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Research Article

An Overview of Erigeron Floribundus Leaf Aqueous Extract's Antidiabetic Properties in A Wistar Rat Model of Type 1 Diabetes Produced by Streptozotocin

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ABSTRACT

Backgroud

The purpose of this study was to assess the antidiabetic effects of the aqueous extract of Erigeron floribundus leaves (AEEF) in diabetic rats. Erigeron floribundus is a herbaceous plant used in traditional Cameroonian medicine to treat diabetes mellitus.

INTRODUCTION

Chronic hyperglycemia and abnormalities in the metabolism of carbohydrates, fats, and proteins are hallmarks of diabetes mellitus, a metabolic disease caused by deficiencies in insulin secretion, action, or both [1]. Diabetes mellitus is currently the largest health issue in the world and is acknowledged as a real public health concern. According to estimates, the prevalence of diabetes increased from 9.3% in 2019 to 10.5% in 2021. The International Diabetes Federation (IDF) estimates that by 2030, this percentage may rise to 11.3%, and by 2045, it may reach 12.2% [2]. An aging population, an imbalanced diet, and a lack of physical activity are all strongly associated with this striking increase in the prevalence of diabetes.

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Serious side effects such myocardial infarction, atherosclerosis, nephropathy, and neuropathy are linked to chronic diabetes mellitus [3]. nsulin injections, oral antidiabetics, and dietary modifications have long been the only options for treating diabetes. Nevertheless, frequent use of these contemporary medications results in a number of unwanted side effects [4]. Additionally, a significant issue for those who are financially disadvantaged is the inaccessibility of generic medications and the steadily rising costs of products. Due to these restrictions, about 80% of people now use herbal medication [5]. Furthermore, a variety of novel antidiabetic medications can be obtained from medicinal plants, which are natural resources. Numerous researchers have assessed the pharmacological action of traditional plants and their interest in traditional medicine in light of the significant rise in the number of diabetics and the adverse effects of anti-diabetic medications. The research on Vitellaria by Miaffo et al. [6] is one example.

Erigeron floribundus (Kunth) Sch. Bip. (Asteraceae) is a herb of 1.5 m in height, with pubescent, lanceolate leaves and vegetation in paleyellow panicles. In Cameroon, it is generally determined as a weed alongside roadsides, and it is used in typical medication to deal with diabetes, angina, lady infertility, dental pain, headaches, and microbial ailments [9,10]. Previous work on this plant has proven that the aqueous extract of E. floribundus leaves includes alkaloids, saponins, tannins, glycosides, phenols, and flavonoids [11]. However, no preceding scientific work has investigated its antidiabetic properties. The goal of the existing work used to be consequently to consider the antidiabetic residences of AEEF in rats rendered diabetic by means of streptozotocin (STZ).

2. MATERIALS AND METHODS

2.1. Animal material

The animals used were male albino rats of the Wi star strain (Rattus norvegicus) provided by the An imal House of the Institute of Health, Nutrition an d Galenic Preparations, University of Ngaoundére , Cameroon. The animals weigh between 150 and 200 grams and are approximately 2 to 3 months o ld. They were adapted to room temperature, 12 ho urs of light and 12 hours of darkness per day. Dri nks and food were provided optionally. Only mal e rats were used in this study because they are les s sensitive to hormone replacement, especially est rogen, which could affect the results.

2.2. Plant material

Leaves of E. floribundus were collected in Octob er 2022 in the Dang region, 15 km from the city o f Ngaoundére, Cameroon (13°34â2 N, 7°27â2 E). After harvesting, E. floribundus was identified by Professor Tchobsala, botanist from the Universit y of Maroua (Cameroon). Samples of this plant w ere identified by comparison with samples with a ccession number 61003/HNC at the Hebiya Natio nal Laboratory in Cameroon. Wash fresh Eucalyp tus multiflorum leaves in tap water, dry them and grind them to a fine powder using a mortar.

