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# Antidiabetic and Antihyperlipidemic Effects of *Calamus rotang* L leaves (Arecaceae) in Streptozotocin-Nicotinamide Induced Diabetic Model

**V Kishor Kumar[1,*], K G Lalitha[2], R Sambath Kumar[3]**

[1]*Department of Pharmacognosy, JKKN College of Pharmacy, B. Kumarapalayam, Namakkal, 638 183, Tamil Nadu, India*
[2]*Department of Pharmaceutical Chemistry, Ultra College of Pharmacy, Madurai, 625 020, Tamil Nadu, India*
[3]*Department of Pharmaceutics, JKKN College of Pharmacy, B. Kumarapalayam, Namakkal, 638 183, Tamil Nadu, India*

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* *Corresponding author.*
V Kishor Kumar
kishorkumar.v@jkkn.ac.in
kishorkpm2006@gmail.com

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ABSTRACT

**Background:** *Calamus rotang* L (Asteraceae), also known as Pirampu in India, has long been employed in Ayurvedic medicinal formulations. It has been used to cure diabetes in folklore medicine for centuries. **Aim:** This Study evaluated the antidiabetic and antihyperlipidemic effects of *Calamus rotang* L leaves in streptozotocin-nicotinamide (STZ-NC) induced diabetic model. **Methods:** Estimation of fasting blood glucose, glycosylated haemoglobin, total haemoglobin, lipid profiles, lipoproteins, hepatic marker enzyme activity, and pancreas histopathology was performed in STZ-NC induced diabetic rats after receiving ethanol extract of *C. rotang* L leaves (100 & 200 mg/kg) for 28 days orally. The data were statistically analysed using one-way analysis (ANOVA) and post hoc multiple comparison tests. **Results:** The ethanol extract of *C. rotang* L leaves was given at doses of 100 and 200 mg/kg showed a substantial drop in fasting blood glucose levels and an increase in body weight. $HbA_1C$, TC, TG, LDL, VLDL, AST, ALT, and ALP levels were dramatically lowered by the ethanol extract of the leaves of *C. rotang* L, whereas Hb, HDL cholesterol levels were significantly increased. Furthermore, in STZ-NC induced diabetes, the *C. rotang* L leaves ethanol extract has a positive impact on pancreas histological alterations. **Conclusions:** For the first time, these findings show that the *C. rotang* L leaves ethanol extract has significant antidiabetic and antihyperlipidemic potential, bolstering the plant's claimed application in the treatment of diabetes and its complications.

**Keywords:** Calamus rotang L leaves; Antidiabetic; Antihyperlipidemic; Glibenclamide

## INTRODUCTION

India produces a lot of herbs and herbal products. Nature around us has provided everything of necessity for mankind. The vast resources of the vegetation, mineral and animal kingdoms have long been used to treat a variety of ailments and other issues.[1] In recent years, there has been a boom in interest in employing herbal medicines to treat a range of ailments since they are typically non-toxic and have been recommended by the World Health Organization as viable alternatives to dangerous contemporary medications. Plant substances having hypoglycaemic properties have been used in ancient medicine and traditional treatment processes all over the world since antiquity.[2] Diabetes and its complications remain a severe public health problem, despite the development of hypoglycaemic drugs derived from natural and synthetic sources.[3] The ethnobotanical community is interested in plants that are used to treat hypoglycaemia and hyperglycaemic diseases since the plants possess excellent medicinal characteristics in many areas.

Traditional diabetes treatment is a combination of diet including exercise and medicinal herbs. Despite the fact that over 1200 different plants have been used to control diabetes, only around 30% of the anti-diabetic herbs were investigated pharmacologically and chemically.[4] Hypoglycaemic drugs on the other hand have the potential to lower blood sugar levels and have been discovered in over 100 plants utilised for antidiabetic therapy. Traditional therapies may provide information that can be used to produce novel oral hypoglycaemic medicines and easy dietary supplements. The Indian system of medicine includes over 100 medicinal plants, including indigenous treatments for treating diabetes that can be used alone or in conjunction with one or more medicinal plants.[5]

