

EFFECTS OF AQUEOUS LEAVE EXTRACTS OF LAUNAEA TARAXACIFOLIA (WILLD.) ON THE HIPPOCAMPAL DAMAGE IN STREPTOZOTOCIN-INDUCED DIABETIC WISTAR RATS

ABSTRACT

This study determined the anti-diabetic effects, assessed the antidepressant properties, and investigated the ameliorative effects of aqueous leaf extract of *Launaeataraxacifolia* (ALELT) on streptozotocin (STZ)-induced diabetic rats. It also evaluated its antioxidant effects on oxidative stress markers in diabetic rats. Forty-two male Wistar rats (110-130 g) were divided into seven groups (A, B, C, D, E, F, and G) of six animals each. Group A was the control, while STZ solution (80 mg/kg) was administered IP to diabetic groups B, C, D, E, and F. At the sixth week of induction, group B was the STZ control; groups C, D, and E rats received 300 mg/kg, 200 mg/kg, and 100 mg/kg per oral (p-o) of ALELT, respectively, for three weeks. Group F received 5 IU/day of insulin subcutaneously; group G received only 300 mg/kg p-o of ALELT for three weeks. After the study, the animals were sacrificed; the hippocampus was excised and fixed in a 10% neutral buffer solution for morphometric analysis. Homogenized samples were used to determine oxidative stress markers, brain derived neurotrophin factor (BDNF) level and insulin concentrations. The results showed varying degrees of hippocampal damage and loss of hilum of Dentate gyrus in the H&E sections, plaque and tangles in the Bielschowsky sections, loss of myelin sheath in the Luxol Fast Blue sections, and dissolution of Nissl bodies in the Cresyl Fast Violet sections, followed by weight loss, abnormal rise in glucose levels, decrease in BDNF, decrease in insulin levels, memory loss in neurobehavioral tests, and decrease in markers of oxidative stress in the negative control rats. These pathologies were reversed in the extract-treated groups and the results were comparable with group A. This study concluded that ALELT demonstrated anti-diabetic effects, mediated by the reduction of fasting blood sugar levels, increased insulin secretion, and elevated BDNF in the hippocampus of diabetic Wistar rat.

Key words: *Launaeataraxacifolia*, Hippocampus, Streptozotocin, Diabetes neuropathy.

1.0 INTRODUCTION

Diabetes mellitus, originating from the Greek word 'diabetes' meaning "to pass through" and Latin 'mellitus' meaning "sweet," is a long-term autoimmune condition where the pancreas cannot produce sufficient insulin needed by the body. Diabetes can lead to secondary complications affecting the brain, kidneys, heart, and eyes. Diabetic brains can suffer from cognitive decline and depression. Behavioral testing has shown a cognitive decline of up to 40% in diabetes patients (Dejgaard *et al.*, 2020). Recently updated systematic reviews have found that diabetes increases the risk of dementia (Ellis *et al.*, 2023). Long-term research indicates a 50-100% higher incidence of dementia in diabetic patients (Lu *et al.*, 2023). The hyperactivity of the hypothalamic-pituitary-adrenal axis (HPA axis) has also been linked to depressive disorders and diabetes (Kalarani *et al.*, 2023). In Africa, botanical remedies have been used as an indigenous health care system since antiquity. *Launaeataraxacifolia* (*Compositae*) is a leafy vegetable found in African nations like Ghana, Senegal, Benin, and Nigeria, known for its cholesterol-lowering and blood pressure-regulating properties (Moussa *et al.*, 2020). The antioxidants and hypoglycemic properties of *L. taraxacifolia* have been documented by (Gbadamosi *et al.*, 2020). An analysis of *Launaeataraxacifolia* extracts in Nigeria and Ghana showed that they possess potassium, calcium, magnesium, ascorbic acid, tannins, and flavonoids. These compounds may be accountable for the plants' antioxidant, hypolipidemic, and glucose lowering properties. The presence of phenolic compounds in *Launaeataraxacifolia* inhibits lipid peroxidation, scavenges (OH) free radicals, chelates metal ions (Fe²⁺), and improves the endogenous antioxidant system (Adedayo *et al.*, 2020). The leaves include leucoanthocyanins, lycopene, phenolic acids, tannins, flavonoids, and beta-carotene in addition to saponins, terpenoids, steroids, and a variety of other compounds. The human body releases endogenous substances that capture free radicals in order to mitigate their effects (d'Avila *et al.*, 2020). *Launaeataraxacifolia* leaf extract has antioxidant qualities that guard against oxidative stress, as shown by studies (Borokiniet *et al.*, 2023). *Launaeataraxacifolia's* antioxidant effectiveness against hydroxyl and

nitric oxide radicals was confirmed by (Adinortey *et al.*, 2019; Gbadamosi *et al.*, 2020). Hence, this study significantly investigates the ameliorative effects of *L. taraxacifolia* leaf extract on hippocampal modification in STZ-induced diabetic rats.

2.0 MATERIALS AND METHODS

2.1 Animal Management

Forty-two healthy male Wistar rats (110–130g) were purchased from the Pharmacology Department at Obafemi Awolowo University in Ile-Ife and acclimated for three weeks in the animal housing of the Department of Anatomy and Cell Biology, Obafemi Awolowo University Ile-Ife. They were housed in clean plastic cages and fed standard rat chow and water *ad libitum*.

2.2 Animal Grouping and Treatment

The animals were randomly divided into seven groups (A-G) of six animals each. Control group A received a single dose of citrate buffer solution with standard rat feed and water *ad libitum*. STZ (80 mg/kg) was administered intraperitoneally under fasting conditions to diabetes groups B, C, D, E, and F. Group G was the *Launaea taraxacifolia* control. At six weeks post-induction, group B was the STZ Negative Control Group; group C received 300 mg/kg p.o. of ALELT; group D received 200 mg/kg p.o. of ALELT; group E received 100 mg/kg p.o. of ALELT; group F received 5 IU/day of insulin subcutaneously; group G received 300 mg/kg p.o. of ALELT only. All treatments followed guidelines from the Committee on Animal Welfare and Protection.

