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Anti-diuretic and anti-glycemic properties of *Jatropha gossypiifolia* L. leave extract on wistar rats

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Abstract

Background: *Jatropha gossypiifolia* L. is a widespread plant in tropical and sub-tropical countries used in traditional medicine. This study investigated the anti-diuretic and anti-hyperglycemia activities of *J. gossypiifolia* leave extract on streptozotocin-induced diabetic rats.

Methods: The leaves was shade dried, pulverized and prepared into extract. 30, 50 and 100 mg/kg of the leaves extracts of *J. gossypiifolia* was subject to diuretics and hyperglycemic properties using established protocol of diuretic and diabetes test on the rat bladders emptied via mild compression in the pelvic region and gently pulling of their tails. 0.5 ml/kg normal saline, reference drug and the tested were administered with a single dose of the various drugs, and Streptozotocin (STZ) was freshly prepared in 0.1 M citrate buffer with pH 4.5 prior to induction, animals were fasted 24 h and single dose of 45 mg STZ per kg body weight was administered intraperitoneally. Urine and blood samples were isolated from rats and centrifuged for the determination of renal function test. Diuretic and antidiabetic indexes where evaluated using adopted method.

Results: This study showed that, graded doses of the extract significantly increased diuretic effect, specifically at 100 mg/kg increased diuretic index at 4.29 and urine volume 5.06 and 10 mg/kg Hydrochlorothiazide with 6.23 ml when compared untreated group (1.18 ml) ($p < 0.0001$). Also, it regulated renal function in homeostatic state. Graded doses at (30, 50 and 100 mg/kg) of the extract significantly reduced streptozotocine induced increased blood glucose level at day 14 (84.00, 60.67 and 42.00 IU/mL) when compared with 20 mg/kg glibenclamide and diabetics control (81.67 and 463.00 IU/mL) ($p > 0.05$). Also, the extract maintained a normal body mass indexes, biochemical and anatomical structure.

Conclusion: The effect associated with *J. gossypiifolia* potentiated its anti-diuretic and anti-hyperglycemic properties as early stated in the ethnomedicinal reports.

Keywords: *J. gossypiifolia*, Anti-diuretic, Anti-hyperglycemic, Streptozotocin

Introduction

Currently, it is estimated that, approximately 80% of the population in developing countries depend on alternative medicine derived from plants and animals as primary sources of health care. The demand and recognition of herbal medicines is rapidly increasing. Approximately 500 medicinal plants used are stated in primordial literature and about 800 of these plants are implicated in aboriginal system of medicine. Herbal drugs derived from plant materials involve the applications of complete plant parts or fractions of plant parts, to care for ailment or diseases [1]. Alternative medicines is known to be the oldest health care provider recognized by humans and have been used as curative herbs either as prophylaxis or curative drugs against illnesses

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and diseases or to enhance physiological and therapeutic conditions [2].

J. gossypiifolia belongs to the family Euphorbiaceae. The name *Jatropha* is derived from the Greek words jatros, which denotes "doctor" and trophe, means "food." It is known for several therapeutic benefits [3]. *J. gossypiifolia* belongs to the Euphorbiacea's family, usually identified as cotton- leaf, physicnut or black physicnut, bellyache bush and a shrub with distinctive latex, mostly used as medicine [4]. The genus *Jatropha* can be alienated in two (2) sub-genera namely; *J. gossypiifolia* The sub-genus *Jatropha* is an extensive distribution with its species originated from Asia, Africa, Central America, South America, Caribbean and West Indies [5], *J. gossypiifolia* had been broadly used in ethno-medicine for treatment of diverse disorders such as; endocrine diseases, cardiovascular diseases, gastrointestinal diseases and central nervous diseases in alternative medicine using its various parts (leaves, seeds, latex, stems and roots). It is generally known as Bellyache-bush, pignut and wild cassava in English; botuje pupa (Yoruba), ake mbogho (Igbo) [6, 7]. This study is based on evaluating the diuretic and antidiabetic properties of *J. gossypiifolia* in the management of water loading hypertension, hypervolemia and hyperglycemia. In this study, antidiuretic and anti-hyperglycemia activities of *J. gossypiifolia* leave extract on streptozotocin-induced diabetic rats was evaluated.

Diuretics are agents that help to promote the rate of urine outflow. Sodium excretion also helps to regulate urine volume with body fluids composition in clinical cases. Medication that induced diuresis can be valuable to several life threatening disorders like the case of nephritic syndrome, congestive cardiac failure, cirrhosis of the kidney failure, pregnancy toxaemia, diabetes and hypertension. Natural occurring diuretics such as alcohol in wine, diverse drinks and beer inhibits Antidiuretic hormone (ADH) secretion and caffeine in tea, cola and coffee which block sodium reabsorption [8]. Diuretics are vital in the treatment of edema during hypertension. These purposes majorly augment the net negative solute and water stability. In the kidney, proximal convoluted tubule reabsorbs approximately 50–66% fluid via passive and active means.

Diabetes mellitus is currently the most significant non infective disorders in the universe [9]. It affects about 5% of the global population [9–12] and amount approximately 10% the entire health care expenses in several countries [13]. Diabetes occurrence in several age-groups brackets globally was anticipated to be 2.8% in 2000 with an estimated increase of about 4.4% in 2030 [14, 15]. *Diabetes mellitus* are part of the leading sources of global death with approximately six deaths in every minute [16]. WHO [17] recorded about 7.1 million mortality caused by high blood pressure, 2.6 million to extreme body mass index and 4.4 million to increased cholesterol worldwide. Type 2 diabetes is linked with aged adults and is recurrent than type 1 diabetes [10, 12, 18]. It is mostly distinguished via peripheral insulin resistivity [15, 19] with insufficient efficient collection of β-cells [10, 20]. The objective of this study includes the evaluation of anti-diuretic and anti-hyperglycemia property of *J. gossypiifolia* leave extract using selected biological markers including lipid profiling, kidney function test, blood sugar level and histology.

Materials and methods

Plant collection and authentication

Fresh leaves of *J. gossypiifolia* were obtained from Ovia East Local Government Area, Benin City. The plant was identified by Dr. O. Timothy in the Department of Plant Biology and Biotechnology, Life Sciences, University of Benin, Nigeria. The plant was authenticated by Dr. H. A. Akinnibosun in the Herbarium Unit of Plant Biology and Biotechnology, Life Sciences, University of Benin, Nigeria with Voucher specimen number UBHA521.

Plant preparation

Freshly prepared leaves of *J. gossypiifolia* were isolated from entire plant, rinsed in distilled water and shade dried in a clean and organized environment to maintain room temperature. The plant materials were further dried using regulated oven at 40 °C for 10 min before being pulverized using British mechanical grinder. Four thousand grams (4000 g) of pulverized leaves was extracted using 10,000 ml n-Hexane via soxhlet extractor. Extracts were then concentrated into semi-solid (HH-S water Bath; Search tech instruments) regulated at standard temperature (45 °C). Percentage yield were calculated via the formula (% Yield = extract weight / powder sample weight × 100/1) [21].

Experimental animals

Adult Wistar male and female rats weighed 190–250 were obtained from the animal house of Biochemistry, University of Benin. They were housed in clean wooden cages and maintained under controlled room temperature (25 ± 1 °C) with relative humidity of 45–55% under 12: 12 h light and dark cycle for one week with free access to food and water ad libitum. All procedures using animals obtained the approval of Life Sciences Institutional Animal Ethical Committee, University of Benin with ethical number (LS20111). The experiment was carried out in compliance with the Guidelines for Committee for the purpose of control and supervision of experiments on animals (CPCSEA).