*Calamus rotang* (commonly referred as Pirampu in Tamil) is a member of the Arecaceae family that may be found in India's central and southern regions (i.e. Maharashtra, Andhra Pradesh, etc.). The vegetation base stretches ten metres vertically and two hundred metres horizontally. Fruits can be eaten raw, but they can also be cooked with pickles and served with meals. Tribals make use of its delicate shoots as anthelmintic.[6] Its sap can be used to cure vision issues.[7] Convulsions and cramps are treated using a saponin found in the stem, an alkaloid found in the leaves, and flavonoids found in the root of *C. rotang*.[8] To cure diabetes mellitus, fresh fruit[1,2] is eaten twice a day for 6–8 weeks.[9–13] A number of pharmacological investigators have found that *C. rotang* L has CNS depressant, analgesic and also anti-inflammatory,[14,15] antioxidant,[16] anti-proliferative,[17] Immunomodulatory[18] and immunosuppressive properties.[19] *C. rotang* has been examined for its immunoadjuvant enhancement,[20] anti-diarrheal, and hypoglycaemic activities.[21]

Bioactive chemical constituents isolated previously in rhizome of *C. rotang* include (+)–Afzelechin.[22] In hexane extract of leaf, GC-MS analysis detected hexadecanoic, octadecanoic, eicosanoic acid methyl ester, while in ethanol extract of plant leaves the presence of pentadecanoic, octadecenoic, heptadecanoic acid methyl ester were found.[23] To our knowledge, the antidiabetic and antihyperlipidemic properties of ethanol extract *C. rotang* L leaves have not been studied. The purpose of this study was to see whether the ethanol extract of *C. rotang* L leaves had any anti-diabetic or anti-hyperlipidemic effects in streptozotocin-nicotinamide induced diabetes rats.

## MATERIALS AND METHODS

### *Drugs and chemicals*

Streptozotocin and Nicotinamide was purchased from Himedia, Mumbai, Glibenclamide gift sample was obtained from Cipla, Mumbai, and ethanol employed to extract the samples was obtained from Pure Chemicals Co from Chennai. Other substances and reagents utilised in this work were of analytical grade, and the enzymatic kits were purchased commercially.

### *Plant material*

In May, the leaves of the *C. rotang* L plant were collected in Kerala's Malappuram District. Prof. P. Jayaraman, Director of the National Institute of Herbal Science in Chennai, recognised the plant, and the Pharmacognosy Department Herbarium retained a voucher specimen (Ref. No. PARC/2012/2178).

### *Extraction preparation*

The leaf 500 gm was pulverised in a fireproof blender then extracted using ethanol in a soxhlet apparatus. The extract was concentrated and dried in a vacuum evaporator (S. K. Appliances, Haryana. Model: DRV60). The dried residue 18 gm was kept in desiccator and utilised in subsequent experiments.

### *Screening for phytochemicals in the preliminary stage*

The dried extract was examined for the presence of various phytoconstituents.[24]

### *Animals used in research*

Wistar albino rats, either sex, weighing between 150 to 200 gm were used in the experiment.[25] Under standard laboratory conditions of temperature (22 ± 2°C) and humidity (45 ± 5°C), the animals were housed in a 12 hour day/12 hour night cycle. The animals were fed a conventional laboratory diet and had access to water at all times. All experimental protocols were approved (JKKMMRFCP/IACE/2012/007) by the Institutional Animal Ethics Committee (IAEC), and all animal research followed the principles and guidelines of India's CPCSEA (Committee for the Purpose of Control and Supervision of Experimentation on Animals).

### *Investigation of oral toxicity (acute)*

The standards 425 of the Organisation for Economic Cooperation and Development (OECD) were used to perform oral toxicity (acute) research.[26]

### *Design of experiment*

To investigate the hypoglycaemic potential of the ethanol extract of *C. rotang* L leaves (EECR) in normal rats, fasting blood glucose (FBG) and oral glucose tolerance test (OGTT) were done at doses of 100 and 200 mg/kg administered orally by gavage. In diabetic rats, the antihyperglycemic effect of the EECR was also tested at dosages of 100 and 200 mg/kg.

