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Research Article
Effect of *Balanites aegyptiaca* Fruit-pericarp Extract on Fructose Induced Hyperglycemia and Hyperlipidemia in Rats

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Abstract

Background and Objective: High fructose intake has been reported to alter metabolisms leading to hyperglycemia and dyslipidemia. This study investigated the effect of *Balanites aegyptiaca* fruit-pericarp extract on high fructose fed rats. **Materials and Methods:** *Balanites aegyptiaca* fruits after collection were dehulled to obtain pericarps, air-dried and pulverized into powdered then extracted with ethanol. Phytochemical content and acute toxicity of the extract were ascertained. The study was conducted on rats divided into 7 groups of 5 each, namely; normal control, extract control (received 600 mg kg^{-1} b.wt., extract), fructose control (received 30% fructose solution), standard drug control (fructose fed rats treated with simvastatin 25 mg kg^{-1}) while group 4-6 were fructose fed rats treated with extract at 200, 400 and 800 mg kg^{-1} b.wt.. After 21 days of extract administration, rats were sacrificed, blood collected and serum separated which was used for the biochemical analysis. **Results:** The study showed pericarp extract possess variety of phytochemical (phenols, flavonoids, saponins, tannins) and is safe with lethal median dose (LD_{50}) assumed at 4000 mg kg^{-1} b.wt., of rats. Lipid profile varies significantly ($p<0.05$) between rats fed fructose untreated and treated whereas, fasting blood glucose and insulin are insignificantly ($p>0.05$) different among all groups. Fructose untreated rats had the highest weight increase at 17% compare to the treated rats. **Conclusion:** The study found pericarp extract of *Balanites aegyptiaca* safe, possess important phytochemicals and able to prevent fructose induced hyperglycemia and hyperlipidemia in rats. It may be a good source for the management of metabolic disorders.

Key words: *Balanites aegyptiaca*, fruit-pericarp, fructose, antihyperlipidemia, antihyperglycemia, rats

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Competing Interest: The authors have declared that no competing interest exists.

Data Availability: All relevant data are within the paper and its supporting information files.

INTRODUCTION

High intake of fructose over long periods has been reported to be hazardous to human beings as well as animals[1,2]. It alter metabolisms resulting to hyperglycemia and hyperlipidemia[3,4,5]. Fructose has been reported to activate gluconeogenesis due to increase in phosphoenolpyruvate carboxykinase (PEPCK) expression[6] and also stimulate de novo lipogenesis[7].

Hyperlipidemia is key factor in the increase prevalence of cardiovascular diseases like atherosclerosis, hypertension, coronary heart disease. Hyperglycemia is a key indicator of diabetes which resulted from either defective or deficient insulin[8]. Natural products particularly from plants had shown some level of protection against cardiovascular diseases and diabetes in several experimental studies[9].

Balanites aegyptiaca plant has long history of traditional uses in treatment of many diseases like jaundice, intestinal worm infection, wounds, malaria, syphilis, epilepsy, dysentery, constipation, diarrhea, hemorrhoid, stomach aches, asthma, diabetes mellitus and fever[10,11]. Extracts from *Balanites aegyptiaca* parts particularly fruit-mesocarp have been found to be a useful source of remedy in the management of hyperglycemia and hyperlipidemia[12]. The plant's fruit-pericarp has not been fully investigated for possible medicinal potentials. This study therefore, investigated *Balanites aegyptiaca* fruit-pericarp extract on fructose induced hyperglycemia and hyperlipidemia in rats.

MATERIALS AND METHODS

Materials

Plant collection and identification: *Balanites aegyptiaca* fruit were collected from Gubi village (latitude 10°45'N and longitude 9°82'E) in Bauchi LGA, Bauchi State, North East of Nigeria and was identified at the Herbarium Unit, Department of Biological Science, Ahmadu Bello University Zaria. A specimen voucher no: 900175 was deposited. After collection of the ripe fruits, the pericarps were obtained by peeling the fruit then air dried.

Chemicals: All chemicals and reagents used were of analytical grade. Reagent kits were obtained from Agappe Diagnostics Switzerland GmbH. Chemical and solvents were obtained from Sigma Aldrich, USA.

Experimental animals: White male wistar albino rats about 3-4 months old were purchased from the Animal House of the University of Jos, Plateau State, Nigeria and kept in clean cages with 12/12 h light/dark photoperiod. Water and feed 'growers mash' (Vital feeds, Jos, Plateau State) were supplied *ad libitum*. Animals were allowed to grow to attain a weight 180-200 g before commencement of the experiment. Experimental protocol was in conformity with national and international laws and guidelines for care and use of laboratory animals as in 'Principle of Laboratory Animal Care'[13].