Evaluation of anti-diuretic

Adult Wistar rats of male and female sexes weighted 190–250 g were randomly divided into five (5) groups ($n = 3$ male and 3 female). Before experimental processes, animals were examined for observable disease signs such as; sneezing, skin and eyes discoloration, runny nose, and lazy in movements). Only healthy animals were randomly selected for this study. The evaluation was done at room temperature (25 ± 5 °C). Prior to the experiment, the rat bladders were emptied via mild compression in the pelvic region and gently pulling of their tails [22, 23]. Group I (untreated) was given a single dose of 0.5 ml/kg normal saline orally. Group II as reference drug received a single dose of 10 mg/kg hydrochlorothiazide orally and the tested groups (III, IV and V) were administered with a single dose of graded doses of *J. gossypiifolia* leaves extract (30, 50 and 100 mg/kg orally per body weight to produce therapeutic effect) derive from the safe doses of acute toxicity study, respectively. More so, a week before the study, Wistar rats were individually housed in a metabolic cages for 6 h to acclimatize them to experimental conditions. In the course of the study, animals were individually transferred to metabolic cages (one animal per cage) for proper urine and faces separation. Volume of collected urine in graduated cylinder was measured at every 6 h, which is expressed as ml/100 g body weight per 6 h [23]. Animals were kept in a quite area to evade stress and some psychological associated effects associated with diuresis.

Determination of renal function test in urine and plasma

Calibrated flame photometer (Coring 410, UK) used for the estimation of sodium (Na+) and potassium (K+) concentration in freshly collected urine samples. Prior to electrolyte concentration estimation, samples were filtered to eliminate shedding and debris. Electrolytes concentration in urine was expressed in parts per million (ppm) [22, 24, 25].

Assay for urea

This test exploits the hydrolysis of urea to ammonia in urease enzyme. 100 µl of reagent 1 was added to 10 µl of serum samples in test tubes. 100 µl solution reagents 1 was added to 10 µl of distilled water as blank. The solutions in test tubes were thoroughly mixed for incubation at 10 min of 37 deg. Celsius. A 2.5 mls of reagents 2 and 3 were added in test tubes. Solutions inside test tubes were properly mixed and further incubated for 10 min at 37 deg. Celsius. Absorbance of samples and standard measurement against blank at 546 nm wavelength. Urea level was calculated as thus:

$$\text{Urea level (mg/dl)} = \text{Absorbance of sample/Absorbance of standard x 80}$$

Assay for creatinine

This test exploits the reaction of creatinine present in alkaline mixture having picric acid to produce colored complex. Complexity of quantity synthesized is directly comparative with creatinine concentration. A 0.2 ml of the sample macro and semi micro was added into test tubes. Absolute amount of 0.2 ml of standard macro with 0.1 ml solution while, semi micro were added into the standard solution tubes. Similarly, 2 mls solution of standard macro, 1 ml solution of semi micro, 2 mls of sample macro and 1 ml of semi micro added to working reagent test tubes. The solutions in the test tubes were mixed. Absorbance of samples and standard measured at 492 nm. Creatinine values were calculated below:

$$\text{Creatinine level units (mg/dl)} = \text{Absorbance of sample/Absorbance for standard x 2.}$$

Assay for electrolytes (sodium, chloride, bicarbonate and potassium)

The assay for bicarbonate exploits the reaction between bicarbonate ions with dilute hydrochloric acid to yield carbon dioxide. Excessive acid is titrated into dilute sodium hydroxide with phenol red indicator. 0.01 N HCl was added to 200 µl of serum sample. Solution was properly mixed and 1 drop of phenol red indicator added. Solution was titrated using 0.01 N sodium hydroxide to attain brick red coloration which serves as endpoint [24]. Bicarbonate was calculated as thus:

$$\text{Bicarbonate (µmol/l)} = 50 - \text{Titre}$$

$$\text{Titre} = \text{Endpoint x 100.}$$

The assay for chloride exploits the formation of chloride precipitate in a sample via mercuric nitrate. Chloride was titrated into solution of standard mercuric ion; undissociated stable mercuric chloride was formed. Surplus mercuric chloride nitrate reaction with diphenylcarbazone produces violet coloration. Two (2) mls deionized water was added to 200 µl serum sample. The solutions were thoroughly mixed and 3 drops of diphenylcarbazone indicator and 1 drop of nitric acid was added. Thereafter, the mixture was titrated with mercuric nitrate to give a violet endpoint. The same procedure was repeated for chloride standard solution [25]. Chloride calculation was as thus:

$$\text{Chloride (µmol/l)} = \text{Titre of sample/Title of standard x 100.}$$

The assay method for sodium and potassium entails the injection of solutions containing elements in flame

leaving solid salt, to dissociate neutral ground position. The atoms became stimulated in flame, therefore moved it to greater energy position. Excited atoms will reverse it to ground state radiating light with distinctive wavelength (590 nm of sodium and 770 nm of potassium). The light transverses via appropriate filter in photosensitive element with quantity measured of current proportional to sodium and potassium quantity present in the sample [25]. Determining the pH of urine calibrated pH meter (Model: WTW-Series pH 720) used to estimate pH of fresh urine samples [22, 26] Computation of diuretic index, Lipschitz value, saliuretic index and Na+/K+ ratio.

The equations were used to calculate these parameters [26, 27].

$$\text{Diuretic index} = (\text{UVt}/\text{UVc}) \quad (1)$$

$$\text{Lipschitz value} = (\text{UVt}/\text{UVr}) \quad (2)$$

$$\text{Saliuretic index} = (\text{CUEt}/\text{CUEc}) \quad (3)$$

$$\text{Na} + /\text{K} + \text{ratio} = (\text{UNa} + /\text{UK}+) \quad (4)$$

Where UVt = Mean urine volume of test group, UVc = Mean urine volume of control group, UVr = Mean urine volume of reference group, CUEt = concentration of electrolytes in urine of test group, CUEc = concentration of electrolytes in urine of control group, UNa^+ = concentration of Na^+ in urine of a group, and UK^+ = concentration of K^+ in urine of a group.

Preparation/ induction of diabetes

Streptozotocin (STZ) was freshly prepared in 0.1 M citrate buffer with pH 4.5. Prior to induction, animals were fasted 24 h and single dose of 45 mg STZ per kg body weight was administered intraperitoneally. Typical diabetic signs such as increased ingestion of water and food, recurrent urination rises in blood glucose level where observed. Selectivity of STZ on induces experimental diabetics with β-cells selectivity, reduced mortality with comparatively prolonged half-life (15 min) of STZ. Diabetes mellitus was established 48 h following STZ administration using Accu-check glucometer machine. Animals having plasma glucose concentration > 200 mg/dl were marked diabetic and integrated into the study as baseline [28].

Treatment protocol

Wistar rats were selected into six (6) groups ($n = 6$). Group I (non-diabetic rats) while other groups are diabetic. Anti-diabetic effect of n-Hexane extract of *J. gossypiifolia* at (30, 50 and 100 mg/kg orally per body weight to produce therapeutic effect) and reference group (10 mg/kg glibenclamide orally per body weight to produce therapeutic effect) were evaluated using blood glucose estimation, body weight, biochemical and histopathological study on the study. Afterwards treatment, the sugar level was observed for day 1, day 7 and 14 days. Blood Glucose levels (mg/dl) being carried out using glucometer (Accu-Chek®, Model-GC, Roche, Germany) across the groups for day 1 (baseline after 3 days induction), day 7 and day 14 after overnight fasting. Blood samples were collected under mild chloroform anesthesia. Blood serum was separated (centrifugation at 10000 speeds for 15 mins) to determines the followings.

Lipid profile

Total cholesterol was determined using enzymatic method using wet reagents diagnostic kits. This was carried out via a modified method of Shrivastava et al. [29] 1000 µl of the reagent being pipetted into distinct three (3) test tubes A, B and C. Distilled water, a standard solution (standard) and plasma (sample) of 10 µl each were pipetted into the same test tubes A, B and C respectively. After mixing, test tubes were allowed to stand for 10 min at room temperature to give room for color change, the absorbance of the blank; samples and the standard measured with 500 nm wavelengths using a UV spectrophotometer. Cholesterol concentration calculated as thus:

$$\text{Cholesterol (mg/dl)} = \text{Absorbance of sample}/\text{Absorbance of standard} \text{ x concentration of standard (mg/dl)}..$$

Total triglycerides were determined using enzymatic method with wet reagent diagnostic kits. This was carried out using a modified method of Umbrae et al. [30]. The reagent (1000 µl) being pipetted in three different test tubes A, B and C and 10 µl each of standard solution (standard) and plasma sample was pipetted in test tubes B and C while test A contained only the reagent (reagent blank). After mixing, the test tubes were left to stand for 10 min at room temperature (25 deg. Celcius) to allow for color change. Furthermore, Absorbance of the blank, plasma from animals and standard were measured using 500 nm wavelength via UV spectrophotometer. This was repeated for all the plasma samples. Concentration of triglyceride in samples was analyzed and expressed as thus:

$$\text{Total Triglyceride (mg/dl)} = \text{Absorbance of sample}/\text{Absorbance of standard} \text{ x concentration of standard (mg/dl)}.$$