### *Hypoglycaemic activity in normal healthy rats.*

The experiment utilized 24 healthy rats that had fasted over night and were divided into four groups of six animals each.

Group I: Normal control + distilled water.

Group II: Normal rats +100 mg/kg EECR.

Group III: Normal rats + 200 mg/kg EECR.

Group IV: Normal rats + 5 mg/kg Glibenclamide.

A single dosage of extract was given to each of the experimental animal groups. After the extract was administered, blood samples were taken from the tail vein at 2, 4, 6, and 8 hours, followed by FBG.

### *OGTT to measure hypoglycemic activity in normal healthy rats.*

A second group of 24 healthy rats was separated and treated similarly to the first group. After measuring the animal's FBG levels, they were given oral glucose (2g/kg) 90 minutes later. Blood samples were taken from the tail vein just before (0h) and 1st, 2nd and 3rd h subsequently following glucose administration and blood glucose levels were calculated.[27]

### *Antihyperglycemic effect in STZ-NC diabetic rats*

The animal model for diabetes mellitus type 2 (NIDDM) was created by administering STZ 60 mg/kg intraperitoneally, succeeded by NC 120 mg/kg 15 minutes later. Hyperglycemia was diagnosed when blood glucose levels were elevated 72 hours after the injection and again on day 7. In the anti-diabetic investigation, only rats with verified persistent NIDDM were employed.[28,29]

On severely diabetic rats, a 28-day treatment was done. Thirty rats were split into five groups, each having six rats.

Group I: Normal control + distilled water,
Group II: Diabetic control + distilled water,
Group III: Diabetic + EECR (100mg/kg),
Group IV: Diabetic + EECR (200mg/kg),
Group V: Diabetic + Glibenclamide (5mg/kg).

Separate suspensions of EECR and glibenclamide were made in 2 % gum acacia. Each dose was given orally through oral gavage on a daily basis for 28 days, based on body weight. In overnight starved animals, body weights and blood glucose levels were assessed weekly using blood glucose test strips and an ACCU CHEK glucometer. The animals were starved overnight after the experiment ended, and blood was obtained for several biochemical tests. Cervical decapitation was used to kill the animals. The pancreas was removed and quickly washed in ice cold saline before being refrigerated for biochemical analysis.[30,31]

### *Biochemical parameter evaluation*

The serum was analysed for haemoglobin (Hb), glycosylated haemoglobin ($HbA_1C$), total cholesterol (TC), triglycerides (TG), high density lipoprotein (HDL), AST (Aspartate Amino Transaminase) or SGOT (Serum Glutamate Pyruvate Transaminase), ALT (Alanine Amino Transaminase) or SGPT (Serum Glutamate Oxaloacetate Transaminase) ALP (Alkaline Phosphatase). Very low density lipoprotein (VLDL) and low density lipoprotein (LDL). Values were calculated using the formula given below.[32–34]

VLDL = TG/5, LDL = TC – (HDL + VLDL).

### *Histopathology examination*

The pancreas was separated, washed in normal saline, then treated in 10% formalin solution for 24 hours and dehydrated with alcohol. Paraffin was used to clean and embed all of the tissues. 5$\mu$ thick slices were cut and stained with haematoxylin and eosin for histological examination.[35]

### *Statistical analysis*

All of the data was expressed using the mean ± standard error mean (SEM). Graphpad Instat version 3.06 computer software was used to run one-way analysis of variance (ANOVA) and Dunnett's post hoc test to find significant differences. At $p<0.05$, differences between the groups was considered significant.

## RESULTS

### *Screening for phytochemicals in the preliminary stage*

In the EECR's phytochemical analysis, carbohydrates, alkaloids, saponins, flavonoids, tannins, and phenolic compounds were discovered.

### *Investigation of oral toxicity (acute)*

In oral toxicity (acute) testing, a sole dose of 2000 mg/kg EECR exhibited no effect on behaviour. There were no fatalities or poisoning symptoms detected over the 24-hour and 14-day monitoring period. The oral $LD_{50}$ of EECR must be more than 2000 mg/kg.