Methods

Plant extraction: The plant fruit after collection were dehulled to obtain the pericarp which were air-dried under shade for a week period then pulverized using pestle and mortar into powdered form and then defatted with hexane as reported by Jung *et al.*[14] followed by extraction with ethanol as described by Govorko *et al.*[15] with modification in choice of the extraction temperature (60°C). Seven hundred and fifty gram (750 g) of pericarp powdered was defatted for 2 h with 250 mL hexane on mechanical shaker and then air-dried. Exact 100 g of defatted sample was mixed with 1000 mL of 80% ethanol and heated to 60°C for 2 h and then kept at 20°C for 10 h. It was filtered through a cheese cloth and the filtrate air-dried. The fruit-pericarp ethanol extract (50.41 g) was kept in a refrigerator in an air tired container until used.

Phytochemical screening: Preliminary phytochemical screening of the ethanolic extract of *Balanites aegyptiaca* fruit-pericarp was done by adopting the methods of Harborne[16] and Sofowora[17].

Acute toxicity study: Acute toxicity study was performed according to guidelines of Organization of Economic Company and Development (OECD)[18] 425. The extracts were administered in a single dose using oral gastric tube. Rats were deprived of food 3 h prior to dosing. After each extract administration, observation was done at 30 min interval for 4 h then after 24 h for behavioral change or death. The dosage; 5, 50, 500, 1000, 2000, 4000 mg kg^{-1} b.wt., were determined and used according to the OECD 425 guidelines with limit between the range of 2000-5000 mg kg^{-1} b.wt.

Bruce[19] up and down procedure for oral acute toxicity study was used to investigate acute toxicity in Wistar albino rats. Briefly, rats were dosed one at a time and observed for survival or death. If a rat survives, the dose for the next rat was increased if it die the dose was decreased. Each rat was observed at least for 24 h before dosing the next rat until the least dose lethal to rat is obtained.

Lethal median dose (LD_{50}) was calculated using the equation:

$$LD_{50} = \text{Apparent least dose lethal to rats-}\left[\frac{a \times b}{N}\right]$$

Where:
N = Number of animal used
a = Dose difference
b = Mortality

Hence, therapeutic doses was calculated as 1/20th, 1/10th and 1/5th of the highest lethal dose.

Animal grouping and treatment: Fructose induced hyperlipidemia and hyperglycemia was determined by method described by Mahmoud *et al.*[20]. Rats were randomly allocated into 7 groups of 5 rats each and treated for 21 days period as follows:

- **Group 1 (Normal control):** Received normal feed and distilled water only
- **Group 2 (Extract control):** Received normal feed+extract (800 mg kg^{-1} b.wt.)
- **Group 3 (Fructose control):** Received normal diet+30% fructose solution
- **Group 4 (Standard drug control):** 30% fructose solution+Simvastatin (25 mg kg^{-1} b.wt.)
- **Group 5 (Fructose fed rats+200 mg extract):** Received normal diet+30% fructose solution+extract (200 mg kg^{-1} bwt.)
- **Group 6 (Fructose fed rats+400 mg extract):** Received normal diet+30% fructose solution+extract (400 mg kg^{-1} b.wt.)
- **Group 7 (Fructose fed rats+800 mg extract):** Received normal diet+30% fructose solution+extract (800 mg kg^{-1} b.wt.)

The extract administered orally using oral gastric tube while 30% fructose solution given in their drinking water daily. Literature shows that rats fed fructose in drinking water for a period of one week or longer has been found to induced hyperglycemia, hyperinsulinemia and hyperlipidemia[20,21].

Measurement of animal body and organs weights: Animal weight was determined weekly by weighing the rats using a weighing scale. The weight was taken in the morning before feeding the rats by properly placing each rat in the weighing pan of the weighing scale and then the weight recorded. Organs (liver, kidney, heart and spleen) excised were drained and weighed using a weighing scale.

Biochemical assays: Serum triglyceride (TG) was determined using the method described by Fossati and Prencipe[22]. Serum total cholesterol was determined spectrophotometrically according to the method of Roeschlau *et al.*[23] while high density lipoprotein Cholesterol (HDL-C) was measured according to the Lopes-Virella *et al.*[24] method. Total Protein was determined by Bradford method[25]. Agappe assay kits were used and procedures were according to the manufacturer's instruction. The LDL-cholesterol and VLDL-cholesterol (VLDL-C) were determined by the formula described by Friedewald *et al.*[26]. The LDL-cholesterol concentration (mg dL^{-1}) = [TC-(HDL-C+Triglycerides/5)] and VLDL-cholesterol concentration (mg dL^{-1}) = [Triglycerides/5].