2.3. Preparation of AEEF

One liter of distilled water was used to macerate one hundred grams (100 g) of powdered E. floribundus for twenty-four hours. Wattman n°1 paper was used to filter the resultant slurry. The filtrate was dried by oven drying it at 45 °C using a Memmert brand UN55. The resulting dry extract had a yield of 5% and weighed 5 g.

2.4. Choice of doses of AEEF

Information gathered from conventional therapists was used to determine dosages. The amount of medicine that a healer administers to a patient on a daily basis has, in fact, vanished in the lab. With the help of the obtained crude extract (5 g), which was assumed to be taken by an adult weighing 70 kg, the human therapeutic dosage (HTD) could be calculated using the following ratio: HTD = 5000 mg/70 kg = 71.42 mg/kg. Calculated using the

method by Shannon et al. [12]: RED = HTD × Human Km/Rat km, where Human Km = 37; Rat Km = 6; Km = specific conversion factor, the rat equivalent dose (RED) was about equivalent to 400 mg/kg. An arithmetic sequence at 100 mg/kg framed the therapeutic doses that were reached (300, 400, and 500 mg/kg).

2.5. Qualitative phytochemical study of AEEF

The several biactive chemicals found in AEEF were identified through phytochemical screening. Using color reactions based on the methodology of N'Guessan et al. [13], several bioactive chemicals were found. They contained phenols (FeCl3 and K3Fe(CN)6), anthraquinones (NH4OH), terpenoids and steroids (acetic anhydride and H2SO4), flavonoids (Shibata reagent and Mg), tannins (FeCl3), alkaloids (Dragendorff reagent and Mayer reagent), and saponines (persistent foam).

2.6. Quantitative phytochemical study of AEEF

2.6.1. Tannin determination

By adding 1000 µL of AEEF or catechin solution (10 mg/mL) and 750 µL of reagent (4% vanillin in methanol) to a tube, the tannin content was ascertained. After five minutes of incubation at 30 °C, the resultant mixture's absorbance at 500 nm was measured. Milligram catechin equivalent per gram of dry extract (mg CE/g) was used to express the tannin content [14].

2.6.2. Flavonoid determination

1 mL of AEEF or quercetin (0–100 µg/mL), 0.2 mL of aluminum chloride solution (10% w/v), 0.2 mL of potassium acetate (1 M), and 5.6 mL of distilled water were added to a tube in order to measure the flavonoid concentration. After 30 minutes of incubation, the resultant mixture's absorbance at 415 nm was measured. Milligrams of quercetin equivalent per gram of dry extract (mg EQ/g) was used to express the flavonoid content [15].

2.6.3. Determination of phenols-

Determine the phenol content by adding 0.5 mL o f AEEF or gallic acid, 2.5 mL of reagent-ciacalteu (10%) and 4 mL of sodium carbonate (7 .5% w/v) to a test tube. The mixture is incubated at room temperature for 30 min and the absorbanc e is measured at 727 nm. The phenol content was expressed as milliequivalents of gallic acid per gr am of dry extract (mgEAG/g) [16].

2.7. Induction of diabetes-

Diabetes was induced by intraperitoneal administ ration of a single dose (60 mg/kg) of STZ (Sigma Aldrich, Saint. Louis) to normal rats before 16 h of fasting. One hour later, all animals were given 3 g/kg D-glucose (Edu-

Lab Biology kit, Bexwell, UK) orally, and 72 h la ter, blood glucose levels of the rats were assessed using the One Touch Ultra Mini glucometer (Life). Screening, USA, Accuracy ± 7.5% and test pap er. Rats with blood glucose levels equal to or grea ter than 150 mg/dL were considered diabetic and selected for testing [17].

2.8. Distribution and treatment of animal-

Thirty (30) male mice (including 5 normal mice a nd 25 diabetic mice) were divided into 6 groups with 5 mice in each group and treated daily for 21 days as follows. Group 1 (normal control) receive d distilled water (10 mL/kg); Group 3 (positive co ntrol) received glyburide (3 mg/kg) orally

IIIGroups 4, 5, and 6 received AEEF (300, 400, a nd 500 mg/kg) orally.< br> Measure parameters s uch as blood sugar, weight, food, and drink every week.

