76.00[c] |
| **4** | 58.80±4.11[a] | 283.20±50.71[a] | 223.00±58.15[c] | 222.00±59.05[c] | 171.20±67.12[c] |
| **5** | 56.80±1.65[a] | 370.20±49.42[a] | 321.75±53.10[c] | 295±112.155[d] | 222.33±62.22[c] |
| **6** | 59.17±6.32[a] | 297.67±43.31[a] | 240.20±70.83[c] | 190.00±55.08[c] | 53.00±12[a] |

Values are expressed as Mean ± SEM. Values with different superscripts in a column are significant at $p < 0.05$.

**Table 4:** Weight of Rats in the Different Groups

| Groups | Initial Body Weight (g) | Final Body Weight (g) | Change in Body Weight (g) |
|---|---|---|---|
| **Control** | 109.53±3.13 | 192.80±14.34 | 83.28±14.49 |
| **Diabetic Control** | 133.75±14.41 | 212.11±17.24 | 78.36±9.15 |
| **Metformin** | 118.33±5.23 | 178.58±11.19 | 66.20±9.74 |
| **100 mg of Extract** | 118.362±12.64 | 176.67±18.24 | 58.31±9.52 |
| **200 mg of Extract** | 112.04±4.43 | 153.99±5.54 | 41.95±1.45 |
| **500 mg of Extract** | 125.81±6.59 | 211.08±15.88 | 85.27±9.29 |

Values are expressed as Mean ± SEM. Values with different superscript in a column are significant at $p < 0.05$

**Table 5:** *In Vivo* Antioxidants Analysis *J. carnea* extract in Streptozotocin-Induced Diabetic Rat

| Activity | Group | | | | | |
|---|---|---|---|---|---|---|
| | **Control** | **Diabetic Control** | **Metformin** | **100 mg (Extract)** | **200 mg (Extract)** | **500 mg (Extract)** |
| **SOD (unit/mg protein)** | 0.98±0.10 | 1.11±0.00 | 1.27±0.00 | 1.14±0.08 | 1.65±0.00* | 2.66±0.00 * |
| **Catalase (unit/mg protein)** | 0.37±0.067 | 0.07±0.00 | 0.47±0.06 | 0.49±0.06 | 0.82±0.00* | 0.95±0.00* |
| **GPx (U/L)** | 2.59±0.35 | 1.77±0.00 | 3.32±0.60 | 3.32±0.41 | 5.71±0.00 * | 6.54±0.00 * |
| **MDA (unit/mg protein)** | 1.50±0.15 | 1.33±0.00 | 1.66±0.42 | 1.86±0.14 | 1.24±0.00 | 4.18±0.00* |

Values are expressed as Mean ± SEM. Values with superscripts show significant differences from the control

## DISCUSSION

Diabetes mellitus, a non-communicable metabolic disorder, is characterized by hyperglycemia and altered metabolism of carbohydrates, fats, and proteins. This condition is often linked to deficiencies in insulin secretion and/or action (Galicia-Garcia *et al*., 2020). One significant consequence of diabetes is the damage to cell membranes, which increases the production of reactive oxygen species (ROS). These ROS play a pivotal role in the pathogenesis of diabetes mellitus. Despite numerous clinical trials aimed at achieving permanent remission, the complexity of diabetes continues to challenge clinicians, researchers, and patients alike. Current efforts focus on enhancing access to advanced diabetes care technologies and affordable insulin analogues (Aloke *et al*., 2022). Streptozotocin (STZ), a glucosamine-nitrosourea compound derived from Streptomyces