The TC/HDL-C and TG/HDL-C ratios were estimated as marker of atherogenic lipid indices[27,28]:

$$\text{TyG index} = \text{Ln}\left[\frac{\text{TG (mg dL}^{-1}) \times \text{FPG (mg dL}^{-1})}{2}\right]$$

The IR was estimated using the homeostasis model assessment for IR (HOMA-IR). The HOMA-IR is expressed as:

$$\text{Fasting glucose (mmol L}^{-1}) \times \text{fasting insulin } (\mu\text{U L}^{-1})/22.5$$

Fasting blood glucose level was determined using glucometer (ACCU-CHEK Active-Roche Diagnostics, Germany).

Glucose enzymes assay: Glucokinase was assayed following Goward's[29] method based on the principle that glucokinase catalyzes the phosphorylation of glucose to glucose 6-phosphate. Glucose-6-phosphate is converted to 6 phosphate-D-gluconate by reduction of β-$NADP^+$ through a reaction with glucose-6-phosphate dehydrogenase. The absorbance of the β-NADPH was read at 340 nm

The activity of the enzymes was by the equation:

$$\text{Units/mg protein} = (A_{340nm}\ \text{Test-}A_{340nm}\ \text{Blank})\ (3) \times df/(6.22)\ (0.1)$$

Where:
6.22 = Molar extinction coefficient of NADPH at 340 nm
3 = Volume of mixture (mL)
0.1 = Volume (mL) of enzyme used
df = Dilution factor

Phosphofructokinase was assayed by Hengartner and Harris[30] method based on the principle that phosphofructokinase catalyzes the conversion of fructose-6-phosphate to fructose-1,6-bisphosphate. The enzyme was assayed based on the rate of reduction of β-NADH through a coupled reaction with pyruvate kinase and lactate dehydrogenase. The absorbance of the β-NAD^+ was read at 340 nm. The activity of the enzymes was determined by the equation:

$$\text{Units mg}^{-1}\text{ protein} = (A_{340nm}\ \text{Test-}A_{340nm}\ \text{Blank})\ (3) \times df/(6.22)\ (0.1)$$

Where:

6.22 = Molar extinction coefficient of NAD+at 340 nm
3 = Volume of mixture (mL)
0.1 = Volume (mL) of enzyme used
df = Dilution factor

Pyruvate kinase was assay by Pogson and Denton[31] method based on the principle that pyruvate kinase catalyzes the conversion of phosphenolpyruvate to pyruvate followed by a reduction of pyruvate in the presence of β-NADH to lactate and β-NAD^+. The activity of the enzyme was determined by the formula stated in phosphofructokinase above.

Phosphoenolpyruvate carboxyl kinase was assay by Berndt and Ulbrich[32] method based on the principle that phosphoenolpyruvate carboxykinase catalyzes the conversion of oxaloacetate to phosphoenolpyruvate coupled by its conversion to pyruvate and lactate in the presence of β-NADH through reactions with pyruvate kinase and lactate dehydrogenase. The activity of the enzyme was determined by the formula stated in phosphofructokinase above.

Fructose-1,6-bisphosphatase was assay by Biswas *et al.*[33] method based on the principle that fructose-1,6-bisphosphatase catalyzes the conversion of fructose-1,6-bisphosphate to fructose-6-phosphate. The enzyme activity was assayed by the measuring of the amount of inorganic phosphate liberated as described by Eibl and Lands[34]. The amount of phosphate was determined by the equation:

$$\text{Units } \mu\text{mole}^{-1}\ P_i\ \text{liberated} = \frac{(A_{840\ nm}\ \text{Test-}A_{840\ nm}\ \text{Blank})(3)}{3.0 \times 0.3}$$

Where:

3 = Total volume (mL) of assay
0.3 = Molar extinction coefficient of inorganic phosphate at 840 nm

Glucose-6-phosphatase was assay by Baginsky *et al.*[35] method based on the principle that glucose-6-phosphatase catalyzes the conversion of glucose-6-phosphate to glucose and inorganic phosphate. The enzyme activity was assayed by the measuring of the amount of inorganic phosphate liberated as described by Biswas *et al.*[33]. The amount of phosphate was determined by the formula as stated in fructose-1,6-bisphosphatase above.

Statistical analysis: Data from the experiments were expressed as mean±standard deviation (SD). Means were analyzed by one way analysis of variance (ANOVA) and compared by Duncan's multiple range test (DMRT)[36]. Significant difference was accepted at $p<0.05$.