2.9. Blood and organ sampling-

Rats were fasted for 16 h, anesthetized with a mix ture of ketamine and diazepam, and then sacrifice d by cervical decapitation. Blood was then collect ed from the rat's carotid artery with heartbeat, pla ced in a dry tube, and centrifuged at 3000 rpm for 15 min. The supernatant was collected and stored in a ±20°C refrigerator (Hisense RT35 320I) for t he determination of biochemical parameters. In a ddition, immediately after sacrifice, the pancreas,

liver, and kidneys of each animal were removed, adipose tissue was removed, and washed in 0.9% NaCl. One part of each organ was stored at ±20° C for oxidative stress, and the other part was stored in 10% formalin for histological distribution.

2.10. Determination of biochemical parameters-

Herbert et al. [18] for the determination of insulin Matthews et al. [19] used the homeostasis model assessment (HOMA-β) = 20 x fasting insulin (U/L)/fasting glucose (mmol/L) - 3.5 to calculate β-cell function. Total fat (TC), low-density lipoprotein cholesterol (LDL-c), low-density lipoprotein cholesterol (VLDL-c) and triglyceride (TG) levels were measured as described by Richmond [20] and Trinder [21]. Obtained by the enzyme colorimetric method. High-density lipoprotein cholesterol (HDL-c) levels were obtained using Weibe et al. [twelve]. Anti-atherosclerotic index (AAI) was calculated according to the method of Kang et al. [23]: AAI = Log(TC/HDL-c). Coronary risk index (CRI) was calculated using the formula of Barter et al. Cardioprotective index (CI) was calculated using the formula of Quantanilha et al. [25]: CI = LDL-c/HDL. Alanine aminotransferase (ALT), aspartate aminotransferase (AST), and creatinine were measured according to the method of Murray [26]. Urea was measured using the method of Kaplan [27]. Oxidative stress markers such as malondialdehyde (MDA), catalase (CAT), reduced glutathione (GSH), and superoxide dismutase (SOD) were assessed using the method of Şehirli et al. [28].

2.11. Histopathology of the pancreas

Cancer cells were placed in vials containing 10% buffered formalin each. Samples were placed on a microtome and sectioned at 5 µm thickness. Sections were mounted on glass slides, dewaxed with xylene and rehydrated with a 95% ethanol dilution, stained with hematoxylin and eosin, and photographed at 100x magnification using a light microscope [29].

2.12. Statistical analysis

Results are expressed as mean ± standard error of the mean (S.E.M.). Data were analyzed using Graphpad prism version 8.0 software. Analysis of variance and Bonferroni test were used to compare data from bivariate tests. Analysis of variance and Turkey's post hoc test were used to compare data from independent tests. The difference is 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. These results revealed the presence of saponins, flavonoids, tannins, phenols, alkaloids, steroids, and terpenoids. However, it is devoid of anthraquinones.

Table 1. Qualitative phytochemical study of AEEF.

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

(+) present; (-) absent.

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.

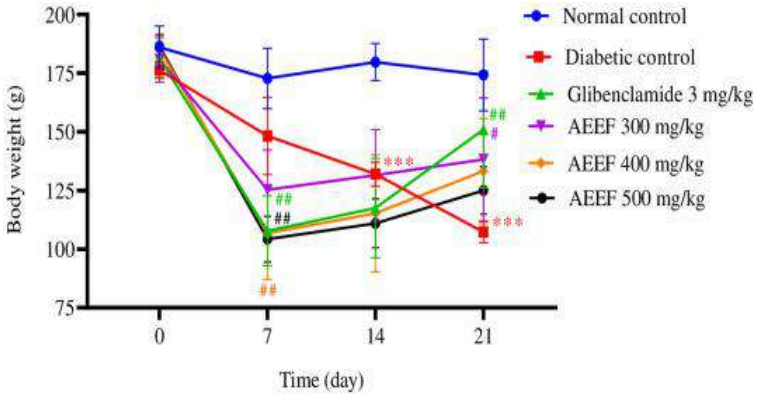
Table 2. Quantitative phytochemical study of AEEF.

