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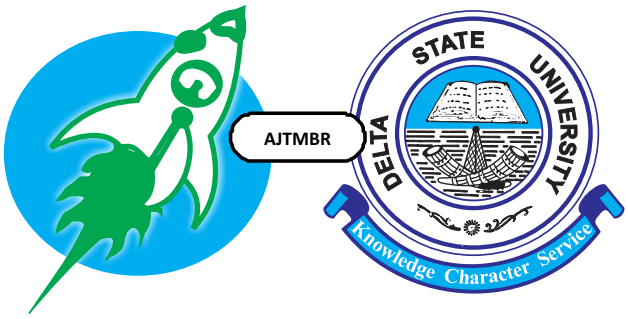

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Focus and Scope

The African Journal of Tropical Medicine and Biomedical Research is a multidisciplinary and international journal published by the College of Health Sciences, Delta State University of Abraka, Nigeria. It provides a forum for Authors working in Africa to share their research findings on all aspects of Tropical Medicine and Biomedical Sciences and to disseminate innovative, relevant and useful information on tropical medicine and biomedical sciences throughout the continent. The journal will publish original research articles, reviews, editorials, commentaries, short reports, case reports and letters to the editor. Articles are welcome in all branches of medicine and dentistry including basic sciences (Anatomy, Biochemistry, Physiology, Pharmacology, Psychology, Nursing etc) and clinical sciences (Internal Medicine, Surgery, Obstetrics and Gynaecology, Dental surgery, Child Health, Laboratory Sciences, Radiology, Community Medicine, etc). Articles are also welcome from social science researchers that document the intermediating and background social factors influencing health in countries of Africa. Priority will be given to publication of articles that describe the application of the principles of primary health care in the prevention and treatment of diseases.

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Original Research- The journal welcomes articles reporting on original research, including both quantitative and qualitative studies. Full-length articles should generally not exceed 3000 words, excluding abstract, tables, figures, and references. The subject matter should be organised under appropriate headings and sub-headings as itemized above.

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Blood Glucose and Hepato-Renal Alterations Following Administration of *Gongronema latifolium* and *Allium sativum* in Diabetic Wistar Rats

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Abstract

Background: *Gongronema latifolium* (GL) and *Allium sativum* (AS) are reported to possess anti-diabetic properties, and preference to its single or concomitant use varies widely.
Objective: The effect of concomitant use of (GL) leaves and (AS) bulb extracts, on the hepato-renal indices of Streptozotocin (STZ) induced hyperglycemic rats was studied.
Materials and methods: Diabetes mellitus was induced by single intraperitoneal dose of (STZ) at 65 mg per kg body weight (bwt) of rats. Thirty female Wistar rats (160 –180 g) were randomly divided into 6 groups of 5 animals each. Groups I and II received 10 mL distilled water per kg bwt and served as normal and diabetic controls [NC and DC] respectively. Group III received Metformin 150 mg per kg bwt of rat, while groups IV, V and VI received 400 mg of AS, GL, and AS + GL extracts per kg body weight respectively. Biochemical analyses were performed after the experimental period of 14 days.
Results: Body weight significantly ($p < 0.05$) increased in animals treated with the extracts compared to DC. Blood glucose levels, aspartate aminotransferase, alanine aminotransferase and alkaline phosphatase concentrations significantly ($p < 0.05$) decreased in the treatment groups, compared to DC. The concentrations of total protein, albumin, sodium, potassium and chloride were significantly increased while urea and creatinine concentrations were significantly decreased when compared to DC.
Conclusion: Extracts of AS and GL singly and in concomitantly use exhibited antihyperglycemic and hepato-renal protective properties, however combined doses outperformed single administration.

