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Research Article

Evaluation of Hypoglycaemic activity of *Combretum roxburghii* on Streptozotocin Induced Diabetic Rats

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Abstract

Diabetes mellitus is a group of chronic, progressive metabolic diseases that have been reducing the biological world. Along with managing one's lifestyle, conventional drugs are used to control diabetes. By proposing numerous objectives, including extraction, *in vivo* anti diabetic research of *Combretum roxburghii*. this study focused on the preventive effect some medicinal plants have on diabetes. There are some convincing indications that the aforementioned plant may have antioxidant, anticancer, antibacterial, and safer conventional medical properties. This significant medicinal plant mentioned above have not been the subject of any antidiabetic investigations. It is thought that increased oxidative stress could hasten the development of diabetes and the effects of antioxidant therapy since external supply of these medicinal plant appears to be advantageous in diabetes situations. The current work examines the extraction, antidiabetic and pancreatic protective activities of a *Combretum roxburghii* in a type 2 diabetes model caused by a high-fat diet (HFD) and streptozotocin (STZ). Treatment with plant resulted in a considerable drop in blood glucose levels that was both time- and dose-dependent. After therapy with plant extracts, which had results similar to those of typical drug-mediated therapeutic effects in the high dose group, glucose tolerance, biochemical markers of plasma lipid profile were all significantly improved. Studies on histopathology showed that extracts with larger and more numerous beta cells had protective effects on pancreatic beta-cells. Our findings show that *Combretum roxburghii* produces the highest/maximum therapeutic advantages and can be a potential treatment for diabetes and its problems.

Keywords: Diabetes; *Combretum roxburghii*; Aerial Parts; Euglycemic; Hyperglycaemia

Introduction

Most widely known as “diabetes” this chronic illness of carbohydrate metabolism is marked by a decreased capacity of the body to make or react to insulin and as a result, maintain healthy levels of blood glucose.

The International Diabetes Federation projects that there will be 643 million individuals worldwide who have diabetes mellitus by 2030 and 784 million (1 in 8 adults) by 2045. In the world’s population, a person is diagnosed with diabetes mellitus every five seconds and 10 people die from it. Therefore, diabetes mellitus is constricting the scope of the biological cosmos. It was estimated that the expense of treating diabetes-related disorders would be 966 billion USD in 2021 and climb to 1,054 billion USD by 2045.

Inflammation, autoimmunity and metabolic stress are risk factors influenced by genetic and environmental factors. These states affect beta-cell mass and/or its function, which eventually prevents insulin levels from adequately meeting insulin demands and results in hyperglycaemia levels high enough to diagnose diabetes [2]. Gene-environment interactions Both genetic and environmental risk factors can occasionally have a direct effect on β-cell mass and/

or its function. Whatever the aetiology of diabetes, persistently elevated blood glucose levels are linked to microvascular and macrovascular problems that raise the morbidity and death rates for diabetics [3]. According to this hypothesis β -cell malfunction or destruction is a necessary component of all diabetes types [4,5].

The Indian subcontinents healthcare system heavily relies on the complementary or traditional medical system as well as a variety of cultural and socioreligious traditions [6]. Up to 90% of people in developing countries utilise plants and their products as traditional medicine for primary healthcare according to the World Health Organization (WHO) [7]. Herbal items are used for more than just nutritional purposes like food and nourishment; they also play a vital part in the treatment of several ailments [8].

Plants can provide both food and medical remedies. India is fortunate to have a long and rich history of cultural traditions. But just 6% of the 250,000–400,000 plant species have had their biological potential examined and only 15% have had their phytochemical potential explored [9]. These customs are linked to the usage of wild plants as herbal medicines. Ethnic groups living in undulating plains and the foothills of dense forests have continued to practice the usage of medicinal herbs [10].

However, for the past few years, medicinal plants have regained widespread acceptance due to a growing belief in herbal therapy because of its fewer side effects than allopathic medication and the need to satisfy the medical needs of growing human population [11].

Materials and Methods

Current work was performed in the Department of Pharmacology, University college of pharmaceutical sciences, Kakatiya university, Warangal. The collection and processing of aerial parts of *Combretum roxburghii* plant material was acquired and authenticated by a taxonomist and plant voucher specimen given number is KUDM-1088 and preserved at departmental museum. All the chemicals and reagent used for this consider were parched research–grade quality and procure in our laboratory according to its preservative conditions. Estimation of glucose, triglycerides, creatinine, cholesterol, Alanine transaminase (ALT) and Aspartate Aminotransferase (AST). Alkaline phosphatase (ALP) were studies by using standard Merck analytical kit methods. (Merck specialities private limited, Mumbai, India).