### *Antidiabetic properties*

Figure 1 depicts the impact of EECR at 100 and 200 mg/kg on fasting blood glucose levels in normal healthy rats. After 6 hours of oral treatment, rats given 200 mg/kg EECR, exhibited a marked reduction of 14 % in FBG, whereas rats given 100 mg/kg had a maximum reductin of 8.6 %. On the OGTT of normal rats, Figure 2 depicts the hypoglycaemic impact of oral therapy at doses of 100 and 200 mg/kg. Three hours after glucose administration, the dose of 200 mg/kg caused a maximum decline of 15.2%, whereas the dose of 100 mg/kg caused a reduction of 6.7%.

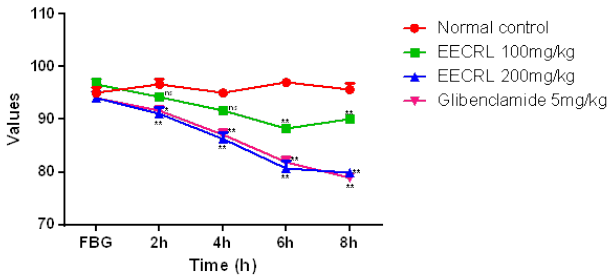


**Fig. 1: Effect of EECR treatment on blood glucose level of normal rats.** The values are expressed as mean ± SEM for groups of six animals each. Values are statistical significant at *P < 0.05, **P < 0.01, ns - not significant as compared with control

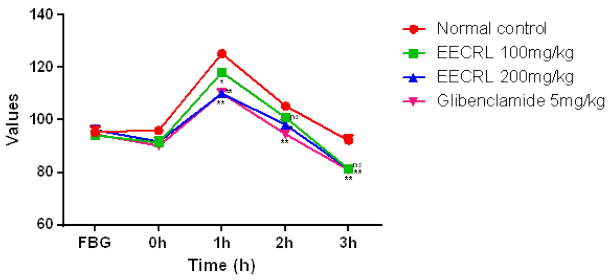


**Fig. 2: Effect of EECR treatment on** blood glucose level of normal rats during OGTT.
The values are expressed as mean ± SEM for groups of six animals each. Values are statistical significant at *P < 0.05, **P < 0.01, ns - not significant as compared with control.

Table 1 shows the antihyperglycemic impact of repeated oral EECR treatment at various dosages on fasting blood glucose levels in STZ-NC diabetic rats. When diabetic rats were given STZ-NC, their blood glucose levels jumped much more than normal controls. When STZ-NC diabetic rats were given different dosages of EECR and glibenclamide, their blood glucose levels dropped considerably ($p<0.01$) when compared to normal control rats, and this was related to the dose and duration of therapy. Blood glucose levels for the 200 mg/kg and 100 mg/kg EECR doses were 66.9% and 63.9%, respectively, at the end of the study (the 28th day). In diabetic rats, the EECR at 200mg/kg was more efficacious than the EECR at 100mg/kg ($p<0.01$).

### *Body weight fluctuations*

STZ-NC animals lost a lot of weight during the trial as compared to normal animals. Although different dosages of EECR and glibenclamide exhibited significant improvements in body weight ($p<0.01$) when compared to diabetic control, which lost 9.51%, 14.63%, and 16.11% respectively, diabetic control lost weight until the conclusion of the trial.

### *Changes in $HbA_1$ C and Hb levels*

$HbA_1C$ levels in STZ-NC diabetic rats were substantially higher ($p<0.01$) than in normal control rats, whereas Hb levels were lower. In STZ-NC diabetic rats, different dosages of EECR and glibenclamide resulted in substantial ($p<0.01$) reductions in $HbA_1C$ levels of 56.38 % and 65.37 %, respectively. When compared to diabetic control rats, the Hb level increased by 26.22 % and 29.80 %, respectively. Glibenclamide, a common drug, led in a 63.64 % decline in $HbA_1C$ and a 29.99 % increase in Hb, which would have been identical to the treatment with 200mg/kg of EECR.