achromogenes, is commonly employed to induce diabetes in experimental models. Streptozotocin selectively destroys pancreatic beta cells, leading to decreased insulin production and subsequent hyperglycemia (Zhu, 2022). Aerobic organisms possess antioxidant defense mechanisms to counteract ROS generated from metabolic processes and external sources. These ROS include hydroxyl radicals (•OH), superoxide anions ($O^{2•-}$), and hydrogen peroxide ($H_2O_2$ (Juan *et al*., 2021). Enzymatic antioxidants such as superoxide dismutase (SOD), glutathione peroxidase (GPx), and catalase, along with non-enzymatic antioxidants like vitamins C and E, glutathione (GSH), β-carotene, and vitamin A, maintain a balance crucial for cellular health (Abu & Onoagbe, 2019; Jomova *et al*., 2024). Superoxide dismutase (SOD) converts superoxide anions to hydrogen peroxide, which is subsequently neutralized by catalase and GPx. Catalase plays a vital role in protecting cells from hydrogen peroxide-induced damage, contributing to cellular tolerance against oxidative stress (Anwar *et al*., 2024). Malondialdehyde (MDA), a marker of lipid peroxidation, indicates oxidative damage to cell membranes (Całyniuk *et al*., 2016). Diabetic kidney disease (DKD) is frequently associated with uncontrolled diabetes mellitus. Oxidative stress is a major factor in the occurrence and progression of DKD. An important key to preventing and managing diabetic kidney disease is defending against oxidative stress and restoring antioxidant defense. Oxidation-antioxidant system imbalance can lead to tissue damage (Ceriello *et.al.,* 1996). Studies have shown that restoring the balance between oxidative stress and antioxidant defenses may be a potential drug target for diabetic kidney disease prevention and treatment (Østergaard *et al*., 2020). An antidiabetic activity has been observed in Kuning ethyl acetate extract by scavenging the DPPH free radical and superoxide anion (Tian *et al.,* [86]. The extracts of Diospyros lotus seeds have anti-lipid peroxidation and hydrogen peroxide free radical scavenging effects and are protective against renal injury Elsaed and Mohamed,2017 [88]. By reducing ROS and oxidative damage to the kidneys, vitamin C maintains kidney function Tian *et.al.,* 2012). Continuous selenium therapy for 12 weeks has reportedly been shown to drastically lower insulin levels in DKD patients (Giannini *et al*., 2007). Resveratrol is a natural antioxidant. Experimental studies have shown that oral resveratrol can improve the level of creatinine clearance and inflammatory markers, and significantly increase SOD, CAT, GSH-Px, and glutathione S transferase (GST) in diabetic patients and diabetic mouse models (Haghighat *et al.,* 2014). Oxidation-antioxidant system imbalance can lead to tissue damage (Ceriello *et.al.,* 1996). Studies have shown that restoring the balance between oxidative stress and antioxidant defenses may be a potential drug target for DKD prevention and treatment [84An antidiabetic activity has been observed in Kuning ethyl acetate extract by scavenging the DPPH free radical and superoxide anion (Tian *et.al.,*2012) [86]. The extracts of Diospyros lotus seeds have anti-lipid peroxidation and hydrogen peroxide free radical scavenging effects and are protective against renal injury (Elsaed and Mohamed,2017 [88]. By reducing ROS and oxidative damage to the kidneys, vitamin C maintains kidney function (Elsaed and Mohamed, 2017). Resveratrol is a natural antioxidant. Experimental studies have shown that oral resveratrol can improve the level of creatinine clearance and inflammatory markers, and significantly increase SOD, CAT, GSH-Px, and glutathione S transferase (GST) in diabetic patients and diabetic mouse models (Yang *et al* 2015) . According to the study, fat-soluble vitamins improve renal injury, inflammation, and overall survival in patients with DKD. This study confirmed that STZ-induced diabetes exacerbates oxidative stress in renal tissues, consistent with previous findings in diabetic rat models (Xu *et al*., 2016). The oxidative imbalance, characterized by increased ROS production and decreased antioxidant defense, underscores the pathological impact of diabetes on renal tissues. Our findings demonstrate significant oxidative responses in Wistar rats exposed to STZ, evidenced by elevated blood glucose levels and enhanced oxidative stress markers characterized by significantly increased activities of CAT, SOD, and GPx in the diabetic-treated groups as well as significantly decreased concentrations of MDA in the treated groups compared with the diabetic control groups.

**CONCLUSION**

This study demonstrated that the methanol extract of *J. carnea* effectively ameliorates oxidative stress induced by STZ in the kidneys of diabetic Wistar rats. The antioxidant properties of the extract play a crucial role in mitigating the oxidative damage associated with diabetes mellitus, suggesting its potential as a therapeutic agent in managing diabetic complications. Further studies are required to elucidate the underlying mechanisms and explore the clinical applications of *J. carnea* in diabetes management.

