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Research Article

EVALUATION OF THE ANTIDIABETIC EFFECTS OF THE HYDROETHANOLIC EXTRACT OF THE TRUNK BARK OF *LANNEA ACIDA* A. RICH. (ANACARDIACEAE) ON FRUCTOSE-INDUCED DIABETIC *WISTAR* RATS

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ABSTRACT

Objectives: Given the increasing consumption of sweet products and the preference for these products. Metabolic disorders such as diabetes appear early in life. This study aimed to evaluate the effect of hydroethanolic extract of *Lannea acida* trunk bark (HEELA) on the impact of daily fructose consumption on the onset of type 2 diabetes.

Methods: Four groups of male Wistar rats were fed a 10% fructose-rich drinking water for 10 weeks to induce diabetes. At the beginning of the 11th week, the three groups were treated with 40. 100 and 200 mg/kg body weight (bw) HEELA for 6 weeks. The negative control group continued to receive fructose without treatment. The fifth group was fed fructose-free drinking water (neutral control). Blood sugar levels were measured every 2 weeks, and biochemical parameters such as lipids and transaminases were assessed. The area under the curve (AUC) was determined. Histopathological sections of the pancreas and liver were also carried out.

Results: The results showed a significant ($p<0.001$) decrease in high-fructose diet-induced increases in blood glucose, relative liver and pancreas weights, AUC, triglyceride, aspartate aminotransferase, and alanine aminotransferase concentrations following HEELA administration at 200 mg/kg bw. Conversely, a significant increase ($p<0.001$) in the fructose-induced decrease in high-density lipoprotein cholesterol. The effects of fructose on liver and pancreas structure were corrected by HEELA.

Conclusion: HEELA improves the blood glucose, lipid profiles, and supports liver and pancreas functions. In addition, it protects against the hepatic and pancreatic tissue damage mediated by the daily fructose consumption.

Keywords: *Lannea acida*, High fructose diet, Diabetes, Hyperglycemia, Pancreas, Area under the curve.

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INTRODUCTION

Diabetes type 2 is a chronic disease that occurs when the pancreas does not produce enough insulin or when the body is unable to use the insulin that it produces efficiently [1]. In recent years, there has been a worldwide increase in obesity, physical inactivity, and a diet rich in energy (sugar, lipids), leading to an upsurge in the number of type 2 diabetes patients [2]. Numerous studies have shown a strong association between the risk of type 2 diabetes and sugar consumption, particularly fructose consumption and sweetened beverages [3,4] showed on an econometric model of repeated cross-sectional data from 175 countries that sugar was significantly associated with an increase in diabetes prevalence in a dose-dependent manner. In Africa, 25 million people live with diabetes. This number is expected to increase by 142% to 59.5 million by 2050 [5]. In Burkina Faso, prevalence was 4.9% nationally and 13.9% in urban areas [6]. In low- and middle-income countries, the rate of premature mortality attributable to diabetes increased between 2000 and 2016 in countries [7].

Experimental studies have shown that the adverse effects of fructose and sugar-sweetened beverages overload in humans and animals manifest as hyperglycemia, insuline resistance, hyperinsulinemia, hypertriglyceridemia, and glucose intolerance, as well as an increase in blood pressure [3,8]. Investigations of animal models with a high-fructose diet on rodents, including medicinal plants attenuating the deleterious effects of fructose, have been carried out [8,9]. Treatment and prevention rely on hygienic-dietary measures, physical, and insulin injections, the use of oral antidiabetics, and bariatric surgery present side effects and are inaccessible due to their high cost and unavailability [10]. Given the difficulties of treating diabetes with conventional medicine, particular attention is being paid to traditional and complementary medicine. Herbal medicines and traditional treatments are said to be the main source of healthcare for millions of people with diabetes due to their affordability, accessibility, and cultural acceptability [11]. In the face of these healthcare problems, the use of plant compounds as a source of drugs for the majority of modern diseases is being promoted in the current drug research [9]. Therefore, users must be informed about their health quality, safety, and efficacy of final plant products [11]. Ethnobotanical surveys have shown that certain medicinal plants, such as *Lannea acida*, help to combat diabetes [12]. Previous pharmacological studies have highlighted certain biological properties of *L. acida* trunk bark [13]. Therefore, evaluating their pharmacological potential based on quality, efficacy, and safety data is necessary. As far as *L. acida* is concerned, no antidiabetic activity has been reported in the literature, particularly on hyperglycemia, dyslipidemia, glucose intolerance, and insulin resistance. This study aimed to evaluate the effect of the hydroethanolic extract of *L. acida* trunk bark on the impact of daily fructose consumption on the onset of type 2 diabetes.