Preparation of plant extract

Extraction processes for medicinal plants were completed by maceration method. The hand- pick medicinal plants is *Combretum roxburghii* were isolated and chopped into slight sections, dried completely at room temperature. The materials from the dried, complete, independent plant were mechanically crushed pulverised into a fine powder and put through a sieve with a 40mm mesh. The above- mentioned independent plant material was ground into a powder and stored in airtight plastic bags. The powdered plant sample weighed 100 g, and 400 ml of methanol was macerated with random agitation for 7 days to extract the compounds. Extract was passed through Whatman's strainer sheet into a separate conical flask after being strained, transferred and cleaned [11]. The methanolic extract of *Combretum roxburghii* was separately dissolved in 1000ml of water and fractionalized with n-hexane, chloroform, ethyl acetate and n-butanol. Under reduced pressure, the substances were separated from the fractions to provide the equivalent extract. All the fractions of *Combretum roxburghii* were divided by separating funnel, evaporated in a rotavapour and used for forward studies. Lastly the *Combretum roxburghii* ethyl acetate portion (EACR), was used for advance pharmacological screening studies [12].

Animals

In accordance with the CPCSEA regulations set forth by the Indian government, animal studies were conducted. The Institutional Animal Ethics Committee (IAEC/08/UCPSC/KU/2020) gave its approval to animal protocols. Wistar albino male rats were utilised to assess the preventive impact of HFD+STZ (the high fat diet plus STZ) caused diabetes paradigm of selected medicinal plant *Combretum roxburghii*. One week before to the experiment, animals were acclimated to the experimental environment. Animals were kept in conventional settings with a 12-hour cycle of day and night, 50–60% relative humidity and unlimited access to food and water.

Acute toxicity study

Studies on acute toxicity were conducted for methanolic extract of *Combretum roxburghii* (Aerial plant extract) extracts were given orally to Wistar albino male rats at dosages of 100, 200, 400, 1000, 2000 mg/kg body weight respectively, suspended in 5% gum acacia. For the first several hours, then every 24 hours for a total of 48 hours, the animals were continuously monitored for any changes in their autonomic or behavioural reactions. Each group experienced mortality at the conclusion of this time.

Assessment of hypoglycaemic activity in euglycemic rats:

The experiment was conducted in compliance with the method outlined in the literature. A total of 30 healthy rats were separated into 5 groups (n = 6) after fasting for 18 hours. The animals in each group had their initial fasting blood samples taken, and then different doses of *Combretum roxburghii* extracts and a standard medicine, Glipizide (10 mg/kg b.w.), drooping in 5% gum acacia, by mouth provided to the various animal arrays to see how they affected blood sugar levels for 24 hours. Their specifics are listed below [13,14].

GP- Groups

Group I – Normal Control,

Group II- Glipizide 10mg/kg (Standard drug)

Group III- Methanolic extract treated group (200mg/kg)

Group IV- Methanolic extract treated group (400mg/kg)

Group V- EACR (100mg/kg)

Group VI – EACR (200mg/kg)

Blood was taken out of the retroorbital plexus of all the groups' rats at 0, 2, 4, 6, 8, and 24 hours following the medication. The specimens were tested for blood sugar levels utilize the glucose oxidase-peroxidase method on the Autoanalyser [15].

Diabetes induction in experimental groups

Wistar albino rats were provided with a HFD before the experiment in order to induce diabetes in all of the study groups. This was followed by a low dosage of streptozotocin (STZ) following the [16]. 58% of HFD calories were fixed as fat, 25% as protein, and 17% as carbohydrates. Rats were given a single STZ injection at a dosage of 45 mg/kg, i.p., following HFD had caused a state resembling the metabolic syndrome. The necessary amount of STZ was weighed into separate Ependorf tubes and dissolved in a citrate buffer with a pH of 4.5. Each tube had citrate buffer added to it just before giving it to the animals. The blood glucose levels were tested using a glucometer 48 hours succeeding the STZ injection. Animals with levels of non-fasting blood sugar larger than 250 mg/dl were deemed to be diabetic. The behaviour of the mice, which displayed polyphagia and polydipsia, further supported the induction of diabetes.