**Conflict of Interest**

The authors declare that they have no conflict of interest related to the publication of this paper.

**Authors' Declaration**

The authors declare that the work presented in this article is original and that they will bear any liability for claims relating to the content of this article.

**REFERENCES**


Abu, O. D., & Onoagbe, I. O. (2019). Biochemical effect of aqueous extract of Dialium Guineense stem bark on oxidative status of normal Wistar rats. *International Journal of Clinical Biology and Biochemistry*, *1*(2), 15-18.

Ebi, H. (1984). Catalase in vitro. *Methods Enzymol*, *105*, 121-126. https://doi.org/10.1016/s0076-6879(84)05016-3

Akbar, S. (2020). Handbook of 200 medicinal plants: a comprehensive review of their traditional medical uses and scientific justifications.

Alamgir, A. (2017). *Therapeutic use of medicinal plants and their extracts: volume 1*. Springer.

Aloke, C., Egwu, C. O., Aja, P. M., Obasi, N. A., Chukwu, J., Akumadu, B. O., Ogbu, P. N., & Achilonu, I. (2022). Current Advances in the Management of Diabetes Mellitus. *Biomedicines*, *10*(10). https://doi.org/10.3390/biomedicines10102436

Anwar, S., Alrumaihi, F., Sarwar, T., Babiker, A. Y., Khan, A. A., Prabhu, S. V., & Rahmani, A. H. (2024). Exploring Therapeutic Potential of Catalase: Strategies in Disease Prevention and Management. *Biomolecules*, *14*(6), 697.

Ayoka, A. O., Akomolafe, R. O., Iwalewa, E. O., Akanmu, M. A., & Ukponmwan, O. E. (2006). Sedative, antiepileptic and antipsychotic effects of Spondias mombin L. (Anacardiaceae) in mice and rats. *J Ethnopharmacol*, *103*(2), 166-175. https://doi.org/10.1016/j.jep.2005.07.019

Beutler, E., Duron, O., & Kelly, B. M. (1963). Improved method for the determination of blood glutathione. *J Lab Clin Med*, *61*, 882-888.

Całyniuk, B., Grochowska-Niedworok, E., Walkiewicz, K. W., Kawecka, S., Popiołek, E., & Fatyga, E. (2016). Malondialdehyde (MDA)–product of lipid peroxidation as marker of homeostasis disorders and aging. Annales Academiae Medicae Silesiensis,

Ceriello A, dello Russo P, Amstad P, and Cerutti P. 1996. High glucose induces antioxidant enzymes in human endothelial cells in culture. Evidence linking hyperglycemia and oxidative stress. Diabetes. 45:471–477. doi: 10.2337/diab.45.4.471.

Davis, S. N. (2006). Insulin, oral hypoglycemic agents and the pharmacology of the endocrine pancreas. *Goodman and Gilmans the Pharmacological Basis of Therapeutics. Brunton, LL (Ed.). McGraw-Hill, New York*, 1613-1645.

Elsaed, W.M, and Mohamed, H.A.2017. Dietary zinc modifies diabetic-induced renal pathology in rats. Ren Fail. 2017;39:246–257. doi: 10.1080/0886022X.2016.1256321

Galicia-Garcia, U., Benito-Vicente, A., Jebari, S., Larrea-Sebal, A., Siddiqi, H., Uribe, K. B., Ostolaza, H., & Martín, C. (2020). Pathophysiology of Type 2 Diabetes Mellitus. *Int J Mol Sci*, *21*(17). https://doi.org/10.3390/ijms21176275

Giannini, C., Lombardo, F., Currò, F., Pomilio, M., Bucciarelli. T., Chiarelli, F., and Mohn, A.2007. Effects of high-dose vitamin E supplementation on oxidative stress and microalbuminuria in young adult patients with childhood onset type 1 diabetes mellitus. Diabetes Metab Res Rev. 23:539–546. doi: 10.1002/dmrr.717.