Keywords: Diabetes mellitus, *Gongronema latifolium, Allium sativum,* hypoglycaemia

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Introduction

Diabetes mellitus (DM) is a metabolic disorder of several etiology characterized by chronic hyperglycemia, resulting from insulin deficiency, malfunction or even both.[1] Diabetes is a complex, chronic ailment requiring continuous medical care with multifactorial risk-reduction approaches beyond glycemic control.[2] Chronic hyperglycemia of diabetes is accompanied with complications like cardiovascular disorder, neurological complications, hepato-renal disorders, muscular system disorder and eventually premature death.[2] The number of people living with diabetes is expected to surge to 300 million or more in the year 2025.[3] Presently, DM is one of the greatest obvious health threats and its incidence is rising swiftly.[4] This has led to the unremitting concern and investigation for various treatment alternatives available to the repertoire of orthodox medications like Insulin, Glibenclamide, Metformin and many others.[5]

Natural medicine involves the use of organic

product/materials with likely less toxic implications sourced from roots, seeds, pulps, stems, barks, leaves in the control, treatment or management of different ailments and diseases with successes.[6] Polyherbal therapy is the mishmash of two or more plant products in the treatment of a particular ailment.[7] Studies have reported that polyherbal therapy produce enhanced therapeutic efficacy with least side effects.[8] The combination of various types of agents from different plant source could have synergistic, antagonistic, potentiative, pharmacological and therapeutic effects.[8] *G. latifolium* and *A. sativum* have been proven to be extremely nutritional and medicinal.[9-10] They are both antidiabetic plants that have been used traditionally as mixture for the management of the disease. Researches have shown that these plants possess pharmacological and therapeutic effects with numerous bioactive compounds.[11-12]

The hypothesis for this study is that combined ethanol extracts of *G. latifolium* and *A. sativum* moderates/attenuates hepatorenal dysfunction of Streptozotocin-induced diabetic Wistar rats, than single extract components.

Materials and Methods

Collection and Identification of Plant Materials

The leaves of *G. latifolium* and bulbs of *A. sativum* were obtained from Akpan Andem Market, Uyo, Akwa Ibom State in July 2020, and were duly authenticated at the Department of Botany and Ecological study, University of Uyo, Uyo, and specimen voucher numbers UUPH 9(a) and UUPH 44(b) obtained for *G. latifolium* and *A. sativum* samples respectively.

Drug Acquisition

Streptozotocin (300 mg) was obtained from Santa Cruz Biotechnology, Inc., U.S.A. Metformin (Glucophage) was obtained from Merck S. L. Poligono Merck Ltd., Barcelona, Spain. Citrate buffer was obtained from Nanjing Shuguang Silane Chemical Co., Ltd., 5611EH Eindhoven, Netherlands. Normal saline and distilled water were obtained from the laboratory of the Department of Biochemistry, University of Uyo, Nigeria.

Preparation of Plant Extract

Matured leaves of *G. latifolium* and *A. sativum* bulbs were washed with clean tap water. The garlic bulbs were peeled and chopped into smaller pieces. These plants were air dried at room temperature for one week to constant weight. The dried plant materials were ground into powder. Each of the powdered samples (500 g) were macerated in 6000 mL of 90 % ethanol for 24 hours, after which the extracts were filtered through a whatman filter paper (No. 1) and crude extract obtained by evaporation in a water bath (Thermo Fisher Scientific, Germany) at 40 ºC. Crude extracts of *G. latifolium* (78.9 g) and *A. sativum* (58.40 g) were obtained as yields and stored in a refrigerator at about 8 ºC.

Experimental Animals

Thirty healthy female Wistar rats weighing between 160 – 180 g were obtained from the Animal House, Faculty of Basic Medical Sciences, University of Uyo, Uyo, Nigeria. The animals were allowed to acclimatize for 2 weeks, before the commencement of the research.

Experimental condition:

They animals were kept in spacious wooden caged under 12 hour light and dark cycle 6:30 am to 6:30 pm, 5 rats were allotted in 6 cages of size 30 cm length, 25 cm width and 15 cm height with clean beddings changed daily. The rats were provided with normal rat feed (Vital® feed, Oyo state, Nigeria) and clean water *ad*

libitum. All experimental protocol were assessed and approved by the Faculty of Basic Medical Sciences Ethical/Research Committee, University of Uyo, Nigeria and followed the Guide for the Care and Use of Laboratory Animals. [13]

Induction of Diabetes and inclusion Criteria

Diabetes was induced by single intraperitoneal dose of Streptozotocin (STZ) (Sigma Aldrich, Germany) at 65 mg/kg b.w of rats, dissolved in 0.1 mL fresh cold citrate buffer pH 4.5 into 12h fasted rats. On the 3rd day post-induction, the rats were fasted for 6 h and blood glucose determined using an On-call-plus glucometer® (Viva Check Laboratories, USA).[12] They rats were alloted selected into 6 groups of 5 rats each and grouped as shown.