MATERIALS AND METHODS

Material

Plant material

L. acida trunk bark was collected and dried under artificial ventilation in the laboratory. Dried bark was ground to a fine powder and stored in a dry place. The sample was identified in the herbarium of the Plant Biology and Ecology laboratory at Joseph KI-ZERBO University. The specimen was deposited under the following identification number: 18052.

Animal material

The tests were carried out on male Wistar rats. On average, they weighed 105.1 g and were 8–12 weeks old. The animals came from the Joseph KI-ZERBO University animal house. They were reared at a temperature of 22±3°C, a relative humidity of 50±10%, and an alternation of 12 h of light and 12 h of darkness. Animals were fed 29% protein-rich pellets. All tests were carried out by the guidelines of the Joseph KI-ZERBO University Ethics Committee under approval number CE-UJKZ/2023-14.

Methods

Diabetes induction

Fructose of 99.5% purity from Carlo Erba reagents was used to induce diabetes. The activity on the curative effect of the hydroethanolic extract of *L. acida* trunk bark was performed by an adapted method of [14,15]. Twenty-five male rats were divided into five groups of five rats. They were treated as follows:

- Group 1 (neutral control): Fructose-free water
- Group 2 (negative control): Fructose-enriched water (10%)
- Group 3: Fructose-enriched water (10%) and hydroethanolic extract of *L. acida* trunk bark (HEELA) at 40 mg/kg bw at week 11
- Group 4: Fructose-enriched water (10%) and HEELA 100 mg/kg bw at week 11
- Group 5: Fructose-enriched water (10%) and HEELA at 200 mg/kg bw at week 11.

The fructose solution was renewed daily to avoid probable fermentation.

The blood glucose levels of each rat were taken every 2 weeks using an Accu-Check glucometer. Animal weights were taken weekly. The experiment lasted 16 weeks.

Sample preparation

At the end of week 16, the animals were deprived of food for 12 h before being necropsied. Blood from the animals was collected by cardiac puncture after anesthesia with lidocaine 20% and ketamine 50 mg/kg intraperitoneally [16]. Blood was centrifuged and serum recovered for biochemical analyses such as glucose level, total cholesterol (TC), triglycerides (TG), high density lipoprotein-cholesterol (HDL-c), transaminases (aspartate aminotransferase [ASAT], alanine aminotransferase [ALAT]). The various activities were carried out by using colorimetric methods. Commercial laboratory kits (Atlas) specific to each parameter were used. After ensuring these parameters, some important organs (such as the liver, heart, pancreas, spleen, adrenal glands, and kidneys) were sampled, rinsed, and weighed on a balance. Relative organ weights were calculated using the following formula: (Absolute organ weight)/(body weight (bw) at sacrifice)*100.

Histopathological examination

The liver and pancreas were preserved in 10% formalin for use as histological sections.

Oral glucose tolerance test

Two days before the end of the fructose-induced diabetes experiment all groups underwent a glucose tolerance test according to the protocol described by [17]. Rats were deprived of food for 12 h. Basal blood glucose was measured at time 0 min using a glucometer (Accu Answer) from the caudal end of the tail. Rats were then given oral glucose at a dose of 2 g/kg or 200 g/L bw in 40% aqueous form. After administration, blood glucose levels were measured at 30, 60, 90, and 120 min from a tail vein [17].

The glucose tolerance curve was made, and the area under the curve (AUC) was calculated using the following formula: AUC=0.25 × (baseline value)+0.5 × (value at 30 min)+0.75 × (value in 1 h)+0.5 × (value in 2 h) [17].

Statistical analysis

Data were analyzed using Excel 2016 and GraphPad Prism software (version 8.4.3). They are presented as mean±standard deviation. One-way analysis of variance was used to compare means between groups. The Tukey test was used to compare two mean values. The significance threshold is set at $p<0.05$. The means in different groups were compared to the neutral and negative control groups.

RESULTS

Rat bw evolution during the treatment

No significant increase in rat bw ($p>0.05$) was observed after 16 weeks of experimentation between the neutral control (tap water). Rats fed only fructose and rats treated with different doses of the extract (Fig. 1).

Effect of HEELA on blood sugar levels in rats

The blood glucose levels of rats fed fructose and neutral controls every 2 weeks remained unchanged until week 8. At week 8, a significant increase ($p<0.01$) was observed in fructose-treated rats compared with neutral controls. This increase continued to be highly significant ($p<0.01$) at week 10. The increase was highly significant ($p<0.001$) at week 12 in rats treated with different doses of the extract and those not treated with the extract. It remained highly significant ($p<0.001$) until week 16 in rats not treated with the extract, negative controls and rats treated with the extract at a dose of 40 mg/kg bw. In contrast, blood glucose levels were significantly ($p<0.01$) reduced in rats treated with 100 and 200 mg/kg bw extract at week 14. In rats treated with 200 mg/kg bw extract, the decrease was highly significant ($p<0.001$) at week 16 compared with negative control rats (Fig. 2).

