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Launaea taraxacifolia LEAF PARTITIONS ATTENUATES HYPERGLYCEMIA VIA REDUCTION IN BLOOD GLUCOSE LEVELS, WITH CONCOMITANT UP-REGULATION OF CARBOHYDRATE METABOLIZING ENZYMES

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Abstract

Diabetes mellitus is a metabolic disorder characterized by chronic hyperglycemia and impaired carbohydrate metabolism. *Launaea taraxacifolia*, a traditional medicinal plant, has demonstrated potential antidiabetic properties, but its effects on key carbohydrate-metabolizing enzymes remain unclear. This study investigated the impact of *L. taraxacifolia* leaf solvent partitions on serum glucose levels and carbohydrate-metabolizing enzymes in streptozotocin (STZ)-induced diabetic rats. Thirty-five Wistar male rats were rendered diabetic via a single intraperitoneal injection of STZ (55 mg/kg). The rats were divided into six groups: untreated diabetic controls, diabetic rats treated with standard drugs (metformin and gliclazide), and those treated with 200 or 400 mg/kg of methanol or n-hexane leaf partitions for 7 days. Fasting blood glucose (FBG) and body weight were monitored, and the activities of key carbohydrate-metabolizing enzymes in the serum were analyzed. Renal tissues underwent histopathological examination. Results showed that the diabetic control group had significant hyperglycemia (FBG > 200 mg/dL) and decreased activities of enzymes such as amylase, glut-6-phosphatase, fructose-1,6-phosphatase, glycogen phosphorylase, ATPase, and ENTPase compared to controls. Treatment with *Launaea taraxacifolia* notably ameliorated hyperglycemia, up-regulated enzyme activities closer to normal levels, and reduced renal lesions. Among the treatments, the low dose of methanol and high dose of n-hexane partitions were most effective, demonstrating potent antihyperglycemic effects possibly through modulation of key metabolic enzymes involved in carbohydrate processing. Findings indicated that partitions of *L. taraxacifolia* exhibited potent antihyperglycemic effects in diabetic rats, which could likely be through modulation of key metabolic enzymes involved in carbohydrate processing.

Keywords: Antihyperglycemic, *Launaea taraxacifolia*, Diabetes mellitus, Fasting blood glucose, Streptozotocin.

Introduction

Diabetes mellitus (DM), a chronic metabolic disorder marked by hyperglycemia, affects 8.8% of adults globally, with projections rising to 700 million cases by 2045 (IDF, 2015; Saeedi et al., 2019). Carbohydrate-metabolizing enzymes are key molecular regulators that determine how the body processes, stores, and utilizes glucose. In normal physiology, these enzymes work in harmony to maintain glucose homeostasis by keeping blood sugar levels within a narrow range despite changes in diet, fasting, or stress. In diabetes, dysregulation of these enzymes contributes significantly to persistent hyperglycemia, oxidative stress,

and tissue damage. For instance, higher amylase activity tends to accelerate the breakdown of carbohydrates, leading to a quicker rise in blood glucose after meals. Conversely, reducing amylase activity can slow this process, helping to moderate the surge in blood sugar that typically follows food intake. (Dineshkumar et al, 2010). Moreover, when the enzymes glucose-6-phosphatase and fructose-1, 6-bisphosphatase are excessively active or overexpressed, the liver tends to release more glucose into the bloodstream. This increase in hepatic glucose production is a major factor driving elevated fasting blood sugar levels commonly observed in diabetes (Golden et al., 1979; Zheng et al., 2022). Furthermore, when ATPase activity is diminished, the cell's ability to manage and utilize energy efficiently becomes compromised. This energy imbalance can interfere with insulin's role in facilitating glucose entry into cells, potentially worsening insulin resistance (Vlad & Popa, 2012). Conventional therapies (e.g., insulin, oral hypoglycemics) often cause adverse effects, prompting interest in plant-based alternatives like *Launaea taraxacifolia* ("African lettuce"). Although studies have highlighted the blood sugar-lowering effect and antioxidant potential of *Launaea taraxacifolia*, due to the presence of certain bioactive compounds like flavonoids, saponins, and so on (Adinortey et al., 2018; Gbadamosi et al., 2020), its specific influence on the enzymes responsible for regulating carbohydrate metabolism and maintaining glucose balance remains largely unexplored.