Group I: Normal control, (NC) received normal rat diet and 10 mL distilled water per kg bwt.

Group II: Negative control, (DC) received normal rat diet and 10 mL distilled water per kg bwt.

Group III: Diabetic + Metformin 150 mg per kg bwt of rats.

Group IV: Diabetic + 400mg *A. Sativum* (AS) extract per kg bwt of rats

Group V: Diabetic + 400 mg*G. latifolium* (GL) extract per kg bwt of rats

Group VI: Diabetic + 200 mg AS + 200 mg GL extracts per kg bwt of rats Administration were performed via oral route using an oral-gauge cannula, and lasted for 14 days.

Phytochemical Screening

The method as described by Trease GE, Evans WC [14] was used in the qualitative screening of the extracts of *G. latifolium* and *A. sativum*

Acute Toxicity Studies

The modified Lorke D.A[15] method was used in the oral toxicity studies of the extracts of GL and AS respectively. Increasing doses of extracts 10 to 5000 mg per kg bwt of swiss mice was investigated for behavioural changes such as writhing, motor dysfunction, a version to feed and water, and mortality within 24 hours.

Body and Organ Weights

The body weights of rats were recorded on a 3 days interval using a digital balance (Reptech, India), while the organ weight was recorded at the end of the study, using an electronic balance (Reptech, India).

Determination of Blood Glucose Concentration

The concentrations of blood glucose in the Wistar rats were determined with On-call-plus glucometer® (Viva Check Laboratories, USA) using strip method.[16] A drop of blood was collected from the tip of the tail of the rats after cutting it with a pair of scissors. The blood was then dropped at one end of the strip on the glucometer. After ten seconds the reading was taken.

Biochemical assays

Alkaline phosphatase (ALP), alanine transaminase (ALT), aspartate transaminase (AST), total bilirubin, albumin, urea, creatinine, Na^+, K^+ and Cl^- concentrations in serum of rats were evaluated using assay kits (Randox Laboratories LTD. United Kingdom).

Statistical Analysis

The data were analysed by one-way ANOVA, using SPSS statistical package. All data were expressed as Mean ± SEM and difference between groups considered significant at ($p < 0.05$.

Results

Phytochemical Analysis of Ethanol extracts of *G. latifolium* **Leaves and** *A. sativum* **Bulb**

A total of 11 phytochemical components were screened for in the leaves of *G. latifolium* and *A. sativum* bulb. Alkaloids and saponins concentrations were higher in *G. latifolium* compared to *A. sativum*. While glycoside was present in *A. sativum* and absent in *G. latifolium*. Similarly, carbohydrate and terpenoids concentrations in *G. latifolium* were higher when compared to *A. sativum*. Protein and steroid concentrations were higher in *A. sativum* when compared to *G. latifolium*. Finally anthraquinones was higher in *G. latifolium* and absent in *A. sativum,* while flavonoids and cardiac glycosides had similar concentrations in both *G. latifolium* and *A. sativum* (Table 1).

Effect of *G. latifolium* **and** *A. sativum* **on Median Lethal Dose Determination**

No behavioral changes such as alertness, breathlessness, restlessness, diarrhoea, convulsion and coma were observed at the administered doses during the acute toxicity testing. The Swiss Mice were physically active and no death was recorded upon the oral administration of extracts up to a dose of 5000 mg/kg body weight. At this point, the process was discontinued and the median lethal dose of the ethanol leaf extract of *G. latifolium* and *A. sativum* was estimated to be over 5000 mg/kg body weight (Table 2).