Effects of the hydroethanolic extract of *L. acida* trunk bark on glucose tolerance and AUC after a high-fructose diet

Before the glucose tolerance test, negative control rats and those treated with extract (40 mg/kg bw) had the highest fasting blood glucose levels. During the tolerance test, after glucose administration, the greatest increases in blood glucose levels were observed between 30 min and 2 h in negative control rats and those treated with extract 40 mg/kg bw. Thirty minutes after glucose administration, blood glucose levels in rats treated with 200 mg/kg bw extract increased non-significantly compared to the neutral control. Low blood glucose

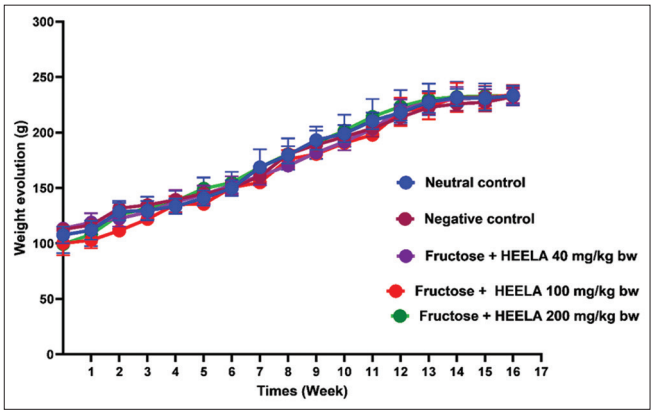

Fig. 1: Body weight gain in rats during the treatment. Values were expressed as mean±standard error; n=5

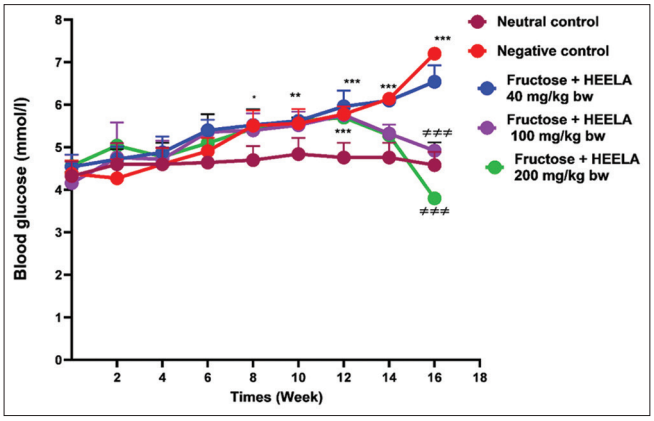

Fig. 2: Blood glucose levels in rats. Values were expressed as mean±standard error; n=5. *p<0.05; **p<0.01; ***p<0.001; p>0.05=ns: comparison with neutral control. ≠p<0.05; ≠≠p<0.01; ≠≠≠ p<0.001: comparison with negative control

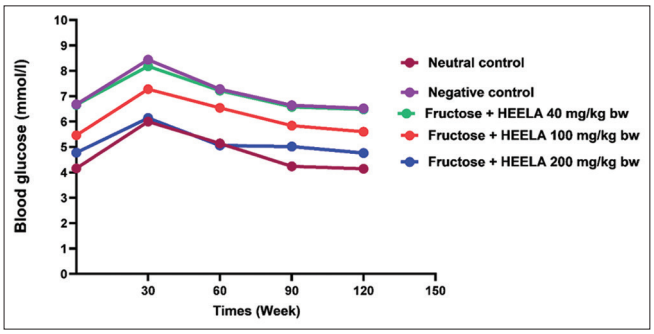

Fig. 3: Effects of the hydroethanolic extract of *Lannea acida* trunk bark on glucose tolerance after a high-fructose diet

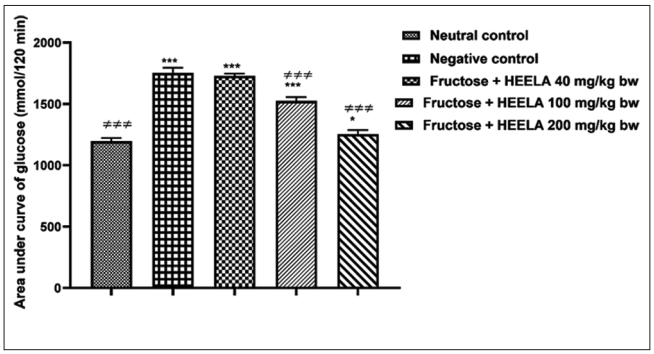

Fig. 4: Area under the curve of glucose tolerance in rats fed in fructose. Values were expressed as mean±standard error; n=5. *p<0.05; **p<0.01; ***p<0.001: Comparison with tap neutral control. ≠p<0.05; ≠≠p<0.01; ≠≠≠p<0.001: comparison with negative control

levels were observed in both neutral control and 200 mg/kg bw extract-treated rats (Fig. 3).