2.3 Extraction of *Launaea taraxacifolia*

The extraction was done using the method described by Gbadamosi *et al.* (2020). Fresh leaves of *L. taraxacifolia* were collected from Pa Jekayin fagarden; it was identified, authenticated, air-dried, and

pulverized at the herbarium of Botany Department, Obafemi Awolowo University with voucher number IFE-18049 issued. Two hundred and fifty g of the powder was macerated in 1.5 liters of distilled water for 72 hours, filtered, and the filtrate was concentrated to dryness using a rotary evaporator at 45°C for 12 hrs.

2.4 Induction and Assessment of Diabetes

Diabetes was induced by a single intraperitoneal dose of 80 mg/kg STZ dissolved in 0.1M citrate buffer (pH 4.5) in 8-hour-fasted diabetic groups (B-F). Normal control rats were injected with citrate buffer alone. Blood glucose levels were evaluated using a glucometer (Adjei *et al.*, 2020).

2.5 Fasting Blood Glucose (FBG) Determination

Fasting blood samples were taken from the tail veins of all rats after induction and monitored throughout the experiment. A fine test glucometer was used to evaluate blood samples for glucose levels. The tail's end was cleansed with an alcohol swab and pierced with a lancet, and the drop was collected using a glucometer strip. Each reading was then appropriately recorded.

2.6 Body Measurement

Body weight was monitored twice weekly using a digital bench top scale. Body weight variations were determined using the weight on the first day of injection as the initial value.

2.7 Memory Exercise for Spatial Navigation

The radial-arm maze and open field maze were used in this test. The objective was to put the navigation memory of the rats to the test, which might be hampered by brain injury. This model was designed to assess spatial navigation memory while considering spatial orientation, perception, and locomotion, as described by Coppolino *et al.*, (2023). The labyrinth was made of gray-painted wood. The radial-arm

maze has a central platform (25 cm diameter) from which eight symmetrical arms (55 cm long 10 cm wide) with four baited arms and four non-baited arms emanated. To eliminate any aroma indications left by the previous subject rat, the chamber was scrubbed with 95% ethanol before. The ethanol was allowed to evaporate entirely before testing. In brief, rats were placed separately on the center platform and permitted to freely navigate the maze for 5 minutes. The time taken by the animal to reach the baited arm served as the memory index. The rats were accustomed to the maze site before the start of the test.

2.8 Mode of Sacrifice and Organ Collection

Rats were humanely sacrificed under diethyl ether anesthesia. The brains were removed, sectioned, and fixed in a 10% neutral buffer solution for histological analysis.

3.0. Biochemical Analysis

3.1 Catalase Activity

The function of CAT was measured using the method described by Johansson and Borg (1988).

3.2 Superoxide Dismutase Activity

The method of (Ijaz et al., 2023) was employed to analyze Superoxide dismutase activity on homogenized brain tissue.

3.3 Insulin Concentrations

An enzyme-linked immunosorbent test (ELISA) kit was used to assess serum insulin concentrations (Crystal Chem, Chicago, IL, USA).

3.4. Brain-Derived Neurotrophic Factor Concentrations

An enzyme-linked immunosorbent test (ELISA) kit was used to assess Brain-derived neurotrophic factor concentrations (Crystal Chem, Chicago, IL, USA) at Biotech Laboratory, Taiwo oke area, Ilorin, Kwuara State, Nigeria.

3.5. Histology and Histochemical Analysis

Histological analysis of the hippocampus was done using the method described by Drury and Wallington (1980). Tissues were sectioned, stained, and analyzed. Tissue blocks were cut into 5µm thick sections and stained.

3.6. Photomicrography and Histomorphometry

Slides were examined using a Leica DM750 microscope, and digital photomicrographs were produced with an attached Leica ICC50 camera. Imported into image J software for histomorphometric analysis were photomicrographs of hematoxylin and eosin dyed sections, an open office.org TM (00o- 4.0 programming software for histomorphometric evaluation.) with a computer system. Digital photomicrographs were taken at x400 and x1000 magnification.

3.7. Statistical Analysis

Data were analyzed using GraphPad Prism 5. One-way ANOVA followed by Tukey's test for multiple comparisons was used. Results were presented as Mean ± SEM, with p-values < 0.05 considered significant.

4.0. RESULTS

4.1 Body Weight Change

There was no significant difference in body weight across groups before induction. STZ caused significant weight loss in diabetic groups. Post-treatment, groups C, D, and E showed weight gain compared to the STZ negative control group. Normal control group A and ALELT control group G gained weight.

Table .1: Body Weight before Induction, Post Induction and Post Treatment

Group (n= 6)	Initial Body Weight (g)	Post Induction Weight (g)	Post treatment Weight (g)	Gained or Loss Weight (g)
Group A	121.6±5.41	187.3±7.67	243.5±3.98	121.9±1.43
Group B	123±6.25	92.3±4.99	97.8±2.34	-25.2±3.91*
Group C	126±4.45	95.5±3.10	154.3±5.23	28.3±0.60
Group D	117.3±5.83	95.8± 4.09	146±5.28	28.7±3.55
Group E	120.6±3.42	97±2.55	129±2.30	9±1.12
Group F	127±4.54	91.5± 6.21	139±6.89	12±2.35
Group G	117.3±4.89	183.6±1.98	250±3.63	133±1.26

Values are mean ± Standard Error of Mean (SEM).*- means group B was significantly different from the normal control and treated groups

Fig.1.A.showing effects of ALELT on total body weight change in the hippocampus of treated diabetic rats

Total body weight changes in group A were 120±2.985 compare to total body weight change in group G 133± 4.431, this showed that group G gained little more weight compare to A, though not significantly different. Total body weight change in A (120±2.985) was significantly different to weight change in B (-20 ± 2.348), C (30 ± 5.237), D (25 ± 5.275), E (11 ± 2.306), and F (6 ± 3.890; p < 0.001). STZ caused significant decrease in the total body weight change in the negative control group B (-20 ±2.348; p

<0.001) compare to treated group CDE and F, 300mg ALELT treated group C (30 ± 5.237) was significant to EFG (11 ± 2.306 , 6 ± 3.890 ; $P < 0.001$), 200mg ALELT treated group D was significant to E and F.