Effect of *G. latifolium, A. sativum* **and their Combination on Body, Liver and Kidney weight of Diabetic and Non-diabetic Rats**

Induction of diabetes mellitus led to drastic loss of body weight of rats during 14 days of experiment. There was no significant ($p > 0.05$) difference between the body weights of animals in all groups at the beginning of the experiment (170.40 ± 0.51 to 186.80 ± 1.62 g). Following treatment, groups on Metformin, extracts (AS and GL) and normal control gained weight significantly ($p < 0.05$) compared to DC group. Initial body weight of treatment groups range from (170.40 ± 0.51 to 180.20 ± 0.49 g), final weight on day 14 of experiment was (179.60 ± 1.44 to188.20 ± 0.58 g) (Table 3).

Liver weight of DC (8.97 ± 0.26 g) increased significantly ($p < 0.05$) compared to the NC (7.32 ± 0.13 g). Liver weight of all diabetic treatments were significantly lower (6.83 ± 0.48, 7.23 ± 0.07, 7.29 ± 0.21 and 6.87 ± 0.31 g) compared to DC (8.97 ± 0.26 g) (Table 3).There was a significant ($p<0.05$) increase in the kidney weights of DC (0.79 ± 0.07) compared to the normal control (0.66 ± 0.03), and the treatment groups (0.65 ± 0.05, 0.69 ± 0.04, 0.67 ± 0.03, and 0.63 ± 0.04) respectively.

Effect of *G. latifolium, A. Sativum* **and their Combination on Blood Glucose Concentration of Diabetic and Non-diabetic Rats**

Blood glucose concentrations of rats were monitored every 3 days following daily treatment with extracts (AS and GL) and Metformin. Induction of diabetes led to significant ($p < 0.05$) increase in blood glucose concentration (325.40to 339.60 mg/dL) in diabetic groups compared to the non-diabetic rats (71.80mg/dL). The blood glucose concentrations of the untreated rats

were high (325.40to 398.20mg/dL) throughout the duration of the experiment compared to the NC and extracts treated groups. Diabetic treatment with Metformin and the different extract groups led to a significant ($p < 0.05$) decrease in blood glucose concentration (331.40 - 155.40 mg/dL), (330.00- 171.00 mg/dL), (328.40-168.40 mg/dL) respectively. Group VI, shows a significant decrease in the blood glucose concentration (339.60- 146.00 mg/dL) when compared to other treatment groups (Table 4).

Effect of G. latifolium, A. Sativum and Their Combination on Liver Enzymes of Diabetic and Non-diabetic Rats

Serum AST, ALT and ALP concentrations were raised significantly ($p < 0.05$) in the DC group (113.20 ± 3.81, 44.80 ± 3.71 and 74.40 ± 4.95) respectively when compared to NC (79.40 ± 0.51, 29.40 ± 0.68 and 45.20 ± 1.39). Singly administered extracts significantly ($p < 0.05$) decreased the activities of AST, ALT and ALP when compared to DC group. However, combined extract treated group improved the activities of AST, ALT and ALP more significantly ($p < 0.05$) compared to groups III, IV and V (Table 5).

Table 1: Phytochemical Constituents of Ethanol Extracts of *G. latifolium* leaves and *A. sativum* bulb

Chemical constituents	*Gongronema latifolium*	*Allium sativum*
Alkaloids	+++	++
Flavonoids	+	+
Saponins	++	+
Glycosides	-	+
Carbohydrates	++	+
Protein	++	+++
Steroids	-	++
Anthraquinones	++	-
Tannins	+	+
Terpenoids	+++	++
Cardiac glycosides	++	++

-, not present;
+, present in small concentration;
++, present in moderately high concentration;
+++, present in high concentration;

Table 2: Median lethal dose of ethanol extracts of *G. latifolium, A. sativum* and combined administered orally

Groups (n=3)	Dose of AS (mg/kg)	Dose of GL (mg/kg)	Dose of AS+GL (mg/kg)	Mice mortality
1	10	10	10	None
2	100	100	100	None
3	1000	1000	1000	None
4	1600	1600	1600	None
5	2900	2900	2900	None
6	5000	5000	5000	None

