ORIGINAL ARTICLE

BIOCHEMICAL INVESTIGATION INTO THE INFLUENCE OF *TELFAIRIA OCCIDENTALIS* ON HEPATIC OXIDATIVE STRESS MARKERS AND PRO-INFLAMMATORY BIOMARKERS INDUCED BY STREPTOZOTOCIN

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ABSTRACT

In rat models of diabetes, this research examined the biochemical impact of *Telfairia occidentalis* (TO) on pro-inflammatory biomarkers and hepatic oxidative stress markers caused by streptozotocin (STZ). There were five experimental groups: G 1 (Normal control) received 0.5 ml of distilled water; G 2 through 5 received 10% fructose for 14 days, after which STZ was administered intraperitoneally once. After the diagnosis of diabetes was confirmed, rats in groups 3 (TO1), 4 (TO2), and 5 (MET) were given 200 mg/kg b.w. TO, 300 mg/kg b.w. TO, and 300 mg/kg b.w. Metformin, respectively, for 28 days. The findings show that STZ significantly ($p<0.05$) increased malondialdehyde (MDA) levels in diabetic rats relative to the control group and significantly ($p<0.05$) decreased the activities of liver antioxidant enzymes such as catalase (CAT), reduced glutathione (GSH), glutathione S-transferase (GST), glutathione peroxidase (GPx), and superoxide dismutase (SOD). On the other hand, administration of TO (200 mg/kg and 300 mg/kg) and Metformin (300 mg/kg) resulted in a significant ($p<0.05$) increase in antioxidant enzyme activities and a significant ($p<0.05$) decrease in MDA levels. Furthermore, the inflammatory biomarkers myeloperoxidase (MPO), interleukin-1beta (IL-1β), tumor necrosis factor-alpha (TNF-α), inducible nitric oxide synthase (iNOS), and cyclooxygenase-2 (COX-2) as well as the apoptotic marker caspase-3 were significantly ($p<0.05$) elevated upon STZ induction; however, these elevations were significantly ($p<0.05$) attenuated upon TO administration, mirroring the effects of Metformin. In conclusion, *Telfairia occidentalis* significantly reduces the oxidative stress markers, inflammatory reactions brought on by STZ, and liver antioxidant status in diabetic rats. These results point to TO's possible therapeutic benefit in reducing diabetes-related liver problems via regulating oxidative and inflammatory pathways.

Keywords: Diabetes mellitus, *Telfairia occidentalis*, antioxidant enzymes, inflammatory biomarkers.

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Introduction

Diabetes is defined by the International Diabetes Federation (1) as a chronic metabolic disorder characterized by elevated blood sugar brought on by insufficiencies in insulin secretion, action, or both. Several studies have shown that diabetes mellitus can cause several consequences, especially in the liver. These issues include increased inflammation, oxidative stress, fibrosis, and changes in the parenchymal cells of the liver (2). Moreover, diabetes leads to problems in glucose homeostasis and lipid metabolism because it negatively impacts the liver's regulation of these processes (3).

Complications associated with diabetes have been linked to liver damage, dysfunction, and potential failure (4, 5). The diabetic condition has also been shown to cause irreversible hepatocellular damage through inflammatory cell recruitment. Moreover, cirrhosis, hepatocellular cancer, cholelithiasis, autoimmune hepatitis, acute liver failure, hepatic inflammation, and non-alcoholic fatty liver disease have all been linked to diabetes-related hepatobiliary illnesses (5).

Streptozotocin (STZ) has been shown to induce diabetes by changing the hepatic biochemical and functional abnormalities that result in oxidative stress, apoptosis, and hepatocellular damage (6). It has been shown that diabetes compounds the effects on liver proteins and enzymes, causing antioxidant enzymes like SOD, CAT, and GPx to become less active. This, in turn, causes oxidative stress and lipid peroxidation (7, 8). Increased oxidative stress associated with STZ-induced diabetes has been related to the etiology of several diseases, including diabetes, anemia, cancer, and cardiovascular disorders (9).

Interestingly, traditional medicinal plants have gained attention for diabetes management due to their therapeutic potency and fewer side effects compared to conventional medications (10). A recent study highlighted those medicinal plants, including *Telfairia occidentalis* (TO), contain flavonoids and saponins relevant for preventing the early-life risk factors for type 2 diabetes (10).