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.

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

Fig. 1 It shows a change in animal weight over time. The graph shows that the body weight of mice in the diabetic control group was significantly reduced on days 14 and 21 compared to the normal control group ($p < 0.001$). On the other hand, animals administered glyburide ($p < 0.01$) and 300 mg/kg AEEF dose ($p < 0.05$) showed an increase in body weight compared to the control group diabetes on day 21 of treatment.



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2. 1. Effect of AEEF on body weight of normal and diabetic rats. Results are expressed as mean ± MSE (n = 5). ***p < 0.001: different from the normal control group. # p < 0.05; ##p < 0.01: different from the diabetic control group. AEEF: Aqueous extract of erigeron leaves. Effect of aqueous extract of E. floribundus leaves on food intake Compared with the normal control group, food intake of the diabetic control group increased on day 14 ($p < 0.05$) and day 21 ($p < 0.001$) of the experiment. However, on day 21 of glyburide and 300, 400 and 500 mg/kg AEEF treatment, food intake was significantly decreased compared to untreated diabetic rats ($p < 0.001$) (Figure 2).

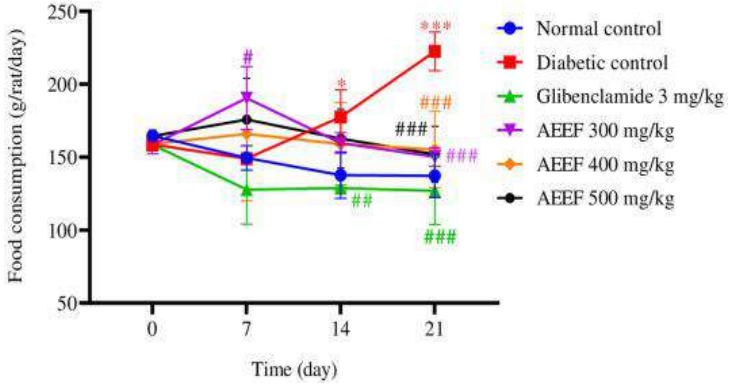

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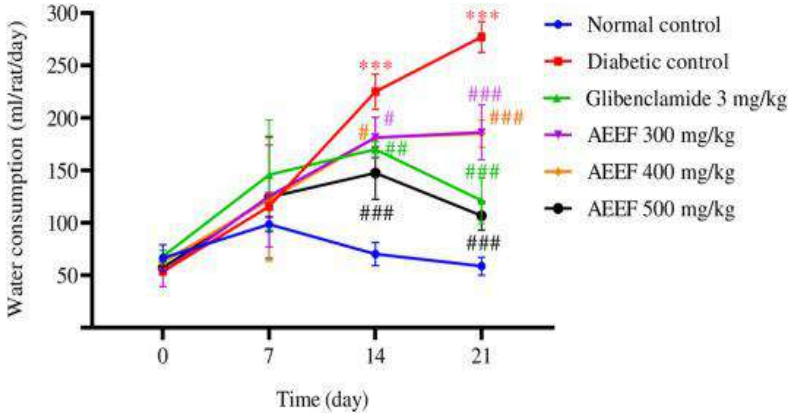
Fig. 2. Effect of AEEF on food consumption in normal and diabetic rats. Results were expressed as mean ± MSE (n = 5). *p < 0.05; ***p < 0.001: significant difference from normal control. #p < 0.05; ##p < 0.01; ###p < 0.001: significant difference from diabetic control. AEEF: aqueous extract of *Erigeron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