Table 3: Effect of *G. latifolium, A. Sativum* and their combination on body weights of diabetic and non-diabetic rats

Groups	Before Induction (g)	Day 0 (g)	Day 3 (g)	Day 6 (g)	Day 9 (g)	Day 12 (g)	Day 14(g)
I (NC)	185.40 ± 1.33	188.20 ± 1.16	190.00 ± 0.45	194.20 ± 1.59	196.80 ± 0.66	200.80 ± 0.58	201.00 ± 1.05
II (DC)	186.80 ± 1.62	186.80 ± 1.07	185.00 ± 0.84	181.00 ± 0.81	179.20 ± 0.58[a]	178.00 ± 1.10[a]	175.60 ± 068[a]
III (Met)	178.00 ± 1.38	176.40 ± 0.93	177.80 ± 1.36	180.00 ± 1.14	181.00 ± 1.05	182.40 ± 1.03	183.80 ± 0.92[b]
IV (AS)	180.20 ± 0.49	178.00 ± 1.26	181.00 ± 0.63	183.40 ± 1.20	184.60 ± 0.81	188.40 ± 1.21b	188.20 ± 0.58[b]
V (GL)	170.40 ± 0.51	168.40 ± 1.03	169.80 ± 0.49	172.60 ± 0.81	174.80 ± 0.80	179.20 ± 1.24	183.00 ± 1.26[b]
VI (AS+GL)	172.40 ± 1.33	170.40 ± 0.81	171.60 ± 1.21	174.40 ± 0.51	178.40 ± 0.24	177.20 ± 0.86	179.60 ± 1.44[b]

Table 3b: Liver and Kidney weights of diabetic and non-diabetic rats

Groups	Liver (g)	Kidney (g)
I (NC)	7.32 ± 0.13	0.66 ± 0.03
II (DC)	8.97 ± 0.26[a]	0.79 ± 0.07[a]
III (Met)	6.83 ± 0.48[b]	0.65 ± 0.05[b]
IV (AS)	7.23 ± 0.07[b]	0.69 ± 0.04[b]
V (GL)	7.29 ± 0.21[b]	0.67 ± 0.03[b]
VI (AS+GL)	6.87 ± 0.31[bde]	0.63 ± 0.04[bde]

[a] = significantly different from group I ($p < 0.05$)
[b] = significantly different from group II ($p < 0.05$)
[c] = significantly different from group III ($p < 0.05$)
[d] = significantly different from group IV ($p < 0.05$)
[e] = significantly different from group V ($p < 0.05$)

Table 4: Effects of *G. latifolium, A. sativum* and their combination on blood glucose concentrations of diabetic and non-diabetic rats

Group	Before Induction (mg/dL)	Day 0 (mg/dL)	Day 3 (mg/dL)	Day 6 (mg/dL)	Day 9 (mg/dL)	Day 12 (mg/dL)	Day 14 (mg/dL)
I (NC)	70.40 ± 0.81	71.80 ± 0.93	70.40 ± 1.08	88.80 ± 1.07	74.20 ± 1.16	76.80 ± 0.97	71.60 ± 1.75
II (DC)	75.60 ± 1.21	325.40 ± 3.36[a]	325.20 ± 2.24[a]	335.40 ± 0.68[a]	333.80 ± 1.24[a]	351.20 ± 0.58[a]	398.20 ± 1.36[a]
III (Met)	73.60 ± 1.47	331.40 ± 3.67[a]	321.40 ± 1.75[a]	297.40 ± 1.91[a,b]	266.40 ± 1.03[a,b]	200.20 ± 2.63[a,b]	155.40 ± 0.51[a,b]
IV (AS)	76.80 ± 1.07	330.00 ± 2.44[a]	312.60 ± 1.47[a]	277.00 ± 0.77[a,b]	251.60 ± 1.69[a,b]	187.08 ± 1.39[a,b]	171.00 ± 3.69[a,b]
V (GL)	71.40 ± 0.51	328.40 ± 3.25[a]	321.20 ± 0.97[a]	296.80 ± 0.80[a,b,d]	269.20 ± 0.97[a,b,d]	172.20 ± 1.32[a,b,c]	168.40 ± 1.47[a,b]
VI (AS+GL)	74.20 ± 2.13	339.60 ± 2.18[a]	327.00 ± 1.34[a]	287.00 ± 1.14[a,b,d,e]	246.20 ± 0.86[a,b,c,d,e]	190.00 ± 2.56[a,b,c,d,e]	146.00 ± 1.26[a,b,d,e]