Fig.1.B. showing effects of ALELT on percentage body weight change on hippocampus of diabetic rats

The percentage body weight change in group A was (100 ± 2.985) compare to percentage body weight change in group G (110 ± 2.431) no notable variance was recorded. Percentage body weight change in A (100 ± 2.985) was significantly different to percentage body weight change in B (-20 ± 2.348), C (30 ± 5.237), D (29 ± 5.275), E (11 ± 2.306), and F (20 ± 3.890 ; $p < 0.001$). STZ caused significant decrease in the percentage body weight change in the negative control group B (-20 ± 2.348 ; $p < 0.001$) compare with treated group C, D, E and F. Group C (30 ± 5.237) was significantly different to E, F and G (11 ± 2.306 , 6 ± 3.890 ; $P < 0.001$), 200mg ALELT treated group D was significant to E and F.

Fig.1.C. showing of ALELT on brain weight change in treated compared to untreated diabetic rats

Group A is significantly different from B ($P < 0.001$), C ($p < 0.05$) E ($P < 0.001$), B is significantly different from D ($P < 0.05$), G ($P < 0.001$) and E is significantly different from group G ($P < 0.001$).

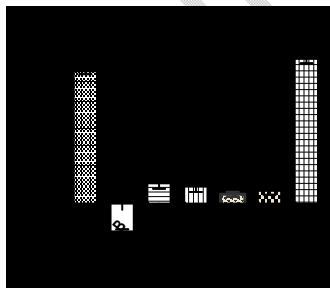


Fig.1.A. Effects of ALELT on total body weight change on hippocampus of treated diabetic rats

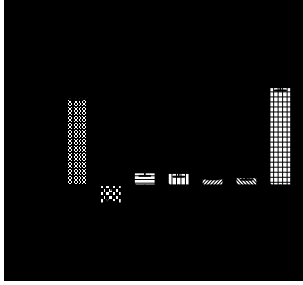


Fig.1.B. Effects of ALELT on percentage body weight change on hippocampus of diabetic rats

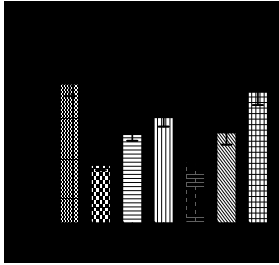


Fig.1.C. Effects of ALELT on brain weight change in treated compared to untreated diabetic rats

Fig.2A. shows that effects of STZ on neurobehavioural activities of the diabetic rats, 4th week of induction

Group A was significantly different from B, C, D, E, and F, but not significantly different from G ($P < 0.001$), Group B, C, D, E, and F were significantly different from G ($P < 0.001$). Memory loss in diabetic groups B, C, D E and F in the first 4th week of induction was found.

Fig.2B. showing effects of ALELT on line crossed in open field maze after the last treatment

Group A was significantly different when compared with groups B, C, D and E ($P < 0.001$), and F ($P < 0.01$). Group B was significantly different from the treated groups C ($P < 0.01$, D, F and (0.001) and to G ($P < 0.001$).

Fig.2C. showing effects of ALELT on time spent before finding food in radial arm maze in diabetic rats

Group A was significantly noteworthy compared with group B, E and F ($p < 0.001$). Group B was significantly noteworthy compared with C ($p < 0.001$), D ($p < 0.001$), E ($p < 0.001$), F ($p < 0.001$) and G ($p < 0.001$). Group C was significantly noteworthy compared to E ($p < 0.001$), group D was statistically noteworthy compared with group E ($p < 0.001$) and F ($p < 0.05$), group E was significantly different from G ($p < 0.001$) and F was significantly different from G ($p < 0.01$).

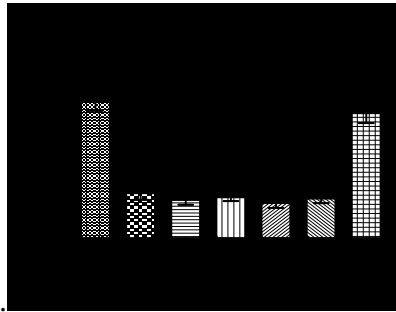


Fig.2A. Effects of STZ on neurobehavioural activities of the diabetic rats, 4th week of induction

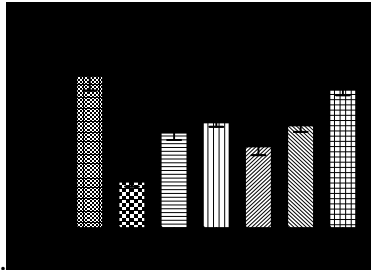


Fig.2B. Effects of ALELT on line crossed in open field maze after the last treatment



Fig.2C. Effects of ALELT on time spent before finding food in radial arm maze in diabetic rats

Effects of ALELT on fasting blood glucose in the hippocampus of STZ-induced diabetic rats

A day before induction of STZ, the glucose levels of the research animals across the group were aligned (97.3 ± 1.80 - 102.7 ± 3.23) with no statistical difference. STZ caused a significant increase in blood glucose levels of diabetic groups after induction (508 ± 26.91). The 200 and 300 mg/ kg of ALELT were able to reverse the diabetic effect of STZ on the hippocampus of the diabetic rats, 200mg/ kg of ALELT appeared to be better treated compared to 300mg/ kg as the glucose level was well regulated by the 200mg / kg of the extract (116 ± 7.39). 5 UI of Insulin control group F showed a surge decrease in the glucose level (76.0 ± 14.63) compared with normal control group (110 ± 3.76).

Table 2. Effects of ALELT on Fasting Blood Glucose Levels

Groups (N=6) Treatment	Initial Glucose (mg/dl)	1st wk of Induction (mg/dl)	2nd wk of Induction (mg/dl)	4th wk of Induction (mg/dl)	6th wk of Induction (mg/dl)	3rd wk Post (mg/dl)
Group A	100±1.66	104.6±2.10	107±2.39	105.9±4.44	97.5±5.70	110±3.76
Group B	100.8±1.60	472±18.10	508±26.91	417±13.0*	397.±32.91	308±27.86
Group C	100±3.40	462.5±28.87	508±23.82	448±24.67	374.2±15.64	135±10.62
Group D	102.7±3.23	468.8± 32.09	441.8±13.07	444.8±28.51	364.8±12.70	116±7.39
Group E	99.5±0.84	473±28.00	449.3±19.05	467±17.80	389±14.60	235±45.00
Group F	100±3.63	459.5±32.00	466±22.82	422.5±13.56	353±14.60	76.0±14.63
Group G	97.3±1.80	103±2.08	100±5.60	102.3±5.60	105±4.21	109±3.38

Table showing the effects of ALELT on fasting blood glucose level before induction, 1st , 2nd, 4th , 6th week of induction and 3rd week post treatment of STZ-induced diabetic rat .