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

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



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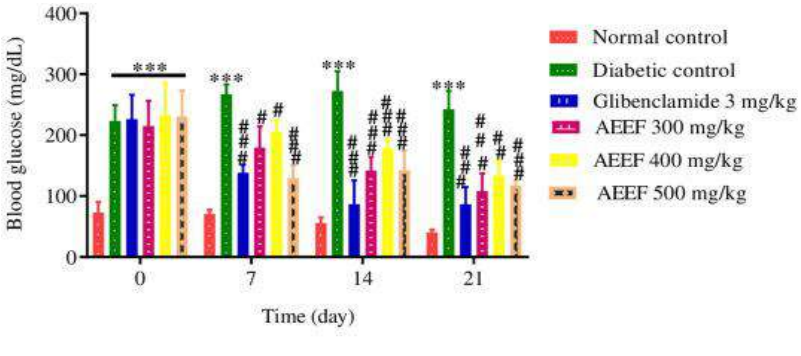
2. 3. Effect of AEEF on water consumption in normal and diabetic rats. Results are expressed as mean ± MSE (n = 5). ***p < 0.001: different from the normal control group. # p < 0.05; ##p < 0.01; ###p < 0.001: There was significant difference between the diabetic control group. AEEF: Aqueous extract of Erigeron leaves. Effects of aqueous extract of Eucalyptus multiflorum on blood glucose and insulin levels

Fig. Figure 4A shows the changes in blood glucose levels in mice over time. As can be seen in this figure, the blood glucose level of all rats increased after STZ injection compared to normal control rats ($p < 0.001$). On days 7, 14 and 21 of treatment, the blood glucose values of rats in the diabetic control group were significantly higher than those in the normal control group ($p < 0.001$). In contrast, blood glucose decreased from day 7 to the end of treatment in rats treated with AEEF and glyburide ($p < 0.05$; $p < 0.001$)**.**



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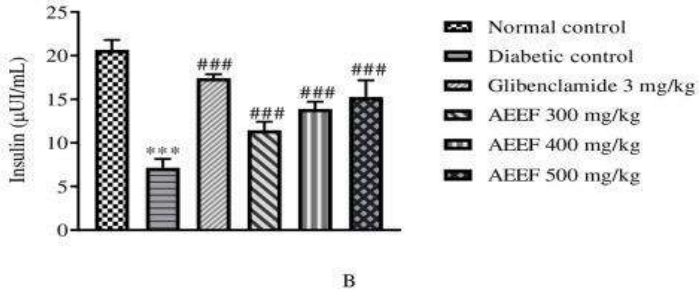

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2. Figure 4. Effect of AEEF on blood glucose (A) and insulin (B) levels in normal and diabetic rats. Results are expressed as mean ± MSE (n = 5). ***p < 0.001: different from normal control group. # p < 0.05; ##p < 0.01; ###p < 0.001: There was a significant difference between the diabetic control group. AEEF: Aqueous extract of Erigeron leaves. In contrast, insulin levels were significantly increased in rats treated with AEEF and glyburide compared with diabetic controls (p < 0.001). Effect of Eucalyptus multiflora aqueous extract on blood lipidsTable 3 shows the effect of AEEF on blood lipid parameters in rats. The results showed that total cholesterol, LDL-c, VLDLc, and TG levels of rats in the diabetic control group were significantly higher (p < 0.001) than in the normal control group. However, HDL-c levels were lower in diabetic controls than in normal controls (p < 0.001). However, all doses of AEEF and glyburide caused a decrease in TC, LDL-c, VLDL-c, and TG levels (p < 0.001) and an increase in HDLc levels (p < 0.001) compared with the diabetic control group.

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) TG (mg/dL)	40.8 ± 0.1 84.3 ± 0.8	127.5 ± 0.6[a] 376.4 ± 0.6[a]	22.1 ± 0.2[c] 125.1 ± 0.3[c]	36.2 ± 0.6[c] 230.1 ± 0.7[c]	24.7 ± 0.1[c] 188.1 ± 0.1[b]	60.6 ± 0.1[c] 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). ap < 0.001: significant difference from normal control. bp < 0.01. cp < 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.