High density lipoprotein (HDL) was determined using the enzymatic method. A precipitating agent consisting of phosphotungstic acid at 0.55 mmol/l and magnesium chloride at 25 mmol/l [31] was used. This was prediluted using ratio 4:1 in distilled water. 500 µls of

reagent was pipetted in two different test tubes A and B. A standard solution (standard) and plasma sample of 200 μls each was pipetted into the same test tube A and B respectively. After mixing, the test tubes were left for 10 min at standard room temperature to allow color change, after samples and standard absorbance measured at 500 nm via UV spectrophotometer. HDL was calculated below:

$$\text{HDL (mg/dl)} = \text{Absorbance of sample/Absorbance of standard} \times \text{concentration of standard (mg/dl)}.$$

Low density lipoprotein (LDL) was calculated as thus: [31].

$$\text{LDL (mg/dl)} = \text{Total cholesterol - Triglycerides/5–HDL}.$$

Histological analysis

The kidney and pancreas were affixed in neutral buffered formalin. Affixed organs were utterly dehydrated with total ethanol in 96% ethanol, 70% ethanol then further washed in distilled water. 4 μm sections prepared with stained in haematoxylin-eosin dye and, stained tissues were observed with the help of Leica MC170 HD, Leica Biosystems, Germany optical photomicroscope, using × 400 magnifications [32].

Statistical analysis

Data were presented as mean ± standard error of mean (SEM). Analysis of variance (ANOVA) and Dunnet's test were used for data determination; $p < 0.05$ taken as statistical significant. The software package, Graph pad prism 7 used for the analysis.

Results

The effect of *J. gossypiifolia* in kidney function parameters (creatinine, urea, bicarbonate, sodium, potassium and chloride) after the occurrence of diuresis across the groups, showed significant differences specifically in the treated groups when compared the untreated control and reference drug ($p < 0.01$). Hence, effect from the extract proved its ability to aid the regulation of kidney function parameters during diuresis as shown in Table 1.

The effect of *J. gossypiifolia* in the animals urine volume and electrolyte subjected to diuresis across the groups, showed significant differences when compared with the untreated control and reference drug ($p < 0.01$) as shown in Table 2. Thereby aid in the regulation and management of imbalance urine volume and its electrolytes.

The effect of *J. gossypiifolia* in the animals blood sugar level subjected to streptozotocine induced hyperglycemia across the groups, showed significant differences by reduction in the sugar level, across reference drug and graded doses of the extract when compared with an increase in the sugar level, in the untreated control drug ($p < 0.01$). Hence, the extract showed the potential in reducing sugar level as shown in Table 3.

Table 4 showed the effect of *J. gossypiifolia* in animal body weight. Day 1 serves as initial body weight before induced with STZ (baseline). The different in the body weight of each group at the beginning were the sizes of rats readily available from the same parent. Day 7 showed reduction in the effect of STZ and onset of treatment, while day14 showed an increased in the body weight after treatment. Hence, values with superscript ^{b} and ^{c} denote significant decrease when compared with day 1 (baseline). The comparison of each group in respect to the difference in baseline body weight is compared across the days of each groups before or after treatment to observed changes in body weight.

The effect of *J. gossypiifolia* in kidney function parameters (creatinine, urea, bicarbonate, sodium, potassium and chloride) induced with streptozotocine across the groups, showed significant differences in the treated groups when compared with untreated control and reference drug ($p < 0.01$). The extract have the ability to regulate and manage kidney malfunction indexes during hyperglycemia as shown in Table 5.

The effect of *J. gossypiifolia* in lipid profile parameters (cholesterol, triglyceride, HDL, VLDL and LDL) induced with streptozotocine across the groups, showed significant differences with reduction in cholesterol, triglyceride, VLDL and LDL but increased in the level of HDL

Table 1 Effect of *J. gossypiifolia* (JG) on renal function test in urine

Groups	Doses (mg/kg)	Creatinine mg/dl Mean ± SEM	Urea mg/dl Mean ± SEM	Bicarbonate (HCO_3) mmol/L Mean ± SEM	Sodium (Na^+) mmol/L Mean ± SEM	Potassium (K^+) mmol/L Mean ± SEM	Chloride (Cl^-) mmol/L Mean ± SEM
Control	NS	0.13 ± 0.01^{a}	22.77 ± 0.72^{a}	13.07 ± 0.39^{a}	92.88 ± 2.00^{a}	22.13 ± 0.77^{a}	52.05 ± 0.95^{a}
Hydro--chlorothiazide	10	0.23 ± 0.02^{b}	48.36 ± 2.53^{c}	18.63 ± 0.78^{b}	110.3 ± 4.75^{c}	19.10 ± 0.82^{a}	65.97 ± 3.92^{b}
J. gossypiifolia	30	0.16 ± 0.01^{a}	37.58 ± 8.22^{b}	16.80 ± 0.46^{a}	100.5 ± 0.56^{a}	19.19 ± 0.31^{a}	66.62 ± 1.37^{b}
J. gossypiifolia	50	0.18 ± 0.01^{a}	24.44 ± 0.47^{a}	18.20 ± 0.46^{b}	102.1 ± 0.47^{b}	18.08 ± 0.32^{a}	64.82 ± 0.58^{b}
J. gossypiifolia	100	0.26 ± 0.01^{b}	37.76 ± 7.37^{b}	20.65 ± 0.38^{b}	104.7 ± 0.19^{b}	18.92 ± 0.05^{a}	64.38 ± 0.32^{b}

Table 2 Effect of *J. gossypiifolia* on urinary volume and electrolyte concentration

Groups	Doses (mg/kg)	Volume of urine (ml) Mean ± SEM	pH	Diuretic Index	Lipschti Z Value	Saliuretic Na^+	Index K^+	Na^+/K^+
Control	NS	1.18 ± 0.61^a	7.02	–	0.19	–	–	4.20
Hydrochlorothiazide	10	6.23 ± 1.02^c	7.53	5.28	–	1.19	0.86	5.78
J. gossypiifolia	30	3.26 ± 0.69^b	6.99	2.76	0.52	1.08	0.87	5.24
J. gossypiifolia	50	4.11 ± 1.00^b	7.04	3.48	0.66	1.10	0.82	5.65
J. gossypiifolia	100	5.06 ± 1.00^c	7.32	4.29	0.81	1.13	0.86	5.53

p-value > superscript ^{a} = 0.05, ^{b} = 0.01, ^{c} = 0.001 showed the level of significant difference when compared with untreated control ($n = 5$). NS---- Normal Saline

(good fat) across the graded doses of the treated groups when compared with untreated control and reference drug ($p < 0.01$). The potential capability of the extract to manage obesity triggered hyperglycemia as shown in Table 6.