These differences were quantified by the AUC of glucose tolerance. This measure showed a highly significant (p<0.001) increase in the AUC of negative control rats compared with the neutral control. This increase was highly significant (p<0.01) in rats treated with 40 and 100 mg/kg bw. The AUC decreased significantly (p<0.001) in rats treated with 200 mg/kg bw compared with negative control rats. The smallest AUC was observed in neutral control rats, followed by those treated with 200 mg/kg bw extract (Fig. 4).

Effect of the hydroethanolic extract of *L. acida* on relative organ weights

The relative weights of the kidneys, spleen, heart, and adrenal glands showed no significant variation (p>0.05) in all rats after 16 weeks of experimentation. However, the relative liver weight of rats fed with negative and those treated with fructose and 40 mg/kg bw of extract (p<0.01 and p<0.05, respectively). A highly significant (p<0.001) increase in relative pancreas weight was observed in rats fed with the negative control and those fed with fructose and 40 mg/kg bw of extract. At 100 mg/kg bw, the relative weight of the pancreas increased very significantly (p<0.01) and no significant variation was observed in the relative weight of the liver and pancreas in fructose-fed rats+extract at 200 mg/kg bw. Fructose-fed rats+the extract at 100 mg/kg bw showed no significant change in relative liver weight.

Relative liver weight decreased significantly in rats treated with 200 mg/kg bw extract compared with rats treated with the negative control (p<0.001). Relative pancreas weight was significantly reduced in rats treated with 200 mg/kg bw extract (p<0.01) compared to those treated with the negative control (Table 1).

Effects of the hydroethanolic extract of *L. acida* on serum lipid HDL-c, TG, TC levels in diabetic rats

HDL-c levels decreased significantly (p<0.001) in negative control rats and those treated with 40 and 100 mg/kg bw extract compared with the neutral control. This decrease was non-significant between the neutral control and rats treated with 200 mg/kg bw extract. The 200 mg/kg bw extract dose resulted in a highly significant (p<0.001) increase in HDL-c levels compared with the negative control.

Triglyceride levels increased significantly (p<0.001) in negative control rats and those treated with 40 and 100 mg/kg bw extract, compared with the neutral control. This increase was non-significant (p>0.05) in rats treated with 200 mg/kg bw extract. The 200 mg/kg bw extract showed a highly significant decrease in serum triglyceride levels compared with the negative control. This decrease was comparable to that of the neutral control.

No significant variation (p>0.05) was observed in TC levels when comparing the negative control group, the groups treated with the extract at doses of 40, 100, and 200 mg/kg bw, and the neutral control rats. The different doses of extract did not cause any significant variation (p>0.05) in cholesterol levels compared with the negative control (Fig. 5).

Table 1: Effects of *Lannea acida* hydroethanolic extract on relative organ weights after 16 weeks of treatment

Relative weights	Liver	Kidneys	Spleen	Heart	Pancreas	Adrenal glands
Treatment (mg/kg)						
Neutral control	3.34±0.30	0.58±0.04	0.21±0.006	0.33±0.04	0.33±0.03	0.02±0.003
Negative control	3.95±0.16**	0.52±0.05	0.23±0.03	0.35±0.03	0.45±0.03***	0.02±0.003
Fructose+HEELA 40 mg/kg	3.86±0.18*	0.55±0.04	0.26±0.03	0.38±0.03	0.44±0.03***	0.02±0.004
Fructose+HEELA 100 mg/kg	3.54±0.30	0.59±0.04	0.21±0.02	0.39±0.01	0.43±0.03**	0.02±0.004
Fructose+HEELA 200 mg/kg	3.14±0.08≠≠≠	0.51±0.03	0.24±0.03	0.35±0.04	0.36±0.03≠≠	0.02±0.002

Values were expressed as mean±standard error; n=5. *p<0.05; **p<0.01; ***p<0.001: comparison with neutral control. ≠≠ p<0.05; ≠≠ p<0.01;≠≠≠ p<0.001: comparison with negative control

Effects of the HEELA on transaminase levels in diabetic rats

A highly significant ($p<0.001$) increase in ALAT levels was observed in the negative control and in the rats treated with the extract at doses of 40 and 100 mg/kg bw compared with the neutral control. The increase in ALAT was non-significant ($p>0.05$) between the neutral control and rats treated with 200 mg/kg bw. ALAT levels were significantly reduced ($p<0.001$) in rats treated with 200 mg/kg bw extract compared with the negative control and in those treated with 40 and 100 mg/kg bw extract compared with the neutral control.

