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Antidiabetic activity of the aqueous extract of *Erigeron floribundus* leaves in streptozotocin-induced type 1 diabetes model in Wistar rats

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ABSTRACT

Backgroud: Erigeron floribundus is a herbaceous plant used in traditional Cameroonian medicine to treat diabetes mellitus. The aim of this study was to evaluate the antidiabetic properties of the aqueous extract of *E. floribundus* leaves (AEEF) in diabetic rats.

Methods: Diabetes was induced by a single intraperitoneal injection of streptozotocin (60 mg/kg) in normal rats fasted for 16 h. Subsequently, 30 diabetic male rats were divided into groups and treated orally for 21 days with distilled water (10 mL/kg), glibenclamide (3 mg/kg) and AEEF (300, 400, and 500 mg/kg). Body weight, food and water intake, blood glucose, insulin levels, lipid and oxidative profiles, as well as some markers of liver and kidney function were assessed. Histological sections of the rats' pancreas were taken.

Results: AEEF and glibenclamide significantly increased ($p < 0.001$) body weight and decreased food and water intake in rats. A decrease in blood glucose ($p < 0.001$) and an increase in insulin levels ($p < 0.001$) were observed in the AEEF and glibenclamide groups. AEEF caused a significant ($p < 0.001$) decrease in the levels of total cholesterol, LDL-c, triglycérides and coronary risk index (CRI), accompanied by a significant ($p < 0.001$) increase in HDL levels and HOMA-β in rats. AEEF showed an improvement ($p < 0.001$) in CAT and SOD activity and GSH levels accompanied by a significant decrease ($p < 0.001$) in malondialdehyde levels. In addition, ALAT and ASAT activity, urea and creatinine levels were significantly reduced ($p < 0.001$) after treatment with AEEF and glibenclamide. The extract also improved the size of Langerhans Islets in the pancreas of diabetic rats.

Conclusion: AEEF contains several bioactive compounds conferring antidiabetic, anti-dyslipidemic and antioxidant properties, thus justifying its therapeutic use in the treatment of diabetes mellitus.

1. Introduction

Diabetes mellitus is a metabolic disorder characterized by chronic hyperglycemia accompanied by disturbances in carbohydrate, lipid and protein metabolism, resulting from defects in insulin secretion, insulin action and/or both [1]. Diabetes mellitus is currently recognized as a genuine public health problem and is the world's biggest health emergency. Worldwide, the prevalence of diabetes was estimated at 9.3 % in 2019, rising to 10.5 % in 2021. According to the International Diabetes Federation (IDF), this figure could reach 11.3 % by 2030 and 12.2 % by 2045 [2]. This remarkable rise in the epidemiology of diabetes is closely linked to an ageing population, unbalanced diet and lack of physical

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activity. Chronic diabetes mellitus is associated with severe complications such as myocardial infarction, atherosclerosis, nephropathy, and neuropathy [3].

The treatment of diabetes has long been restricted to dietary changes, insulin injections and oral antidiabetics. However, the regular administration of these modern drugs generates many undesirable side effects [4]. In addition, constantly rising product prices and inaccessibility to generic drugs are a major problem for financially deprived populations. These limitations have led almost 80 % of the population to turn to herbal medicine [5]. Moreover, medicinal plants are natural resources and can offer a wide range of new antidiabetic drugs. In view of the considerable increase in the number of diabetics and the side effects of anti-diabetic drugs, many researchers have evaluated the pharmacological action of traditional plants and their interest in traditional medicine. Examples include the work of Miaffo et al. [6] on *Vitellaria paradoxa*, Prawej et al. [7] on *Haritiera fomes*, Nyangono et al. [8] on *Cesaria barteri*, and many others.

Erigeron floribundus (Kunth) Sch. Bip. (Asteraceae) is a herb of 1.5 m in height, with pubescent, lanceolate leaves and flowers in paleyellow panicles. In Cameroon, it is commonly found as a weed along roadsides, and it is used in traditional medicine to treat diabetes, angina, female infertility, dental pain, headaches, and microbial diseases [9,10]. Previous work on this plant has shown that the aqueous extract of *E. floribundus* leaves contains alkaloids, saponins, tannins, glycosides, phenols, and flavonoids [11]. However, no previous scientific work has investigated its antidiabetic properties. The aim of the present work was therefore to evaluate the antidiabetic properties of AEEF in rats rendered diabetic by streptozotocin (STZ).

2. Materials and methods

2.1. Animal material

The animals used were male albino rats of Wistar strain (Rattus norvegicus), supplied by the animal house of the Laboratory of Medicinal Plants, Health and Galenic Formulation of the University of Ngaoundéré (Cameroon). The animals weighed between 150 and 200 g and were approximately 2–3 months old. They were acclimatized to room temperature, with 12 h of light and 12 h of darkness per day. Drinking water and a standard diet were provided ad libitum. Only male rats were used in this study because they are less prone to hormonal fluctuations, particularly estrogen, which can interfere with the results.

2.2. Plant material

E. floribundus leaves were harvested in October 2022 in the locality of Dang, 15 km from the town of Ngaoundéré, Cameroon (13°34′N 7°27′E). After harvesting, E. floribundus was identified by Prof. Tchobsala, Botanist at the University of Maroua (Cameroon). A sample of this plant was authenticated at the Herbier National du Cameroun by comparison with a specimen registered under number 61003/HNC. Fresh E. floribundus leaves were washed in tap water, dried and ground to a fine powder using a mortar.

2.3. Preparation of AEEF

One hundred grams (100 g) of *E. floribundus* powder was macerated in 1 L of distilled water for 24 h. The resulting mixture was filtered through Wattman n°1 paper. The filtrate was oven-dried (Memmert brand UN55) at 45 °C until dry. The dry extract obtained weighed 5 g, giving a yield of 5 %.

2.4. Choice of doses of AEEF

The determination of doses was made using information collected from traditional therapists. Indeed, the quantity of remedy that the healer gives to a patient per day has been evaporated in the laboratory. The crude extract obtained (5 g) assumed to be consumed by an adult weighing 70 kg, made it possible to determine the human therapeutic dose (HTD) by the ratio: HTD = 5000 mg/70 kg = 71.42 mg/kg. The rat equivalent dose (RED) was approximately equal to 400 mg/kg, calculated according to the Shannon et al. [12] formula: RED = HTD × Human Km/Rat km where Human Km = 37; Rat Km = 6; Km = specific conversion factor. The therapeutic doses obtained (300, 400, and 500 mg/kg) were framed by an arithmetic sequence at 100 mg/kg.