In tropical areas like Nigeria, growing abundantly, *Telfairia occidentalis* (TO), often known as fluted pumpkin or "Ugu," is a popular plant. Proteins, carotenoids, polyunsaturated fatty acids, tocopherol, and phytosterols are abundant in its seeds. (11). The TO seed extracted with methanol has also been shown to include anthraquinones, flavonoids, alkaloids, saponins, phenolics, and tannins. (12). The plant has been associated with hepatoprotective effects, enhancement of male fertility activity, immunomodulatory, anticancer, and anti-inflammatory effects, as well as antioxidant activities (13). There are little or no reports on the antioxidants and pro-inflammatory roles of *Telfairia occidentalis* leaf extracts in managing diabetic conditions in rats. Therefore, the current inquiry's objective is to ascertain whether T. occidentalis can protect rat models of liver damage caused by streptozotocin.

Materials and Methods

Plant Extract Preparation

In Okuku, Nigeria's Cross River State, the leaves of *Telfairia occidentalis* (TO) were gathered from a neighboring farm. With voucher number UIH 63457, the plant was botanically recognized at the Department of Botany Herbarium at the University of Ibadan. After being allowed to air dry, the TO leaves were crushed mechanically. TO leaves were soaked in a (1:3) ratio of 100% ethanol for 72 hours. The filtrate was then concentrated at 40ºC using Whatman paper size 1.

Animal Model

Ethical approval for the treatment and handling of experimental animals was obtained from the Faculty of Basic Medical Science Animal Ethical Committee University of Cross River State with an approval number; 114BCM262. Thirty-five (35) male albino rats weighing between one hundred and two hundred grams were obtained from the University of Cross River State's Faculty of Basic Medical Sciences' animal holding facility. They were put in five groups of seven rats each in plastic cages with wire nets and good ventilation. Before the trial started, the rats were given 14 days to become used to their new environment and were given unlimited access to drinking water and rodent feed.

The Design of Experiment

The rats were divided into five groups, each consisting of 7

rats, at random. The course of treatment is outlined below:

G 1: Got distilled water for 14 days and acted as the control group.

G 2: Functioned as the group with diabetes and was given 10% fructose for 14 days before receiving a single dose of 40 mg/kg of streptozotocin (STZ).

G 3 Was given 10% fructose for 14 days before receiving a single 40 mg/kg dose of streptozotocin (STZ) and then receiving a 28-day treatment with 200 mg/kg body weight TO (10).

G 4: Was given 10% fructose for 14 days before receiving a single 40 mg/kg dose of streptozotocin (STZ) and 28 days of treatment with 300 mg/kg body weight TO.

G 5: Was given 10% fructose for 14 days before receiving a single dose of 40 mg/kg of streptozotocin (STZ) and 28 days of therapy with 300 mg/kg body weight of metformin.

Animal Sacrifice and the Creation of the Liver Homogenate's Post-Mitochondrial Fraction Within 24 hours of the final treatment, all rats were killed. The plasma was acquired by centrifuging the blood at 3000 RPM for 15 minutes after cardio-puncturing it into EDTA. Following the liver's removal, it was homogenized in 0.1 M phosphate buffer (pH 7.4) and washed with 1.15% potassium chloride solution. Subsequently, the homogenates underwent a 10-minute, 10,000-g centrifugation at 4°C to separate the post-mitochondrial fraction required for the laboratory test. [14].

Measuring Hepatic Oxidative Stress Biomarkers Using Clairborne's (1995) approach, the catalase (CAT) activity was assayed. Britten et al. (1992) techniques were followed to determine Glutathione S-transferase and glutathione (GSH) (GST). The activity of glutathione peroxidase (GPx) was measured using Rotruck's (1973) technique. We measured superoxide dismutase (SOD) by applying the procedure Fridovich and Misra (1972) outlined. The Granell et al. (2003) approach was utilized to ascertain the activity of myeloperoxidase (MPO). The Malondialdehyde (MDA) was measured using the technique that Farombi et al. (2008) reported. The content of colonic nitrites, a stable byproduct of nitric oxide (NO), was utilized to gauge the amount of NO present. using a nitrite of sodium curve as a reference, the colonic nitrite concentration was calculated in μm of nitrites/mg protein. (21).

Measuring Liver Inflammatory and Apoptotic Biomarkers

As directed by the manufacturer (CUSABIO Life Science Inc., Wuhan, China), the amounts of COX-2, caspase-3, iNOS, TNF-α, and IL-1β were measured in the liver homogenate supernatant using ELISA kits.

RESULTS

The results in Figure 1-6 revealed that Streptozotocin (STZ) injection in rats resulted in a substantial ($p<0.05$) decrease in the activities of liver SOD, GSH, GST, GPx, and CAT, along with a higher concentration of MDA in the livers of diabetic rats than of control rats. When comparing rats treated with 200mg/kg and 300mg/kg of *Telfairia occidentalis* (TO) to those exposed to STZ alone, the treatment significantly ($p<0.05$) restored the activities of SOD, GSH, GST, GPx, and CAT with a corresponding drop in MDA level. Moreover, a comparable pattern was seen when metformin (300 mg/kg) was administered. with (200mg/kg and 300mg/kg) *T. occidentalis* treated groups when compared with rats exposed to STZ as shown in Figures 1-6.