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

STZ caused an increase in CRI, CI and AAI (p < 0.001) and a decrease in HOMA-β (p < 0.001) in diabetic rats compared with normal control rats. Conversely, AEEF treatment in rats resulted in a decrease in CRI, CI and AAI (p < 0.001) and an increase in HOMA-β (p < 0.001) compared with untreated diabetic rats (Table 4).

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

Empty Cell	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). ap < 0.001: significant difference from normal control.

bp < 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.

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 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.

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 ± 0.31	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). ap < 0.001: significant difference from normal control.

bp < 0.001: significant difference from diabetic control. MDA: malondialdehyde; GSH: reduced glutathione; SOD: superoxide dismutase; CAT: catalase.

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.

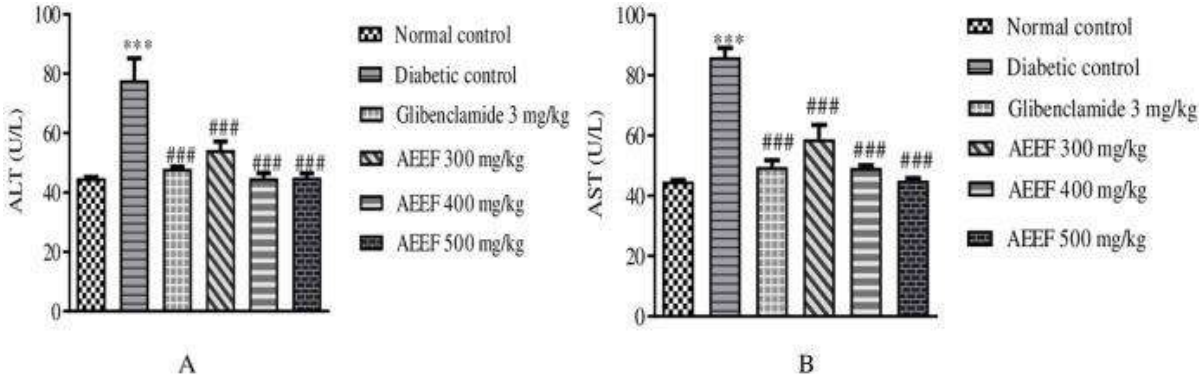

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Fig. 5. Effect of AEEF on ALAT (A) and ASAT (B) activities in normal and diabetic rats. Results were expressed as mean ± MSE (n = 5). ***p < 0.001: significant difference from normal control. ###p < 0.001: significant difference from diabetic control.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

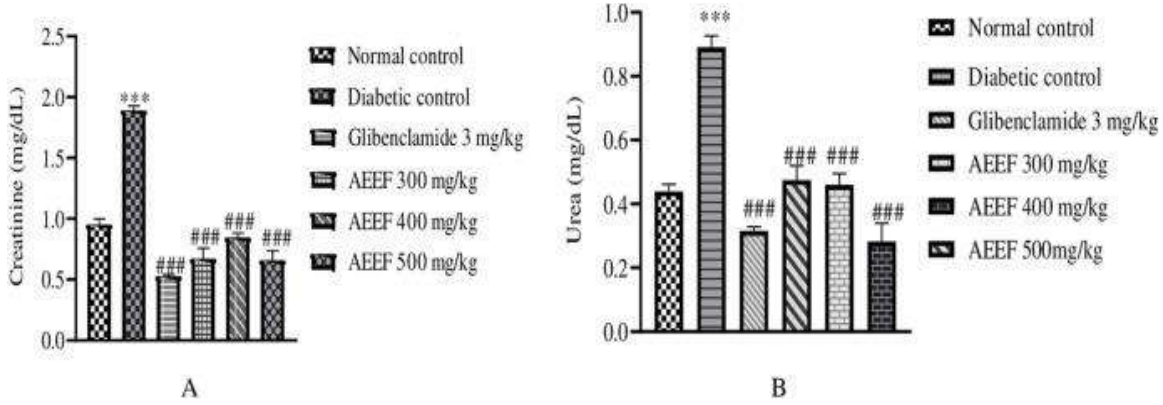

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Fig. 6. Effect of AEEF on creatinine (A) and urea (B) levels in normal and diabetic rats. Results were expressed as mean ± MSE (n = 5). ***p < 0.001: significant difference from normal control. ###p < 0.001: significant difference from diabetic control.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

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

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.