2.5. Qualitative phytochemical study of AEEF

Phytochemical screening was carried out to identify the various biactive compounds present in AEEF. These bioactive compounds were identified using color reactions based on the method of N'Guessan et al. [13]. They included flavonoids (Shibata reagent and Mg), tannins ($FeCl_3$), alkaloids (Dragendorff reagent and Mayer reagent), terpenoids and steroids (acetic anhydride and H_2SO_4), saponines (persistent foam), phenols ($FeCl_3$ and K3Fe(CN)$_6$) and anthraquinones (NH_4OH).

2.6. Quantitative phytochemical study of AEEF

2.6.1. Tannin determination

Tannin content was determined by introducing 1000 µL of AEEF or catechin solution (10 mg/mL) and 750 µL of reagent (4 % vanillin in methanol) into a tube. The resulting mixture was incubated at 30 °C for 5 min and absorbance measured at 500 nm. Tannin content was expressed as milligram catechin equivalent per gram dry extract (mg CE/g) [14].

2.6.2. Flavonoid determination

Flavonoid content was determined by adding 1 mL AEEF or quercetin (0–100 µg/mL), 0.2 mL aluminum chloride solution (10 % w/v), 0.2 mL potassium acetate (1 M) and 5.6 mL distilled water to a tube. The resulting mixture was incubated for 30 min and absorbance measured at 415 nm. Flavonoid content was expressed as milligram quercetin equivalent per gram dry extract (mg EQ/g) [15].

2.6.3. Determination of phenols

Phenol content was determined by adding 0.5 mL AEEF or gallic acid, 2.5 mL reagent-ciacalteu (10 %) and 4 mL sodium carbonate (7.5 % w/v) to a tube. The mixture was incubated for 30 min at room temperature and absorbance measured at 727 nm. Phenol content was expressed as milligrams of gallic acid equivalent per gram of dry extract (mgEAG/g) [16].

2.7. Induction of diabetes

Diabetes was induced by administration of a single dose (60 mg/kg) of STZ (Sigma-Aldrich, Saint. Louis) intraperitoneally in normal rats previously fasted for 16 h. One hour after, 3 g/kg of D-glucose (Edu-Lab Biology kit, Bexwell, UK) was administered *per os* to each animal, and 72 h later, the rats' blood glucose levels were assessed using a One Touch Ultra Mini glucometer (Life Scan, USA, accuracy ±7.5 %.) and test strips. Rats with blood glucose levels greater than or equal to 150 mg/dL were considered diabetic and selected for the experiment [17].

2.8. Distribution and treatment of animal

Thirty (30) male rats including 5 normal and 25 diabetic were divided into 6 groups of 5 rats each and treated daily for 21 days as follows.

- Group 1 (normal control) received distilled water (10 mL/kg) orally;
- Group 2 (diabetic control) received distilled water (10 mL/kg) orally;
- Group 3 (positive control) received glibenclamide (3 mg/kg) orally;

- Groups 4, 5, and 6 received AEEF (300, 400 and 500 mg/kg) orally, respectively.

Parameters such as blood glucose, body weight, food and water consumption were measured weekly.

2.9. Blood and organ sampling

Rats were fasted for 16 h, anesthetized with a combination of ketamine and diazepam, then sacrificed by cervical decapitation. Blood was then collected by cardiac puncture from the jugular vein of the rats, collected in dry tubes and centrifuged at 3000 rpm for 15 min. The supernatant obtained was collected and stored at −20 °C in the refrigerator (Hisense brand RT35 320I) for the determination of biochemical parameters. In addition, the pancreas, liver and kidneys of each animal were removed immediately after sacrifice, cleared of adipose tissue and cleaned in 0.9 % NaCl. Part of each organ was stored at −20 °C for oxidative stress parameters, and the other part was preserved in 10 % formalin for histological sections.

2.10. Determination of biochemical parameters

The method of Herbert et al. [18] was used for the determination of insulin rate. The method of Matthews et al. [19] was used to calculate the Homeostasis Model Assessment of β-cell function (HOMA-β) = 20 x fasting insulin (U/L)/fasting blood glucose (mmol/L) - 3.5. Total cholesterol (TC), low density lipoprotein cholesterol (LDL-c), very low density lipoprotein cholesterol (VLDL-c), and triglyceride (TG) levels were obtained using the enzymatic colorimetric method described by Richmond [20] and Trinder [21]. High density lipoprotein cholesterol (HDL-c) levels were obtained using the method of Weibe et al. [22]. The anti-atherogenic index (AAI) was calculated using the formula of Kang et al. [23]: AAI = Log (TC/HDL-c). The coronary risk index (CRI) was calculated using the formula of Barter and al [24].: CRI = Total cholesterol/HDL-c. The cardioprotective index (CI) was calculated using the formula of Quantanilha et al. [25]: CI = LDL-c/HDL. Alanine amino transaminase (ALT), aspartate aminotransferase (AST), and creatinine were determined according to the method of Murray [26]. Urea was determined by the method of Kaplan [27]. Oxidative stress markers such as malondialdehyde (MDA), catalase (CAT), reduced glutathion (GSH), and superoxide dismutase (SOD) were assessed using the method of Sehirli et al. [28].

2.11. Histopathology of the pancreas

Rat pancreas fragments were placed in small vials each containing 10 % buffered formalin. Samples were fixed on a microtome and cut to 5 µm thickness. The sections were mounted on glass slides and subsequently dewaxed with xylene and rehydrated with 95 % ethanol dilutions, then stained with hematoxylin and eosin and photographed with a light microscope at 100× magnification [29].

2.12. Statistical analysis

Results were expressed as mean ± standard error on the mean (S.E.M.). Data were analyzed using Graphpad prism version 8.0 software. Analysis of variance followed by Bonferroni's test was used to compare data from bivariate tests. Analysis of variance followed by Turkey's posttest was used to compare data from single-variable tests. The difference was significant at the 5 % probability level.

