

Neuroprotective and Antioxidative Potentials of Aqueous Crude Extract of *Sterculia Tragacantha* Leaf in Streptozotocin-Induced Diabetes in Rats

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ABSTRACT

Background: In the western part of Nigeria, different medicinal plants including *Sterculia tragacantha* has been proved in managing diabetes mellitus with no scientific basis. This research focus on the neuroprotective and antioxidative potential of aqueous crude extract from *S. tragacantha* leaf (AESTL) using streptozotocin-induced diabetes using albino rat model.

Methodology: AESTL was prepared (w/v) and its effect on biomarkers of inflammation; together with some oxidative stress, markers on the brain of streptozotocin-induced diabetic rats were evaluated.

Results: The results showed that diabetic rats treated with AESTL exhibited an inhibitory effect on the neurotransmitters: acetylcholinesterase (AChE), butyrylcholinesterase (BChE), dopamine, serotonin, NO and Na⁺K⁺ ATPase, in a dose dependent manner, on the brain of the animals when compared with diabetic control. Furthermore, the results revealed that no similar effect was observed in the activities of catalase (CAT) and superoxide dismutase (SOD) in the brain of the control and diabetic rats treated with (150 and 300 mg/kg of AESTL). Also, this was observed on metformin (standard drug) group with similar effect with the control group but the vehicle (untreated diabetic group) when compared with the control group and diabetic rats treated with (150 and 300 mg/kg of AESTL) in CAT and SOD showed significant ($p < 0.05$) increase within the stipulated days of the experiments. In addition, brain content of the glutathione (GSH), glutathione-S-transferase (GST) and glutathione peroxidase (GPx) were significantly increased with co-administration of the AESTL doses when compared with the vehicle.

Conclusion: Inhibitory effect of AChE, BChE and some other biomarkers of inflammation and antioxidative potentials by AESTL could be the major breakthrough in the management of diabetes mellitus.

Keywords: AESTL; Biomarkers of inflammation; Metformin; Neurotransmitters; Oxidative stress markers; *Sterculia tragacantha*; Inhibitory effect

The research work was designed to evaluate neuroprotective and antioxidant potentials of crude extract of *Sterculia tragacantha* (AESTL) in streptozotocin-induced diabetes in rats. Knowing that diabetes mellitus has been globally proved to be involved in oxidative stress in which the pathological changes in central nervous system caused memory lost and affective retardation which later increase the risk of vascular depletion in both human and rat brain [1]. The use of medicinal plants or herbal medicines is gaining momentum in the management of diabetes mellitus and

major advantages of herbal medicine seem to be their potency and minimal side effects [2].

Therefore, enzymes play important roles when measured in different tissues and cells by investigating and diagnosing their notable role in diseases [3]. Most of the enzymes activities in the tissues like brain and others tissues serve as builder to discover toxicity of harmful effects of administered compounds (streptozotocin) into body [4].

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Our results showed that AESTL lowered the glucose levels in diabetic rats probably due to antioxidant nature of the extract. This is in agreement with earlier reports [5,6]. The finding in this research corroborates the earlier finding, that streptozotocin induced significant increase in glucose levels in untreated diabetic rats [7].

In neurodegenerative diseases as well as other age-related diseases, the imbalance that occurred between the ROS production and reduction in antioxidative potential causes the oxidative stress, which makes it more, implicated [8]. Synaptic cleft is one of the major cholinergic builder protein required for maintenance of acetylcholine levels and helps the neurons functioning in the AchE. This is a product of serine protease that forms choline and acetate when acetylcholine is hydrolyzed thereby causing an effect on cholinergic transfer of impulse between neurons. In this present study, the notable reduction caused by AESTL on AChE with no alteration in all treated groups could be suggestive that the plant has potential therapeutic importance. Therefore, this validates the result obtained in experimental rats. Thus, the reduction caused by AChE activity via the crude extract from *Steculia tragacantha* could be traceable to the rise in acetylcholine levels in the synaptic cleft, which could lead to an elevation in cholinergic transfer of impulse between neurons in the rats. The hydrolysis of AchE and BChE causes by modulatory immune response of acetylcholine result in services of the brain for poor-quality systemic inflation. In addition, this study supported where an increase in cholinesterase activities and inflammation is validated. This now revealed that in diabetic rats, there is inactivation of Ach when AChE and BChE, which could eventually aggravate the diabetic condition, activate inflammation. Treatment with 300 mg/kg body weight of AESTL ameliorated the alteration caused to the enzymes' activity in streptozotocin-induced diabetes in rats. Depletion of NO and uncoupling eNOS function is caused by increase in arginase activity which caused damage to endothelium-dependent vaso-relaxation via reduction in L-arginine available to eNOS [8].