Evaluation of selected fraction's anti-diabetic MECR in sub acute study (28 days) of Diabetic rats generated by streptozotocin:

Overnight fasted rats with diabetes were separated into six-rat groups. The vehicle 5% gumacacia, standard drug and the test extract fractions (EACR) were administered orally to the animals every day for 28 days.

Group I – Diabetic group

Group II- Glipizide 10mg/kg (Standard drug)

Group III- Methanolic extract treated group (200mg/kg)

Group IV- Methanolic extract treated group (400mg/kg)

Group V- EACR (100mg/kg)

Group VI – EACR (200mg/kg)

After 7, 14, 21, and 28 days of therapy, the animals' body weights and blood sugar volumes were calculated during the investigation period. The first and final 28 days of treatment were used to estimate serum levels of cholesterol, triglycerides, insulin, ALP, creatinine, and total protein[17]. After the investigation was over, animals were sacrificed by being given an ether overdose. To investigate the histological alterations, the pancreas was isolated.

Assessment of diabetogenesis in all experimental animals

By designing the plasma sugar levels each week, the prevalence of diabetes was assessed in all experimental animals. By picking a drop of blood from a rat tail, an automatic glucometer was utilized to decide the blood sugar volumes. Rats were treated diabetic when their blood glucose levels surpassed 250 mg/dl, and the proportion of diabetes was computed.

Measurement of pancreatic weights in all experimental animals

Day 28 of the 4-week post-STZ experimental period (the first 2-weeks of HFD are regarded as the pre-experimental period), blood glucose levels were evaluated in all experimental animals. Blood was drawn to separate the plasma, which was then used for a biochemical study of the levels of triglycerides and total cholesterol. High doses of anaesthesia were used to kill the animals and each animal's pancreas was gently removed and its wet mass was noted [16].

Estimation of biochemical parameters in all experimental groups

All of the experimental groups had their plasma profiles predicted values for metabolic components such plasma triglycerides and total cholesterol. These estimates were made using biochemical kits that can be purchased commercially from Accurex, Biomedical (Mumbai, India).

Histopathological evaluation of pancreas in all experimental animal groups

After sacrificing all experimental animals, it was decided to extract some pancreatic tissue and fix it in 10% formalin saline. The typical histological tissue processing protocol was followed when working with formalin-fixed specimens [16]. These steps of processing entail gradually rising alcohol concentrations to dehydrate tissues, with 100% being the last step (absolute alcohol). Following the xylene cleaning process on the tissues, a paraffin wax infiltration stage was carried out, and paraffin embedded blocks were created. Leica, a German company, provided a microtome to slice these blocks into 5 m-thin sections, which were then smeared with hematoxylin and eosin (H&E). Below a light microscope, specimens were checked for histological alterations. Each slide's pancreatic beta cell count, and size were analysed, and quantification was done.

Statistic evaluation

To demonstrate all experimental values, the average and the mean standard deviation were utilised (SEM). After analysis of the variance in one direction, Turkey's multiple comparison test was employed to see if a statistically significant distinction existed betwixt the groups (ANOVA). If the P value is less than 0.05, statistical findings are deemed significant.

Results and Discussion

Table 1 at three test dosages (100,200 and 400 mg/kg b.w.) after 2hr of administration, *Combretum roxburghii* extracts (MECR) significant ($P < 0.05$) drop in blood sugar levels in euglycemic rats up to 16 hours of the longer hypoglycaemic impact were studied. At 4, 6 and 8 hours into the trial, all test doses had a significant outcome with a P value of $P < 0.01$. After 4 hours of extract administration at all test doses, the maximum percentage depletion in blood glucose levels ranged from 14.1% to 26.3%. MECR exhibited a maximal hypoglycemic effect of 26.3% at 4 hours after administration, which was comparable to the effects produced by Glipizide (10mg/kg), an established medication.