3. Results

3.1. Qualitative phytochemistry of AEEF

Table 1 shows the results of the phytochemical screening of AEEF.

Table 1
Qualitative phytochemical study of AEEF.

Compounds	Results
Flavonoids	+
Alkaloids	+
Tannins	+
Steroids	+
Triterpenes	+
Saponins	+
Anthraquinones	−
Phenols	+

(+) present; (−) absent.

These results revealed the presence of saponins, flavonoids, tannins, phenols, alkaloids, steroids, and terpenoids. However, it is devoid of anthraquinones.

3.2. Quantitative phytochemistry of AEEF

Table 2 shows the content of flavonoids, tannins and phenols in AEEF. The table shows that flavonoids (61.45 mgEQ/g) were higher than tannins (11.34 mgEC/g) and phenols (31.72 mgEAG/g) in the extract.

3.3. Effect of aqueous extract E. floribundus leaf on body weight

Fig. 1 shows the variation in body weight of the animals as a function of time. The figure shows that the body weight of rats in the diabetic control group decreased significantly ($p < 0.001$) on days 14 and 21 compared with the normal control group. On the other hand, on treatment day 21, a significant increase in body weight was observed in animals treated with glibenclamide ($p < 0.01$) and AEEF at a dose of 300 mg/kg ($p < 0.05$), compared with the diabetic control.

3.4. Effect of aqueous extract E. floribundus leaf on food consumption

Food consumption in the diabetic control group significantly increased on days 14 ($p < 0.05$) and 21 ($p < 0.001$) of the experiment, compared with the normal control group. However, food consumption was significantly reduced ($p < 0.001$) on day 21 of treatment with glibenclamide and AEEF at 300, 400, and 500 mg/kg compared with untreated diabetic rats (Fig. 2).

3.5. Effect of aqueous extract E. floribundus leaf on water intake

The water intake of diabetic rats increased significantly ($p < 0.001$) on days 14 and 21 of the experiment compared with the normal control group (Fig. 3). In contrast, water intake decreased significantly ($p < 0.05$; $p < 0.001$) in rats treated with AEEF at doses of 300, 400 and 500 mg/kg and glibenclamide ($p < 0.01$) on treatment day 14, compared with the diabetic control. This decrease was significant ($p < 0.001$) at all doses of AEEF and glibenclamide on day 21 of the experiment.

3.6. Effect of aqueous extract of E. floribundus leaf on blood glucose and insulin levels

Fig. 4A shows the variation in rat blood glucose levels as a function of

Table 2
Quantitative phytochemical study of AEEF.

Compounds	Phenols (mgGAE/g)	Flavonoids (mgQE/g)	Tannins (mgCE/g)
Content	31.72 ± 0,14	61.45 ± 0,16	11.34 ± 0,12

Each value represents the mean ± MSE (n = 3). mgGAE/g: mg Gallic Acid Equivalent/g; mgQE/g: mg Quercetin Equivalent/g; mgCE/g: mg Catechin Equivalent; n = number of repetitions.

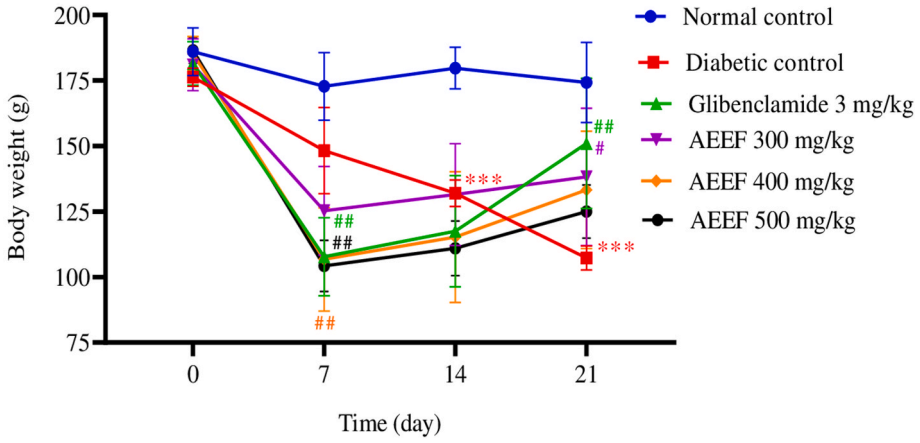

Fig. 1. Effect of AEEF on body weight in normal and diabetic rats. Results were expressed as mean ± MSE (n = 5). ***p < 0.001: significant difference from normal control. #p < 0.05; ##p < 0.01: significant difference from diabetic control. AEEF: aqueous extract of *Erigeron floribundus* leaves.

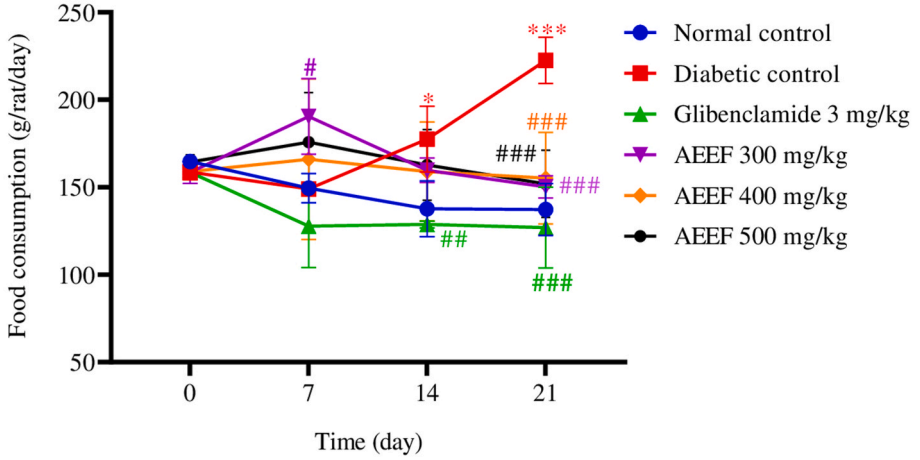

Fig. 2. Effect of AEEF on food consumption in normal and diabetic rats. Results were expressed as mean ± MSE (n = 5). *p < 0.05; ***p < 0.001: significant difference from normal control. #p < 0.05; ##p < 0.01; ###p < 0.001: significant difference from diabetic control. AEEF: aqueous extract of *Erigeron floribundus* leaves.