Similarly, STZ induction markedly increased the level of inflammatory biomarkers such as Myeloperoxidase (MPO), Interleukin-1 beta (IL-1β), Tumor Necrosis Factor-alpha (TNF-α), inducible Nitric Oxide Synthase (iNOS), Cyclooxygenase-2 (COX-2) and caspase-3 in contrast to the control group. Interestingly, in comparison to control, the administration of Telfairia occidentalis (TO) significantly ($p<0.05$) reduced the levels of inflammatory biomarkers and caspase-3 in the liver of diabetic rats. as shown in Figures 7-13.

DISCUSSION

Numerous researches have been done on the detrimental consequences of diabetes-related issues over time. (22). It has been demonstrated that diabetes is linked to decreased metabolic function, which affects liver integrity, both anatomically and functionally. Therefore, the current investigation's objective is to assess the effectiveness of T.

occidentalis in rat models of liver damage caused by diabetes. (23) Important antioxidant enzyme activity was shown to be significantly ($P<0.05$) decreased after administering streptozotocin (STZ) to cause diabetes, including SOD, CAT, GPx, and GST. As a result, there was also an increase in MDA and a drop in GSH concentration. The results of Airaodion et al. (2019), which demonstrated decreased serum antioxidant enzymes following diabetes induction in rat models, are consistent with the considerable drop in the concentration of these important antioxidant enzymes, GSH, and increased MDA levels in the liver of diabetic rats produced by STZ.

Furthermore, the present outcomes are consistent with those of Geens et al. (2012), who evaluated the effectiveness of Naringin against STZ-induced toxicity in adult rats and observed a considerable drop in GPx, SOD, CAT, and GSH. The results of Meeker et al. (2010), who reported a significant ($p<0.05$) decrease in the concentration of antioxidant enzymes such GPx, SOD, and CAT upon induction of STZ, are consistent with the current experiment. This result also confirms the findings of Sakaue et al. (2007), who observed in adult male rats exposed to STZ a reduction in antioxidant enzymes (GPx, SOD, and CAT), changes in GSH level, and changes in sperm shape. On the other hand, the current data support the findings of Aja et al. research (2022), which showed that exposure to BPA led to a reduction in antioxidant enzymes, GSH, semen quality, elevated MDA, and impaired spermatogenesis.

Fascinatingly, the treatment of T. occidentalis raised the concentration of antioxidant enzymes (GPx, SOD, GST, and CAT) and restored them to a substantial extent ($p<0.05$). The medicinal efficacy and protective potential of *T. occidentalis*, which has been shown to comprise a variety of bioactive compounds with demonstrated antioxidant qualities, such as flavonoids and phenolic acids, may be the cause of the rise in these enzymes. (29,22). Similarly, *T. occidentalis* has been shown to contain vitamin E and vitamin A, which play a pivotal role in the antioxidant defense mechanism. Antioxidants are located throughout the cell and protect against ROS toxicity. SOD, CAT, and GPx lessen the oxidative damage that ROS cause to testicular cell membranes while shielding the living system from their damaging effects. (22). Decreased CAT activity impairs the liver cells' capacity to remove H2O2 generated by exposure to STZ. Reducing SOD activity may lead to the buildup of superoxide radicals, Thus, the CAT enzyme is inhibited (30). H2O2 can quickly oxidatively destroy DNA, proteins, and lipids. Therefore, the heme-containing enzyme catalase helps to break down hydrogen peroxide into water and oxygen (31), acting as a vital antioxidant enzyme safeguarding cells against oxidative damage from reactive oxygen species (30). Glutathione Peroxidase (GPx) on the other hand is a selenium-containing enzyme, that participates in the diminution of hydrogen peroxide and lipid hydroperoxides to water and alcohols, respectively (32). It stands as another crucial antioxidant enzyme, shielding cells from oxidative damage (33). On the other hand, glutathione-S-transferase (GST) helps conjugate GSH to electrophilic substances. This process enhances their water solubility, facilitating their excretion from the body. GST is essential to the xenobiotics' detoxification process, encompassing drugs, carcinogens, and environmental pollutants (34). Therefore, Studies by Osukoya et al. (2016) and Eseyin et al. (2014) have stated the hepatoprotective effects of *Telfairia occidentalis* in managing diabetic rats, emphasizing its role in reversing structural and functional liver abnormalities induced by diabetes.