### *Activity against hyperlipidemia*

Table 2 represents the levels of TC, TG, HDL, LDL, and VLDL in the control group and experimental groups. The serum concentrations for TC, TG, LDL, and VLDL were considerably greater ($p<0.01$) in STZ-NC diabetic rats while comparing to a normal control group, although serum HDL levels were significantly lower ($p<0.01$). The alteration in lipid metabolism was partially attenuated that after administration of different doses of EECR and glibenclamide, as evidenced by significant ($p<0.01$) declines in serum TC (43.72 %, 51.35 %, and 52.65 %), TG (47.11 %, 56.94 %, and 58.81 %), LDL (59.09 %, 70.18 %, and 72.24 %), and VLDL (47.10 %, 56.93 %, and 58.81% ) levels and by elevation in HDL level (40.14 %, 46.41%, and 48.70%), respectively while comparing with diabetic control rats. When comparing to other dosages of EECR 100 mg/kg and glibenclamide 5 mg/kg, EECR 200 mg/kg was more effective in enhancing the level of lipid parameter.

### *Changes in AST, ALT, and ALP levels*

When comparing the diabetes control group to the normal control group, the diabetes control group had substantially ($p<0.01$) higher hepatic marker enzyme activity, such as AST, ALT, and ALP. While comparing to the diabetic control group, treatment with various doses of EECR and glibenclamide resulted in significant ($p<0.01$) reductions in AST (72.66%, 78.44%, and 78.00%), ALT (71.60%, 74.90%, and 74.48 %), and ALP (58.83%, 61.51%, and 63.14%) (Table 3). In STZ-NC diabetic rats, the EECR 200 mg/kg dose, rather than the 100 mg/kg dose, caused the highest reduction in liver enzymes such as AST, ALT, and ALP.

### *Pancreas histopathological analysis*

Photomicrographs of the islets of Langerhans in the pancreas of normal control groups revealed normal acini and cellular populations (Figure 3 A). Glibenclamide restored the normal cellular population size of islets having hyperplasia (Figure 3B), as well as the significant loss of pancreatic $\beta$-cell mass associated with Atrophic acini and the islets of diabetes control groups (Figure 3C). At the dosage level of 200 mg/kg (Figure 3D), EECR revealed a pancreas with acini and normal islets, $\beta$-cell regeneration, and notably normal regenerated and preserved cells, as well as noticeable proliferating and regenerated $\beta$-cells in comparison to the lower dose level of 100 mg/kg (Figure 3E).

## DISCUSSION

Use of STZ for inducing diabetes in rodent models is well recognized. STZ-induced diabetes has been shown to match human DM[36] with glycosuria, hyperglycemia, polyphagia, polydipsia, and weight loss.[37] STZ has a cytotoxic impact on pancreatic beta cells, reducing endogenous insulin synthesis

**Table 1: Effect of 28 days EECR treatment on fasting blood glucose level of control and experimental groups of rats**

| Group | Treatment | Dose (mg/kg) | Fasting blood glucose level (mg/dL) | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | | Treatment days | | | | | |
| | | | 0 day | 3 days after STZ | 1st week | 2nd week | 3rd week | 4th week |
| I | Normal control | —– | 93.33 ± 2.02 | 95.00 ± 1.15 | 92.33 ± 4.05 | 95.00 ± 1.15 | 93.66 ± 2.33 | 95.00 ± 1.73 |
| II | Diabetic control | — — | 91.00 ± 1.52 | 295.66 ± 4.48 | 307.00 ± 4.93[a] | 323.33 ± 3.48[a] | 335.00 ± 5.68[a] | 346.33 ± 3.52[a] |
| III | EECRL | 100 | 93.33 ± 0.88 | 294.00 ± 5.50 | 246.66 ± 4.48[b] | 205.00 ± 6.08[b] | 156.00 ± 6.65[b] | 106.00 ± 2.30[b] |
| IV | EECRL | 200 | 93.00 ± 1.52 | 295.33 ± 6.11 | 204.33 ± 3.18[b] | 165.33 ± 4.66[b] | 130.66 ± 2.60[b] | 97.66 ± 1.45[b] |
| V | Glibenclamide | 5 | 89.66 ± 1.76 | 304.00 ± 2.51 | 191.66 ± 4.33[b] | 153.00 ± 5.03[b] | 112.66 ± 1.76[b] | 96.33 ± 1.20[b] |