Group and Treatment	Blood glucose level (mg/dl) at different time intervals							
	0 h	1h	2 h	4 h	6 h	8 h	16 h	24 h
Control	88.5 ± 4.9	88.8 ± 6.08 (0.33%)	87.2 ± 6.05 (1.46%)	82.5 ± 6.2 (6.77%)	84.7 ± 7.3 (4.29%)	82.3 ± 6.3 (7%)	83.01 ± 4.6 (6.20%)	83.4 ± 5.3 (5.76%)
Standard Group (Glipizide10mg/kg)	88.6 ± 5.3	81. 0 ± 3.9 (8.57%)	71.32 ± 2.3* (19.50%)	60.15 ± 3.2** (32.11%)	72.77 ± 6.0 (17.8%)	77.4 ± 4.5 (12.6%)	81.72 ± 4.4 (7.76%)	82.9 ± 3.7 (6.43%)
MECR (200mg/kg)	87.8 ± 3.4	87.2 ± 5.7 (2.89%)	81.4 ± 4.9 (8.24%)	76.1 ± 4.6 (14.14%)	75.1 ± 5.0 (15.2%)	78.3 ± 5.7 (11.6%)	80.7 ± 4.1 (10.13%)	82.07 ± 4.6 (7.49%)
MECR (400mg/kg)	89.5 ± 4.2	88.5 ± 6.3 (1.11%)	83.2 ± 5.4 (8.15%)	66.9 ± 3.8 (26.36%)	70.3 ± 3.2* (21.4%)	75.7 ± 4.0 (14.3%)	81.1 ± 4.3 (8.26%)	82.4 ± 2.9 (7.93%)
EACR (100mg/kg)	90.4 ± 3.7	87.0 ± 3.8 (2.62%)	83.7 ± 3.4 (7.33%)	74.1 ± 2.6 (17.83%)	75.7 ± 3.9 (16%)	81.6 ± 3.4 (11.8%)	82.6 ± 2.6 (8.53%)	84.7 ± 2.5 (6.23%)
EACR (200mg/kg)	90.3 ± 4.5	85.6 ± 5.9 (4.09%)	77.6 ± 4.9 (12.95%)	70.8 ± 3.2* (20.48%)	72.8 ± 6.3* (19.3%)	80.0 ± 6.11 (11.4%)	81.8 ± 2.8 (8.30%)	85.1 ± 3.1 (4.65%)

Table 1: Effect of *Combretum roxburghii* extracts regarding fasting blood sugar levels in euglycemic rats.

The data were shown as mean ± SEM (n = 6) Statistically significant* $p < 0.05$, ** $p < 0.01$, compared to the control group.

Group and Treatment	Blood glucose level (mg/dl) at different time intervals							
	0 h	1h	2 h	4 h	6 h	8 h	16h	24 h
Control (Diabetic)	281.9 ± 9.7	279.1 ± 11.2 (0.81%)	276.8 ± 10.3 (0.15%)	268.1 ± 10.4 (4.89%)	264.8 ± 22.5 (6.06%)	265.2 ± 17.8 (5.92%)	268.0 ± 17.1 (4.93%)	271.1 ± 9.41 (3.83%)
Standard Group (Glipizide10mg/kg)	265.95 ± 11.9	249.3 ± 9.4 (6.26%)	217.69 ± 14.0* (15.54%)	175.79 ± 18.6** (33.9 ± 6.8)	189.3 ± 17.1** (28.82%)	227.9 ± 19.73 (14.30%)	242 ± 14.7 (9%)	257 ± 9.2 (3.36%)
MECR (200mg/kg)	261.9 ± 22.0	237.5 ± 15.7 (9.31%)	223.6 ± 17.4 (19.60%)	213.4 ± 17.6* (18.41%)	232.8 ± 8.1 (11.11%)	250.7 ± 5.7 (4.27%)	271.71 ± 8.5 (3.75%)	279.7 ± 8.6 (1.15%)
MECR (400mg/kg)	278.2 ± 11.2	263.6 ± 9.5 (5.24%)	229.6+10.5* (14.87%)	196.71 ± 6.0** (29.29%)	214.4 ± 12.9* (22.93%)	229.8 ± 8.2 (17.39%)	255.6 ± 9.0 (8.12%)	274.1 ± 4.6 (1.47%)
EACR (100mg/kg)	286.0 ± 4.3	263.6 ± 3.5 (7.83%)	230.9 ± 10.3* (18.7%)	198.7 ± 14.2** (30.52%)	223.7 ± 9.6* (21.78%)	239.6 ± 8.0 (16.22%)	257.4 ± 7.9 (10%)	279.1 ± 7.7 (2.41%)
EACR (200mg/kg)	264.26 ± 17.5	248.7 ± 16.3 (5.88%)	223.4 ± 14.2 (17%)	187.8 ± 8.0* (28.93%)	240.4 ± 4.6 ((9.02%)	251.2 ± 4.5 (4.94%)	268.0 ± 4.5 (1.41%)	278.0 ± 4.7 (0.51%)

Table 2: *Combretum roxburghii* extract's impact on diabetic rats produced by streptozotocin fasting blood glucose levels.