RESULTS

Phytochemical content and toxicity of pericarp extract: The result of the phytochemical screening of *Balanites aegyptiaca* fruit-pericarp extract showed the presence of tannins, phenols, flavonoids and saponins. Results of acute toxicity study showed no death or treatment-related mortality at all the tested doses, no significant changes in behavior such as apathy, hyperactivity and morbidity in the treated rats. The pericarp extract seems to be safe up to a dose of 4000 mg kg^{-1} b.wt., where, the LD_{50} value for acute toxicity is considered to be greater than 4000 mg kg^{-1} b.wt.

Anti-hyperlipidemic effect of pericarp extract: Effect of *Balanites aegyptiaca* fruit-pericarp extract on lipid profile in rats fed fructose solution is presented in Table 1. There was a significant difference ($p<0.05$) in triglyceride and cholesterol contents of fructose fed untreated rats (304.53±11.49 mg dL^{-1}) and (293.75±53.80 mg dL^{-1}) in comparison to the treated rats groups (<219.20±12.02 mg dL^{-1}) and (<177.92±6.00 mg dL^{-1}) in a dose dependent manner. Significant elevation ($p<0.05$) in HDL content was observed in fructose fed rats that received the extract (>33.17±6.07 mg dL^{-1}) in comparison to fructose fed untreated rats (30.40±10.29 mg dL^{-1}).

Anti-atherogenic effect of pericarp extract: Effect of *Balanites aegyptiaca* fruit-pericarp extract on atherogenic and anti-atherogenic indexes in rats fed fructose solution is given in Table 2. A significant ($p<0.05$) change was recorded in their atherogenic indexes 1 and 2 from fructose fed control rats (10.52±3.42 mg dL^{-1}) and (7.36±2.93 mg dL^{-1}) in a comparable manner to fructose fed treated rats' groups

Table 1: Effect of ethanolic extract of *Balanites aegyptiaca* fruit-pericarp on lipid profiles of normal and fructose fed rats

	Groups						
Parameters (mg dL^{-1})	Normal control	Extract control	Fructose control	Standard drug control	Fructose fed rats+ 200 mg extract	Fructose fed rats+400 mg	Extract fructose fed rats+ 800 mg extract
Triglyceride	114.67±11.43^{a}	117.60±8.40^{a}	304.53±11.49^{bcde}	143.47±4.86^{b}	219.20±12.02^{bcd}	175.73±27.66^{bc}	169.33±34.78^{bc}
Cholesterol	167.92±72.18^{a}	185.00±22.94^{a}	293.75±53.80^{b}	167.92±19.18^{a}	177.92±6.00^{a}	156.67±7.99^{a}	138.33±7.60^{a}
High density lipoprotein	40.59±2.76^{abc}	46.34±1.43^{b-e}	30.40±10.29^{a}	37.82±9.27^{abc}	33.17±6.07^{ab}	42.57±4.01^{bc}	52.77±11.16^{b-f}
Low density lipoprotein	104.39±7.81^{b}	115.14±4.04^{b}	202.45±9.45^{bc}	101.40±7.15^{b}	100.91±10.30^{b}	78.95±9.02^{ab}	51.69±6.68^{a}
Very low density lipoprotein	22.93±2.29^{a}	23.52±1.68^{a}	60.91±2.30^{b-e}	28.69±0.97^{b}	43.84±2.40^{bcd}	35.15±5.53^{bc}	33.87±6.96^{bc}

Values are Mean±SD of 5 determinations, values with different superscript across the rows are significantly different ($p<0.05$)

Table 2: Antiatherogenic effect of ethanolic extract of *Balanites aegyptiaca* fruit-pericarp of normal and fructose fed rats

	Groups						
Parameters (mg dL^{-1})	Normal control	Extract control	Fructose control	Standard drug control	Fructose fed rats+ 200 mg extract	Fructose fed rats+ 400 mg extract	Fructose fed rats+ 800 mg extract
Atherogenic index 1	4.11±1.68^{ab}	4.00±0.53^{ab}	10.52±3.42^{cd}	4.60±0.83^{ab}	5.51±1.03^{c}	3.71±0.41^{ab}	2.70±0.48^{a}
Atherogenic index 2	2.55±1.72^{ab}	2.49±0.55^{ab}	7.36±2.93^{cd}	2.78±0.70^{ab}	3.16±0.83^{c}	1.88±0.32^{ab}	1.05±0.48^{a}
Anti-atherogenic	39.76±7.71^{b}	34.33±6.92^{b}	12.78±8.09^{a}	29.46±8.22^{b}	23.15±5.48^{ab}	37.72±6.52^{b}	63.25±9.51^{bc}