A highly significant ($p<0.001$) increase in ASAT levels was observed in the negative control group and those treated with the extract at doses of 40 and 100 mg/kg bw, compared with the neutral control. The increase in ASAT levels was non-significant ($p>0.05$) between the neutral control and rats treated with 200 mg/kg bw. ASAT levels were significantly ($p<0.001$) reduced in rats treated with 100 and 200 mg/kg bw extract compared with the negative control (Fig. 6).

Histopathological examination of liver and pancreas

Neutral control rats show normal liver structure, with normal hepatic parenchyma consisting of portal vein, hepatic artery, biliary canaliculus, and well-individualized hepatocytes. Negative control rats showed leukocyte infiltration. Rats treated with the highest dose of extract showed less leukocyte infiltration than negative control rats (Fig. 7).

Histopathological sectioning of the pancreas showed in neutral control rats a normal structure with normal pancreatic parenchyma consisting of well-individualized exocrine and endocrine pancreas. In negative control rats, the structure showed a regression in pancreatic islet size. In contrast, in rats treated with the highest dose of the

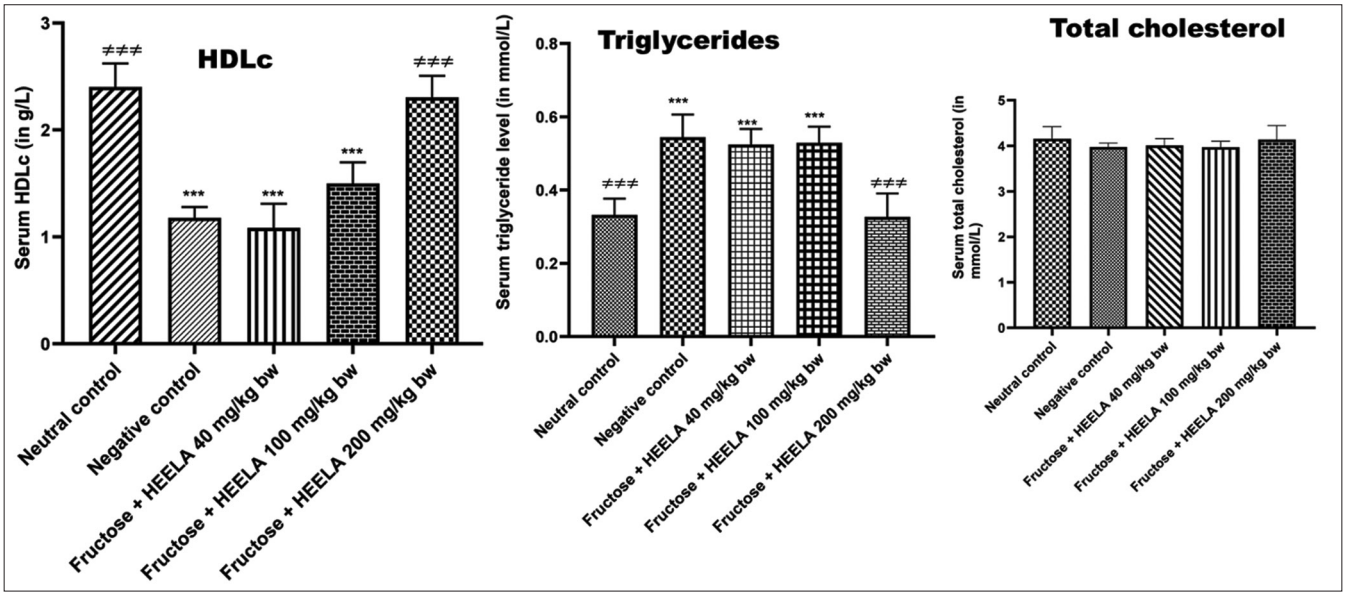

Fig. 5: Concentration of high density lipoprotein-cholesterol, triglycerides, total cholesterol in rats after 16 weeks of experimentation. *p<0.05; **p<0.01; ***p<0.001; p>0.05=ns: comparison with neutral control. ≠p<0.05; ≠≠p<0.01; ≠≠≠p<0.001: Comparison with negative control