Fig.3. shows that effects of ALELT on SOD concentration of STZ- induced diabetic rats

Normal control group A was significantly different from group B ($p < 0.001$) and E ($p < 0.01$), and group E was significantly different from G ($p < 0.05$). Superoxide dismutase level was brought down in the STZ-control group compared with other treated groups.

Fig.4. showing Effects of ALELT on catalase activities

Group A was significantly different from B ($p < 0.001$), E ($p < 0.05$), group B was significantly different from C ($p < 0.05$), D ($p < 0.01$) and G ($p < 0.001$), group E was significantly different from G ($p < 0.05$)

Fig.5. showing effects of ALELT on insulin activities

Group A was significantly different compared with B ($p < 0.01$), and group B was significantly different from C, D, F and G ($p < 0.001$). Group E was significantly different compared with group F ($p < 0.01$) and group G ($p < 0.05$).

Fig.6. showing effect of ALELT on BDNF activities in STZ-induced-diabetic rats

Group A was significantly different to B ($P < 0.001$), C ($p < 0.05$), E ($p < 0.001$) and F ($p < 0.05$). B was significantly different from C, D, F, and G ($P < 0.001$), and group D was significantly different compared to E (0.01) and G ($P < 0.001$).

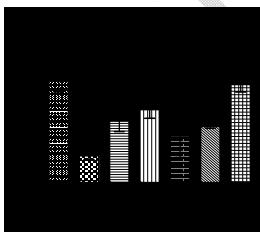


Fig.3. Effects of ALELT on SOD concentration of STZ-induced diabetic rats

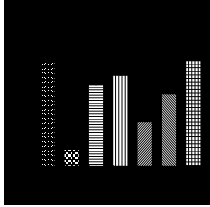


Fig.4. : Effects of ALELT on catalase activities

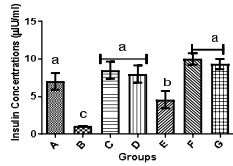


Fig.5. Effects of ALELT on insulin activities

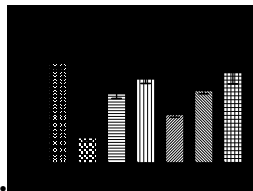


Fig.6. Effect of ALELT on BDNF activities in STZ-induced diabetic rats

Fig.7. showing effects of ALELT on total neuronal density of CA 1 in STZ- induced diabetic rats

Group A was at variance compared with B ($P < 0.001$), C ($P < 0.05$), E ($p < 0.001$), and F ($p < 0.05$). Group B was significantly different from C, D, F, G with ($p < 0.001$), D was statistically significant from E and G ($p < 0.01$)

Fig.8. showing effects of ALELT on total neuronal density of CornusAmmonis 2 (CA2) in diabetic rats

Group A was significantly different from B and E with the P value ($P < 0.001$), B was significantly noteworthy to C, D, E, F and G ($p < 0.001$) and E was at variance from G ($P < 0.001$)

Fig.9. showing effects of ALELT on total neuronal density of CA3 neurons in diabetic rats

Group A was at variance from B ($p < 0.001$), C ($p < 0.05$), E ($p < 0.001$) and F ($p < 0.01$). Group B was statistically significant from C, D ($p < 0.001$) E ($p < 0.01$), F ($p < 0.001$) and G ($p < 0.001$). Group D was significantly different from E ($p < 0.05$), and G ($p < 0.01$), E was significantly different from G ($p < 0.05$).

Fig.10. showing effects of ALELT of total neuronal density of dentate gyrus in STZ- induced rats

Group A was at variance from B, C, D, E, F and G ($p < 0.001$). Group B was significantly different from, C, D, E, F and G ($p < 0.001$), C was at variance from G ($p < 0.05$), D was statistically noteworthy compared to G ($p < 0.01$), group E was significant different from G ($p < 0.001$) and F was at variance from G ($P < 0.001$)

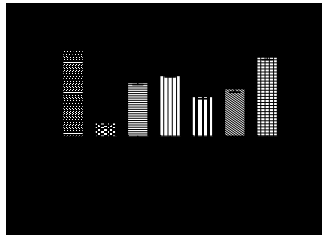


Fig.7. Effects of ALELT on total neuronal density of CA 1 in STZ- induced diabetic rats

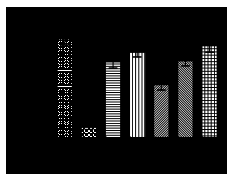


Fig.8. Effects of ALELT on total neuronal density of CornusAmmonis 2 (CA2) in diabetic rats

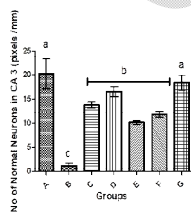


Fig.9. Effects of ALELT on total neuronal density of CA3 neurons in diabetic rats

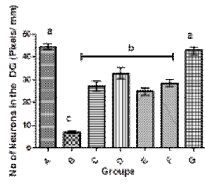


Fig.10. Effects of ALELT of total neuronal density of Dentate Gyrus in STZ- induced rats