[a] = significantly different from group I ($p < 0.05$)
[b] = significantly different from group II ($p < 0.05$)
[c] = significantly different from group III ($p < 0.05$)
[d] = significantly different from group IV ($p < 0.05$)
[e] = significantly different from group V ($p < 0.05$)

Table 5: Effects of *G. latifolium, A. sativum* and their combination on liver enzymes of diabetic and non-diabetic rats

Groups	AST(U/L)	ALT (UL)	ALP (U/L)
I (NC)	79.40 ± 0.51	29.40 ± 0.68	45.20 ± 1.39
II (DC)	113.20 ± 3.81[a]	44.80 ± 3.71[a]	74.40 ± 4.95[a]
III (Met)	90.40 ± 4.19[b]	27.20 ± 3.73[b]	53.80 ± 4.81[b]
IV (AS)	99.00 ± 0.84[b]	37.20 ± 1.32[b]	59.60 ± 1.96[b]
V (GL)	93.80 ± 1.69[b]	35.60 ± 1.69[b]	58.00 ± 1.30[b]
VI (AS + GL)	83.67 ± 0.70[b,c,d,e]	29.00 ± 1.00[b,d,e]	45.33 ± 0.33[b,c,d,e]

[a] = significantly different from group I ($p < 0.05$)
[b] = significantly different from group II ($p < 0.05$)
[c] = significantly different from group III ($p < 0.05$)
[d] = significantly different from group IV ($p < 0.05$)
[e] = significantly different from group V ($p < 0.05$)

Table 6: Effect of *G. latifolium, A. sativum* and their combination on renal enzymes of diabetic and non-diabetic rats

Group	Total protein (g/dL)	Albumin (g/dL)	Urea (mmol/L)	Creatinine (mmol/L)	Na^+ (mmol/L)	K^+ (mmol/L)	Cl^- (mmol/L)
I (NC)	64.20 ± 0.73	38.20 ± 0.58	4.38 ± 0.19	68.38 ± 0.19	141.58 ± 1.01	6.64 ± 0.11	95.66 ± 0.45
II (DC)	49.40 ± 0.68[a]	22.00 ± 0.89[a]	7.28 ± 0.34[a]	85.40 ± 4.37[a]	123.70 ± 3.66[a]	4.04 ± 0.25[a]	87.10 ± 1.81
III (Met)	60.60 ± 1.91[b]	37.40 ± 0.75[b]	5.12 ± 0.51[b]	72.00 ± 3.79[b]	145.36 ± 3.11[b]	6.24 ± 0.45[b]	92.30 ± 1.63
IV (AS)	54.20 ± 1.56[b]	34.80 ± 0.80[b]	5.58 ± 0.20[b]	75.00 ± 1.38[b]	135.70 ± 2.91[b]	6.94 ± 0.23[b]	98.16 ± 1.81[b]
V (GL)	58.40 ± 1.14[b]	32.60 ± 0.24[b]	5.71 ± 0.30[b]	74.60 ± 1.08[b]	132.58 ± 0.83[b]	6.66 ± 0.28[b]	95.90 ± 1.86
VI (AS+GL)	61.33 ± 0.50[b]	38.00 ± 0.58[b,e]	4.21 ± 0.54[b,c,d,e]	71.80 ± 0.58[b]	142.43 ± 0.80[b,d,e]	6.43 ± 0.48[b]	94.63 ± 1.39

[a] = significantly different from group I ($p < 0.05$)
[b] = significantly different from group II ($p < 0.05$)
[c] = significantly different from group III ($p < 0.05$)
[d] = significantly different from group IV ($p < 0.05$)
[e] = significantly different from group V ($p < 0.05$)