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.

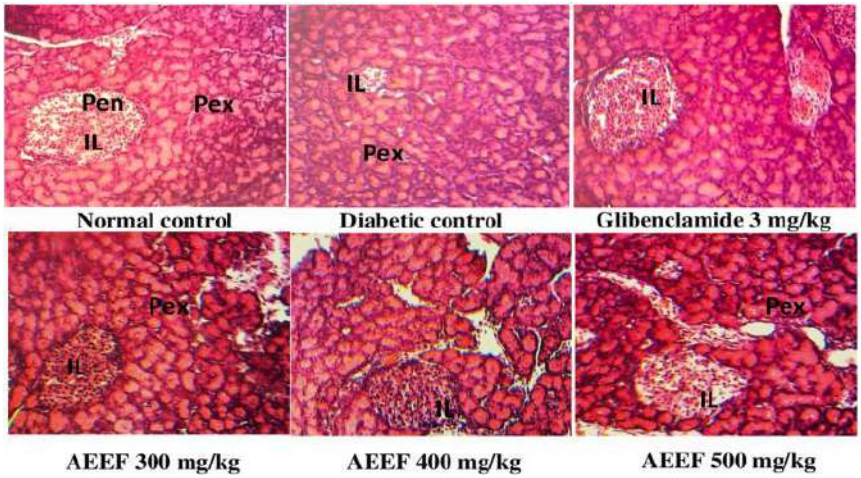

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Fig. 7. Histological section of rat pancreas in normal and diabetic rats. Pen = endocrine pancreas; Pex = exocrine pancreas; IL = Islet of Langerhans. AEEF: aqueous extract of *Erigeron floribundus* leaves.

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], 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 Studies have also shown that untreated diabetic ra ts develop polydipsia compared to normal rats. T he polydipsia seen in these animals may be due to the high amount of sugar in the renal filtrate; this sugar acts as an osmotic diuretic and inhibits tubu lar reabsorption of water, causing dehydration, th us stimulating thirst in the hypothalamus of medi umsized animals [37]. However, reduced water in take was observed in rats treated with AEEF and glyburide. The reason for the reduced water intak