Values are Mean±SD of 5 determinations, values with different superscript across the rows are significantly different ($p<0.05$)

Table 3: Effect of ethanolic extract of *Balanites aegyptiaca* fruit-pericarp on some biochemical indices of normal and fructose fed rats

	Groups						
Parameters	Normal control	Extract control	Fructose control	Standard drug control	Fructose fed rats+ 200 mg extract	Fructose fed rats+ 400 mg extract	Fructose fed rats+ 800 mg extract
FBG (mmol L^{-1})	5.50±0.21^{a}	5.62±0.51^{ab}	7.16±0.05^{bcde}	6.22±0.33^{bcd}	6.26±0.40^{bcd}	6.04±0.23^{bc}	5.72±0.22^{ab}
Insulin (μU L^{-1})	4.12±0.82^{a}	5.35±0.36^{b}	8.04±0.73^{bcd}	5.23±0.47^{b}	5.46±0.45^{b}	6.02±0.41^{b}	6.94±1.22^{bc}
HOMA-IR	1.01±0.19^{a}	1.33±0.16^{b}	2.56±0.24^{bcde}	1.44±0.18^{bc}	1.77±0.38^{bcd}	1.62±0.11^{bc}	1.52±0.18^{bc}
Total protein (mg g^{-1} Liver)	28.42±8.13^{b}	26.83±5.92^{ab}	27.86±2.36^{b}	23.93±3.42^{a}	26.34±5.23^{ab}	26.94±5.24^{ab}	22.46±4.26^{a}

Values are Mean±SD of 5 determinations, values with different superscript across the rows are significantly different ($p<0.05$)

(<5.51±1.03 mg dL^{-1}) and (<3.16±0.83 mg dL^{-1}) while an increase in antiatherogenic index of extract treated rats groups was recorded (>23.15±5.48 mg dL^{-1}) compared to fructose fed control rats (12.78±8.09 mg dL^{-1}).

Effect of pericarp extract on insulin and blood glucose: Fasting blood glucose, insulin, total protein concentrations of the treated and untreated fructose fed rats were presented in Table 3. The study recorded a significant difference ($p<0.05$) in fasting blood glucose level from fructose control rats and the fructose fed treated rats and non-fructose fed rats groups. Insulin level and HOMA-IR were significantly ($p<0.05$) high in fructose fed control rats (8.04±0.73 μU L^{-1})and (2.56±0.24) in comparison to fructose fed treated rats (<5.46±0.45 μU L^{-1}) and (<1.77±0.38). Albumin concentration was not significantly different ($p>0.05$) in all the rats' groups but total protein concentration showed a slightly different among the rats' groups.

Effect of pericarp extract on glucose metabolic enzymes: Effects of *Balanites aegyptiaca* fruit-pericarp extract on key glycolytic enzymes: glucokinase (GK), phosphofructokinase (PFK) and pyruvate kinase (PK) activities in liver tissues of streptozotocin-induced diabetic rats is presented in Table 4. Significant changes ($p<0.05$) were observed in the activities of these enzymes. The extract enhance the activities of glycolytic enzymes in a dose dependent manner, glucokinase (from 1.96±0.28 to >2.15±0.17 U min^{-1} mg^{-1} protein), phosphofructokinase (from 0.38±0.05 to 1.79±0.29 min mg^{-1} protein) and pyruvate kinase (from 0.24±0.11 to >1.23±0.02 U min^{-1} mg^{-1} protein).

The activities of glyconeogenic enzymes (phosphoenol pyruvate carboxykinase, fructose-1,6-bisphosphatase and glucose-6 phosphatase assayed are presented also in Table 4. The study recorded a significantly ($p<0.05$) depression in the activities of the gluconeogenic enzymes; fructose-1,6-bisphosphatase (from 0.98±0.19 to <0.64±0.16 μmole P_i liberated), glucose-6-phosphatase (from 10.61±0.14 to <0.56±0.02 U min^{-1} $μmole^{-1}$ P_i liberated) and phosphenolpyruvate carboxyl kinase (from 0.47±0.04 to <0.45±0.04 U min^{-1} mg^{-1} Protein).

Effect of pericarp extract on body weight: Figure 1 shows the effect of *Balanites aegyptiaca* fruit-pericarp extract on body weight of rats fed fructose solution while percentage weigh gained is present in Fig. 2. The study recorded an increase in body weight of fructose fed control rats at about 17% against 9-12% increase by the fructose fed treated and normal control rats, Organs weight of rats fed fructose solution following administration of extract of *Balanites aegpytiaca* fruit-pericarp showed no significant different among all rats groups (Fig. 3).