This research study revealed an increase in the level of nitric oxide in diabetic rats. This suggests that an increase in nitric oxide production can lead to a decrease in arginase activity thereby causing alteration of nitric oxide production. Therefore, amelioration of the diseased condition by reducing the nitric oxide using this plant (AESTL) could suggest the fact that AESTL exhibited an inhibitory effect on nitric oxide activity. Majorly, there is great stress from diabetes mellitus. Norepinephrine (NE) and epinephrine (E) serve as anti-stress chemicals in the body by which epinephrine is involved in increasing the power of muscles and elongating the action of muscle, by its ability to activate the release of glucose from glycogen [34]. Therefore, basal levels of NE and E seem to be higher in diabetic untreated groups than diabetic treated rats with reduction in NE and E on the brain. These findings agree with previous report. An attenuated response of NE and E to AESTL treatment was observed in groups, standard drug and borderline control group.

Furthermore, the most important proteins responsible for the maintenance of ion homeostasis through active transport and control of delicate chemical gradient that is necessary for the optimal function of the central nervous system is membrane-bound ATPases and any alteration caused to the membrane lipid components of brain leads to inactivation of these membrane-bound enzymes. Inactive forms of ATPases are involved in the development of numerous diseases like neurological diseases,

diabetes mellitus, coronary artery diseases, stroke and tumor. The cation transport across the neuronal membrane, which is mediated by the ATPases, is involved in many biological processes. Impairment of cellular energy metabolism could result in neurons vulnerability by excitotoxic damage especially when neurons are subjected to additional stresses of A β and tau accumulations. It has been proposed that alterations in Na⁺/K⁺-ATPase activity may represent an important neurotoxic mechanism for neurons. Therefore, the ameliorative effects of AESTL on streptozotocin-induced diabetes in rats with respect to Na⁺-K⁺-ATPase recorded in this work further suggest that AESTL has potential active compounds necessary to maintain ion gradients across biological membranes and thus confer significant protection to the brain by stabilizing the functional integrity of the membrane. Our present observations strongly support the earlier research findings wherein it was suggested that administration of *Bacopa monniera* could possess beneficial therapeutic strategy in ameliorating diabetes mellitus, cognitive dysfunctions and other related neurological disorders [41]. Dopamine, a major precursor of norepinephrine plays a major key role in reward and movement regulation in the brain. In the reward pathway, the production of DA takes place in the ventral tegmental area (VTA), in nerve cell bodies. From there, it is released into the nucleus accumbens and prefrontal cortex. It is of interest the loss of dopamine was reversed by AESTL in diabetic rats in this work. This is probably due to the cumulative effect of the bioactive principles in AESTL. Knowing that insulin and glucose metabolism play an important role in brain serotonin release, the information that affect central 5-HT functions may be associated with the impairment of insulin signaling, leading to the development of diabetes. Interestingly, our results show that the serotonin reduction was seen in AESTL and metformin treated groups, which might be linked to cumulative effects of all the bioactive compounds present in AESTL. One of the major mechanisms in cell injury of any aerobic organism that is subjected to oxidative stress is lipid peroxidation and this in turn is linked with loss of membrane fluidity and permeability increase that result in loss of structure and function [2, 3]. Furthermore, intrusion of foreign agents like streptozotocin caused damage to cell thereby resulting into reactive oxygen species (ROS) in diabetic condition.

Present study, as shown in Figure 5a, revealed that AESTL ameliorates the damage done in all treated group when compared with untreated group. This finding is in agreement with previous study in association with an increase in thiobarbituric acid reactive substances (TBARS) in the tissue. Alteration in any antioxidative defense system induces lipid peroxidation and oxidative stress. Enzymes such as SOD, catalase, glutathione peroxidase, glutathione-s-transferase as well as glutathione form the defense system, which usually protects the cell against oxidative damage. In this research study, most of the oxidative stress markers were significantly decreased in streptozotocin-induced rats as shown in Figures 5b, 6 and 7. This is attributable to the medicinal values in AESTL treatment. It has been established that CAT, SOD and GPx play important roles as protective enzymes against free radical formation in tissues. The present studies validate protective roles of the extract (AESTL) in reducing peroxidation level and restore the damaged levels of antioxidant enzymes system.

CONCLUSION

It can be concluded from this study that AESTL showed great potentials in ameliorating the diabetic conditions, thereby play a

protective role on the brain against diabetogenic-oxidative stress causing change in the levels of peroxidation thereby decreasing activities of oxidative markers. Therefore, in reducing diabetes-associated oxidative stress; AESTL could be very helpful in diabetes mellitus management.

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