Discussion

J. gossypiifolia leaves Hexane extract has several chemical components that is partly or fully liable for increased diuresis and moderate natriuretic property. Results showed increase acceleration removal of extreme fluid via urinary hypo-osmolality and fairly increase natriuretic property. Possible results revealed n-Hexane leaves extract of *J. gossypiifolia* at (30, 50 and 100 mg/kg) with moderate diuretic property. Increase in natriuresis is a response to acute treatment by the extract may partly explain the increase in diuresis [8, 33]. The extracts as well as Hydrochlorothiazide caused urinary increase in rat Na^+ and Cl^-. Increase in Na^+ excretion decrease glomerular filtration rate via increasing Na + load readily available for Na^+/K^+ exchange, exciting further exchange of hyperaldosteronism (Tables 1 and 2) to causes reduction in blood level [34, 35] Increase in Na^+ in *macula densa blocked* rennin secretion; to increase GFR and reduce blood level resulted in increased rennin secretion. Glomerular filtration recorded by creatinine clearance does not fluctuate as observed in the treatment when compared with the controls (Table 1), suggesting an increase in diuresis which possible have tubular origin as appeared to show clearance of free water (Table 2). It is significantly reduce in animals that are administered with the plant extract when compared with the controls ($p < 0.05$). Single dose of Hydrochlorothiazide 10 mg/kg was orally administered to observe the diuretic effect on hepatic or kidney deficiency. It acts via inhibiting reabsorpted Na^+ and Cl^- in ascending branch of loop of Henle. Also, it has wide peripheral and free renal vascular activity [36]. Inhibition of reabsorpted sodium. Primarily, it triggered urinary sodium excretion of significant chloride. Also, it promotes tubule-glomerular feedback inhibition devoid of essential increase on filtration (Tables 1 and 2). Major modification occurs in pore pressure and interstitial volume with total proximal reabsorption remains constant hydrochlorothiazide (10 mg/kg) induces the removal of harmful water and salt via kidneys excretion from the body through urine [37]. It is as well active in the inner medullary collectors causing increase influx and decrease reabsorption of sodium, chloride and water ions. Secretion of potassium is low probably could be associated with increase in potassium. *J. gossypiifolia* extract stimulated decrease in K+ excretion when compared with hydrochlorothiazide (10 mg/kg) ($p < 0.05$), suggesting n-Hexane leaves extract of *J. gossypiifolia* mimics possible action of hydrochlorothiazide. Since it is known that, hypervolemia brings about hypertension [37], thereby; hypotensive property of *J. gossypiifolia* can be explained via the mechanisms of diuretic properties. Increased in sodium level in hydrated animals with n-Hexane leaves extract of *J. gossypiifolia* at (30, 50 and 100 mg/kg) in (Tables 1 & 2) could serves

Table 3 Effect of *J. gossypiifolia* in blood sugar level

Groups	Doses (mg/kg)	Baseline (mg/dl) Mean ± SEM	7 days of treatment (mg/dl) Mean ± SEM	14 days of treatment (mg/dl) Mean ± SEM
Control (STZ)	40	281.70 ± 12.73a	303.30 ± 5.90^a	463.00 ± 85.11^a
Gliberclamide	10	263.70 ± 3.18a	99.67 ± 2.19^c	81.67 ± 7.31^c
Normal control	DW	66.67 ± 3.18c	62.33 ± 6.23^c	57.00 ± 7.51^c
J. gossypiifolia	30	226.00 ± 20.21a	145.30 ± 21.11^b	84.00 ± 13.28^c
J. gossypiifolia	50	253.70 ± 18.85a	108.70 ± 4.98^b	60.67 ± 5.18^c
J. gossypiifolia	100	235.00 ± 12.17a	58.00 ± 5.20^c	42.00 ± 12.17^c

p-value > superscript ^{a} = 0.05, ^{b} = 0.01, ^{c} = 0.001 showed the level of significant difference when compared with untreated control ($n = 5$). DW---- distilled water

Table 4 Effect of *J. gossypiifolia* on body weight on hyperglycemic animals

Groups/days	Control (STZ) 40 mg/kg Mean ± SEM	Gliberclamide 10 mg/kg Mean ± SEM	Normal control Mean ± SEM	30 mg/kg *J. gossypiifolia* Mean ± SEM	50 mg/kg *J. gossypiifolia* Mean ± SEM	100 mg/kg *J. gossypiifolia* Mean ± SEM
Body Weight For Day 1	217.70 ± 26.44^{a}	274.30 ± 6.74^{a}	177.00 ± 4.16^{a}	249.30 ± 22.24^{b}	227.70 ± 9.68^{a}	266.00 ± 18.56^{a}
Body Weight For Day 7	181.70 ± 18.22^{b}	216.00 ± 20.55^{c}	173.70 ± 2.19^{a}	217.70 ± 26.30^{b}	181.70 ± 17.68^{c}	204.70 ± 44.25^{c}
Body Weight For Day 14	162.70 ± 18.27^{c}	240.00 ± 7.00^{b}	199.00 ± 1.15^{b}	218.30 ± 20.67^{b}	193.00 ± 14.53^{b}	231.30 ± 22.75^{b}

P-value > superscript ^{a} = 0.05, ^{b} = 0.01, showed the level of significant difference when compared across the days, ($n = 5$). DW---- distilled water, JG--- *J. gossypiifolia*

as the secondary intensity of diuresis occurrence from plasma compartment contraction. Difference in diuresis could rise with disparity in clearance. Certainly, it is implicit that, at a given uremia, clearance and diuresis varies in certain ways, with reduced clearance for low urinary flow rates associated with a major urea reabsorption occurred around the pelvis [8]. Increase in Na^{+}, K^{+}, and Cl^{-} stimulated by extracts to caused alkalization of urine, to show a strong blocking effect of carbonic anhydrase and saluretic. A single dose oral administration of n-Hexane leaves (30, 50 and 100 mg/kg) of *J. gossypiifolia* significantly increased urine volume within 24 h after treatment. In addition, treated groups increased, with dose dependent, excretion of K^{+}, Cl^{-} and Na^{+} to cause decrease in urine osmolarity. The extract elicited increased in diuresis and moderate natriuresis elevation in tubular origin.

Animal pre-exposed to 45 mg/kg dose of streptozotocine induced hyperglycemia, showed that *J. gossypiifolia* leaves n-Hexane extract at (30, 50 and 100 mg/kg) significantly decreased in blood glucose levels on days 7 for leaves extract (145.30, 108.70 and 58.00 mg/dl) and day 14, the leaves extract exhibited (84.00, 60.67 and 42.00 mg/dl) when compared with diabetic control for day 7 and 14 (303.30 and 463.00 mg/dl) ($p < 0.05$) (Table 3). Therefore, it was recommended that the effect potentiates the extracts ability to control hyperglycemia and diabetes insipidus when compared with reference drugs (gliberclamide). Similar study was carried out by Saleem et al. [28] which showed that in vitro studies on antidiabetic and anti-ulcer potentials of *J. gossypiifolia* (Euphorbiaceae) was carried out. Also the reports of Owolabi et al. [38] showed blood glucose reducing cause of *Newboudia laevis* ethanol leaves extracts on days 4, 8 and 14 of treatment. Higher doses (50 and 100 mg/kg) of *J. gossypiifolia* leaves extract showed significant reduction in blood glucose on days 7 and more effective on prolong treatment at day 14 ($p < 0.05$). This finding scientifically validates n-hexane extract with a better effect on blood glucose levels. Its efficacy could be recommended for ethnotherapeutic approach against hyperglycemia disorders at higher doses [39]. The lowering effect of *J. gossypiifolia* leaves and root extracts on blood glucose level thus validated its uses. Certain saponins and alkaloids could be responsible for the supportive effect [40]. Certain bio-constituents synergized to develop symptoms removal in *Diabetes mellitus* such as, flavonoids, polyphenols etc. It is significant to note that insulinotrophic effects of certain flavonoids are implicated. Viable actions of this extract bring about reducing effect in blood glucose measurement. Flavonoids has been stimulated with decrease in blood glucose via changing insulin sensitivity and discharge, glucose transporters, PPAR-γ, liver glucose synthesis and peripheral glucose uptake [41]. Kameswaararao et al. [42] from his reports suggested its actions might be due to residual stimulation of pancreatic beta cell mimicking sulphonylurea. Odetola et al. [40] work showed similar result with *J. gossypiifolia* extracts anti-hyperglycaemic effect via extra-pancreatic mechanism attributed to the quantity of 0.8770 mg/kg saponins, 0.380 mg/kg flavonoids and 0.600 mg/kg alkaloids were present, owing to their ability to scavenge free radicals as antioxidant. This supports Odetola et al. [40] findings but against Owira et al. [43].