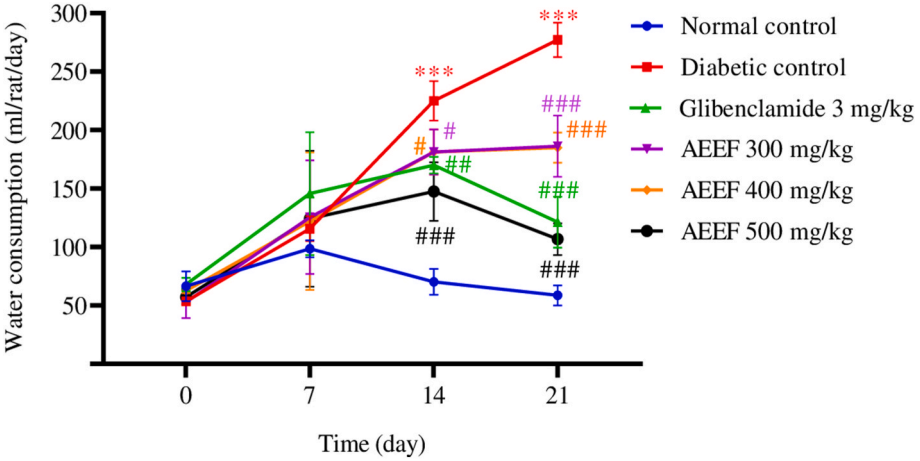

Fig. 3. Effect of AEEF on water consumption in normal and diabetic rats. Results were expressed as mean ± MSE (n = 5). ***p < 0.001: significant difference from normal control. #p < 0.05; ##p < 0.01; ###p < 0.001: significant difference from diabetic control. AEEF: aqueous extract of *Erigeron floribundus* leaves.

time. From this figure, it can be seen that the blood glucose levels of all rats increased significantly (p < 0.001) after STZ injection compared with rats in the normal control group. On days 7, 14 and 21 of treatment, blood glucose levels in diabetic control rats increased significantly (p < 0.001) compared with the normal control. In contrast, blood glucose levels in AEEF and glibenclamide-treated rats decreased (p < 0.05; p <

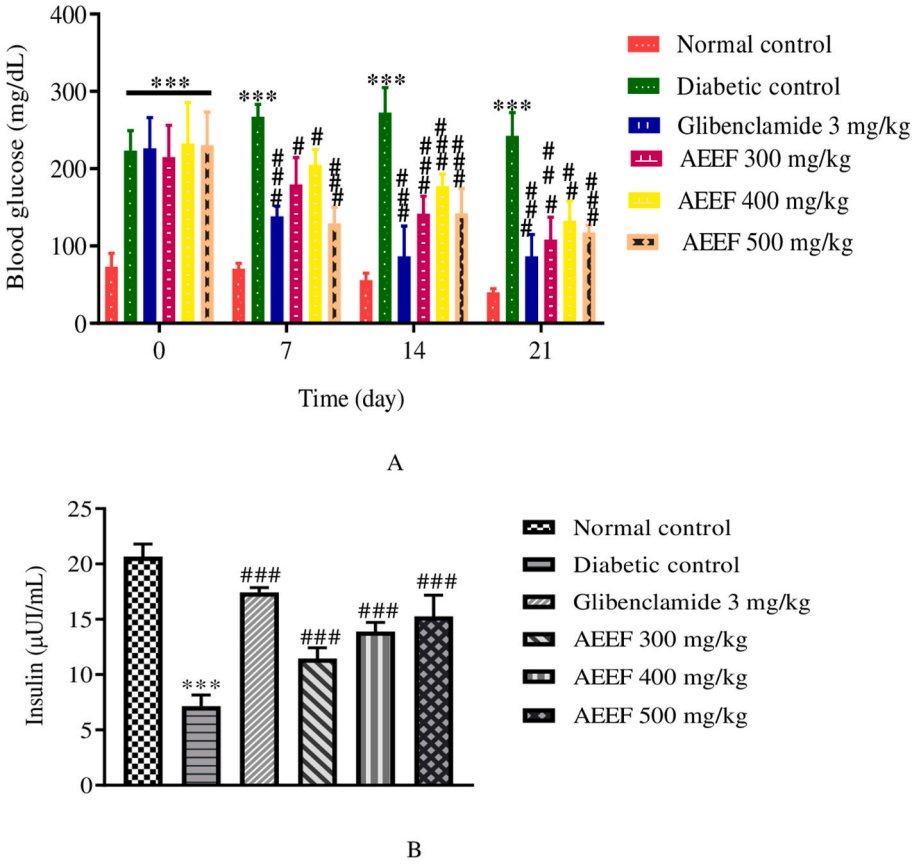

Fig. 4. Effect of AEEF on blood glucose (A) and insulin (B) levels in normal and diabetic rats. Results were expressed as mean ± MSE (n = 5). ***p < 0.001: significant difference from normal control. #p < 0.05; ##p < 0.01; ###p < 0.001: significant difference from diabetic control. AEEF: aqueous extract of *Erigeron floribundus* leaves.

0.001) from day 7 to the end of treatment.

Insulin levels in untreated diabetic rats were significantly ($p < 0.001$) lower than in the normal control (Fig. 4B). In contrast, insulin levels in AEEF and glibenclamide-treated rats increased significantly ($p < 0.001$) compared with the diabetic control.

3.7. Effect of aqueous extract of E. floribundus leaf on lipid profile

Table 3 shows the effects of AEEF on lipid parameters in rats. The table shows that total cholesterol, LDL-c, VLDL-c and TG levels of rats in the diabetic control group were significantly ($p < 0.001$) higher than in the normal control group. However, HDL-c levels in the diabetic control group showed a significant decrease ($p < 0.001$) compared with the normal control group. However, AEEF at all doses and glibenclamide resulted in a significant decrease ($p < 0.001$) in TC, LDL-c, VLDL-c and TG levels and an increase ($p < 0.001$) in HDL-c levels compared with the diabetic control.