Moreover, Metformin, a well-known antidiabetic agent, has been documented to have anti-inflammatory qualities (35). The similarity in effects observed between TO and Metformin in attenuating antioxidant enzymes and inflammatory biomarkers supports TO's potential as an anti-inflammatory agent.

In this investigation, rats receiving STZ showed a considerable decline in glutathione (GSH) levels, which was found to be statistically significant ($p < 0.05$). This conclusion is in line with the results of Ahangarpour et al. (2016b), who observed a notable decline in GSH levels in response to GSH exposure, as well as decreased concentration of CAT and SOD (36).

Furthermore, the present investigation validates the results of Xie et al. (2017), who observed a noteworthy reduction in the

activities of GSH, CAT, and SOD within the liver of male rats. following the administration of STZ. However, the observed reduction in GSH levels implies an accumulation of free radicals and a decrease in the activities of antioxidant enzymes. Administration of *T. occidentalis* however, resulted in a significant restoration and increase in GSH levels ($p < 0.05$). This effect could be attributed to the reducing properties and potentials of *T. occidentalis* occasioned by its antioxidant features or the crucial role of GSH in controlling the permeability of the inner membrane and preserving the decreased state of sulphydryl groups (36).

In this current study, a statistically significant increase in malondialdehyde was observed in the group treated with STZ. This finding aligns with the observations of Oboh and Ademiluyi. (2012) noted that STZ administration leads to rapid lipid degradation, resulting in high malondialdehyde concentrations (MDA) and inducing oxidative stress in testicular tissue.

The observed rise in MDA concentrations may be attributed to the accumulation of ROS, causing oxidative degradation of lipids. This mechanism involves free radicals abstracting electrons from cell membrane lipids, leading to cellular harm. This process, which affects polyunsaturated fatty acids with numerous double bonds between the methylene bridges (-CH2-), which include extremely reactive hydrogen atoms, is based on a free radical chain reaction mechanism. (37).

In contrast, treatment with T. occidentalis exhibited anti-lipid peroxidation activity, significantly decreasing the level of MDA. Thus, the restoration of structural and functional integrity of membrane phospholipids may be attributed to the therapeutic efficacy and antioxidant properties of T. occidentalis (38). Therefore, Malondialdehyde (MDA) serves as a byproduct of lipid peroxidation, generated when Polyunsaturated fatty acids in cell membranes are attacked by reactive oxygen species (ROS). (38). MDA functions as a biomarker of oxidative stress and is frequently utilized to assess the extent of lipid peroxidation in tissues and cells. The notable finding is that treatment with *Telfairia occidentalis* at doses of 200mg/kg body weight and 300mg/kg body weight significantly decreases the activities of MDA compared with the streptozotocin (STZ) induced group. Similar positive effects were observed with Metformin, a known antidiabetic agent. This aligns with other studies that have demonstrated the antioxidant properties of TO (11).

In furtherance to this, Streptozotocin (STZ) induction significantly ($P<0.05$) elevated the level of inflammatory biomarkers such as MPO, IL-1β, TNF-α, iNOS, COX-2, and caspase-3. Thus, this finding is concurrent with the work of Tolman et al. (2004) and Friedman. (2008) who reported the deleterious increase in IL-1β, TNF-α, iNOS, COX-2, and caspase-3 upon Streptozotocin administration.

Interestingly, *Telfairia occidentalis* administration significantly ($P<0.05$) decreased the levels of Myeloperoxidase (MPO), Interleukin-1 beta (IL-1β), Tumor Necrosis Factor-alpha (TNF-α), inducible Nitric Oxide Synthase (iNOS), Cyclooxygenase-2 (COX-2), and caspase-3. Hence, MPO, IL-1β, TNF-α, iNOS, COX-2, and caspase-3 signify a cascade of events associated with inflammation, oxidative stress, and apoptotic processes (38). Myeloperoxidase (MPO) is an enzyme present in neutrophils and is involved in the defense against pathogens (9). Increased MPO levels often indicate heightened neutrophil activity, suggesting an inflammatory response thus, STZ-induced diabetes leads to an influx of inflammatory cells, contributing to increased MPO levels (9). Conversely, Interleukin-1 beta (IL-1β) is a pro-inflammatory cytokine that plays a key role in the immune response thus, elevated IL-1β indicates an inflammatory state (37). STZ-induced diabetes can trigger the release of pro-inflammatory cytokines, contributing to the inflammatory milieu (37).