Thus, the current study explores the therapeutic value of methanol and n-hexane fractions of *Launaea taraxacifolia* leave extract on streptozotocin-induced diabetic rat model. The research specifically examines how these extracts influence blood glucose regulation, the activity of key carbohydrate-metabolizing enzymes, and structural changes in kidney tissue.

Materials and Methods

Collection, identification, and preparation of plant materials

Plant Preparation and Partitioning:

Fresh *L. taraxacifolia* leaves were authenticated, air-dried, and powdered. Methanol extraction (72-hour cold maceration) yielded a crude extract. The crude methanol extract of *L. taraxacifolia* was partitioned with n-hexane through continuous stirring and decantation. Both partitions were concentrated using a rotary evaporator (40°C) and vacuum oven (600 mmHg), yielding 7.77 g (methanol) and 8.32 g (n-hexane). These were stored refrigerated (4°C) in airtight containers until use.

Animal Model:

Forty male Wistar rats (150–170 g) were acclimatized for two weeks. Diabetes was induced via streptozotocin (55 mg/kg, i.p., citrate buffer pH 4.5); fasting glucose ≥200 mg/dL confirmed diabetes.

Ethics statement

All experimental procedures were approved and supervised by the University of Ibadan Animal Care and Use Research Ethics Committee (UI-ACUREC) with the approval number UI-ACUREC/075-0821/4. All animal procedures were done in conformity with established principles of institutional guidelines for the Care and Use of Laboratory Animals. Also, the experiment was conducted in compliance with the most recent regulations and standards for the care of laboratory animals (NRC, 2011).

Animals

A total of forty male Wistar rats weighing between 150 and 170 g were procured from the animal house, Department of Physiology, University of Ibadan, Nigeria. The animals were acclimatized for two weeks at the animal house of the Department of Zoology,

University of Ibadan. The rats were kept in well-ventilated cages, free of pathogens, at room temperature (25±2°C) and had free access to standard diet (commercial pellet) and water throughout the experiment.

Induction of diabetes

After overnight fasting, basal blood glucose was measured (Accu-check). Rats (except controls) received 55mg/kg streptozotocin (i.p., in citrate buffer pH 4.5). Five (5) mortalities were recorded after induction with STZ. After 72h, fasting glucose ≥ 200mg/dL confirmed diabetes. Controls received citrate buffer only. Diabetic rats were used for experiments.

Experimental design

Thirty-five diabetic rats were divided into seven groups (n=5): Group 1 (diabetic control), Group 2 (normal control), Group 3 (metformin+gliclazide), Groups 4-5 (methanol partition 200/400 mg/kg), and Groups 6-7 (n-hexane partition 200/400 mg/kg).

Organ collection for biochemical analysis and histopathology

Treatments lasted for seven (7) days with monitoring of body weight and blood glucose levels. After overnight fasting, rats were euthanized by cervical dislocation (Donovan and Brown, 2006). Kidneys were excised post-euthanasia for both biochemical analysis and histopathological studies..

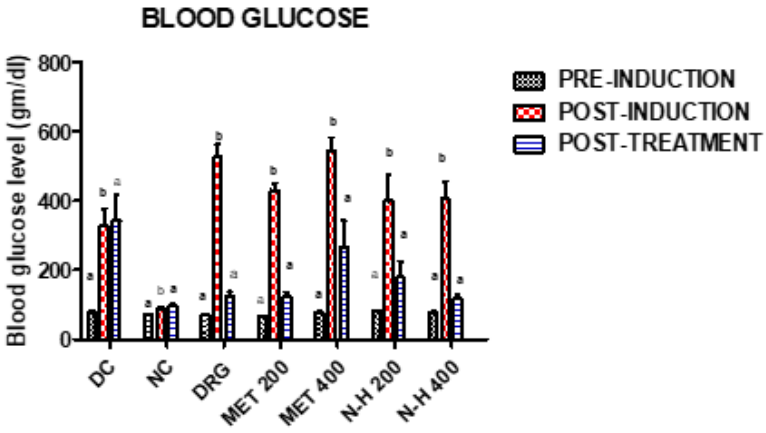
Data analysis

Data were analyzed by one-way ANOVA with Tukey's post-hoc test using GraphPad Prism 7.0 (mean ± SEM; $p<0.05$ significant).