The data were shown as mean ± SEM (n = 6) *Statistically significant $p < 0.05$, ** $p < 0.01$ when compared to the control group that was normal (n = 6).

Group	Body weight		Blood glucose level (mg/dl)	
	1st Day	28th Day	1st Day	28th Day
Control (Diabetic)	213.3 ± 10.4	178.2 ± 6.7	252.1 ± 7.6	291.1 ± 6.6
Standard Group (Glipizide10mg/kg)	202.5 ± 8.2	230 ± 8.4 (13.58%)	281.6 ± 4.6	140.4 ± 5.8** (50.14%)
EACR(200mg/kg)	208 ± 6.4	217.7 ± 6.5 (4.66%)	274.3 ± 4.8	158.4 ± 5.4 (42.25%)

Table 3: Effect of ethyl acetate fractions of *Combretum roxburghii* on the body weight and blood glucose levels in STZ induced diabetic rats.

The data were shown as mean ± SEM (n = 6) *Statistically significant $p < 0.05$, ** $p < 0.01$ when compared to the control group that was normal (n = 6).

Group	Insulin (µIU/ml)		Serum Cholesterol (mg/dl)		Serum triglycerides (mg/dl)	
	1st Day	28th Day	1st Day	28th Day	1st Day	28th Day
Control	8.66 ± 0.5	8.06 ± 0.4	132.4 ± 6.7	145.2 ± 3.5	163.2 ± 10.6	170.2 ± 8.6
Standard Group Glipizide10mg/kg	9.08 ± 0.8	16.4 ± 0.6** (80.61%)	138.2 ± 2.8	80.1 ± 5.2** (42.04%)	170.1 ± 1.7	96.1 ± 8.4** (43.50%)
EACR (200mg/kg)	8.42 ± 1.5	13.2 ± 1.3** (56.7%)	150.3 ± 3.4	95.3 ± 3.2** (36.59%)	168.3 ± 5.2	95.7 ± 4.3** (43.13%)

Table 4: Effect of ethyl acetate fractions of *Combretum roxburghii* on insulin, serum cholesterol and triglycerides in STZ induced diabetic rats.

The data were shown as mean ± SEM (n = 6) *Statistically significant $p < 0.05$, ** $p < 0.01$ when compared to the control group that was normal (n = 6).

Group	ALT (IU/L)		AST(IU/L)		ALP (IU/L)	
	1st Day	28th Day	1st Day	28th Day	1st Day	28th Day
Control (Diabetic)	186.4 ± 4.5	192.8 ± 3.6	119.6 ± 3.2	128.3 ± 3.6	246.9 ± 9.2	263.5 ± 3.6
Standard Group (Glipizide 10mg/kg)	175.3 ± 3.9	84.9 ± 3.9** (51.56%)	128.3 ± 2.6	72.46 ± 2.8** (43.52%)	296.7 ± 6.4	156.5 ± 5.8** (47.25%)
EACR (200mg/kg)	176.2 ± 4.2	90.2 ± 4.5** (48.80%)	128.2 ± 2.5	82.3 ± 3.5** (35.80%)	280.2 ± 3.7	168.3 ± 5.8** (40%)

Table 5: Effect of ethyl acetate fractions of *Combretum roxburghii* on ALT, AST and ALP in STZ induced diabetic rats.

The data were shown as mean ± SEM (n = 6) *Statistically significant $p < 0.05$, ** $p < 0.01$ when compared to the control group that was normal (n = 6).