DISCUSSION

The medicinal potential of *Balanitesa egyptiaca* fruit-pericarp extract was investigated on fructose induced hyperglycemia and hyperlipidemia in rats. Phytochemicals like saponin, tannins, phenols and flavonoids were identified from the pericarp extract. The pericarp extract was found to be safe at concentration up to 4000 mg kg^{-1} b.wt. The study discover pericarp extract of *Balanites aegyptiaca* fruit possess anti-hyperlipidemic activity. It also exerts glucose enzymes

Table 4: Effect of ethanolic extract of *Balanites aegyptiaca* fruit-pericarp on enzymes of carbohydrate metabolism of normal and fructose fed rats

	Groups						
Parameters	Normal control	Extract control	Fructose control	Standard drug control	Fructose fed rats+ 200 mg extract	Fructose fed rats+ 400 mg extract	Fructose fed rats+ 800 mg extract
Glucose 6-Phosphatase (U min^{-1} µmole^{-1} P_i liberated)	0.22 ± 0.03^{a}	0.49 ± 0.03^{bcd}	0.61 ± 0.14^{bcd}	0.37 ± 0.15^{bc}	0.56 ± 0.02^{bcd}	0.39 ± 0.06^{bc}	0.36 ± 0.07^{bc}
Fructose-1,6-bis-phosphatase (U min^{-1} µmole^{-1} P_i liberated)	0.06 ± 0.02^{a}	0.18 ± 0.06^{ab}	0.98 ± 0.19^{bcde}	0.40 ± 0.02^{bc}	0.64 ± 0.16^{bcd}	0.21 ± 0.06^{b}	0.12 ± 0.06^{ab}
Phosphoenolpyruvate carboxykinase (U min^{-1} mg^{-1} protein)	0.05 ± 0.00^{a}	0.33 ± 0.03^{bcde}	0.47 ± 0.04^{bcdefg}	0.22 ± 0.02^{bc}	0.45 ± 0.04^{bcdefg}	0.37 ± 0.03^{bcdef}	0.27 ± 0.02^{bcd}
Glucokinase (U min^{-1} mg^{-1} protein)	2.42 ± 0.12^{bc}	2.53 ± 0.04^{bcd}	1.96 ± 0.28^{a}	2.43 ± 0.03^{bc}	2.15 ± 0.17^{b}	2.42 ± 0.13^{bc}	2.63 ± 0.02^{bcd}
Phosphofructokinase (U min^{-1} mg^{-1} protein)	2.13 ± 0.14^{bcd}	1.49 ± 0.44^{b}	0.38 ± 0.05^{a}	1.80 ± 0.37^{bc}	1.79 ± 0.29^{bc}	2.13 ± 0.14^{bcd}	2.35 ± 0.08^{bcd}
Pyruvate kinase (U min^{-1} mg^{-1} protein)	1.34 ± 0.05^{bc}	0.85 ± 0.34^{b}	0.24 ± 0.11^{a}	0.86 ± 0.24^{b}	1.23 ± 0.02^{bc}	1.32 ± 0.03^{bc}	1.33 ± 0.04^{bc}

Values are Mean±SD of 5 determinations, values with different superscript across the rows are significantly different ($p<0.05$)