The values are expressed as mean ± SEM for groups of six animals each. Values are statistical significant at ap < 0.01when compared to the corresponding values of the normal control. bp < 0.01when compared to the corresponding values of the diabetic control.

**Table 2: Effect of 28 daysEECR treatment on total cholesterol, triglycerides, HDL, LDL and VLDL of control and experimental groups of rats.**

| Group | Treatment | Dose (mg/kg) | Total cholesterol (mg/dL) | Triglycerides (mg/dL) | HDL (mg/dL) | LDL (mg/dL) | VLDL (mg/dL) |
|---|---|---|---|---|---|---|---|
| I | Normal control | —– | 124.00 ± 2.08 | 82.00 ± 1.73 | 52.00 ± 1.73 | 55.60 ± 2.15 | 16.40 ± 0.34 |
| II | Diabetic control | —— | 257.66 ± 2.60[a] | 213.66 ± 3.38[a] | 27.33 ± 2.02[a] | 187.60 ± 4.83[a] | 42.73 ± 0.67[a] |
| III | EECRL | 100 | 145.00 ± 3.46[b] | 113.00 ± 2.08[b] | 45.66 ± 1.85[b] | 76.73 ± 4.06[b] | 22.60 ± 0.41[b] |
| IV | EECRL | 200 | 125.33 ± 2.02[b] | 92.00 ± 1.73[b] | 51.00 ± 1.15[b] | 55.93 ± 2.90[b] | 18.40 ± 0.34[b] |
| V | Gliben-clamide | 5 | 122.00 ± 1.15[b] | 88.00 ± 5.03[b] | 52.33 ± 2.72[b] | 52.06 ± 2.40[b] | 17.60 ± 1.00[b] |

The values are expressed as mean ± SEM for groups of six animals each. Values are statistical significant at a p < 0.01when compared to the corresponding values of the normal control. bp < 0.01when compared to the corresponding values of the diabetic control.

**Table 3: Effect of 28 days EECR treatment on AST, ALT and ALP of control and experimental groups of rats**

| Group | Treatment | Dose (mg/kg) | AST (IU/L) | ALT (IU/L) | ALP (IU/L) |
|---|---|---|---|---|---|
| I | Normal control | —– | 33.66 ± 2.02 | 41.00 ± 1.15 | 108.00 ± 2.30 |
| II | Diabetic control | —— | 150.00 ± 3.60[a] | 162.00 ± 2.08[a] | 286.66 ± 1.45[a] |
| III | EECRL | 100 | 41.00 ± 1.15[b] | 46.00 ± 1.73[b] | 118.00 ± 2.08[b] |
| IV | EECRL | 200 | 32.33 ± 1.85[b] | 40.66 ± 1.20[b] | 110.33 ± 0.88[b] |
| V | Glibenclamide | 5 | 33.00 ± 1.52[b] | 41.33 ± 2.02[b] | 105.66 ± 2.02[b] |

The values are expressed as mean ± SEM for groups of six animals each. Values are statistical significant at a p < 0.01when compared to the corresponding values of the normal control. bp < 0.01when compared to the corresponding values of the diabetic control.