Moreover, Tumor Necrosis Factor-alpha (TNF-α) is a cytokine involved in inflammation and immune regulation hence, increased TNF-α levels signify an inflammatory response (39). STZ-induced diabetes can stimulate the release of TNF-α, contributing to the inflammatory cascade and potential tissue damage (39).

Hence, Inducible Nitric Oxide Synthase (iNOS) produces nitric oxide (NO), which has various physiological functions therefore, in diabetes, excessive NO production can contribute to oxidative stress and tissue damage (13).

However, an enzyme called cyclooxygenase-2 (COX-2) is needed for the production of prostaglandins. during inflammation thus, increased COX-2 expression suggests an inflammatory response (23). STZ-induced diabetes has been reported to upregulate COX-2 thus, contributing to the inflammatory processes associated with diabetes (23). Finally, Caspase-3 is a key enzyme in apoptosis (programmed cell death) therefore, elevated caspase-3 levels indicate an increase in apoptotic activity (4). STZ-induced diabetes can trigger apoptotic pathways, potentially leading to cell death, particularly in tissues such as the liver (40).

Furthermore, the elevation of MPO, IL-1β, and TNF-α suggests an inflammatory state in response to STZ-induced diabetes thus, inflammation is a key component of diabetic complications, and increased iNOS and COX-2 has been shown to contribute to the process that produces reactive oxygen species (ROS), which causes oxidative stress (41). This oxidative stress is a common feature in diabetes and the rise in caspase-3 levels indicates an activation of apoptotic pathways (41,42). Excessive apoptosis can contribute to tissue damage and dysfunction, a common outcome in diabetic complications (43). The elevation of these biochemical parameters in response to STZ-induced diabetes signifies a complex interplay of inflammatory, oxidative, and apoptotic processes that contribute to the etiology of problems associated with diabetes (43). Thus, the observed attenuation of inflammatory biomarkers by *Telfairia occidentalis* suggests a comprehensive modulation of the inflammatory pathways induced by STZ. The anti-inflammatory effects of TO align with its antioxidant properties, collectively contributing to the amelioration of diabetes-associated liver complications thus, these findings reinforce the concept that oxidative stress and inflammation are interconnected processes in diabetes-related liver damage (4).

Hence, Ujong and Nkanu. (2021) highlighted the therapeutic potential of plants with medicinal properties in diabetes treatment. The present study contributes to this narrative by specifically emphasizing the therapeutic value of Telfairia occidentalis in mitigating liver complications associated with diabetes (42).

On the other hand, metformin is a biguanide antidiabetic drug that effectively reduces type 2 diabetes in rats. It does this by inhibiting gluconeogenesis and increasing the body's use of glucose in the liver, muscles, and intestines. (42). Consequently, metformin had synergistic effects in this study by raising inflammatory marker levels and antioxidant enzyme activity (43).

Therefore, it has been demonstrated that STZ causes hyperglycemia, which leads to oxidative stress that kills pancreatic beta cells (44). Consequently, it has been demonstrated that TO, an antioxidant, reverses this effect and shields beta cells from STZ's oxidative impact. (42).

.CONCLUSION

To sum up, *Telfairia occidentalis* has a great deal of promise as a treatment for liver problems brought on by diabetes. The modulation of oxidative and inflammatory pathways positions *Telfairia occidentalis* as a holistic intervention in addressing the multifaceted challenges posed by diabetes in the liver. These results add to the increasing amount of available data supporting the utilization of TO in complementary or alternative strategies for managing diabetes-related liver disorders.

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TABLES AND FIGURE

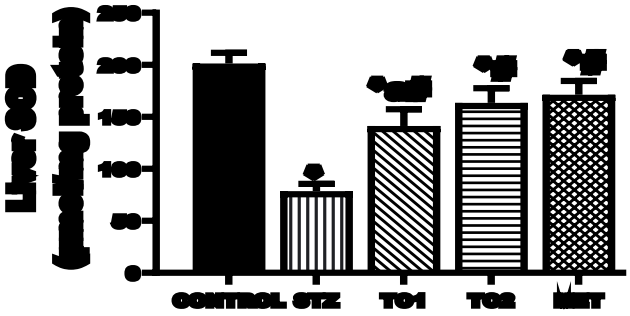

Figure 1: Effect of *T. occidentalis* (TO) on activities of SOD in the liver of streptozotocin-induced diabetic rats. Data is expressed as mean ± SEM; n = 7, p< 0.05, * = significantly different compared with Control, a = significantly different compared with STZ, and # = significantly different compared with MET.

Figure 2: Effect of *T. occidentalis* (TO) on activities of GSH in the liver of streptozotocin-induced diabetic rats. Data is expressed as mean ± SEM; n = 7, p< 0.05, * = significantly different compared with Control, a = significantly different compared with STZ, and # = significantly different compared with MET.