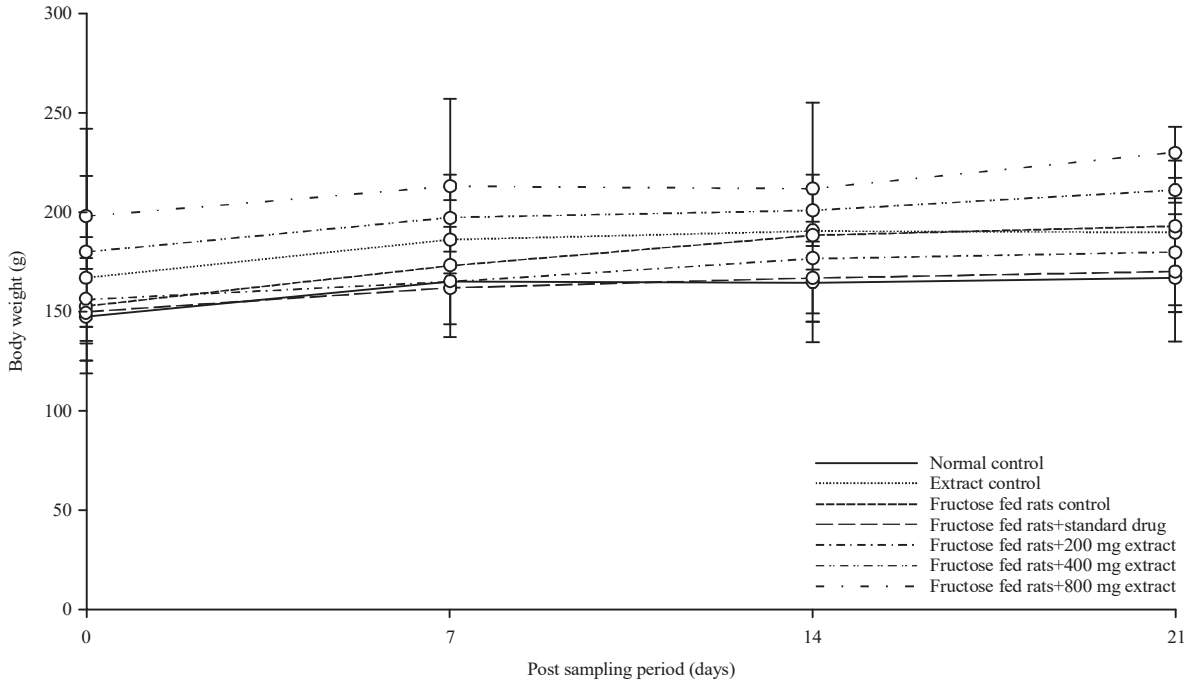

Fig. 1: Effect of ethanolic extract of *Balanites aegyptiaca* fruit-pericarp on body weight of normal and fructose fed rats

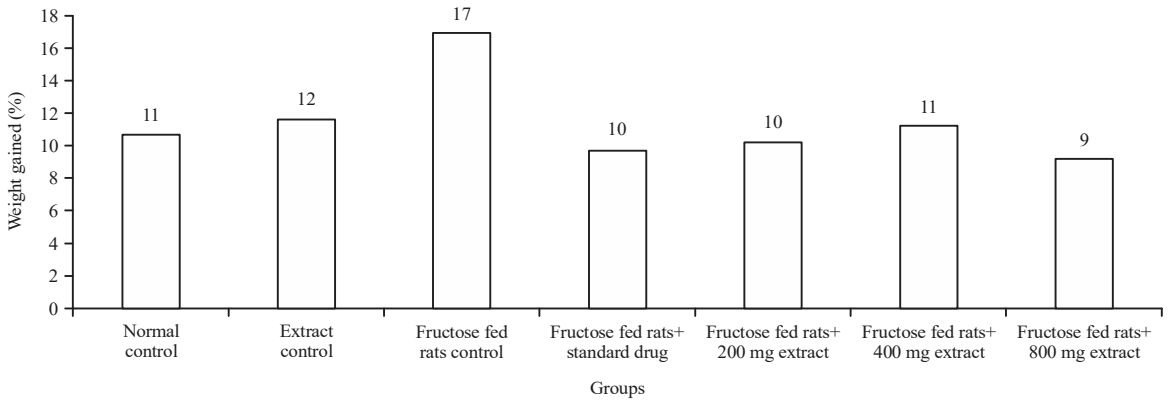

Fig. 2: Percentage body weight gained of normal and fructose fed rats following treatment with ethanolic extract of *Balanites aegyptiaca* fruit-pericarp
n = 5

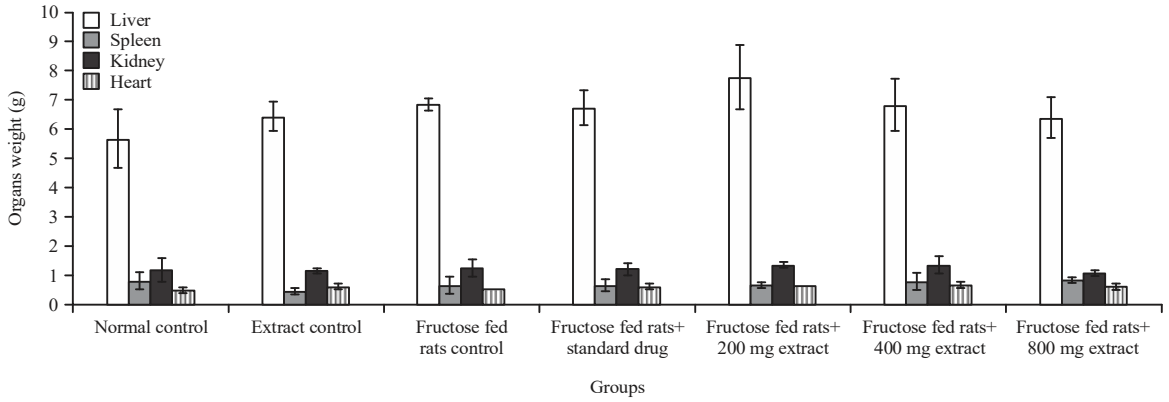

Fig. 3: Effect of ethanolic extract of *Balanites aegyptiaca* fruit-pericarp on organs weight of normal and fructose fed rats
n = 5