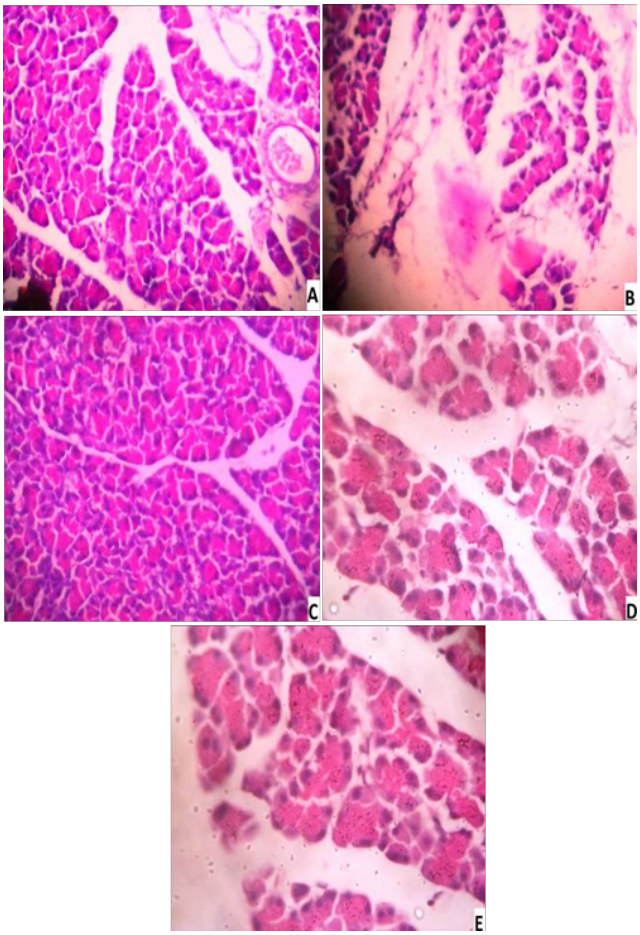


**Fig. 3: Effect of 28 days EECR treatment on cellular damage in pancreas of control and experimental groups of rats.** A = Normal control (Normal acini with islets of $\beta$-cells), B = Diabetic control (Atrophic acini and reduction of $\beta$-cell size; Shows degreased islets), C = Glibenclamide (Markedly normal regenerated and preserved cells; with marked proliferated and regenerated $\beta$-cells), D = EECRL 100mg/kg (shows hyperplastic condition; with marked increased proliferation of (hyperplastic) $\beta$-cells), E = EECRL 200mg/kg (Shows pancreas with acini and normal islets. $\beta$-cell regeneration and markedly normal regenerated and preserved cells; with marked proliferated and regenerated $\beta$-cells).

and raising blood glucose levels as a result.[38] NC is an antioxidant that protects type 2 DM, which produces pancreatic $\beta$-cell mass, from the cytotoxic effects of STZ by scavenging free radicals and causing very mild damage.[28]

EECR had a dose-dependent hypoglycemic impact in normoglycemic rats after 3 hours in our investigation. EECR 200 mg/kg demonstrated a significant enhancement in glucose tolerance in the oral glucose tolerance test. In diabetic rats, EECR treatment reduced blood glucose levels in a dose-dependent manner, with a dosage of 200 mg/kg having a similar impact as glibenclamide, which is a common antidiabetic drug used to compare the anti-diabetic properties of a variety of bioactive substances in STZ-induced mild diabetes.[39,40] The effect of glibenclamide is to increase insulin production in the Langerhans islets $\beta$-cell. Two suggested mechanisms of action for the EECR are insulin potentiation from the $\beta$-cell and increased peripheral glucose absorption.[41] Previous findings suggest that EECR works in a similar way as glibenclamide. In this situation, researchers have already demonstrated antidiabetic effect with an increase in insulin release from $\beta$-cells.[42] According to a recent research, diabetic rats treated with *C. rotang* L seed methanol extract demonstrated a substantial ($p<0.01$) drop in fasting blood glucose after 7 days of therapy compared to diabetic control rats who were not treated.[43]