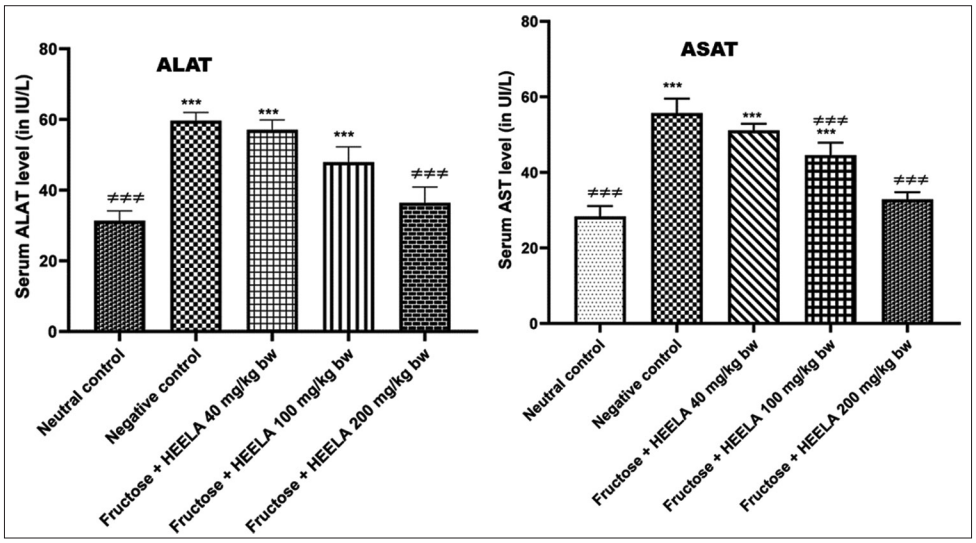

Fig. 6: Concentration of alanine aminotransferase and aspartate aminotransferase in rats after 16 weeks of experimentation. *p<0.05; **p<0.01; ***p<0.001: Comparison with neutral control. ≠p<0.05; ≠≠p<0.01; ≠≠≠p<0.001: Comparison with negative control

extract, the size of the pancreatic islet was well individualized, as in neutral control rats (Fig. 8).

DISCUSSION

Fructose metabolism is controlled by fructokinase or ketohexokinase C and aldolase B in enterocytes, hepatocytes, proximal tubule cells of the kidney, and pancreas [18,19]. Ketohexokinase phosphorylates fructose to fructose-1-phosphate. This phosphorylation, typical of fructose in position 1, uniquely bypasses the phosphorylation-dependent control step of the glycolytic pathway with phosphofructokinase, thus avoiding excessive glycolysis [20]. Excessive fructose consumption over the body's energy requirements leads to vascular endothelial dysfunction, increased intrahepatic lipids, glucose production, hypertriglyceridemia and increased hepatic insulin resistance, and activation of the inflammation cascade [19].

Fructose administration resulted in hyperglycemia in rats not treated with the extract. Our results corroborate previous studies that revealed hyperglycemia in animals fed a fructose-rich diet [14,21]. Six weeks of treatment with different doses of the extract showed that, in addition to its anti-hyperglycemic effect, the extract possesses an antidiabetic effect. This dose-dependent antidiabetic effect could be attributable to the concentration of the extract's various essential secondary metabolites and also to their activity. The antidiabetic effect of *L. acida* may be attributed to the presence of phenolic compounds, which play a key role in reducing diabetes by regulating plasma glucose levels and hepatic metabolism, which may inhibit digestive enzymes [22]. Indeed, flavonoids may be involved in reducing blood glucose levels by regulating adenosine 5'-monophosphate-activated protein kinase activity, regulating peroxisome proliferator-activated receptor γ, and inhibiting α-glucosidase (α-Glu) activity [10]. Alkaloids have been reported to delay glucose absorption through inhibition of digestive enzymes such as α-Glu [23]. Our previous studies have shown that HEELA contains the phenolic compounds.