regulatory effect as evident from the improve activity of key enzymes in glycolysis but depress gluconeogenic enzymes in rats treated with the extract.

The normalcy and insignificant changes in parameters observed following the oral toxicity study of *Balanites aegyptiaca* fruit-pericarp extract agrees with the report that some medicinal plants extract or preparation has less or no toxic effects[10,37]. Similar findings has been reported by the author in a previous study with extracts from leaves, stem-bark and fruit-mesocarp of *Balanites aegyptiaca*[38].

In this study, high levels of cholesterol and triglycerides from fructose fed control rats is an indication that fructose adversely affect lipid metabolism resulting in the increase accumulation of these lipids[7]. Declined in serum triglyceride level of fructose fed rats treated with pericarp extract of *Balanites aegyptiaca* suggest ability of extract to reverse hypertriglyceridemia induced by fructose. It has been reported that plant extract lower cholesterol by either decreasing cholesterol absorption from the intestine via binding with bile acids and increasing bile acids excretion[39] or by inhibition of HMG-CoA reductase activity[40]. The low cholesterol from the fructose fed rats treated with pericarp extract seems to agree with the above statement.

Increase in the level of serum LDL-cholesterol and VLDL-cholesterol in fructose fed control rats in this study is an indication of cardiovascular disease development associated with insulin resistance. While, low serum LDL-cholesterol and VLDL-cholesterol levels with concomitant increase in HDL-cholesterol in the fructose fed rats treated withpericarp extract suggest inhibition of hyperlipidemia which is due the phytochemicals identified. Similar trend have been observed in one of the author previous study by Mhya *et al.*[41] and other studies with extracts from *Balanites aegyptiaca* parts[12].

High intake of fructose has been reported to disturb carbohydrate metabolism resulting to hyperglycemia[3]. Hyperglycemia is mainly resulted from increased gluconeogenesis by the fructose via activation of adenosine monophosphate kinase in the hypothalamus resulting in the secretion of corticosterone which acts in the liver to increase phosphoenolpyruvate carboxykinase expression[6]. Depress activity of phosphoenolpyruvate carboxykinase among other gluconeogenic enzymes in rats treated with pericarp extract might have slow gluconeogenesis resulting in normal blood glucose as compare to the slight increase observed in fructose fed control rats. *Balanites aegyptiaca* fruit-mesocarp extract has been reported to have slowed gluconeogenesis by decreasing the activities of enzymes, such as glucose-6-phosphatase, fructose-1, 6-diphosphatase, phosphoenolpyruvate carboxykinase and pyruvate carboxylase[42].

The activities of glucokinase, phosphofructokinase and pyruvate kinase were depressed in fructose fed control rats. Reduced activities of these enzymes in this study are consistent with other studies on glycolytic enzymes[43,44]. Decrease in the activities of the glycolytic enzymes in this study is likely due to insulin resistance caused by fructose intake which might be the reason for slightly increase in blood glucose levels recorded in same rats' groups. However, increase activities of the glycolytic enzymes in rats received pericarp extract may be the result of the extract. Literature survey have showed that several plants extract were able to promote the activities of similar enzymes in glycolysis[45,46].

CONCLUSION

In conclusion, ethanol extract of *Balanites aegyptiaca* fruit-pericarp is safe and contain some medicinal important phytochemicals. It exerts anti-hyperlipidemia, anti-hyperglycemia and glucose enzymes regulatory activity in rats fed fructose solution. The activities exhibited may likely be due to some of the phytochemicals identified. Results from this study showed *Balanites aegyptiaca* fruit-pericarp a good source with diverse medicinal potentials which may be recommended for use in the management of metabolic disorders. Further research leading to isolation, identification and elucidation of active molecule from fruit-pericarp is recommended.

SIGNIFICANCE STATEMENT

This study discover pericarp of *Balanites aegyptiaca* possess molecules which has medicinal values that can be beneficial for management of several metabolic disorders. Findings from this study may serve as a platform for the use of this plant part and an open door toward unveiling active molecules for novel drug discovery.

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