Table 5 Effect of *Jatropha gossypiifolia* L. on renal function test on day 14

Groups	Doses (mg/kg)	Creatinine mg/dl Mean ± SEM	Urea mg/dl Mean ± SEM	Bicarbonate (HCO_3) mmol/L Mean ± SEM	Sodium (Na^{+}) mmol/L Mean ± SEM	Potassium (K^{+}) mmol/L Mean ± SEM	Chloride (Cl^{-}) mmol/L Mean ± SEM
Control (STZ)	40	0.28 ± 0.00 ^{a}	37.17 ± 5.52^{a}	13.50 ± 0.87^{a}	101.1 ± 1.31^{a}	19.40 ± 0.65^{a}	78.22 ± 3.19^{a}
Gliberclamide	10	0.18 ± 0.02^{b}	27.50 ± 1.44^{a}	19.17 ± 0.48^{b}	105.1 ± 0.95^{a}	23.08 ± 0.35^{a}	65.77 ± 4.39^{a}
Normal control	DW	0.21 ± 0.01^{b}	27.59 ± 2.55^{a}	18.50 ± 1.44^{b}	109.5 ± 1.78^{b}	22.00 ± 1.34^{a}	64.00 ± 4.07^{b}
J. gossypiifolia	30	0.23 ± 0.01^{a}	24.41 ± 0.05^{b}	19.75 ± 0.05^{b}	109.3 ± 0.14^{b}	24.56 ± 0.32^{b}	64.25 ± 1.11^{b}
J. gossypiifolia	50	0.22 ± 0.01^{b}	23.79 ± 0.36^{b}	18.98 ± 0.01^{b}	109.2 ± 0.43^{b}	25.50 ± 0.29^{b}	63.18 ± 0.15 ^{b}
J. gossypiifolia	100	0.26 ± 0.00^{a}	27.88 ± 0.26^{a}	17.34 ± 0.01^{a}	108.5 ± 0.64^{b}	25.32 ± 0.18^{b}	78.92 ± 0.44^{a}

p-value > superscript ^{a} = 0.05, ^{b} = 0.01 showed the level of significant difference when compared with untreated control, (n = 5). DW---- distilled water

Table 6 Effect of *J. gossypiifolia* on lipid profile test on day 14

Groups	Doses (mg/kg)	Cholesterol mg/dl Mean ± SEM	Triglyceride mg/dl Mean ± SEM	HDL mg/dl Mean ± SEM	VLDL mg/dl Mean ± SEM	LDL mg/dl Mean ± SEM
Control (STZ)	40	91.60 ± 0.92^{a}	284.4 ± 2.33^{a}	9.18 ± 0.10^{a}	69.85 ± 1.05^{a}	36.37 ± 5.88^{a}
Gliberclamide	10	62.10 ± 0.06^{c}	187.2 ± 1.61^{b}	18.07 ± 0.25^{c}	37.43 ± 0.32^{c}	6.03 ± 0.39^{d}
Normal control	DW	76.08 ± 1.51^{b}	194.0 ± 6.58^{b}	12.33 ± 0.20^{b}	41.96 ± 0.09^{b}	21.92 ± 1.58^{b}
J. gossypiifolia	30	78.29 ± 0.03^{b}	237.6 ± 1.41^{a}	10.39 ± 0.16^{a}	47.61 ± 0.23^{b}	20.39 ± 0.41^{b}
J. gossypiifolia	50	78.49 ± 0.29^{b}	232.7 ± 0.41^{a}	10.48 ± 0.03^{a}	46.54 ± 0.08^{b}	21.47 ± 0.40^{b}
J. gossypiifolia	100	84.18 ± 0.36^{a}	227.6 ± 0.35^{a}	12.06 ± 0.04^{b}	45.52 ± 0.07^{a}	26.60 ± 0.32^{a}

P-value < 0.05 showed the level of significant difference when compared with untreated control, (n = 5). DW---- distilled water

Weight loss is a general attribute seen in *Diabetes mellitus* due to breakdown of structural proteins and muscle wasting [44]. The study showed that n-hexane leaves extract at graded doses slightly increased at day 14 after treatment as shown in Table 4 ($p < 0.05$). This shows that, the extract reversed weight loss caused hyperglycemia when compared with untreated control. This result contradict the findings of Murunga et al. [45] which showed naringin, a component in grapefruit ameliorates weight loss in streptozotocin induced diabetic rats. Several biochemical indices are distorted in hyperglycemic state such as, renal function parameters and lipid profiles. Plants with anti-hyperglycemic activity shown to elicit its effects on renal function and serum cholesterol. A significant reduction in urea levels of the treated groups in leaves (24.41, 23.79 & 27.88 mg/dl) extracts when compared with untreated group (37.17 mg/dl) ($p < 0.05$) as shown in Table 5. Creatinine levels in relative to diabetics showed significant reductions in treated rats at graded doses of leaves (0.23, 0.22 and 0.26 mg/dl) extract when compared with untreated group (0.28 mg/dl) ($p < 0.05$). Creatinine and urea levels show that the extract

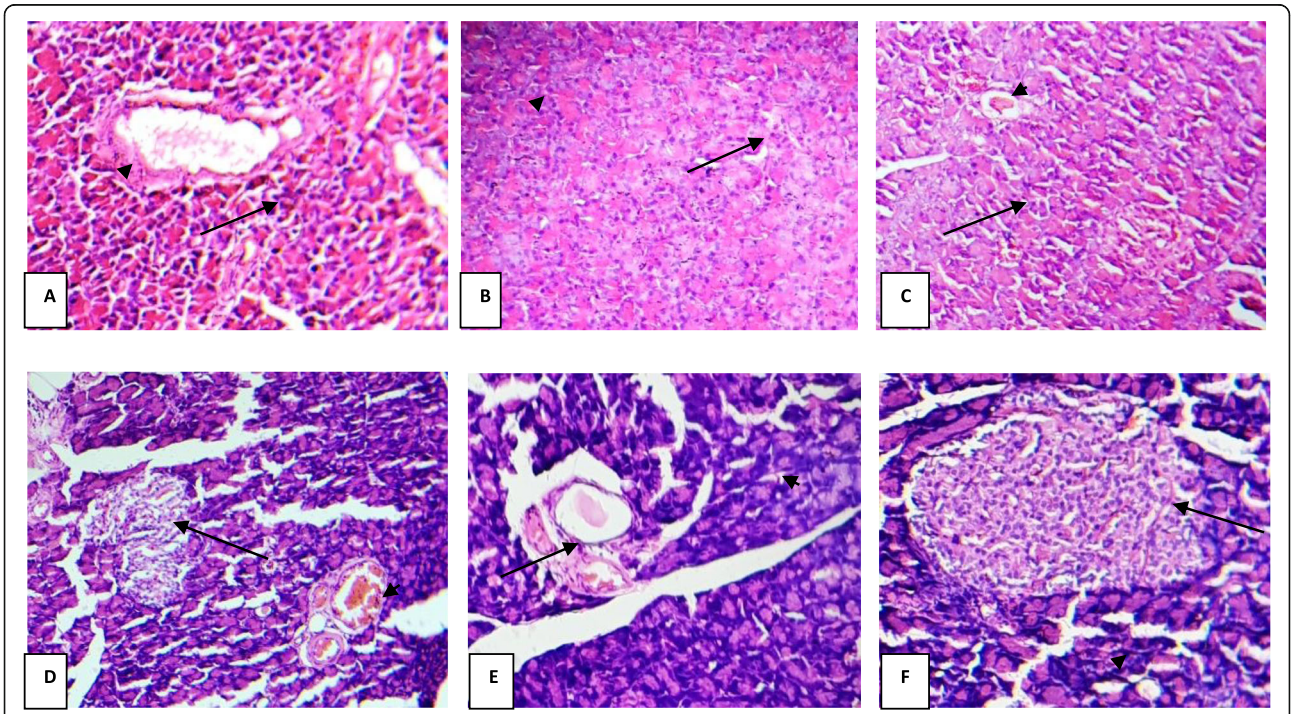

Fig. 1 Effect of n-Hexane leave extracts of *J. gossypiifolia* on the pancrease. **A =** untreated group: Pancrease features show several acinar cells having islet-cells with mildly despaired pyknotic Nuclei via Lymphocytic infiltrates and visible intralobular duct appearing fatty. B = 10 mg/kg Gliberclamide: Pancrease reveals features with several acinar cells in islet-cells showed mildly despaired pyknotic nuclei with mild dispersed Lymphocytic infiltrates. C = Normal control: Pancrease reveals secreterory acini pancreatic islet. Histology reveals intralobular duct on low power. D = 30 mg/kg extract: Pancrease reveals secreterory acini with bulky pancreatic islet. The histology reveals intralobular duct. E = 50 mg/kg extract: Pancrease character showed certain acinar cells having islet-cells exhibiting mildly despaired pyknotic nuclei. The histology reveals intralobular duct. F = 100 mg/kg extract: Pancrease reveals secreterory acini with bulky pancreatic islet. The nucleus appears pyknotic. Using haematoxylin-eosin dye with X 40 magnification