Results

Effects of methanol and n-hexane partitions of *L. taraxacifolia* on blood glucose & body weight:

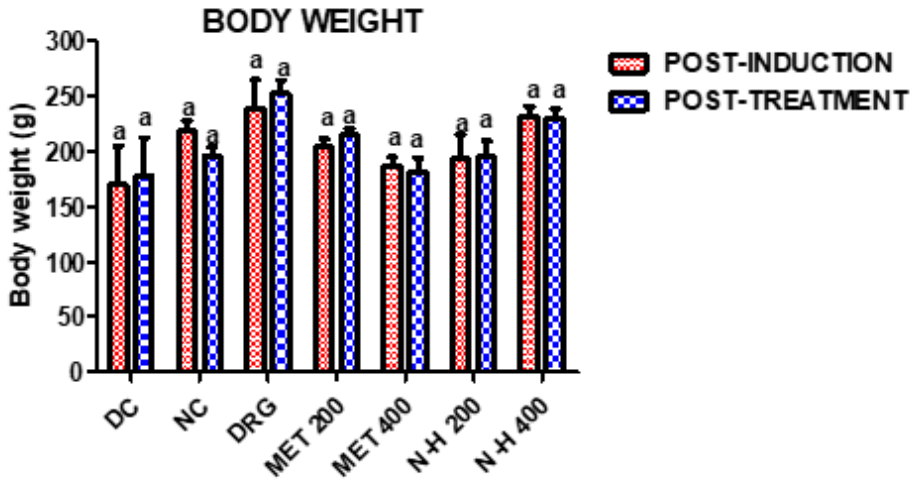
Diabetic rats showed significant hyperglycemia ($p < 0.05$) compared to controls. *L. taraxacifolia* partitions (especially 400 mg/kg n-hexane) reduced glucose levels dose-dependently (Figure 1). No significant weight changes occurred post-treatment (Figure 2).



Bars represent the mean ± SEM (n=5). Bars with different labels are statistically significant at $p < 0.05$.

Figure 1: Blood glucose levels of rats pre-diabetes induction and treatment with partitions of *L. taraxacifolia* leaf.

DC: Diabetes Control (diabetic untreated rats); **NC:** Normal Control; **DRG:** Drug Control; **MET 200**: Methanol 200mg/kg; **MET 400:** Methanol 400mg/kg; **N-H 200**: n-Hexane 200mg/kg; **N-H 400**: n-Hexane 400mg/kg



Bars represent the mean ± SEM (n=5). Bars with different labels are statistically significant at $p < 0.05$. **Figure 2: Body weights of rats at post-induction and post treatment after treatment with different partitions of *L. taraxacifolia* leaf**
DC: Diabetes Control (diabetic untreated rats); **NC:** Normal Control; **DRG:** Drug Control; **MET 200**: Methanol 200mg/kg; **MET 400:** Methanol 400mg/kg; **N-H 200**: n-Hexane 200mg/kg; **N-H 400**: n-Hexane 400mg/kg

Effects of treatment with *L. taraxacifolia* leaf extract and partition on the serum carbohydrate metabolizing enzymes in diabetic rats

Administration of both methanol and n-hexane fractions of *Launaea taraxacifolia* leaf extract led to noticeable enhancement in the activity of several carbohydrate-metabolizing enzymes in diabetic rats. Among the treatment regimens, the 400 mg/kg dose for each fraction demonstrated the most pronounced effects. While the n-hexane extract appeared to be more effective in restoring enzymes linked to nucleotidase function, the methanol extract showed greater influence on ATPase activity and the regulation of fructose-1,6-bisphosphatase.