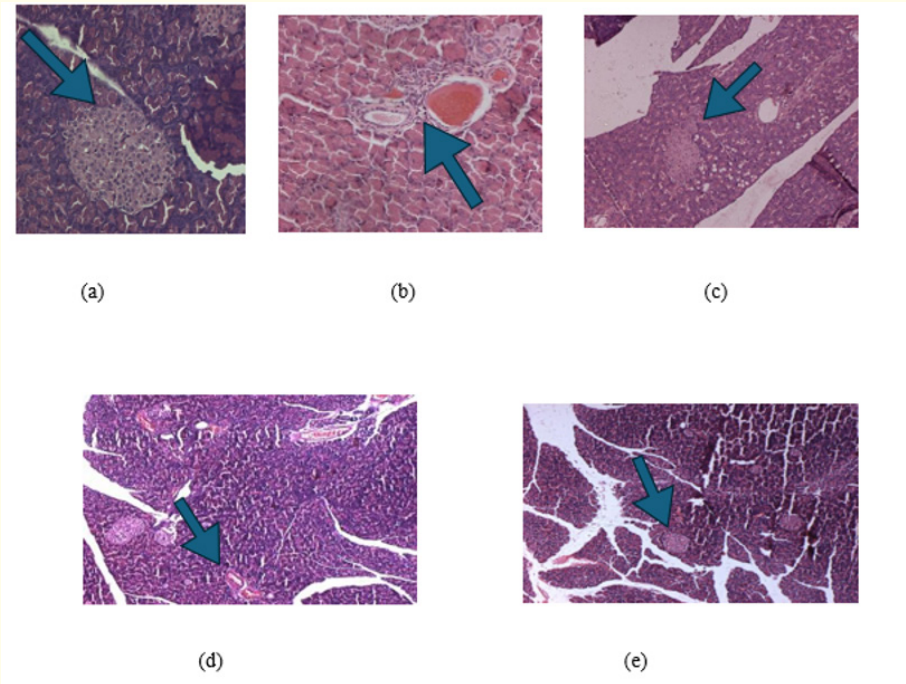

Figure 1: Effect of Methanolic extract of Combretum roxburghii (MECR) and Ethyl acetate fractions of Combretum roxburghii (EACR) on histological alterations in diabetic rats (a) normal control rat, (b) diabetic rat, (c) diabetic rat treated with glipizide (10 mg/kg), (d) diabetic rat treated with MECR (400 mg/kg) and (e) diabetic rat treated with EACR (200 mg/kg) are shown in the histology of the rat pancreas (H&E staining, 40X magnification).

The outcomes of the investigation are demonstrated in Table-2. MECR at test dose (100, 200, and 400 my/kg b. w.) exhibited significantly ($P < 0.05$) decreased the fasting blood sugar level 2hr after the medication and continued to have an impact for 24 hr after the investigation. The maximal depletion ($P < 0.01$) in blood glucose level was discovered in both the test and standard drug groups after 4hr of administration. The percentage depletion in blood glucose level was elevated with 100 mg/kg b.w. Of EACR (30.5%) The significant ($P < 0.01$) antihyperglycemic effect and percentage depletion in blood glucose level with 100 mg/kg was remarkably comparable to the reference drug, Glipizide (10mg/kg) at any time interval of the investigation.Both the test extracts and the reference drug, Glipizide caused after 28 days of the trial, substantially ($p < 0.01$) enhanced serum insulin level. This indicates that the test extracts might have exhibited the antihyperglycemic effect like Glipizide, trigger the insulin release by beta cells of the pancreatic islets have some of their potassium channels blocked. Diabetes has been linked to elevated levels of triglycerides and hyperlipidemia, according, which leads to coronary artery diseases.

The maximum percentage reduction in serum cholesterol and triglycerides level was observed in EACR treated group with 36.3% and 43% respectively and was nearer to the value (42% and 43.5%) found in standard drug, Glipizide treated group. As a result, it is reasonable to say that these extracts may lower blood lipid levels via increasing insulin sensitivity in the tissues or by releasing insulin. Thus, it substantiates the antihyperglycemic effect of the extracts. After 28 days of the trial, there was a substantial ($P < 0.01$) decrease in ALT, AST, and ALP levels in the rats treated with EACR and it was very equivalent to that of the reference drug, Glipizide. Diabetes is associated with an increased risk of cirrhosis and ketogenesis, which may be brought on by the high levels of these hepato-specific enzymes' activity. Therefore, the decrease in ALT, AST, and ALP levels following supplementation with EACR further reinforces the extracts' antidiabetogenic effects.

After 28 days of therapy, blood total proteins increased significantly ($P < 0.01$) in both the extracts and the Glipizide reference drug treated groups. Diabetes results in modifications to protein metabolism, which lower serum total proteins because of an insulin shortage. Insulin increases protein synthesis and amplifies the uptake of amino acids into muscle. As a result, the extract's elevated serum protein levels account for their anti- diabetogenic effects.