3.8. Effect of aqueous extract of E. floribundus leaf on CRI, AAI, CI, and HOMA-β

STZ caused a significant increase ($p < 0.001$) in CRI, CI and AAI and a significant decrease ($p < 0.001$) in HOMA-β in diabetic control rats compared with normal control rats. In contrast, AEEF treatment of rats resulted in a significant reduction ($p < 0.001$) in CRI, CI and AAI and a significant increase ($p < 0.001$) in HOMA-β of animals compared with untreated diabetic animals (Table 4).

3.9. Effect of aqueous extract E. floribundus leaf on markers of oxidative stress

Table 5 shows hepatic and renal concentrations of MDA, GSH and the

Table 3
Effect of AEEF on lipid profile in normal and diabetic rats.

Parameters	Normal Control	Diabetic Control	Glibenclamide 3 mg/kg	AEEF 300 mg/kg	AEEF 400 mg/kg	AEEF 500 mg/kg
TC (mg/dL)	287.1 ± 0,1	354.5 ± 0.7[a]	213.9 ± 0.8[c]	224.3 ± 0.1[c]	207.9 ± 0.4[c]	259.1 ± 0/9[c]
LDL-c (mg/dL)	153.2 ± 0,5	173.2 ± 0.9[a]	106.0 ± 1.6[c]	118.6 ± 0.8[c]	92.9 ± 0.1[c]	101.2 ± 1.2[c]
VLDL-c (mg/dL)	40.8 ± 0.1	127.5 ± 0.6[a]	22.1 ± 0.2[c]	36.2 ± 0.6[c]	24.7 ± 0.1[c]	60.6 ± 0.1[c]
TG (mg/dL)	84.3 ± 0.8	376.4 ± 0.6[a]	125.1 ± 0.3[c]	230.1 ± 0.7[c]	188.1 ± 0.1[b]	103.7 ± 1.1[c]
HDL-c (mg/dL)	92.9 ± 0.7	53.7 ± 0.5[a]	85.7 ± 0.3[c]	69.5 ± 0.8[b]	90.3 ± 1.1[c]	96.7 ± 0.8[c]

Results were expressed as mean ± MSE (n = 5).
[a] $p < 0.001$: significant difference from normal control.
[b] $p < 0.01$.
[c] $p < 0.001$: significant difference from diabetic control. TC: total cholesterol; LDL-c: low-density lipoprotein cholesterol; VLDL-c: very-low-density lipoprotein cholesterol; TG: triglyceride; HDL-c: high-density lipoprotein cholesterol.

Table 4
Effect of AEEF on coronary risk, anti-atherogenic, cardioprotective, and HOMA-β indices in normal and diabetic rats.

	Normal Control	Diabetic Control	Glibenclamide 3 mg/kg	AEEF 300 mg/kg	AEEF 400 mg/kg	AEEF 500 mg/kg
CRI	3.10 ± 0.29	6.59 ± 0.13[a]	2.49 ± 0.17[b]	2.30 ± 0.15[b]	2.31 ± 0.17[b]	2.67 ± 0.13[b]
AAI	0,49 ± 0.20	0.81 ± 0.15[a]	0.39 ± 0.13[b]	0.51 ± 0.13[b]	0.36 ± 0.21[b]	0.42 ± 0.11[b]
CI	1,64 ± 0.18	3.22 ± 0.16[a]	1.23 ± 0.13[b]	1.70 ± 0.22[b]	1.21 ± 0.11[b]	1.05 ± 0.12[b]
HOMA-β	164.50 ± 3.62	35.43 ± 1.82[a]	90.23 ± 3.59[b]	65.25 ± 1.49[b]	79.50 ± 2.10[b]	87.75 ± 2.98[b]

Results were expressed as mean ± MSE (n = 5).
[a] $p < 0.001$: significant difference from normal control.
[b] $p < 0.001$: significant difference from diabetic control. CRI: coronary risk index; AAI: antiatherogenic index; CI: cardioprotective index; HOMA-β: homeostatic model assessment of insulin resistance.

activities of SOD and CAT in rats. Compared with the normal control group, this table shows a significant increase ($p < 0.001$) in MDA levels and a significant decrease ($p < 0.001$) in GSH levels, SOD and CAT activity in rats in the diabetic control group. However, in the AEEF and glibenclamide-treated groups, there was a reduction ($p < 0.001$) in MDA followed by an increase ($p < 0.001$) in GSH, SOD, and CAT activity compared with the diabetic control.

3.10. Effect of aqueous extract E. floribundus leaf on transaminase activity

The ALAT and ASAT activities of diabetic control animals were significantly increased ($p < 0.001$) compared with the normal control (Fig. 5). Compared to the diabetic control, AEEF caused a significant decrease ($p < 0.001$) in transaminase activities (ALT and AST) in diabetic rats treated with glibenclamide and different doses of AEEF.

3.11. Effect of aqueous extract E. floribundus leaf on creatinine and urea levels

Fig. 6 shows the effects of AEEF on rat creatinine (A) and urea (B) levels, respectively. The results showed a significant ($p < 0.001$) increase in creatinine and urea levels in diabetic rats compared with normal rats. In contrast, there was a significant reduction ($p < 0.001$) in these parameters in AEEF- and glibenclamide-treated rats compared with untreated diabetic rats.

3.12. Effect of aqueous extract E. floribundus leaf on histopathology of pancreas

Fig. 7 shows a histological section of the pancreas of diabetic rats treated with AEEF for 21 days. On this figure, we can see that the size of the Langerhans islets in the pancreas of diabetic control rats has decreased compared with that of normal control rats, whose size is normal and large. In rats treated with AEEF at doses of 300, 400 and 500 mg/kg and glibenclamide, the size of their islets increased significantly after treatment compared with that of diabetic control rats.

4. Discussion

Phytochemical analysis of AEEF revealed the presence of saponins, flavonoids, tannins, phenols, alkaloids, steroids and terpenoids. These results concur with those obtained by Asongalem et al. [11], who also showed the presence of these same compounds in AEEF. Bioactive molecules in plants are generally known for their diverse biological and pharmacological activities. According to Mangambu et al. [30],

Table 5
Effect of AEEF on oxidative stress in normal and diabetic rats.