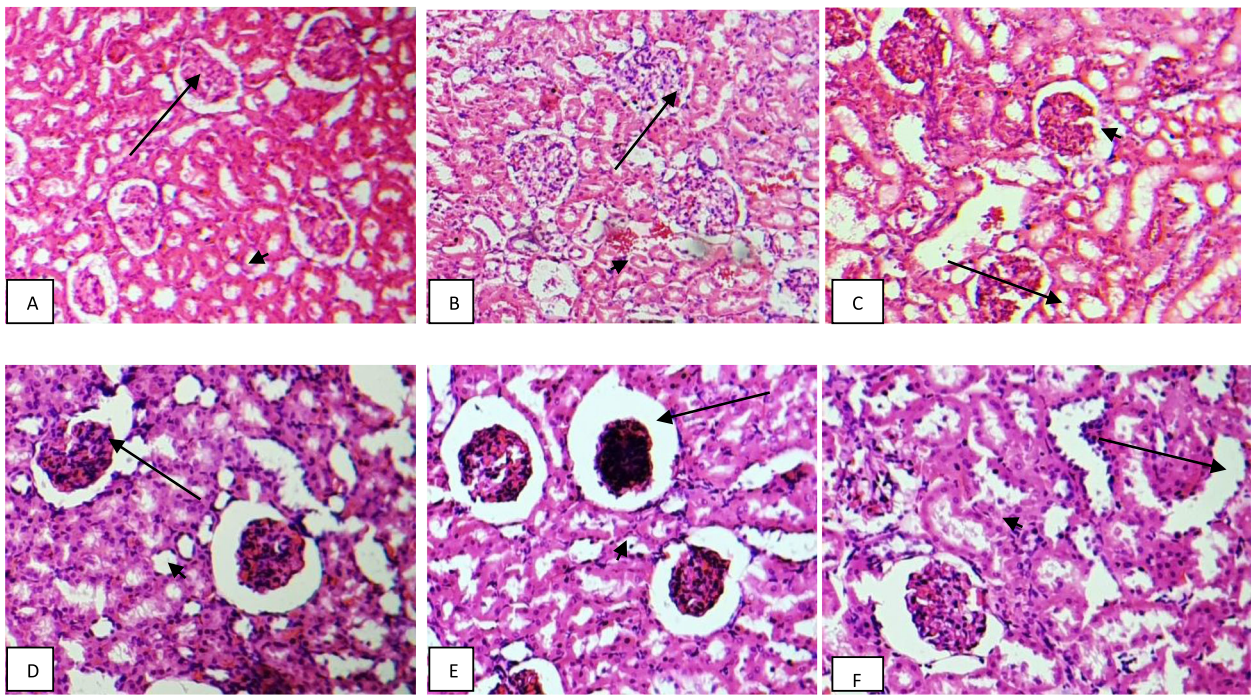

Fig. 2 Effect of n-Hexane leaves extracts of *J. gossypiifolia* on the kidney. A = untreated group: Kidney reveals visible renal corpuscle and interstitial space and tubules showing tubular necrosis. B = 10 mg/kg Gliberclamide: Kidney reveals visible renal corpuscle and interstitial space and tubules with diffused mononuclear infiltrate. C = Normal control: Kidney reveals visible renal corpuscle and interstitial space and tubules. D = 30 mg/kg extract: Kidney reveals visible atrophied renal corpuscle with distortion in the tubules. E = 50 mg/kg extract: Kidney reveals visible atrophied renal corpuscle with distortion in the. F = tubules and mononuclear infiltrates. 100 mg/kg extract: Kidney reveals visible slightly atrophied renal with mild tubular necrosis and mild mononuclear infiltrates. Using haematoxylin-eosin dye with X 40 magnification

possess nephroprotective effect as confirmed from urea and creatinine reduction in treated rats. This finding concurred with Chukwuma et al. [46] reports. Kidney being a vital organ involved in waste products elimination. Renal function tests helps to confirm renal dysfunction. Creatinine and urea are the major renal injury indicators. Hyperglycaemia could be responsible for some increments seen in diabetes [47]. High urea levels are attributed to gluconeogenesis used as substitute source for glucose due to insulin deficiency [48]. Gluconeogenesis rate increased due to raised proteolysis that produces glucogenic amino acids subsequently undergo deamination of the liver leading to elevated urea [48]. Similar effects reported by Osigwe et al. [49] in alloxan induced diabetic rats exposed to *Newboudia laevis* extracts for 21 days. The effects of *J. gossypiifolia* proposed renoprotection owning to antihyperglycaemic activity to enhanced insulin sensitivity thus decreased gluconeogenesis and proteolysis. *J. gossypiifolia* treated groups maintained its bicarbonate levels in graded doses. This elicited that, the extract prevent bicarbonate reduction. Low bicarbonate levels characterize diabetic ketoacidosis which is observed in type 1 and 2 *Diabetes mellitus* under certain conditions of metabolic stress [14]. Hyponatraemia is a frequent feature seen in *Diabetes mellitus* due to osmotic diuresis [50]. Sodium levels in untreated group is low compared with treated groups (*J. gossypiifolia*), showed significant increase in sodium levels signifying a modulation in sodium levels due to decreased osmotic diuresis ($p < 0.05$). Potassium levels in treated groups showed a significant increase ($p < 0.05$) in the leaves extract at graded doses (30, 50 and 100 mg/kg) when compared with untreated group. Hyperkalaemia has significant values of diabetic patients due to hyporeninemic hypoaldosteronism caused by diabetic nephropathy [50]. Hyperchloraemia is a common feature in defectively controlled diabetes related with hyperglycaemia, ketosis and acidosis. It is an indicator of progressive renal defects. Chloride ion levels, showed significant reduction in treated groups (*J. gossypiifolia*) chloride level at lower doses in leaves extract when compared with control group (Table 5). Usually, it is affirmed from the endpoints that, the extracts showed renoprotective effects in treated rats. The effects of extract on renal indices in line with Chukwuma et al. [46] and Osigwe et al. [49] works showed renoprotective effects of *Citrus paradisci* juice and *Newbouldia laevis* leaf extract respectively in alloxan induced diabetic rats. Goldberg, [51] reported that deficits in insulin production or sensitivity are linked with lipid anomaly causative

to conditions includes; atherosclerosis and fatty hepatic disease. This was remarked from the significant difference across triglyceride, HDL, total cholesterol and LDL between *J. gossypiifolia* extract treated groups and untreated groups ($p < 0.05$). The extracts significantly reduced TC, TG, VLDL and LDL, whereas, a significant increase in HDL as shown in Table 6. This report concurred to Castilla [52] and Odetola et al. [40] work respectively, showed the hypolipidaemic effect of *Citrus paradisi* juice and aqueous extract of fermented *Parkia biglobosa* in alloxan induced diabetic rats. Also, a study carried out by Owolabi et al. [38] on hypolipidaemic effects of *Napoleona vogelis* methanol leaf extract. An increase in HDL termed 'good cholesterol' and the decrease in LDL termed 'bad cholesterol' by these extract either individually or in combination enhances the dietary supplements role used to prevent cardiovascular complications associated with diabetes [40]. Histopathological examination of untreated kidney reveals an intact architecture devoid of atrophy, necrosis or inflammation, when compared with the treated kidneys, which showed atrophy of renal corpuscles and visible inflammatory infiltrates. It explain that Streptozotocin induced diabetes enhances nephrotoxic [53] (Figs. 1 & 2). The treated kidneys at 30, 50 and 100 mg/kg n-hexane leaves extract of *J. gossypiifolia* had a better architecture than untreated group devoid of atrophy, necrosis or inflammation (Figs. 1 & 2). This suggests that the plant extracts are nephroprotective and it is supported by renal biochemical parameters with significant difference ($p < 0.05$). These observations might be attributed to the presence of antioxidant and anti-inflammatory principles present in the extract, just as the report of Fuji et al. [54] showed that proanthrocyanidins had the strongest protective effect against high glucose mediated oxidative stress on the cultured kidney cells. The treated pancreas revealed a well architecture devoid of lymphocytic infiltration, congestion or atrophy when compared with the pancreas of untreated group revealed lymphocytic infiltrations and pyknotic cell congestion. This observation is in line with cytotoxic effects of streptozotocin induced diabetes that damage pancreatic cells (β cell) with consequent hyperglycaemia [53]. The pancreas of the treated group at 30, 50 and 100 mg/kg *J. gossypiifolia* leaves extract revealed marked improvements over untreated group (Figs. 1 & 2). These observations are similar to the work of Florence et al. [55] showed that *Annona muricate* aqueous extract have a protective effect on pancreas with consequently improves glucose metabolism.