Table 1 Effects of treatment with *L. taraxacifolia* leaf extract and partition on the serum carbohydrate metabolizing enzymes in diabetic rats

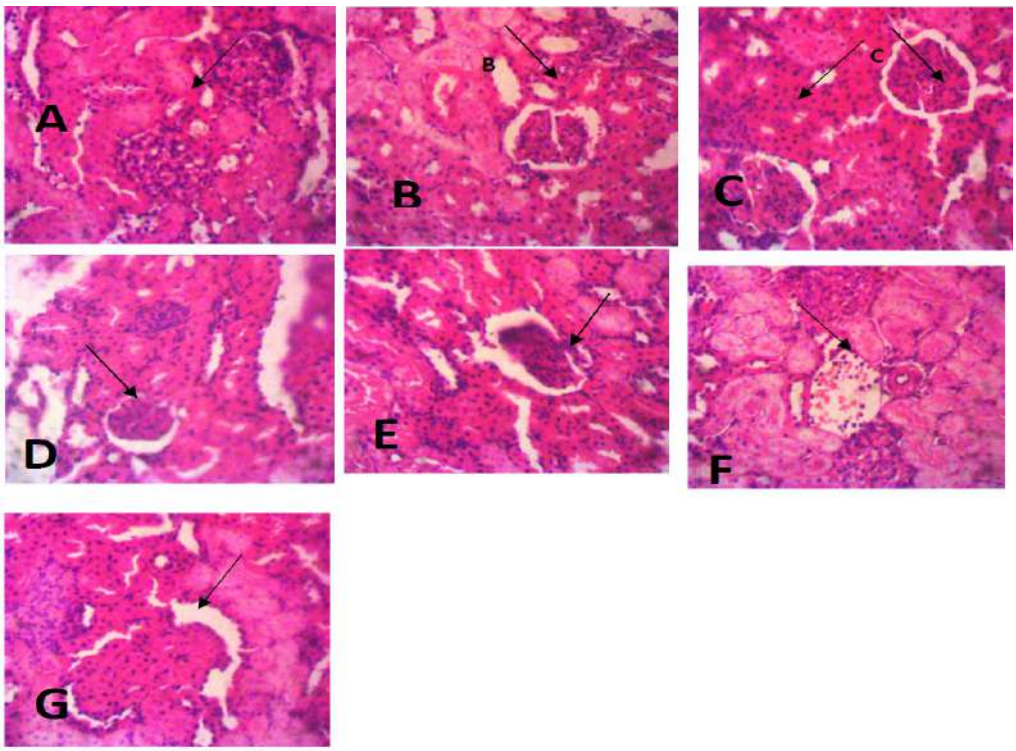
Groups	Amylase	Glu-6-P	Fructose-1,6-P	Glyco P	ATPase	ENTpdase	5' Nucleotidase
NC	2.3227 ± 1.0536^{ab}	2.6910 ± 1.0563	4.4880 ± 2.0283^{c}	4.8278 ± 2.0735^{b}	3.5508 ± 0.0200^{ab}	5.6673 ± 2.0475^{c}	4.6180 ± 1.0176^{b}
DC	2.3142 ± 1.0070^{ab}	3.0237 ± 1.0190	2.5388 ± 1.0327^{a}	2.0213 ± 1.0352^{a}	2.6728 ± 0.0292^{a}	2.8108 ± 1.0117^{a}	2.7118 ± 1.0391^{a}
DRG	2.8172 ± 1.0487^{c}	3.0930 ± 1.4295	3.6035 ± 1.0728^{b}	2.2405 ± 1.3732^{a}	2.6795 ± 0.1034^{a}	2.9185 ± 1.2224^{a}	4.8043 ± 2.1241^{b}
MET 200	2.2743 ± 1.0032^{a}	1.8920 ± 1.1536^{a}	4.2377 ± 2.0507^{c}	4.1558 ± 1.1461^{b}	3.3558 ± 0.0543^{ab}	3.3312 ± 1.0585^{ab}	4.5542 ± 1.0096

MET 400	2.8417 ± 1.0103 ^{c}	2.9367 ± 1.1100	5.5005 ± 1.0421 ^{d}	4.1158 ± 2.0895 ^{b}	4.5930 ± 0.0356 ^{b}	3.9292 ± 1.0636 ^{ab}	4.5992 ± 1.0477 ^{b}
N-H 200	2.5230 ± 1.0906 ^{b}	1.8032 ± 1.1589 ^{a}	4.2013 ± 1.0418 ^{c}	4.1258 ± 1.1555 ^{b}	3.2677 ± 0.0796 ^{ab}	3.2487 ± 1.0580 ^{ab}	4.3277 ± 1.0738 ^{b}
N-H 400	2.6530 ± 1.0922 ^{b}	2.1248 ± 0.9026 ^{b}	5.2582 ± 2.0499 ^{d}	4.5265 ± 1.2345 ^{b}	4.2695 ± 0.0542 ^{b}	4.3735 ± 1.0733 ^{b}	5.3728 ± 1.0745 ^{c}