Plate 1: Effects of ALELT on general histoarchitecture of CA1

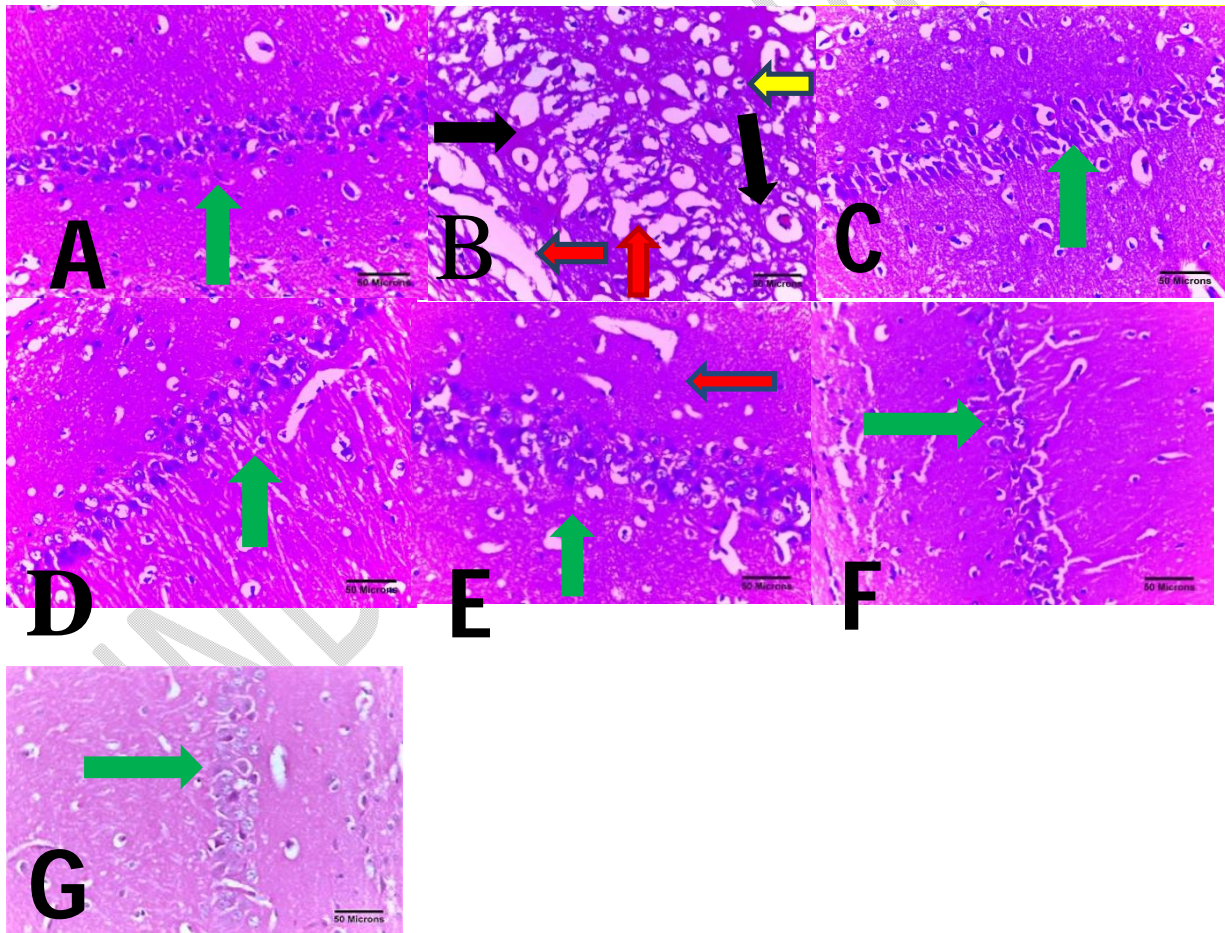


Plate 1 showing Selected photomicrographs of CA1 region of hippocampus of the A, B, C, D, E, F, and G. The red arrow identifies the damage area, the black arrow identifies eosinophilic necrosis, the yellow arrow identifies pyknotic nucleus amid associated vacuolations. By contrast, the green arrow identifies relatively normal neurons, and the blue arrow identifies myelin sheath. H & E \times 400. (Scale bar 50 μ m)

Plate 2: GENERAL HISTOARCHITECTURE OF CA2 IN DIABETIC RATS.

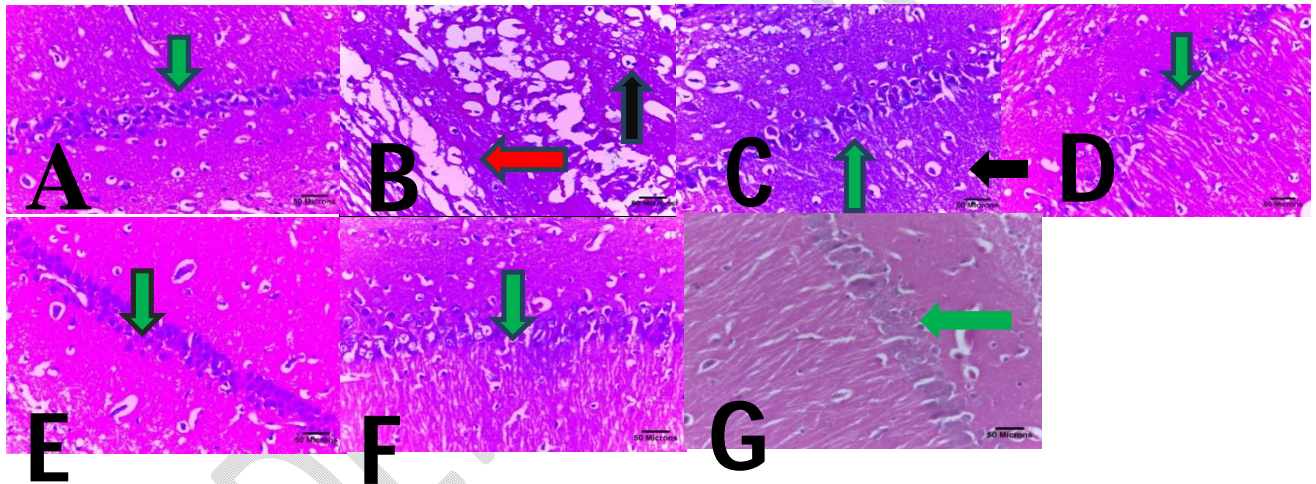


Plate 2 describe Selected photomicrographs of the CA2 region of hippocampus of group A, B, C, D, E, F, and G. The black arrow identifies eosinophilic necrosis, the red arrow identifies pyknotic nucleus amid associated vacuolations. By contrast, the green arrow identifies relatively normal neurons, and the red arrow identifies basophilic-substance in the cytoplasm. H&E \times 400. Scale bar 50 μ m).