Increased fructose consumption leads to fructose intolerance. Indeed, our results showed glycemic changes after glucose loading during the glucose tolerance test and an increase in the AUC in control rats. Our results are in line with those of [24], who observed glucose intolerance in rats fed 7% fructose for 12 weeks. Glucose intolerance could be due to an alteration in pancreatic ß-cells and their function. This alteration can be observed on histopathological sections of the pancreas of negative control rats, showing a regression in pancreatic islet size. According to Miranda *et al*. [24], low fructose consumption can induce changes in pancreatic cells with the onset of glucose intolerance. Furthermore, the relative pancreas weight revealed hypertrophy in negative control rats. This hypertrophy could be due to inflammation caused by fructose consumption. Indeed, a fructose-rich diet can lead to infiltration of inflammatory cells into the pancreas [25]. Early and progressive alteration of pancreatic ß-cells is implicated in the pathogenesis of type 2 diabetes [26]. The treatment of rats with the extract showed poor glucose tolerance and a decrease in the AUC. This could suggest that *L. Acida* extract plays an insulin-sensitizing role [27]. Furthermore, treatment revealed morphologically normal pancreatic

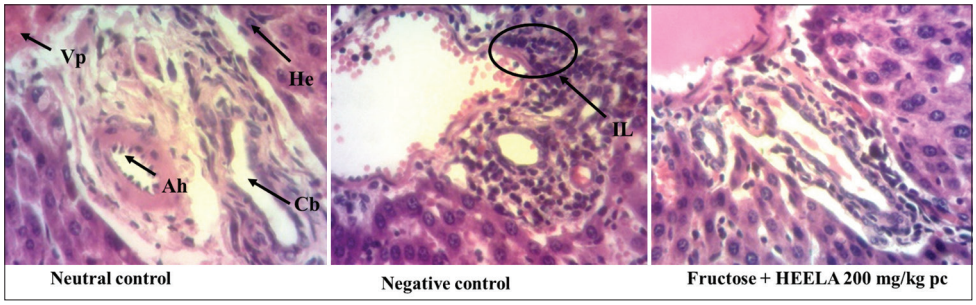

Fig. 7: Liver structure after 16 weeks of experimentation. Ah: Hepatic artery. Cb: Bile duct, He: Hepatocytes, IL: Leukocyteinfiltrates, VP: Portal vein

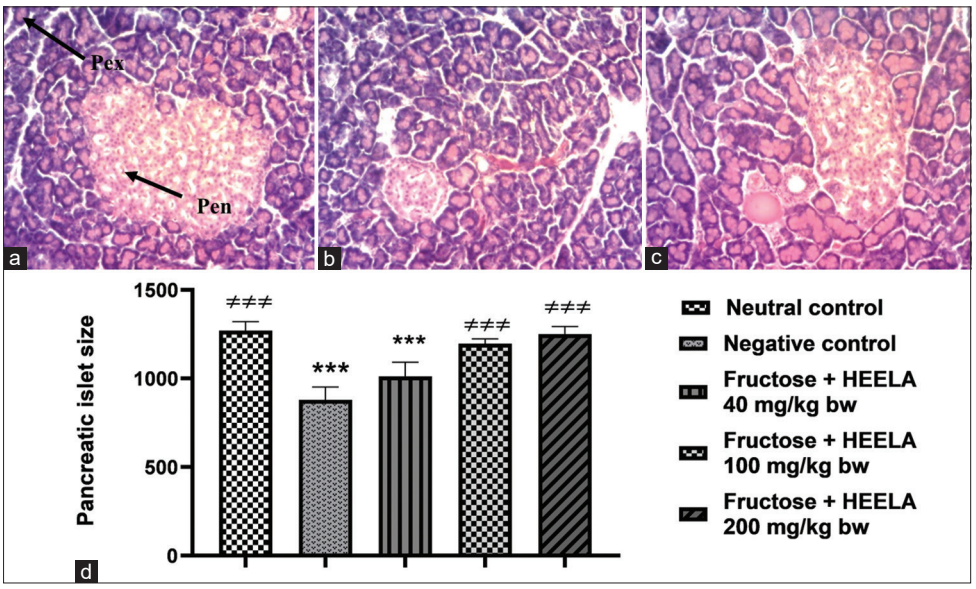

Fig. 8: Structure of the pancreas after 16 weeks of experimentation. Pex: Exocrine pancreas. Pen: Endocrine pancreas. a, b, c Pancreas structures in neutral control, negative control and EHELA 200 mg/kg bw rats, respectively. d: Pancreatic islet size. *p<0.05; **p<0.01; ***p<0.001; p>0.05=ns: comparison with neutral control. ≠p<0.05; ≠≠p<0.01; ≠≠≠p<0.001: comparison with negative control

islets and a decrease in relative pancreatic weights. The extract could prevent damage to the pancreas by averting glucose intolerance. The protective effects on the pancreas could be attributed to the compounds identified in the extract, namely tannins, polyphenols, coumarins, alkaloids, triterpenes and steroids, and flavonoids. These effects could also be due to HEELA's high antioxidant capacity [23]. Phenolic compounds would act through mechanisms such as protecting pancreatic β-cells from glucotoxicity and oxidative stress, inhibiting carbohydrate digestion and absorption in the gut, reducing glucose release from the liver, improving glucose utilization by the liver and insulin-sensitive peripheral tissues (muscle, adipocytes) by activating insulin receptors [28,29].