Values are expressed as mean ± S.E.M. Values along the same column having different superscripts are significantly different ($p < 0.05$), while those without superscripts are not significantly correlated. **NC:** Normal Control; **DC:** Diabetes Control (diabetic untreated rats); **DRG:** Drug Control; **MET 200**: Methanol 200mg/kg; **MET 400:** Methanol 400mg/kg; **N-H 200**: n-Hexane 200mg/kg; **N-H 400**: n-Hexane 400mg/kg

Effect of treatment with *Launaea taraxacifolia* leaf partitions on histopathology of diabetic rats.

Untreated diabetic rats showed severe glomerular/tubular lesions (Figure 4, Plate A). *L. taraxacifolia* treatments (especially 400 mg/kg n-hexane) ameliorated damage, with near-normal kidney morphology (Plates C–G). Mild inflammation persisted in the 200 mg/kg n-hexane group (Plate F).



Hematoxylin and Eosin (H & E); magnification: 400x

Figure 4 (plates A-G): Histopathological examination of the kidney

Plate A (Diabetic untreated rats): Appearance of glomerular and tubular lesions with severe proliferative glomerulopathy and congestion of glomerular capillaries, **Plate B (Normal control):** No observable lesion, **Plate C**

(Diabetic rats/Drugs): No structural defects observed, **Plate D (Diabetic rats/200mg/kg methanol partition):** No structural defects observed, **Plate E (Diabetic rats/400mg/kg methanol partition):** No structural defects observed, **Plate F (Diabetic rats/200mg/kg n-hexane partition):** moderate glomerulonephritis (an inflammation of tiny filters in the kidney) with mesangial hyperplasia, **Plate G (Diabetic rats/400mg/kg n-hexane partition):** No structural defects observed.

Discussion

This study revealed that both methanol and n-hexane partitions of *Launaea taraxacifolia* significantly improved the activities of key carbohydrate-metabolizing enzymes in diabetic rats. Enzymes such as ATPase, amylase, glucose-6-phosphatase, and fructose-1,6-bisphosphatase, typically disrupted in diabetic states, were positively modulated following treatment. Among the tested doses; the 400 mg/kg dose produced the most pronounced results. The methanol extract showed greater enhancement of ATPase and fructose-1,6-bisphosphatase activities, implying better energy utilization and suppression of hepatic glucose production (Golden et al., 1979; Vlad & Popa, 2012). Conversely, the n-hexane extract exerted stronger effects on nucleotidase-linked enzymes, suggesting an influence on purinergic signaling and insulin responsiveness (Lunkes et al., 2004). These results indicate that *L. taraxacifolia* does not merely act as a blood glucose-lowering agent but also contributes to broader metabolic correction via enzyme modulation.

While the present study offers valuable insights, it is not without constraints. The intervention period was limited to just seven days, a choice made to capture the early biochemical and tissue-level changes following *Launaea taraxacifolia* treatment, and to reduce the risk of mortality associated with prolonged hyperglycemia in streptozotocin-induced diabetic rats. This short timeframe allowed for controlled observation of acute effects but prevented evaluation of whether the observed benefits would persist or potentially diminish over the long term. The relatively small sample size per experimental group also represents a limitation. This was primarily due to ethical considerations for animal use and the need to balance statistical power with the principle of reduction in animal experimentation. While the results were consistent enough to detect meaningful differences, a larger cohort would increase the robustness of statistical analyses and improve confidence in the generalizability of the findings.

Conclusion

This study investigates the therapeutic potential of *Launaea taraxacifolia* leaf partitions in managing hyperglycemia. The findings demonstrate that leaf partitions significantly attenuate elevated blood glucose levels by reducing glucose concentrations. Additionally, treatment with *Launaea taraxacifolia* partitions promotes the up-regulation of key carbohydrate-metabolizing enzymes, thereby enhancing glucose utilization and metabolic function. These results suggest that *Launaea taraxacifolia* leaf partitions could serve as a beneficial natural intervention for hyperglycemia management through modulation of glucose homeostasis and enzymatic activity.

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