Discussion

The medicinal potentials of plants lie in its bioactive phytochemical constituents that elicit physiological response in the human body.[17] The Phytochemical analysis of the plant extracts of AS and GL revealed the presence of tannins, flavonoids, saponins, terpenoids, cardiac glycosides and alkaloids, which are known to exhibit pharmacological activities. The therapeutic potentials of plants have been linked with their antioxidant potentials.[18] Flavonoids are potent antioxidants and free radical scavengers that mitigate oxidative cell damage, possess strong anticancer activities, anti-inflammatory activities and defensive against the different degree of carcinogenesis.[19-20] Most plants containing glycosides, alkaloids, terpenoids, flavonoids and carotenoids are also frequently implicated as possessing antidiabetic activities.[21] Tannins is important in the treatment of inflamed or ulcerated tissues, burns, wounds, pneumonia and dysentery, while saponins have antitumor and anti-mutagenic activities by preventing cancer cells from growing.[22] Alkaloids have analgesic and anti-inflammatory effects.[23]

In the acute toxicity study carried out, it was observed that the oral administration of *G. latifolium* and *A. sativum* singly, and in combination did not present any mortality in the test animals even at its highest concentration of 5000 mg/kg that these extracts were safe and non-toxic for use after administering them on the experimental animals up to 5000 mg per kg body weight. They reported on the individual acute toxicity studies of extracts of *G. latifolium* and *A. sativum* respectively.[25] The result of this study indicates that the combined extract is safe and non-toxic, as the acute toxicity test showed an LD_{50} value of greater than 5000 mg per kg body weight of mice, which is also consistent with its popular use.

Streptozotocin induced diabetes is typically characterized by severe loss in body weight, and this reduction is due to degeneration of structural proteins.[26] In this study, the induction of experimental diabetes elicited markedly significant decrease in body weight of rats when compared to NC group. The animals gained weight in the course of treatment with the extract, which may be due to the efficacy of the plant extracts and or benefits from the herb-herb interaction. This result is in agreement with the report of [9] who demonstrated that the combined extracts of *Gongronema latifolium* and *Ocimum gratissimum* were effective in restoring the body weights of experimental animals to normal.

The effects of DM on weight of some internal organs have been reported in many studies. The extracts (GL and AS) and metformin effectively restored the derangement on the organ weight caused by STZ. The result shows that diabetes increases weight of liver and kidney.[9,27] The enlargement of the liver and kidney due to induction of experimental diabetes is due to hepatopathy and nephropathy which causes lesion on the liver and kidney.[28] Treatment with *G. latifolium* and *A. sativum* normalized the weight of liver and kidney. This results support that reduction in the weight of the liver and kidney after treatment with leaf extract as a consequence of the removal of the challenge of hyperglycemia. The result indicates that once hyperglycemia is corrected, there is possibility of subsequent normalization of the weight of the internal organs.

The reduction on the blood sugar concentrations elicited by the combined extract was significantly similar to the reduction in the group treated with Metformin. Though *G. latifolium, A. sativum*

and the combined extracts all proved effective in this study, the combined extract had the maximum capacity to restore blood glucose to near normal concentrations. The hypoglycemic activity of the extracts and composite may be due to its protective action against STZ-mediated damage to the pancreatic ß-cells, and also possibly through regeneration of damaged ß-cells or increased insulin release or secretion.[29] Some of these bioactive compounds (saponins, flavonoids, tannins and alkaloids) are thought to be responsible for the blood glucose lowering activities of these plants.[30] This result is in consonance with reports by [31, 32] who demonstrated the hypoglycemic effect of combined extracts of *Vernonia amygdalina, Ocimum gratissimum* and *Gongronema latifolium*.