Fructose stimulates lipid secretion, contributing to dyslipidemia. Analysis of lipid parameters showed dyslipidemia characterized by a decrease in HDL-c and an increase in TG in negative control rats. These results are in line with other studies that have shown that concentrations of 10–35% fructose as drinking water in rats lead to lipid disorders and hepatic steatosis [21,30]. This dyslipidemia is thought to result from a deficit in insulin secretion and/or insulin resistance, which are distinctive features of type 2 diabetes. HEELA improved dyslipidemia induced by the high-fructose diet in rats. The antihyperlipidemic effect of the extract would be due to its anti-hyperglycemic effect through the presence of flavonoids, polyphenols, coumarins, tannins, alkaloids, triterpenes, and sterols recognized as bioactive in the management of diabetes [31,32]. The extract could prevent the risk of diabetes-related cardiovascular complications. The extract is thought to participate in lipid metabolism and protective function against the incidence of lipid peroxidation and cardiovascular disease [33].

Hyperlipidemia-induced damage to liver tissue affects its transport function and membrane permeability, leading to leakage of enzymes into the extracellular environment. As a result, a significant release of transaminases, ALAT and ASAT, into the blood is a sign of severe liver tissue damage [22], as was the case in this study with negative control rats. These results are in line with those obtained by [22] by exposing female Wistar rats to a fructose-rich diet for 70 days. Relative liver weight also increased in negative control rats. Similar results have been obtained in previous studies [30]. The elevation of these parameters could be due to fructose-induced steatosis, with the accumulation of fat in the liver. In this case, steatosis causes liver damage and oxidative stress, with inflammation of the hepatocytes resulting in the marked release of ASAT and ALAT [30].

Hepatocyte inflammation was revealed by histopathological sections of the liver showing leukocyte infiltration. Treatment of rats with the extract showed a reduction in transaminase levels, an attenuation of relative liver weight, and a normal liver structure. These results may confer a hepatoprotective effect on *L. acida* extract. The extract's hepatoprotective effect could be attributed to polyphenols, tannins, and flavonoids, which are recognized for their antioxidant activity and hepatoprotective effect [34]. Phenolic compounds could act by attenuating fat accumulation in the liver and restoring insulin sensitivity in the liver [35]. Our previous studies have shown the antioxidant properties of HEELA.

A fructose-rich diet causes inflammation in organs such as the liver and pancreas. Several studies have shown that inflammation is linked to the onset of insulin resistance and type 2 diabetes [36]. Thus, the rise in blood glucose levels could be due to the development of insulin resistance and the onset of type 2 diabetes. This involvement of inflammation in diabetes raises the question of how anti-inflammatories can be taken into account in the search for antidiabetic agents [36]. In addition, previous studies have highlighted the anti-inflammatory properties of *L. acida* trunk bark [37]. The decrease in the relative weight of the liver and pancreas of rats treated with the highest dose of the extract could confirm the anti-inflammatory effect of the hydroethanolic extract of *L. acida* trunk bark in the onset of diabetes.

CONCLUSION

The present study evaluated the antidiabetic effect of the hydroethanolic extract of *L. acida* trunk bark on a fructose-rich diet in male Wistar rats. Sixteen weeks after the induction of diabetes and treatment of rats, HEELA was found to have antidiabetic effects. These effects were reported by the restoration of lipid parameters, the decrease of blood glucose levels, and the AUC at the highest dose of the extract. In addition, the extract at the highest dose restored liver and pancreas structures altered by diabetes induction. Finally, the relative weights of liver, pancreas decreased in rats at the highest dose of HEELA compared with diabetic rats. The study also needs to be continued to assess the effect on oxidative stress and insulin resistance. And to elucidate the mechanisms by which extracts respond to glucose intolerance and insulin resistance.

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AUTHOR'S CONTRIBUTION

Abdelaziz Koussoube: Conceptualization, methodology, formal analysis, data curation, writing- original draft. Filkpièrè Léonard DA: Supervision, formal analysis, data curation. Maya Doukoure: Methodology, writing - review and editing. Basile Tindano: Methodology, Writing - Review and Editing. Balé BAYALA: Conceptualization, validation, resources, project administration, funding acquisition. We declare that all authors contributed significantly towards the research study to the conception, design and/or analysis and interpretation of data and to the drafting of the article or revising it critically for important intellectual content. All authors gave final approval of the version to be published and agreed to be accountable for all aspects of the work, ensuring its accuracy and integrity.

DECLARATION OF INTERESTS

Authors declare no conflict of interest.

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