e in rats treated with AEEF is that the extract inhi bits hypothalamic thirst in these animals, thus pre venting the development of polydipsia. Insulin de ficiency causes hyperglycemia within two days [3 8]. In fact, this study showed that all untreated dia betic rats developed hyperglycemia with hypoins ulinemia compared to normal control rats. Howev er, treatment of diabetic rats with AEEF (300, 40 0 and 500 mg/kg) and glibenclamide (3 mg/kg) re duced blood sugar levels. The reduction in blood sugar may be explained by the presence of flavon oids in AEEF, since flavonoids have been shown to activate the phosphoinositide 3-
kinase (PI3K) signaling pathway, activating those responsible for the effects of insulin, thereby pro moting glucose uptake and inhibiting hepatic gluc ose synthesis, thereby inhibiting gluconeogenesis in tissues and reducing hyperglycemia [39] or AE EF, acting by the same mechanism as glyburide, s timulates pancreatic β-
cells to release insulin. In fact, glyburide binds to receptors on the surface of the pancreatic β-
cell membrane, causing the cell membrane to dep olarize, which then opens calcium channels, allo wing calcium to enter the cell. The influx of calci um causes insulin release, which in turn leads to a decrease in blood sugar. These results are consist ent with those obtained by Miaffo et al. [41] also observed a decrease in blood sugar levels in diabe tic rats treated with an aqueous extract of Vitellari a paradoxa skin. -
c increases TG concentration and decreases HDL-c levels [42]. The results of this study showed tha t untreated diabetic controls had increased TC, T G and LDL-c levels, while HDL-
c levels were decreased compared to normal contr ols. The increase in blood lipids in these animals could be explained by the hypoinsulinemia presen t in mice, since insulin is responsible for lipid acc umulation in adipose tissue [43]. In contrast, thes e lipid parameters improved in rats treated with A EEF. This could be due to the fact that the extract suppresses lipoprotein lipase or inhibits HMG-coA reductase, two major enzymes involved in tri glyceride metabolism and cholesterol synthesis, t hus preventing the development of dyslipidemia a nd arteriosclerotic processes [44]. Also, this study showed that untreated diabetic rats had a significa nt risk factor (CRI) compared to normal rats. Incr eased CRI indicates the risk of coronary atheroscl erosis [45]. In contrast, CRI decreased in rats trea ted with AEEF. The decrease in CRI in these ani mals may be due to the effect of polyphenols fou nd in AEEF, since these molecules act as cardiopr otective agents for cells against oxidative damage [46]. The relationship between stimuli [47] In fac, hyperglycemia is one of the main causes of high f ree radical levels, followed by the production of r eactive oxygen species, which can lead to strong l ipid peroxidation, and the resistance to blocking a ntioxidant is not good and further affects glucose metabolism in biological organisms [48]. This stu dy showed that diabetic animals had increased M DA levels and decreased SOD, CAT and GSH act ivities. In contrast, animals treated with AEEF ha d decreased MDA levels and increased SOD, CA T and GSH activities. These results may be explai ned by the fact that the extract prevents the forma tion of reactive oxygen species by combating the oxidation of macromolecules such as proteins. Th is inhibitory effect may be due to the presence of some antioxidants (e.g. flavonoids) in the extract, since flavonoids have been shown to have ironch elating and stabilizing properties that significantl y reduce oxidative free radicals [49]. In addition, flavonoids in AEEF are thought to be effective in preventing lipid peroxidation due to their ability t o absorb hydrogen from the CH2 group of polyun saturated fatty acids [50]. This result confirms the results of Saker et al. [51] found that rosemaryex tract has the same effect. An increase in their acti vity above plasma level indicates the presence of hepatocyte lysis or lipid infiltration in the liver [5 2]. In addition, studies have shown that liver cells

are destroyed in STZ-induced diabetic rats, resulting in the release of ALAT and ASAT into the blood [53]. The results obtained in this study indeed show that increasing the levels of ALAT and ASAT in the blood is effective in controlling diabetes. In contrast, a decrease in these parameters was observed in the AEEF and glyburide treatment groups. The restoration of ALT and AST activity in AEEF treated rats can be explained by the improvement of lipid parameters, which can prevent liver damage in animals. This effect may be due to the presence of flavonoids in the extract, which are hepatoprotective agents. These results are consistent with the study of Kolefer et al. [55] who also found that serum ALAT and ASAT activities were reduced in diabetic rats treated with Ficus vallis-choudae Delile leaf aqueous extract. [56] This study showed that plasma urea and creatinine levels were increased in untreated diabetic rats compared to normal rats, but these parameters were lower in AEEF-treated rats than in diabetic rats.

5. CONCLUSION

The present study shows that AEEF contains many bioactive compounds with antidiabetic, antidyslipidemic and antioxidant properties, thus proving its use in diabetes treatment. Moving forward, we plan to study the activity of this extract on type 2 diabetes samples to elucidate additional mechanisms of action.

6. Limitations of the study and clinical applications

This study has some limitations. In fact, all molecular level information is required to optimize the mechanism by which AEEF lowers blood sugar. In addition, toxicological studies are important to ensure the safety of AEEF. In medical use, anti-diabetic drugs extracted from Asarum erigeron for human use in the treatment of diabetes will be produced.

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