Parameters		Normal Control	Diabetic Control	Glibenclamide 3 mg/kg	AEEF 300 mg/kg	AEEF 400 mg/kg	AEEF 500 mg/kg
MDA (nmol/g)	Liver	8.61 ± 0.23	18.12 ± 0.31[a]	8.89 ± 0.08[b]	11.23 ± 0.31[b]	11.08 ± 0.73[b]	8.51 ± 0.30[b]
	Kidneys	7.54 ± 0.14	16.23 ± 0.03[a]	7.45 ± 0.02[b]	10.54 ± 0.20[b]	10.21 ± 0.32[b]	9.65 ± 0.01[b]
GSH (nmol/g)	Liver	12.4 ± 0.82	5.99 ± 0.51[a]	8.75 ± 0.51[b]	7.49 ± 0.38[b]	9.44 ± 0.30[b]	11.27 ± 0.61[b]
	Kidneys	13.55 ± 0.18	5.32 ± 0.21[a]	10.32 ± 0.02[b]	8.96 ± 0.22[b]	8.54 ± 0.06[b]	10.87 ± 0.44[b]
SOD (U/mg)	Liver	23.12 ± 0.63	10.81 ± 0.89[a]	14.66 ± 0.54[b]	12.54 ± 0.41[b]	14.03 ± 0.81[b]	21.42 ± 0.41[b]
	Kidneys	21.87 ± 0.13	9.66 ± 0.43[a]	22.55 ± 0.22[b]	19.66 ± 0.22[b]	17.22 ± 0.05[b]	19.66 ± 0.12[b]
CAT (μmol/mg)	Liver	17.35 ± 0.51	7.25 ± 0.23[a]	11.66 ± 0.77[b]	15.58 ± 0.28[b]	11.99 ± 0.25[b]	16.15 ± 0.86[b]
	Kidneys	23.22 ± 031	10.55 ± 0.01[a]	21.75 ± 0.65[b]	19.44 ± 0.31[b]	20.12 ± 0.04[b]	22.32 ± 0.05[b]

Results were expressed as mean ± MSE (n = 5).
[a] $p < 0.001$: significant difference from normal control.
[b] $p < 0.001$: significant difference from diabetic control. MDA: malondialdehyde; GSH: reduced glutathione; SOD: superoxide dismutase; CAT: catalase.

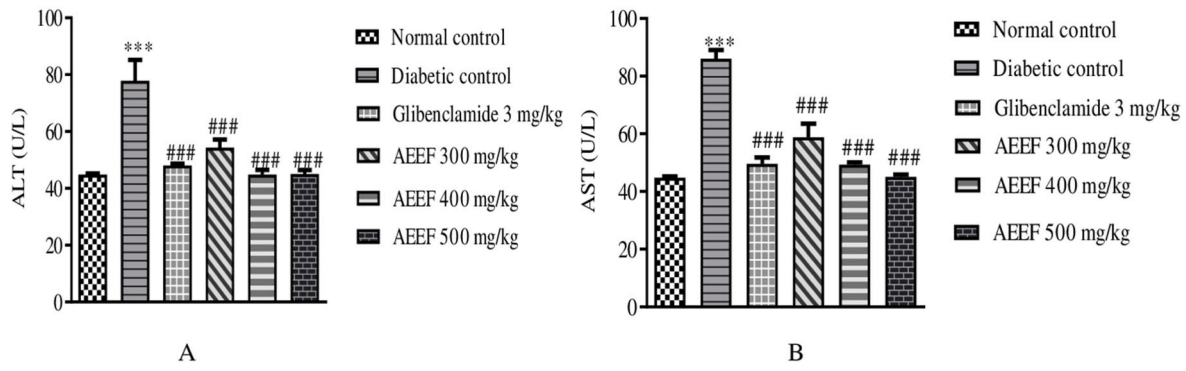

Fig. 5. Effect of AEEF on ALAT (A) and ASAT (B) activities in normal and diabetic rats. Results were expressed as mean ± MSE (n = 5). ***$p < 0.001$: significant difference from normal control. ###$p < 0.001$: significant difference from diabetic control. AEEF: aqueous extract of *Erigeron floribundus* leaves.

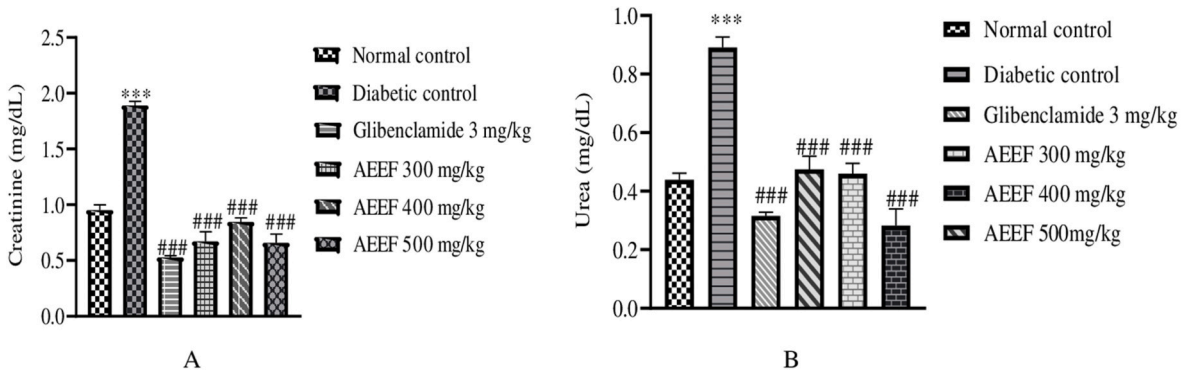

Fig. 6. Effect of AEEF on creatinine (A) and urea (B) levels in normal and diabetic rats. Results were expressed as mean ± MSE (n = 5). ***p < 0.001: significant difference from normal control. ###p < 0.001: significant difference from diabetic control. AEEF: aqueous extract of *Erigeron floribundus* leaves.