Figure 3: Effect of *T. occidentalis* (TO) on activities of GST in the liver of streptozotocin-induced diabetic rats. Data is expressed as mean ± SEM; n = 7, p< 0.05, * = significantly different compared with Control, a = significantly different compared with STZ, and # = significantly different compared with MET.

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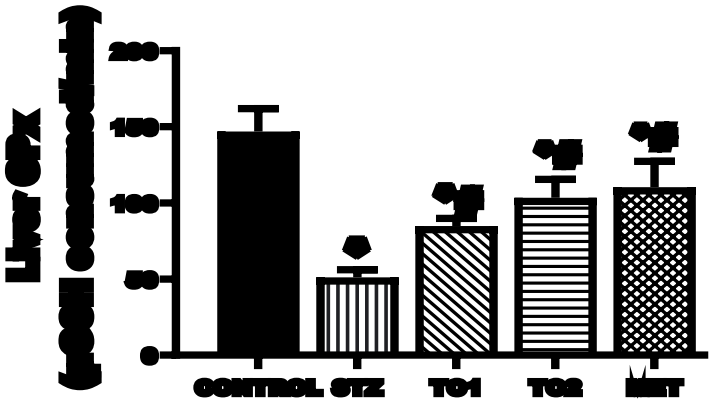

Figure 4: Effect of *T. occidentalis* (TO) on activities of GPx in the liver of streptozotocin-induced diabetic rats. Data is expressed as mean ± SEM; n = 7, p< 0.05, * = significantly different compared with Control, a = significantly different compared with STZ, and # = significantly different compared with MET.

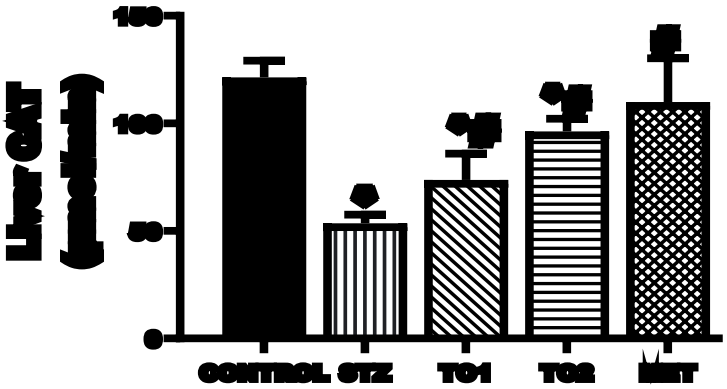

Figure 5: Effect of *T. occidentalis* (TO) on activities of CAT in the liver of streptozotocin-induced diabetic rats. Data is expressed as mean ± SEM; n = 7, p< 0.05, * = significantly different compared with Control, a = significantly different compared with STZ, and # = significantly different compared with MET.

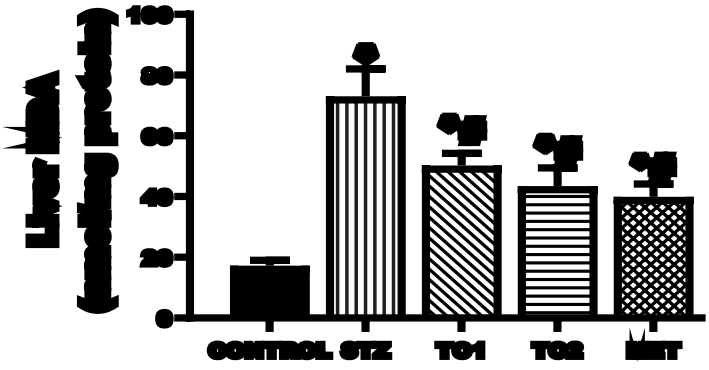

Figure 6: Effect of *T. occidentalis* (TO) on activities of MDA in the liver of streptozotocin-induced diabetic rats. Data is expressed as mean ± SEM; n = 7, p< 0.05, * = significantly different compared with Control, a = significantly different compared with STZ, and # = significantly different compared with MET.