Conclusion

In conclusion, the effect is associated with *J. gossypiifolia* with potential anti-diuretic and anti-hyperglycemic properties as stated in its ethnomedicinal reports.

Abbreviations

J. gossypiifolia: *Jatropha gossypiifolia*; L: Llinneus; mg/kg: Miligram/ kilogram; ml: Mililiter; ADH: Antidiuretic hormone; β-cells: Beta cell; ^{0}C: Degree Celcius.; Hr: Hour; CPCSEA.: Committee for the purpose of control and supervision of experiments on animals; Na+: Sodium; K+: Potassium; µl: Microliter; dl: Decilitre; N HCl: Normal hydrochloric acid; µmol/l: Micromole/litre; nm: Nanometer; STZ: Streptozotocin; UV spectrophotometer: Ultraviolet spectrophotometer; HDL: High density lipoprotein; LDL: Low density lipoprotein; VLDL: VERY Low density lipoprotein; DW: Distilled water; PPAR-γ: Peroxisome proliferator-activated receptor

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Authors' contributions

Gabriel Ogunma Benjamin carried out the research work (antidiuretic and antidiabetic) under the supervision of MacDonald Idu. The authors read and approved the final manuscript.

Authors' information

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Availability of data and materials

Data where obtained from this research study and statistically analysed as shown in the result Tables, Figures and Plates. Materials such as chemicals, drugs, kits and animals where ordered from necessary stores within and out the country.

Declarations

Ethical approval and consent to participate

All procedures using animals obtained the approval of Life Sciences Institutional Animal Ethical Committee, University of Benin with LS20111 ethical number.

Consent for publication

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Competing interests

No competing interest.

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References

1. Zhao A, Yang XY. New coumarin glucopyranosides from roots of *Angelica dahurica*. Chin Herbal Med. 2018;10(1):103–6. https://doi.org/10.1016/j.chmed.2018.01.008.
2. Simon OR, West ME. The past and the present use of plants for medicines. West Indian Med J. 2006;55:217–21.
3. Sabandar CW, Ahmat N, Jaafar FM, Sahidin I. Medicinal property, phytochemistry and pharmacology of several Jatropha species [*Euphorbiaceae*]: a review. Phytochem. 2013;85:7–29. https://doi.org/10.1016/j.phytochem.2012.10.009.
4. Apu AS, Hossain F, Rizwan F, Bhuyan SH, Matin M, Jamaluddin ATM. Study of pharmacological activities of metanol extract of *Jatropha gossypifolia* fruits. J Basic Clin Pharm. 2013;4(1):20–4. https://doi.org/10.4103/0976-0105.109404.
5. Félix-Silva J, Giordani RB, Silva AA, Zucolotto SM, Fernandes-Pedrosa MF. *Jatropha gossypiifolia* L. (Euphorbiaceae): A review of traditional uses, phytochemistry, pharmacology, and toxicology of this medicinal plant. Evidence-Based Complemen Altern Med. 2014;5:1–32.