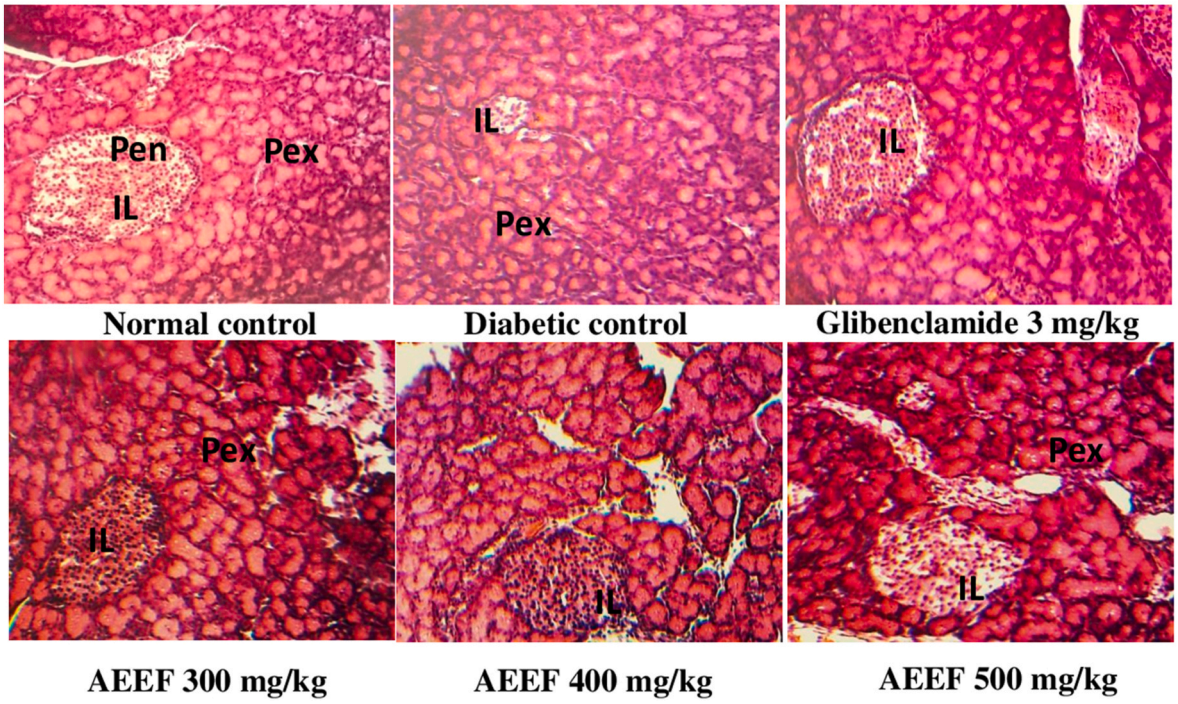

Fig. 7. Histological section of rat pancreas in normal and diabetic rats. Pen = endocrine pancreas; Pex = exocrine pancreas; IL = Islet of Langerhans. AEEF: aqueous extract of *Erigeron floribundus* leaves.

substances such as flavonoids and tannins are known to have hypoglycemic effects. Saponins and alkaloids, known for their antioxidant (free radical scavenging), antihyperlipidemic, and hepatoprotective properties [31,32].

Diabetes is a disease characterized by polyphagia and severe body weight loss that can lead to several complications [33]. In our study, the results indeed showed a significant decrease in body weight in animals rendered diabetic by STZ compared to normal animals. This loss of body weight in the diabetic group could be explained by the result of lipid and structural protein catabolism due to the lack of hydrated carbons used as an energy source [34]. In contrast, AEEF-treated groups showed improvement in body weight. The recovery of body weight in these rats could be explained by the ability of the extract to reduce hyperglycemia induced by STZ by stimulating insulin secretion; which would have contributed to this weight gain [35]. This result is similar to those obtained by Maidadi et al. [36], who also showed an increase in body weight in diabetic rats treated with aqueous extract of *Rytigynia senegalensis*.

Compared with normal rats, untreated diabetic rats showed polyphagia. This result could be explained by the fact that these animals used their lipid and protein reserves for their energy metabolism in the absence of glucose as an energy source. In contrast, rats treated with AEEF and glibenclamide showed a reduction in food intake. This reduction in food intake is thought to be due to AEEF acting like glibenclamide in stimulating insulin secretion, enabling rats to use glucose as an energy source.

This study also showed polydipsia in untreated diabetic rats compared with normal rats. The polydipsia observed in these animals would be due to the presence in the renal filtrate of an excess of glucose which has the effects of an osmotic diuretic, inhibiting water reabsorption by the renal tubules, causing dehydration and thus stimulating the hypothalamic thirst centers of these animals [37]. However, in rats treated with AEEF and glibenclamide, a decrease in water intake was observed. This decrease in water intake in AEEF-treated rats could be explained by the fact that the extract inhibited the hypothalamic thirst centers of these animals, thus preventing the occurrence of this polydipsia.

STZ is a substance that causes pancreatic β-cell necrosis and severe

insulin deficiency, with established diabetic hyperglycemia within two days [38]. Indeed, this study showed hyperglycemia accompanied by hypoinsulinemia in all untreated diabetic rats compared with normal control rats. However, treatment of diabetic rats with AEEF (300, 400, and 500 mg/kg) and glibenclamide (3 mg/kg) reduced blood glucose levels. This reduction in blood glucose levels could be explained either by the presence of flavonoids in AEEF, as flavonoids have been shown to activate the phosphoinositide 3-kinase (PI3K) signalling pathway, whose activation leads to an insulin-mimetic action that stimulates glucose uptake and glycogen synthesis, thereby inhibiting gluconeogenesis in target tissues and reducing hyperglycemia [39] or that AEEF acts via the same mechanism as glibenclamide, stimulating insulin secretion by pancreatic beta cells. In fact, glibenclamide binds to its receptors on the surface of the pancreatic beta cell membrane, causing depolarization of the membrane, followed by the opening of calcium channels leading to the entry of calcium into the cell. This entry of calcium results in the release of insulin, inducing a drop in blood glucose levels [40]. These results concur with those obtained by Miaffo et al. [41], who also demonstrated a significant reduction in blood glucose levels in diabetic rats treated with aqueous extract of *Vitellaria paradoxa* trunk bark.