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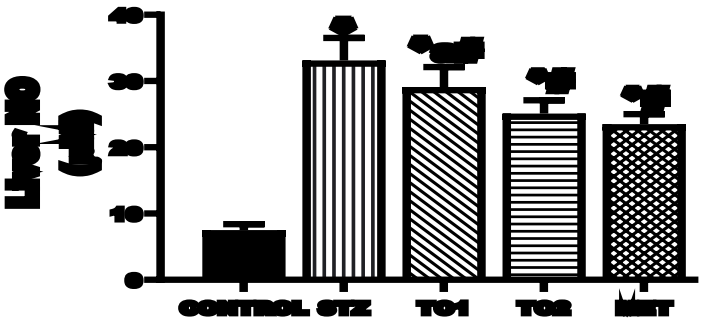

Figure 7: Effect of *T. occidentalis* (TO) on activities of NO in the liver of streptozotocin-induced diabetic rats. Data is expressed as mean ± SEM; n = 7, p< 0.05, * = significantly different compared with Control, a = significantly different compared with STZ, and # = significantly different compared with MET.

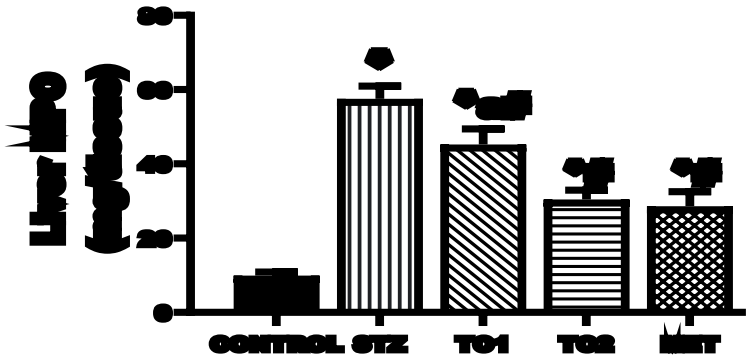

Figure 8: Effect of *T. occidentalis* (TO) on activities of Myeloperoxidase MPO in the liver of streptozotocin-induced diabetic rats. Data is expressed as mean ± SEM; n = 7, p< 0.05, * = significantly different compared with Control, a = significantly different compared with STZ, and # = significantly different compared with MET.

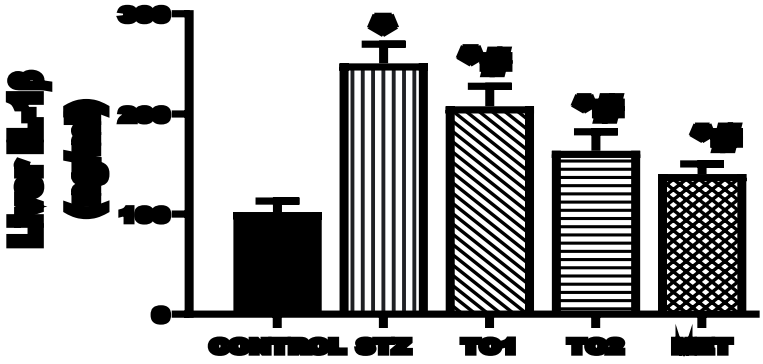

Figure 9: Effect of *T. occidentalis* (TO) on activities of Interleukin-1 beta (IL-1β) in the liver of streptozotocin-induced diabetic rats. Data is expressed as mean ± SEM; n = 7, p< 0.05, * = significantly different compared with Control, a = significantly different compared with STZ, and # = significantly different compared with MET.

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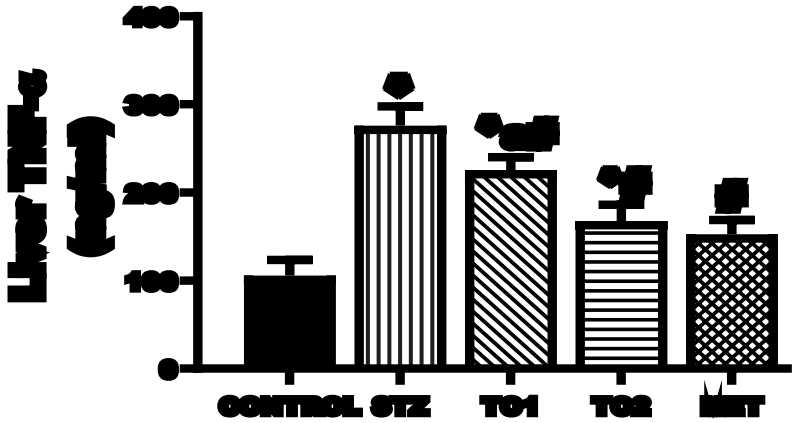

Figure 10: Effect of *T. occidentalis* (TO) on activities of Tumor Necrosis Factor-alpha (TNF-α) in the liver of streptozotocin-induced diabetic rats. Data is expressed as mean ± SEM; n = 7, p< 0.05, * = significantly different compared with Control, a = significantly different compared with STZ, and # = significantly different compared with MET.