Plate 3: EFFECTS OF ALELT ON GENERAL HISTOARCHITECTURE OF CA3.

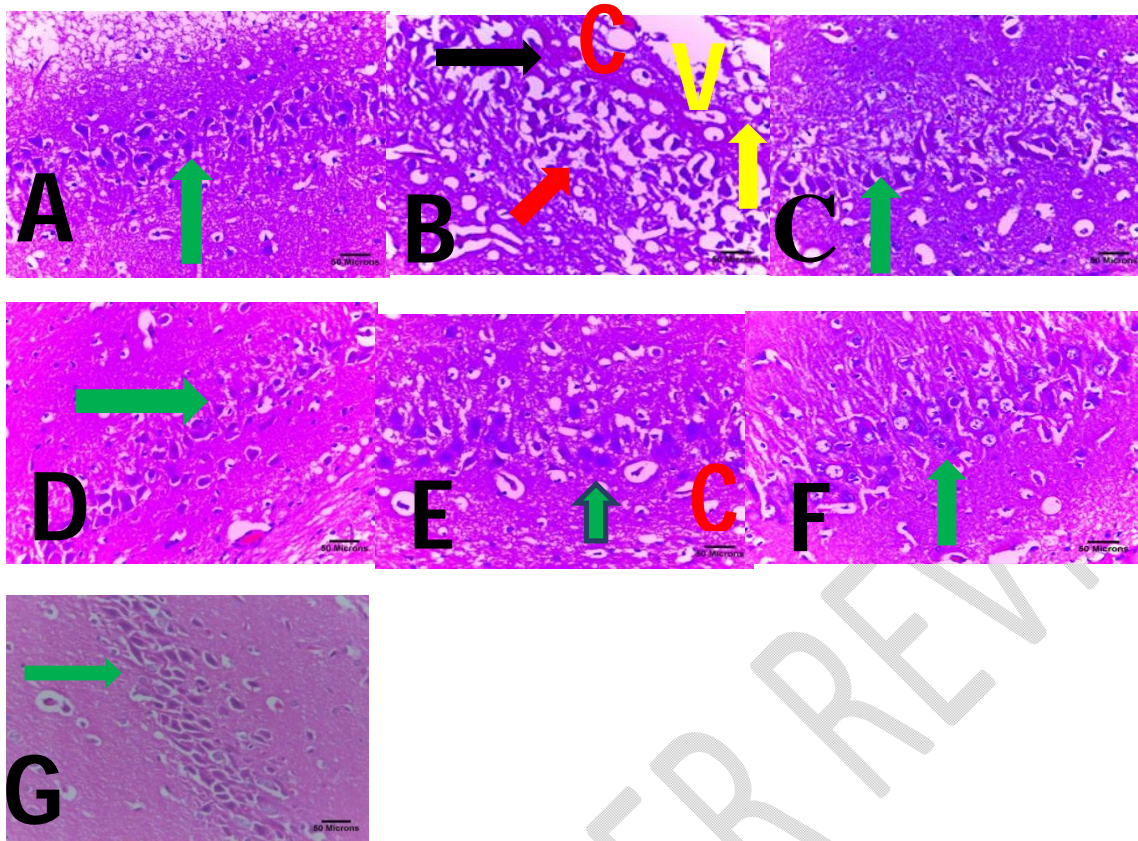
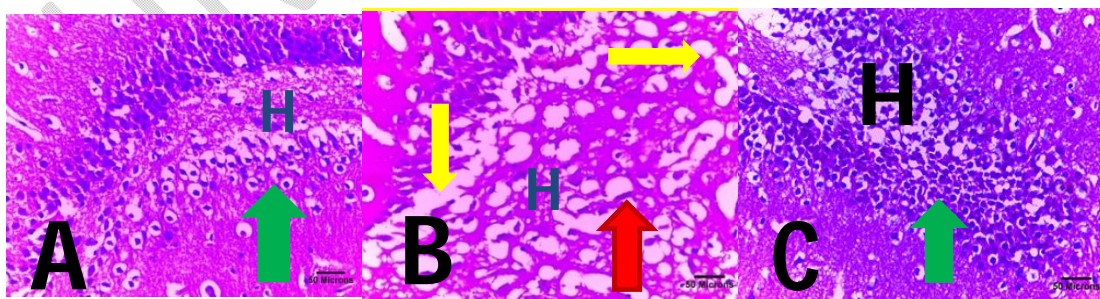


Plate 3 shows that photomicrographs of CA3 region of hippocampus of group A, B, C, D, E, F, and G. The black arrow identifies eosinophilic necrosis, the yellow arrow identifies pyknotic nucleus amid associated vacuolations (V) and total chromatolysis connoted with red C. By contrast, the green arrow identifies relatively normal neurons, and the red arrow identifies basophilic-substance. (H &E \times 400, Scale bar 50 μ m).