Diabetes is associated with disorders of plasma lipid and lipoprotein metabolism, characterized by elevated TC, LDL-c and TG concentrations and reduced HDL-c levels [42]. The results of this study showed an increase in TC, TG and LDL-c levels accompanied by a decrease in HDL-c levels in the untreated diabetic control compared with the normal control. The increase in lipemia in these animals could be explained by the hypoinsulinemia present in these rats, since insulin is responsible for lipid accumulation in adipose tissue [43]. In contrast, AEEF-treated rats showed an improvement in these lipid parameters. This may be due to the fact that the extract stimulated lipoprotein lipase or inhibited HMG-coA reductase, two key enzymes involved in triglyceride metabolism and cholesterol synthesis, thus preventing the onset of dyslipidemia and arteriosclerotic processes [44]. Furthermore, this study showed a significant increase in coronary risk index (CRI) in untreated diabetic rats compared to normal rats. Increased CRI is indicative of coronary atherogenic risk [45]. In contrast, AEEF-treated rats showed a decrease in CRI. This reduction in CRI in these animals is probably due to the action of the polyphenols present in AEEF, as these molecules have been recognized as cardioprotective agents for cells against oxidative damage [46].

It has been recognized that there is a correlation between diabetes and oxidative stress [47]. Indeed, hyperglycemia is one of the main causes of high levels of free radicals, followed by the production of reactive oxygen species, which can lead to increased lipid peroxidation and impaired antioxidant defense and further impair glucose metabolism in the biological system [48]. This study showed an increase in MDA levels and a decrease in SOD, CAT and GSH activity in diabetic animals. In contrast, AEEF treated animals showed a decrease in MDA levels and an increase in SOD, CAT and GSH activity. This result could be explained by the fact that the extract inhibited the formation of reactive oxygen species by opposing the oxidation of macromolecules such as proteins. This inhibition would be due to the presence of certain antioxidant substances in the extract such as flavonoids, as flavonoids have been shown to possess iron chelating and stabilizing properties to reduce highly oxidizing free radicals [49]. In addition, flavonoids present in AEEF are also thought to be effective in preventing lipid peroxidation, as they are able to extract hydrogen from the CH2 groups of polyunsaturated fatty acids [50]. This result corroborates those of Saker et al. [51], who demonstrated the same effects with Rosmarinus officinalis extract.

Transaminases (ALAT and ASAT) are markers of abnormal liver function. An increase in their activity to higher-than-normal plasma levels suggests hepatic cytolysis or lipid infiltration in the liver [52]. In addition, studies have shown that the liver cells of STZ-induced diabetic rats are irreversibly destroyed, resulting in the release of ALAT and ASAT into the blood [53]. The results obtained in this study did indeed show an increase in plasma ALAT and ASAT levels in the diabetic control. In contrast, a decrease in these parameters was observed in the AEEF and glibenclamide-treated groups. The restoration of ALT and AST activity in AEEF-treated rats could be explained by the improvement of their lipid parameters, which would have prevented liver damage in the animals. This effect would probably be due to the presence in the extract of flavonoids, which are hepatoprotective agents [54]. This result is in line with the work of Kolefer et al. [55], who also showed a decrease in plasma ALAT and ASAT activities in diabetic rats treated with the aqueous extract of *Ficus vallis-choudae* Delile leaves.

Elevated plasma urea and creatinine levels are an indicator of renal dysfunction induced by the hyperglycemia that accompanies diabetes [56]. This study showed an increase in plasma urea and creatinine levels in untreated diabetic rats compared with normal rats. In AEEF-treated rats, however, these parameters were significantly lower than in diabetic rats. This drop in urea and creatinine levels in AEEF-treated rats could be explained by the fact that AEEF may have protected the rats' kidney tissues either by reducing their hyperglycemia or by the presence of certain nephroprotective agents such as the alkaloids, phenols and tannins present in AEEF [57]. In addition, AEEF is said to act on oxidative stress by preserving the activity of antioxidant enzymes at renal level [58]. This result is similar to those of Prakasam et al. [59], who also showed a reduction in plasma urea and creatinine levels in rats made diabetic by STZ and treated with *Casearia esculenta* root extract at doses of 200 and 300 mg/kg orally respectively for 45 days.

Histopathological findings in the pancreas of diabetic rats showed atrophy of their islets. In fact, STZ is a substance that is taken up by the β-cell and, thanks to GLUT 2 transporters, causes cell death via DNA fragmentation [60]. However, in rats treated with AEEF, an improvement in islet size and HOMA-β of rats was observed. This effect in these animals would be due to the lowering of blood sugar levels by AEEF, which allowed reversibility and restoration of the architecture of the rats' pancreatic islets [61]. This result is similar to those of Gupta et al. [62], who also showed a restoration of the histoarchitecture of rat pancreatic tissues induced by STZ and treated with the methanolic extract of *Moringa oleifera* leaves for 21 days.

5. Conclusion

The present study has shown that AEEF contains several bioactive compounds conferring antidiabetic, antidyslipidemic, and antioxidant properties, thus justifying its therapeutic use in the treatment of diabetes mellitus. Looking ahead, we plan to study the activity of this extract on a type 2 diabetes model to elucidate other mechanisms of action.

6. Limitations of the study and clinical applications

This study has some limitations. Indeed, any data at the molecular level would be needed to better elucidate the mechanisms by which AEEF relieves diabetes mellitus. In addition, a toxicological profile study would also be important to ensure the safety of AEEF. In clinical applications, it will have the development of an antidiabetic drug derived from *Erigeron floribundus* which will be used by the population for the management of diabetes mellitus.

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Data availability

We have the data of this research article and can provide it as per the request.

CRediT authorship contribution statement

Boutou Masky: Writing – original draft, Resources, Project administration, Methodology, Investigation, Funding acquisition, Conceptualization. **Hamadjida Adjia:** Validation, Resources, Project administration, Methodology, Investigation. **David Miaffo:** Writing – review & editing, Writing – original draft, Validation, Resources, Methodology. **Bibi Farouck Aboubakar Oumarou:** Validation, Resources, Methodology. **Harquin Simplice Foyet:** Writing – review & editing, Validation, Supervision, Methodology, Investigation, Conceptualization. **Kakesse Maguirgue:** Validation, Resources, Methodology. **Ernest Rodrigue Talla:** Project administration, Methodology, Investigation, Formal analysis. **Angele Kopodjing Bello:** Methodology, Formal analysis. **Christian Bonabé:** Methodology, Formal analysis. **Fidèle Ntchapda:** Writing – review & editing, Writing – original draft, Validation, Supervision, Resources, Project administration, Methodology, Conceptualization.

Declaration of competing interest

The authors declare no conflict of interest.

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