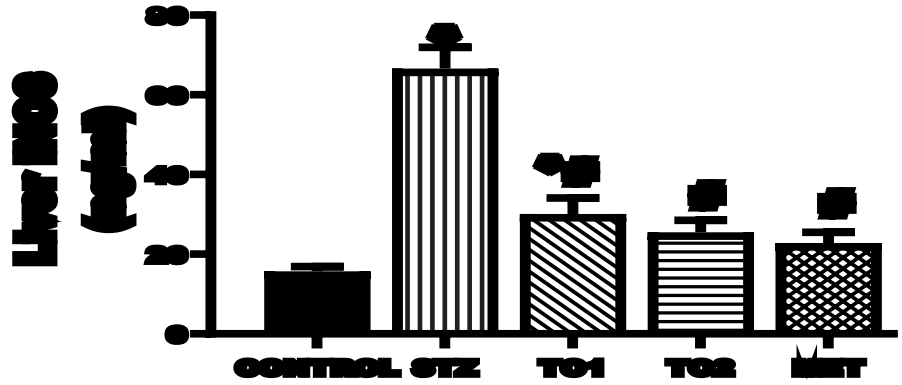

Figure 11: Effect of *T. occidentalis* (TO) on activities of inducible Nitric Oxide Synthase (iNOS) in the liver of Streptozotocin-induced diabetic rats. Data is expressed as mean ± SEM; n = 7, p< 0.05, * = significantly different compared with Control, a = significantly different compared with STZ, and # = significantly different compared with MET.

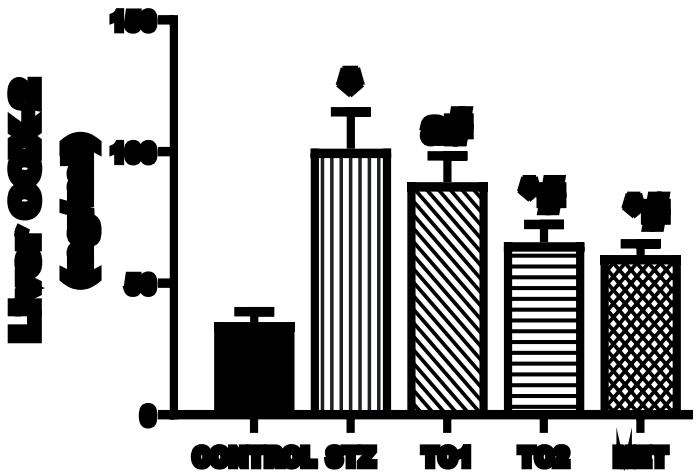

Figure 12: Effect of *T. occidentalis* (TO) on activities of Cyclooxygenase-2 (COX-2 in the liver of Streptozotocin-induced diabetic rats. Data is expressed as mean ± SEM; n = 7, p< 0.05, * = significantly different compared with Control, a = significantly different compared with STZ, and # = significantly different compared with MET.

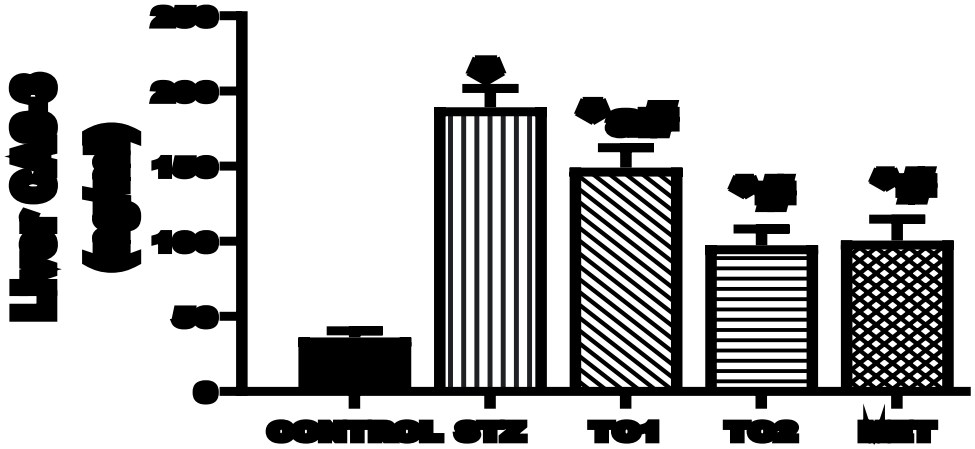

Figure 13: Effect of *T. occidentalis* (TO) on activities of caspase-3 in the liver of Streptozotocin-induced diabetic rats. Data is expressed as mean ± SEM; n = 7, p< 0.05, * = significantly different compared with Control, a = significantly different compared with STZ, and # = significantly different compared with MET.