Plate 4: GENERAL HISTOARCHITECTURE OF DENTATE GYRUS



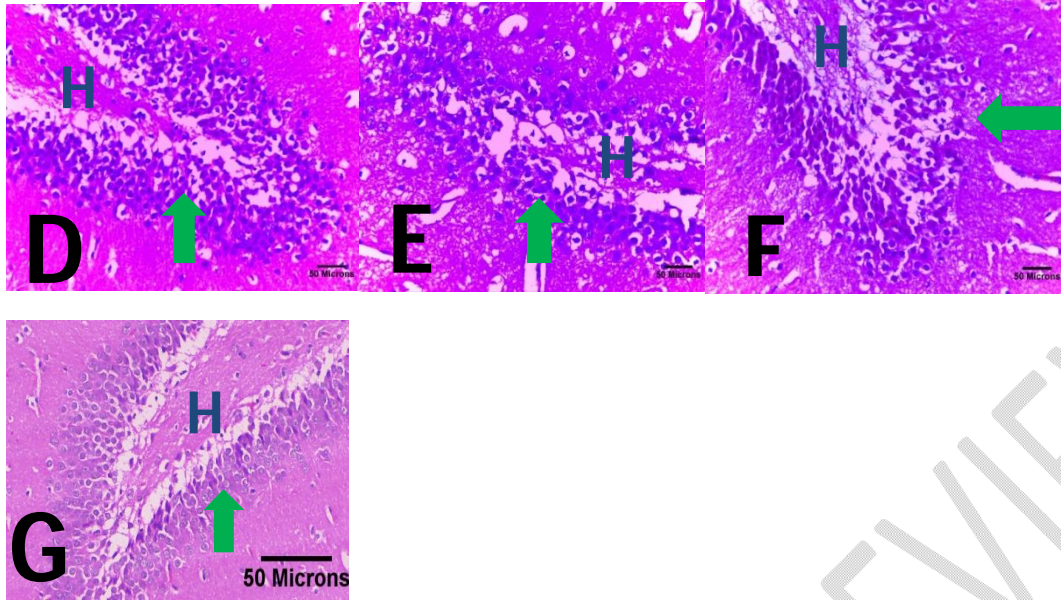


Plate 4 describe Selected photomicrographs of the DG region of the hippocampus of A, B, C, D, E, F, and G. The red arrow identifies eosinophilic necrosis, and the yellow arrow identifies pyknotic nucleus amid associated vacuolations. By contrast, the green arrow identifies relatively normal granular neurons. Group (A) showed numerous neuronal granular cells indicated with green which are well aligned on the Dentate Gyrus (DG) with preserved density and preserved hilum of the DG. Group (B) showed loss of neuronal density, loss of hilum of the DG vacuolations, neuronal dispersal, neuronal atrophy, presence of eosinophilic necrotic cells and chromatolysis. Group (C) showed restored neuronal density, preserved DG hilum, numerous granular cells were restored. Group (D) showed preserved granular cells indicated with blue arrow, restored neuronal density and preserved hilum of the Dentate Gyrus(H). Group (E) showed some levels of recovery with preserved hilum of the DG amidst vacuolations. Group (F) showed restored neuronal density with preserved hilum of the dentate gyrus. Group (G) showed preserved granular cells and hilum of the DG. H&E $\times 400$ (Scale bar 50 μ m).

Plate5: EFFECTS OF ALELT ON MYELIN SHEATH CONTENT IN CA1

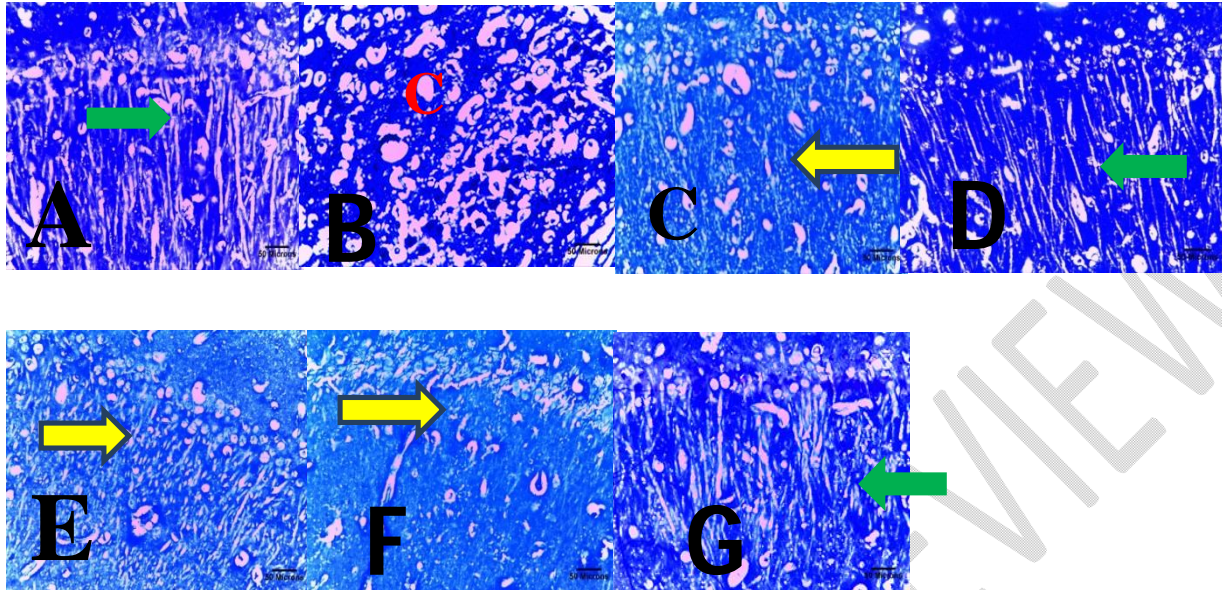
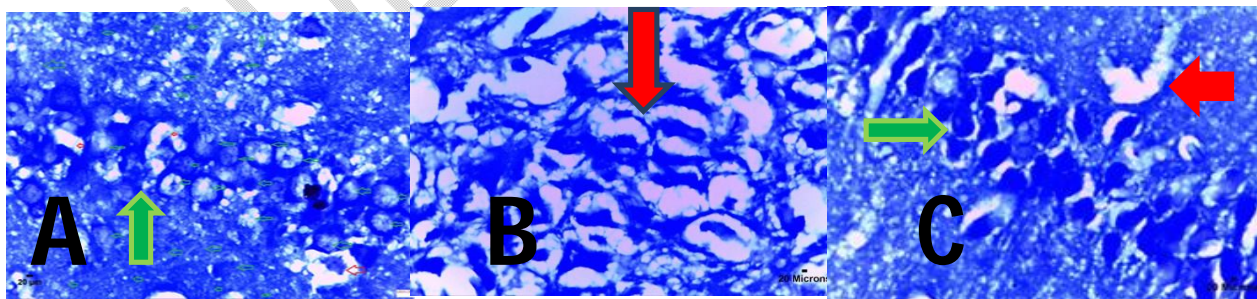


Plate 5: Selected photomicrographs of the CA1 region of the hippocampus of groups A, B, C, D, E, F, and G. The red arrow identifies pyknotic nucleus amid associated vacuolations and demyelination. The red circle identifies the fibrous scar and area of total chromatolysis. By contrast, the green arrow identifies relatively normal neurons and strands of myelin sheath while the yellow arrow shows some level of recovery from demyelination. LFB $\times 1000$. Scale bar $20\mu\text{m}$.