STZ-NC induced diabetes results in weight loss in rats because of protein wastage in the absence of glucose as just a source of energy.[44] After 28 days of EECR therapy, glycemic control improved considerably, avoiding weight loss. Improved glucose control or structural protein creation might explain the increase in body weight.[45] Hyperglycemia is a significant contributor to the onset of cardiovascular disease (CVD). Hyperglycemia causes protein glycation and peroxidation, which damages arterial walls, according to animal studies.[46] Diabetics have a 2-8 times higher risk of all forms of cardiovascular disease than non-diabetics. Accelerated coronary heart disease (CHD) has emerged as a leading cause of morbidity and death in diabetics across the world.[47] Diabetic hyperlipidemia is defined by elevated TG, TC, LDL, and VLDL cholesterol levels, and also reduced HDL cholesterol levels. As a result of these changes, diabetic patients are more likely to develop coronary heart disease. LDL-C has a positive relationship with the risk of cardiovascular disease, whereas HDL-C has a negative relationship.[48,49] When compared to normal control rats, STZ-NC therapy resulted in alterations in normal lipid profiles, including greater TC, TG, LDL, and VLDL levels, along with lower HDL levels. The abnormal lipid profile in STZ-NC diabetic rats was recovered following treatment with both EECR and glibenclamide. This cholesterol-lowering action might be attributable to a good stabilisation of glucose levels following EECR therapy, which could help to restore diabetic rats impaired lipid metabolism. As a consequence, EECR's capacity to prevent CVD disorders associated with diabetes is supported by its hypolipidemic action in diabetic rats.

Liver is the primary organ for metabolism, detoxification, storage, and excretion of xenobiotics and their metabolites. The liver enzymes AST, ALT, and ALP give excellent idea of how well the liver is functioning.[50] The liver of STZ-induced diabetic rats was necrotized. Increased AST, ALT, and ALP activity in plasma may be due to the leakage of these enzymes from the liver cytosol into circulation, indicating that STZ has a hepatotoxic impact.[51] The effect of such enzymes in plasma was lowered in diabetic rats that were given EECR, lowering the liver damage caused by

STZ-NC induced diabetes. The activity of these enzymes was significantly reduced in diabetic rats administered with EECR, indicating that it had a hepatoprotective impact in reducing diabetes complications.

Damage to pancreatic islets, in addition to insulin resistance, is another essential factor in the onset and development of diabetes.[52] The damage to diabetic rats' pancreatic islets produced by STZ-NC was a major contributor in the animals' hyperglycemia. In our study, histopathological examinations demonstrated that EECR therapy expanded the amount of pancreatic islets in a dose-dependent manner. These findings suggested that EECR may be able to preserve or promote the regeneration of pancreatic $\beta$-cells, both are beneficial to DM.

## CONCLUSION

The EECR demonstrated good antihyperglycemic and antihyperlipidemic effects in the STZ-NC generated diabetes model, according to the above findings. Moreover, this study has offered scientific support for the safety and usefulness of CR leaves by traditional practitioners in diabetes treatment. However, further research is needed to isolate, purify and characterise the beneficial compounds in EECR, as well as to determine their mechanism of action at molecular level in diabetes and diabetic complications.

We reveal that we have not received any funding from any source for this research.

## CONFLICT OF INTEREST

We declare that we have no conflicts of interest.

## ABBREVIATIONS

STZ: Streptozotocin; NC: Nicotinamide; $HbA_1C$: Glycosylated haemoglobin; Hb: Haemoglobin; TC: Total cholesterol; TG: Triglycerides; HDL: High density lipoprotein; LDL: Low density lipoprotein; VLDL: Very low density lipoprotein; AST: Aspartate Amino Transaminase; ALT: Alanine Amino Transaminase; ALP: Alkaline Phosphatase; CNS: Central nervous system, GC-MS: Gas chromatography - Mass spectrometry, IAEC: Institutional Animal Ethics Committee; CPCSEA: Committee for the Purpose of Control and Supervision of Experimentation on Animals; OECD: organization for economic cooperation and development; EECR: ethanol extract of *Calamus rotang* L leaves; FBG: Fasting blood glucose; OGTT: Oral glucose tolerance test; NIDDM Non-insulin dependent diabetes mellitus; SEM: Standard error mean; $LD_{50}$: Lethal dose 50; DM: Diabetes mellitus, CVD: Cardiovascular disease; CHD: Coronary heart disease.

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