The liver is a large, complex organ that plays a central role in biomolecule metabolism.[33] The liver encloses several enzymes within the hepatocytes. Most of the enzymes found in the hepatocytes can be measured in the serum and are used as tests of liver function, such as the aminotransferases.[34] Raised liver enzymes concentration in the blood, may point to inflammation or injury to cells in the liver. Injury to the liver ultimately results in a rise in serum concentrations of aminotransferases.[33] The increase in serum enzyme activities are roughly relative to the degree of tissue harm.[35]

The significant increase in the serum AST, ALT and ALP observed in diabetic rats (Table 5) is consistent with studies by [36], indicating possible liver damage due to STZ mediated action, which may cause leakage of these enzymes from the liver cytosol into the blood.[37] Treatment with *G. latifoium* and *A. sativum* significantly decreased the raised levels of AST, ALT and ALP. The highest reduction was observed in the combined extract treated group, followed by *G. latifoium and A. sativum* treated groups for AST and ALP levels, while *A. sativum* and *G. latifoium* for ALT levels. The decrease in AST, ALT and ALP in rats given the combined extract indicates the possible hepatoprotective effect of the plant extracts. This study confirms reports by[12], who demonstrated the hepatoprotective activity of the extracts on diabetic rats.

The renal system plays a major role in the regulation of electrolyte/fluid balance, the pH buffer system and in the elimination of waste products such as urea and creatinine. When kidney function declines, obviously these processes become impaired.[38] Kidney disease is one of the most common and severe complications of diabetes.[39] Overtime, individuals with diabetes can develop a condition called diabetic nephropathy. Total protein, albumin, creatinine and urea are markers alongside electrolyte balance used in the assessment of kidney functions.[38] One major problem with diabetes is that the amount of glucose in the blood can offset the proportion of serum electrolytes.

Treatment with ethanol extracts of *G. latifoium, A. sativum*, composite and Metformin brought about a significant increase in serum protein and albumin and a decrease in urea concentration of DC. This increase may be as a result of renal dysfunction which results in elevated urea concentration. Decrease of serum protein concentration in diabetic control rats may be due to impaired protein turnover and muscle wasting in diabetic condition. The uncontrolled diabetes is associated with severe muscle wasting.[40] A significant increase in albumin concentration was observed in the composite treated group. This may be due to inhibition of proteolytic activity which enhance insulin secretion and proper

utilization of blood glucose. Similar effect was reported by [41]. Decrease in serum total protein and albumin concentration was also reversed upon the administration of the single and combined extracts as seen in the treatment groups.

Creatinine is a metabolite of muscle creatine, whose amount in serum is proportional to the body's muscle mass. The amount of creatinine is usually constant, as elevated levels indicate diminished renal function, since it is easily excreted by the kidneys. Treatment with combined extracts of G. *latifolium*, A. *sativum*, brought about a significant decrease in the creatinine concentration of diabetic rats to near normal.[38,12]

Sodium, potassium and chloride (Cl-) are essential in maintaining cellular and extracellular homeostasis. They are regulated by the kidney. Most metabolic processes are dependent on, or affected by these electrolytes. Some of the functions of these electrolytes are; maintenance of osmotic pressure and water distribution in various body fluid compartments.[42] Diabetes is characterized by increased volume and metabolites excretions via the kidney, usually in excess of normal thresholds. This usually gives rise to derangement in homeostatic balance with respect to electrolytes.[43] Interestingly the concentrations of these electrolytes were brought to near normal state by treatment with the combined extracts of G. *latifoium* and A. *sativum*. The result of this study shows that the extract treatment has significant improvement in electrolyte imbalance and raised the electrolyte concentrations of diabetic animals to normal compared to the DC group and is in line with the findings.[44]

Conclusion

Oral administration of *A. sativum* and *G. latifolium,* at 400 mg per kg body weight of rats for 14 days, has the potential to restore the altered concentrations of these liver and kidney enzymes and thus modulate diabetic hepatic and renal perturbations. This restoration was observed more in the combined extract than in the single extracts. From the results of this study, it can be concluded that the combined extracts of *A. sativum* and *G. latifolium* possesses better hypoglycemic and hepato-renal protective activities than the individual extracts. Therefore it may be gainful in managing diabetes and its related complications, thus supporting the claim of the local use of the combined extracts of both plants in the treatment of diabetes mellitus.

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Conflicts of Interest

There are no conflicts of interest.

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