Histopathological evaluations of pancreas in all experimental animal groups were studied and treatment with test extracts MECR and the standard drug Glipizide was found to regenerate the depleted cells and enhancing the pancreatic tissue. All the selected fractions showed better activity improved morphology of islets of langerhans cells and restored the normal configuration of pancreas.

Conclusion

The results generated in this *In vivo* studies are vital in order to Develop EACR as therapeutic agent in several disease conditions. As we see in this study, EACR produced beneficial effects in diabetic conditions. It is universally believed that stress from oxidation plays a pivotal part in the development of diabetes and is a primary mediator for all the diabetes associated complications. Therefore, it is very much possible that *Combretum roxburghii* (EACR) probably will be effective in combating against incidence of diabetes and its complications. More detailed molecular studies and isolation of active constituents and evaluation of phytochemical constituents from this plant may further provide vital information to explore Phytochemicals for clinical studies. However, these studies suggest that MECR might be designed to develop of new antidiabetic formulations.

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Conflict of Interest

The author declares no conflict of interest.

Bibliography

1. American Diabetic Association. "Diagnosis and classification of diabetes mellitus". *Diabetes Care* 42.1 (2019): 13-28.

2. Josephine M Forbes and Mark E Cooper. "Mechanism of Diabetes Complications". *Physical Review* 93.13 (2013): 137-188.

3. Bindu Jacob Narendhirakannan RT. "Role of medicinal plants in the management of diabetes mellitus: a review". *Biotech* 9.2 (2019): 4-8.

4. Fatmah A Matough., *et al*. "The role of oxidative stress and Antioxidants in Diabetic complications". *SQU Medical Journal* 12.1 (2012): 5-18.

5. Deepa Rajendran., *et al*. "A Review on role of Antioxidant in Diabetic". *Assam Journal of Pharmaceutical and clinical Research* 11.2 (2012): 48-53.

6. Uttpal Anand., *et al*. "Ethnodermatological use of medicinal plants in india: from Ayurvedic formulations to clinical perspectives- A review". *Journal of Ethnopharmacology* 7.3 (2022): 22-28.

7. Syed Ibrahim Rizvi and Neetu Mishra. "Traditional Indian Medicines used for the management of Diabetes mellitus". *Journal of Diabetes Research* 5.3 (2013): 1-11.

8. Hira Choudhury., *et al*. "An update on natural compounds in the remedy of diabetes mellitus: A systematic review". *Journal of Traditional and complementary Medicine* 8.3 (2018): 361-376.

9. Rajeev Rattan., *et al*. "Preliminary phytochemical screening, Antioxidant and Antifungal activity of Lepidagathis cuspidate". *International Journal of Drug Development and Research* 8.1 (2016): 001-003.

10. Rajiv Gandhi G and P Sasikumar. "Antidiabetic effect of Merremia emarginata Burm. F. in streptozotocin induced diabetic rats". *Asian Pacific Journal of Tropical Biomedicine* 2.4 (2012): 281-286.

11. Chandra Prakash Kala., *et al*. "Developing the medicinal plants sector in northern India: Challenges and opportunities". *Journal of Ethnobiology and Ethnomedicine* 2.1 (2006): 32-36.

12. Gangola S., *et al*. "India as the Heritage of Medicinal plants and their use". *Current Trends in Biomedical Engineering and Biosciences* 4.4 (2017): 0050-0051.

13. Praneetha P., *et al*. "Invitro and In vivo hepatoprotective studies on methanolic extract of aerial parts of Ludwigia hyssopifolia G. Don Excel". *Pharmacognosy Magazine* 14.59 (2018): 546.

14. Ahmad U and Ahmad RS. "Antidiabetic property of aqueous extract of Stevia rebaudiana Bertoni leaves in Streptozotocin induced diabetes in albino rats". *BMC complementary and Alternative Medicine* 18.1 (2018): 1-11.

15. Tinder P. "Determination of blood glucose using an oxidase-peroxidase system with a non-carcinogenic chromogen". *Journal of Clinical Pathology* 22.4 (1969): 158-161.

16. Sunitha Thalugula and Narsimha Reddy Yellu. "Pancreatic beta cell protective effects of Flemengia strobilifera extracts in combination model of high fat diet and streptozotocin induced type 2 Diabetes". *International Journal of Pharmaceutical Sciences and Research* 10.12 (2019): 5723-5732.

17. Mansoor F., *et al*. "Incidence of traumatic injection neuropathy among children in Pakistan". *Eastern Mediterranean Health Journal* 11.4 (2005): 798-804.