6. Ogundare OA. Antimicrobial effect of *Tithonia diversifolia* and *Jatropha gossypifolia* leaf extracts. Trends App Sci Res. 2007;2(2):145–50. https://doi.org/10.3923/tasr.2007.145.150.
7. Sharaibi OJ, Ogundipe OT, Afolayan AJ, Aworinde DO. Ethnobotanical survey and phytochemical analysis of medicinal plants used for the treatment of hyperprolactinemia in Lagos state. Nigeria J Med Plant Res. 2014;8(43):1284–8.
8. Devi P, Meera R, Muthumani P, Chilakalapudi R, Thota VK, Duddu VD, et al. Antidiuretic hormone (ADH) secretion and caffeine in tea, cola and coffee block sodium reabsorption. Intern J Pharm Bio Arch. 2010;1(4):331–4.
9. Szkudelska K, Nogowski L, Szkudelski T. Adipocyte dysfunction in rats with streptozotocin-nicotinamide induced diabetes. Intern J Exper Pathol. 2014; 95(2):86–94. https://doi.org/10.1111/iep.12073.
10. Sergio G, Norman B, Alis G, Fernando E. Hypoglycemic effects of flavonoids and extracts from *Jatropha gossypiifolia*. Molecules. 2015;20(4):6181–93. https://doi.org/10.3390/molecules20046181.
11. Palsamy P, Subramanian S. Ameliorative potential of resveratrol on proinflammatory cytokines, hyperglycemia mediated oxidative stress, and pancreatic beta-cell dysfunction in streptozotocin-nicotinamide-induced diabetic rats. J Cell Physiol. 2010;224(2):423–32. https://doi.org/10.1002/jcp.22138.
12. Szkudelski T. Streptozotocin-nicotinamide-induced diabetes in the rat. Characteristics of the experimental model. Exper Bio Med. 2012;237(5):481–90. https://doi.org/10.1258/ebm.2012.011372.
13. Pari L, Saravanan R. Beneficial effect of succinic acid monoethyl ester on erythrocyte membrane bound enzymes and antioxidant status in streptozotocin-nicotinamide induced type 2 diabetes. Chem Bio Interact. 2007;169(1):15–24. https://doi.org/10.1016/j.cbi.2007.04.010.
14. Wild S, Roglic G, Green ASR, King H. Global prevalence of diabetes estimates for the year 2000 and projections for 2030. Diabetes Care. 2004;27(5):1047–53. https://doi.org/10.2337/diacare.27.5.1047.
15. Kodama S, Horikawa C, Fujihara K, Yoshizawa S, Yachi Y, Tanaka S, et al. Quantitative relationship between body weight gain in adulthood and incident type 2 diabetes: a meta-analysis. Obesity Rev. 2014;15(3):202–14. https://doi.org/10.1111/obr.12129.
16. Li HT, Wu XD, Davey AK, Wang J. Antihyperglycemic effects of baicalin on streptozotocin – nicotinamide induced diabetic rats. Phytother Res. 2011; 25(2):189–94. https://doi.org/10.1002/ptr.3238.
17. WHO. Laboratory diagnosis and monitoring of diabetes mellitus. World health organization report. Geneva, Netherlands. 2002; 5–7.
18. Olabanji SO. PIXE analysis of some Nigerian anti-diabetic medicinal plants [II]. Nuclear Instrum Methods Phys Res Beam Interact Mater Atom. 2014;318: 187–90. https://doi.org/10.1016/j.nimb.2013.06.052.
19. Islam MS, Wilson RD. Animal models: method for experimentally induced rodent models of type 2 diabetes. In: Joost HG, Al-Hasani H, Schürmann A, editors. . New York: Humana Press; 2001. p. 61–74.
20. Masiello P. Animal models of type 2 diabetes with reduced pancreatic beta-cell mass. Int J Biochem Cell Bio. 2006;38(5-6):873–93. https://doi.org/10.1016/j.biocel.2005.09.007.
21. Mukherjee PK. Quality control of herbal drugs (an approach to evaluation of botanicals). Bus Horiz New Delhi. 2002:380–421.
22. Asif M, Atif M, AMS AM, Zahari CD, Irshadm A, Ashfaq A. Diuretic activity of *Trianthema portulacastrum* crude extract in albino rats. Trop J Pharmacol Res. 2013;12(6):967–72. https://doi.org/10.4314/tjpr.v12i6.15.
23. Ratnasooriya WD, Pieris KP, Samaratunga U, Jayakody JR. Diuretic activity of Spilanthes acmella flowers in rats. J Ethnopharmacol. 2004;91(2-3):317–20. https://doi.org/10.1016/j.jep.2004.01.006.
24. Sathianarayanan S, Jose A, Rajasekaran A, George RM, Chittethu AB. Diuretic activity of aqueous and alcoholic extracts of *Wrightia tinctoria*. Phytomed. 2011;2:7–8.
25. Adeosun OG, Oduola T, Fagbomedo FA. Suitability of stem latex of *Jatropha gossypiifolia* as a protein precipitant for biochemical analysis. Indian J Clin Biochem. 2014;29(2):210–2. https://doi.org/10.1007/s12291-013-0342-z.
26. Abdala S, Martín-Herrera D, Benjumea D, Gutiérrez SD. Diuretic activity of some *Smilax canariensis* fractions. J Ethnopharmacol. 2012;40(2):227–81. https://doi.org/10.1016/j.jep.2012.01.017.
27. Danamma KAK, Jayasimha BG, Basha SN. Diuretic activity and study of biochemical parameters in the methanol extract of *Hibiscus esculentus* (okra) fresh fruits. Intern J Pharmacol Bio Sc. 2011;1:160–9.
28. Saleem H, Ahmad I, Ashraf M, Shoaib MAG, Nadeem MF, Shahid MN, et al. In vitro studies on antidiabetic and antiulcer potentials of *Jatropha gossypiifolia* [Euphorbiaceae]. Trop J Pharm Res. 2016;5(1):121–5. https://doi.org/10.4314/tjpr.v15i1.17.
29. Shrivastava R, Solanki SS, Tomar V. Effect of polyherbal combination on hypolipidemic activity. Intern J Pharm Sci and Drug Res. 2009;1(1):9–12.
30. Umbrae RP, Patil SM, Mate GS, Dongare SS. Hypolipidemic activity of *Orthosiphon stamnineus* Benth bark extract. J Pharm Res. 2009;2(11):1735–8.
31. Yakubu MT, Afolayan AJ. Effect of aqueous extract of *Bulbine natalensis* baker stem on haematological and serum lipid profile of male wistar rats. Indian J Exper Bio. 2009;47:283–8.
32. Drury RAB, Wallinton EA. Carletons: histological technique. 16th ed. London: Oxford University Press; 2013. p. 124–36.
33. Tahri A, Yamani S, Legssyer A. Acute diuretic, natriuretic and hypotensive effects of a continuous perfusion of aqueous extract of *Urtica dioica* in the rat. Ethnopharmaco J. 2000;73(1–2):95–100. https://doi.org/10.1016/S0378-8741(00)00270-1.
34. Jouad H, Lacaille-Dubois MA, Eddouks M. Chronic diuretic effect of the water extract of *Spergularia purpurea* in normal rats. J Ethnopharmacol. 2001;75(2–3):219–23. https://doi.org/10.1016/S0378-8741(01)00193-3.
35. Vargas SR, Perez GRM. Diuretic and urolithiatic activities of the aqueous extract of the fruit of *Randia echinocarpa* on rats. J Ethnopharmacol. 2002; 83(1–2):145–7. https://doi.org/10.1016/S0378-8741(02)00091-0.
36. Mustapha E, Khadija B, Saad E, Faiza M, Abdellatif S. Effet diur'etique de l'infusion de fleurs de *lavandula officinalis*. Reprod Nutri Develop. 2001;41(5): 393–9. https://doi.org/10.1051/rnd:2001139.
37. Ojewole JAO. Analgesic, anti-inflammatory and hypoglycemic effects of ethanol extract of Zingiber officinale (roscoe) rhizomes (Zingiberaceae) in mice and rats. Phytother Res. 2006;20(9):764–72. https://doi.org/10.1002/ptr.1952.
38. Owolabi OJ, Amaechina FC, Okoro M. Effect of *Newboulda laevis* ethanol leaf extract on blood glucose levels in diabetic rats. Trop J Pharm Res. 2011; 10(3):249–54. https://doi.org/10.4314/tjpr.v10i3.12.
39. Glynn J, Bhikha K. Combining herbs: synergy in action. In: Tibb institute editor, a science of medicine: The art of cure; 2012. p. 162–70.
40. Odetola AA, Akinloye O, Egunjobi C, Adekunle WA, Ayoola AO. Possible antidiabetic and antihyperlipidaemic effect of fermented Parkia biglobosa (Jacq) extract in alloxan induced diabetic rats. Clin Exper Pharm Physiol. 2006;33(9):808–12. https://doi.org/10.1111/j.1440-1681.2006.04444.x.
41. Mahmoud AM, Hussein OE. Effect of naringin as an anti-diabetic and insights in molecular mechanisms. Diabetes Obes Intern J. 2016;1(5):000128.
42. Kameswaararao B, Kesavulu MM, Apparao C. Diabetes mellitus. Fitoterapia. 2003;74:7–13.
43. Owira PMO, Ojewole JAO. Grapefruit juice improves glycaemic control but exacerbates metformin-induced lactic acidosis in diabetic rats. Meth Find Exp Clin Pharmacol. 2009;31(9):563–70.
44. Oyedemi SO, Adewusi EA, Aiyegoro OA, Akinpeanolu DA. Effect of *Afzelia africana* (smith) aqueous stem bark extract in diabetic and hematological indices on streptozocin-induced diabetic wister rats. Asian Pacific J Trop Biomed. 2011;1(5):353–8. https://doi.org/10.1016/S2221-1691(11)60079-8.
45. Murunga AN, Miruka DO, Driver C, Nkomo FS, Cobongela SZZ, Owira PMO. Grapefruit derived flavonoid naringin improves ketoacidosis and lipid peroxidation in type 1 diabetes rat model. PLoS One. 2016;11(4):e0153241. https://doi.org/10.1371/journal.pone.0153241.
46. Chukwuma OO, Chidozie EA, Ikenna IK, Augusta NC, Jeremiah OS. Anti-diabetic and renal protective effect of the fruit juice of *Citrus X Paradisi* on alloxan induced diabetic male albino wistar rats. Pharm Lett. 2016;8(19):32–8.
47. Alarcon C, Wicksteed B, Prentki M, Corkey BE, Rhodes CJ. Preferential metabolic stimulus-coupling, a signal for glucose-induced proinsulin biosynthesis translation. Diabetes. 2002;51(8):2496–504. https://doi.org/10.2337/diabetes.51.8.2496.
48. Abdulazeez MA, Ibrahim K, Bulus K, Babvoshia HB, Abdullahi Y. Effect of combined use of *Ocimum gratissimum* and *Vernonia amygdalina* extract on angiotensin converting enzyme, hypolipidemic and *in-vivo* antioxidant in streptozocin-induced diabetic rats. Afr J Biochem Res. 2013;7:165–73.
49. Osigwe CC, Akah PA, Nworu CS. Biochemical and haematological effects of the leaf extract of *Newbouldia laevis* in alloxan- induced diabetic rats. J Biosci Med. 2017;5:18–36.
50. Liamis G, Liberopoulos E, Barkas F, Elisaf M. Diabetes mellitus and electrolyte disorders. World J Clin Case. 2014;2(10):488–96. https://doi.org/10.12998/wjcc.v2.i10.488.
51. Goldberg J. Causes and consequences of diabetic and dyslipidemia. J Clin Endocrinol Metab. 2001;86(3):3–9. https://doi.org/10.1210/jcem.86.3.7304.
52. Castilla PE. Diuretic. American J Clin Nutri. 2006;84(1):252–62. https://doi.org/10.1093/ajcn/84.1.252.

53. Eleazu CO, Iroaganachi M, Eleazu KC. Effect of cocoyam (*Colocasia esculenta* L.) and unripe plantain (*Musa paradisiaca* L.) on relative tissue weights of streptozotocin-induced diabetic rats. J Diabetes Res. 2013;2013(160964):8.
54. Fuji H, Yokozawa T, Kim YA, Tohga C, Nonaka G. Proanthrocyanidins protective effect in high glucose mediated oxidative stress in cultured kidney cells. Mini Reviews in Med Chem. 2006;7:663–78.
55. Florence NT, Benoit MZ, Jonas K, Alexandra T, DDP D, Pierre K, et al. Antidiabetic and antioxidant effects of *Annona muricata* (Annonaceae), aqueous extract on streptozotocin-induced diabetic rats. J Ethnopharmacol. 2014;151(2):784–90. https://doi.org/10.1016/j.jep.2013.09.021.

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