Gutteridge, J. M. (1981). Thiobarbituric acid-reactivity following iron-dependent free-radical damage to amino acids and carbohydrates. *FEBS Lett*, *128*(2), 343-346. https://doi.org/10.1016/0014-5793(81)80113-5

. Haghighat, N, Vafa, M, Eghtesadi, S, Heidari, I, Hosseini, A,and Rostami, A. 2014. The effects of tocotrienols added to canola oil on microalbuminuria, inflammation, and nitrosative stress in patients with type 2 diabetes: a randomized, double-blind, placebo-controlled trial. Int J Prev Med. 5:617–623.

Jomova, K., Alomar, S. Y., Alwasel, S. H., Nepovimova, E., Kuca, K., & Valko, M. (2024). Several lines of antioxidant defense against oxidative stress: antioxidant enzymes, nanomaterials with multiple enzyme-mimicking activities, and low-molecular-weight antioxidants. *Archives of Toxicology*, *98*(5), 1323-1367. https://doi.org/10.1007/s00204-024-03696-4

Juan, C. A., Pérez de la Lastra, J. M., Plou, F. J., & Pérez-Lebeña, E. (2021). The Chemistry of Reactive Oxygen Species (ROS) Revisited: Outlining Their Role in Biological Macromolecules (DNA, Lipids and Proteins) and Induced Pathologies. *Int J Mol Sci*, *22*(9). https://doi.org/10.3390/ijms22094642

Ochekwu, E. B., Ekeke, C., Nwadiaro, P. O., & Christopher, S. (2015). Phytochemical evaluation of leaves of some medicinal plants from parts of Niger Delta.

Organization, W. H. (2001). *Legal status of traditional medicine and complementary*. World Health Organization.

. Østergaard, J.A., Cooper, M.E. and Jandeleit-Dahm K.A.M.2020. Targeting oxidative stress and anti-oxidant defence in diabetic kidney disease. J Nephrol. 33:917–929. doi: 10.1007/s40620-020-00749-6

Petrovska, B. B. (2012). Historical review of medicinal plants' usage. *Pharmacogn Rev*, *6*(11), 1-5. https://doi.org/10.4103/0973-7847.95849

Popov, I., & Lewin, G. (1999). Photochemiluminescent detection of antiradical activity. VI. Antioxidant characteristics of human blood plasma, low density lipoprotein, serum albumin and amino acids during in vitro oxidation. *Luminescence*, *14*(3), 169-174. https://doi.org/10.1002/(SICI)1522-7243(199905/06)14:3<169::AID-BIO539>3.0.CO;2-K

Rendra, E., Riabov, V., Mossel, D. M., Sevastyanova, T., Harmsen, M. C., & Kzhyshkowska, J. (2019). Reactive oxygen species (ROS) in macrophage activation and function in diabetes. *Immunobiology*, *224*(2), 242-253.

Taylor, J., Rabe, T., McGaw, L., Jäger, A., & Van Staden, J. (2001). Towards the scientific validation of traditional medicinal plants. *Plant growth regulation*, *34*, 23-37.

Tian, S., Tang, J., Liu, H., Wang, L., Shen. J, Li, J.and Gan, Y. 2012.Propyl gallate plays a nephroprotective role in early stage of diabetic nephropathy associated with suppression of glomerular endothelial cell proliferation and angiogenesis. Exp Diabetes Res. 2012:1–8. doi: 10.1155/2012/209567.

Xu, L., Shen, P., Bi, Y., Chen, J., Xiao, Z., Zhang, X., & Wang, Z. (2016). Danshen injection ameliorates STZ-induced diabetic nephropathy in association with suppression of oxidative stress, pro-inflammatory factors and fibrosis. *International Immunopharmacology*, *38*, 385-394.

Yang, H., Xu, W., Zhou, Z., Liu, J., Li, X, Chen, L., Weng, J. and Yu, Z.2015. Curcumin attenuates urinary excretion of albumin in type ii diabetic patients with enhancing nuclear factor erythroid-derived 2-like 2 (Nrf2) system and repressing inflammatory signaling efficacies. Exp Clin Endocrinol Diabetes. 2015;123:360–367. doi: 10.1055/s-0035-1545345

Zhu, B. T. (2022). Pathogenic Mechanism of Autoimmune Diabetes Mellitus in Humans: Potential Role of Streptozotocin-Induced Selective Autoimmunity against Human Islet β-Cells. *Cells*, *11*(3). https://doi.org/10.3390/cells11030492