Plate 6. EFFECTS OF ALELT ON NISSL SUBSTANCE CONTENT OF CORNU AMMONIS 1



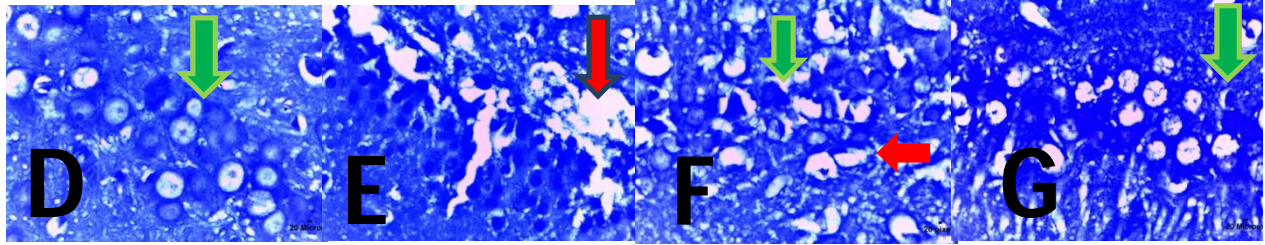


Plate 6 describe Selected photomicrographs of the CA1 region of the hippocampus of groups A, B, C, D, E, F, and G. The red arrow identifies degenerated neurons amid associated vacuolations. By contrast, the green arrow identifies relatively normal neuron nissl body in Cresyl Fast Violet $\times 1000$ staining (Scale bar $20\mu\text{m}$).

Discussion

It has been suggested that the development of diabetes-related problems began with the mitochondrial generation of free radicals triggered by hyperglycemia (Bolzán *et al.*, 2018). Numerous diabetes-related pathophysiological issues may start and worsen as a result of a surge in free radical generation and a decrease in antioxidant reactions, according to research conducted on diabetic patients (Zheng *et al.*, 2022). According to Adinortey and colleagues, *Launaea taraxacifolia* contains useful quantities of minerals and phytochemicals like calcium, iron, magnesium, potassium, flavonoids, terpenoids, tannins, and saponins. *Launaea taraxacifolia* effects on blood glucose have been reported by a few researchers (Adinortey *et al.*, 2019). Studies have found that doses as low as 5 g/ kg were extremely safe and tolerable, with no animal deaths reported. In the present study, STZ-induced diabetes caused notable weight loss across the diabetic groups compared with normal control group (A). This may be due to breakdown of tissues proteins in diabetic rats. Hyperglycemic state was confirmed on the 3rd day of induction with fasting glucose ranging from 500mg/ dl and above, at the 6th week of STZ-induction, hyperglycemic state was sustained at 280 mg /dl and above across the diabetic group. This corresponded to the report by (Fagbohun *et al.*, 2020 and Adjei *et al.*, 2022) that diabetes was confirmed on the 3rd

day of STZ induction and was sustained in the diabetic group with blood glucose concentration typically greater than 250mg/dl. A significant decrease in fasting blood glucose was observed in the 200 mg/ kg and 300 mg/ kg body weight doses of ALELT treated groups C and D compared with the non- treated diabetic group B. This may be due to the presence of quercetin in *Launaea taraxacifolia*; a natural flavonoid found abundantly in vegetables and fruits that inhibit gut enzymes, such as alpha-glucosidase, an enzyme found at the borders of the intestinal brush that is essential for transforming complex sugars into glucose for easy absorption as reported by. This corroborated with the report of (Gbadamosi *et al.*, 2020) that ALELT at 300 mg/ kg had greater blood glucose lowering effects when compared with glibenclamide treated group. This reduction was also noted in the insulin treated group F. It was observed that 5 I.U /day of insulin caused excessive fall in glucose level below 70 mg/ dl in group F. This was contrary to (Pinheiro *et al.*, 2022) who considered insulin at 5 IU/ day as efficient for keeping the glycemic levels close to normal in rat. A notable fall in insulin level was observed in the STZ control group (B) compared to normal control group A and the treated group C, D, E, F and G. This may be due to the destruction of beta cells that are responsible for the production of insulin in the pancreatic islet of Langerhans; it may also be as a result of the decrease in glucose level. Image J analysis of photomicrographs stained sectioned (LFB) revealed that there was total distortion of myelin sheath in CA1 in group B, which may be responsible for the inhibition of impulse transmissions in group B compared with group A and the treated group C and D. Shorten and thicken processes of myelin sheath was observed in group E and F, the myelin sheath in group D showed rapid recovery compared to group C, E and F. There was evidence of demyelination in group B and E. This may be the reason for the uncoordinated movement during an open field maze test and the rats of group B took more time in the radial arm maze before they could recognize the baited arm. This corroborated with the findings of Edwards *et al.*, who stated that the relationship between diabetes and depression was reciprocal as

depression was also considered a risk factor for the development of diabetes (Edwards *et al.*, 2023). A very notable novel in this research work is the potential of *Launaea taraxacifolia* being able to restore the hilum of DG which was lost in the STZ-group. The study demonstrated the protective effects of *L. taraxacifolia* against STZ-induced hippocampal damage in diabetic rats, evidenced by improvements in body weight, glucose levels, insulin, BDNF, and oxidative stress markers. The histological analysis corroborated these findings, showing less hippocampal damage in treated groups.

Conclusion

This study concluded that ALELT poses anti-diabetic effects and its extract possibly exerts these effects by reducing fasting blood sugar levels, increased insulin secretion or decreased intestinal glucose absorption. Further studies are warranted to elucidate more on its mechanisms and therapeutic potential.

Ethical Approval

Ethical clearance was granted by the Health Research and Ethics Committee (HREC) of the Institute of Public Health, OAU Ile-Ife, Nigeria (Reference No: IPH/OAU/12/2111).

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Author(s) hereby declare that NO generative AI technologies such as Large Language Models (ChatGPT, COPILOT, etc.) and text-to-image generators have been used during the writing or editing of this manuscript.

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