# EVALUATION OF ANTIDIABETIC ACTIVITY OF *CRESSA CRETICA* LINN IN ALLOXAN INDUCED DIABETES IN RATS

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**Summary**

The study was undertaken to investigate the folkloric claim of *Cressa cretica* (CC) (Family: convolvulaceae) for antidiabetic effect of single oral administration of ethanolic extract to alloxan induced diabetic rats. The maximum glucose lowering effect of 11.86% was observed at 12 hour after the administration of 300mg/Kg .Repeated oral treatment with ethanolic extract of Cressa cretica(EECC) (300mg/Kg/day) for two weeks significantly reduced blood glucose, serum cholesterol and improved HDL-cholesterol and albumin as compared to diabetic control group. These results clearly indicates that alcoholic extract of *Cressa cretica* have high antidiabetic potential.

**Key words**: *Cressa cretica*, convolvulaceae, Antidiabetic, alloxan

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## Introduction

Diabetes is a metabolic disorder characterized by hyperglycemia, glycosuria, hyperlepemia,negative nitrogen balance and sometimes ketonemia[1]. Currently there are 190 million people with diabetes in the world and their number may double in next three decades[2].Out of total diabetics about 85-90% suffer from type 2 diabetes mellitus, which is now recognized as vascular disease[3] .Diabetes is also one of the costliest disease to the community. In 2002 American diabetic association estimated the cost of diabetic treatment, its complication and hospitalization to be $132 billion [4-5].

Traditional medicines are gaining popularity in the treatment of diabetes and its complications due to their efficacy, minimal side effects and low cost. The world health organization has also recommended the evaluation of plant effectiveness in conditions where we lack safe modern drugs [6].This has lead to an increase in the demand of research on antidiabetic natural products which produce minimal or no side effects. *Cressa cretica* (Linn) belonging to family Convolvulaceae, commonly known as Rudravanti is a erect, small, dwarf shrub, which is used traditionally in asthma, bronchitis, dyspepsia, flatulence, colic, anorexia, diabetes, leprosy, tonic, aphrodisiac, antibilious and general debility[7-8].Chloroform extract of Cressa cretica is found to be effective against dermatophytic fungi and some basic elements such as Al,Ca,Cu, Fe, Mg,Mn,P,S,&Zn has been determined from Cressa cretica[9] . The air dried powdered whole plant gave n-octacosanol, scopoletin, umbelliferon, isopimpinellin,β sitosterol and its D(+) glucoside, quercetin[10]. A new syringaresinol-β-D glucoside from *Cressa cretica* has been reported[11].
The objective of present investigation is to study the effect of EECC on blood glucose and biochemical parameters such HDL-cholesterol, total protein, albumin, triglyceride, and alkaline phosphatase in normal and alloxane induced diabetic Wistar rats.

## Material and Methods

### Plant Material

Fresh plant was collected from sandy shores along mangrove creeks near Devanampattinam Beach, Cuddalore Taluk, Tamilnadu (India) and authenticated by Dr K Ravi kumar FRLHT, Bangalore. A voucher specimen of the plant was preserved in the herbarium of FRLHT for further reference and study.

### Extraction

The plant washed with water and dried in shade and successive solvent extraction was done using soxhlet with Pet ether (60-80$^0$ C), chloroform(yield7%), and ethanol(yield 15%) . All the extracts were dried below 45$^0$ C in rotary evaporator and stored in airtight containers in refrigerator below 10$^0$ C. The various extracts obtained were tested phytochemically for the presence of various active constituents. Alcoholic extract showed the presence of alkaloids, glycosides and flavonoids. Alcoholic extract was chosen for animal study.

### Animals

Adult albino wistar rats of either sex weighing 150-200 gm were acclimatized for a period of 10 days at room temperature 50 % relative humidity, at 12 hr light and day cycle and were maintained on a standard pellet and water *ad libitum* .The animal described fasted were deprived of food for 18 hr but had free access to water. The study was approved by animal ethical committee of the university.

### Induction of Diabetes

The fasted rats were divided into 5 groups of 6 animals each. After 18hr of overnight fasting animals were made diabetic by single intraperitonial administration of cold freshly prepared solution of alloxan (Sigma Chem. Co. St Louis,USA) at a dose of 120mg/kg in 2mM citrate buffer (pH-3.0). After one week, animals with fasting blood glucose of 250 mg/dl or more were considered diabetic and were employed in the study

**Single Dose treatment**

.The rats were divided into 5 groups of 6 animals each.
Group I- control diabetic rat, untreated
Group II,III,IV- treated with single oral dose of ethanolic extract of Cressa cretica with a concentration 100,200,300 mg/kg respectively
Group V- diabetic rats treated with glibenclamide (10mg/kg)
The blood glucose was measured at 0,4,8, and 12 hr after treatment using standard kits of Bayers diagnostic private limited[12].

**Repeated dose treatment**

The diabetic rats (Blood glucose>250mg/dl) of group I, IV,&V were selected for repeated dose treatment. Animals were treated once a day for 2 weeks with saline (0.1ml), EECC(300mg/Kg) and glibenclamide (10mg/Kg) respectively. The blood glucose was measured on 14$^{th}$ day.

**Biochemical assays**

Animals chosen for repeated dose treatment were sacrificed six hours after the last treatment on 14$^{th}$ day, whole blood was collected by cardiac puncture under mild ether anesthesia and serum was seprated for estimation of cholesterol, HDL-cholesterol, total protein, albumin, triglyceride, and alkaline phosphatase(ALP). All assays were carried out using standard kits of Bayer diagnostic Ltd India.

**Statistical Analysis**

The data is represented as mean±SEM and statistical significance between treated and control group was analyzed by means of student t test. $p<0.05$ implies significance[13]

## Results

In the present study antidiabetic effect of ethanolic extract of *Cressa cretica* was measured by administering single dose of EECC in different concentration and it was found that 300mg/Kg of EECC has lowered the the blood glucose level up to 11.86% after 12 hr of administration (Table-I, & Fig-I).Diabetes is also characterized by hyperlipemia, negative nitrogen balance and increase in level of alkaline phosphatase[14]. For an effective treatment it is expected that any drug should not only lower the blood glucose but also affect all the biochemical parameters affected by this disease.So the same dose (300mg/Kg) is administered for 14 days to see the extent of glucose lowering with repeated administration and change in the biochemical parameters. Blood glucose was found to be reduced by 18% in repeated dose treatment experiment (Table-II& FigII), so it signifies that EECC has dose dependent lowering of blood glucose with passage of time.

**Table I-** Effect of single dose treatment ethanolic extract of whole plant of *Cressa cretica* in alloxan induced hyperglycemia

| Treatment | Plasma glucose concentration (mg%) | | | |
|---|---|---|---|---|
| | Time after treatment hour | | | |
| | 0 hr | 4hr | 8hr | 12hr |
| Control diabetic Saline 10 ml/kg | 275.86±1.0 | 275.3±0.89 | 275.10±0.73 | 275.08±0.76 |
| Ethanolic extract of C.C 100mg/kg | 273.38±0.57 | 270.86±0.65[a] (1.61%) | 264.64±1.47[b] (3.83%) | 259.53±1.49[b] (5.65%) |
| Ethanolic extract of C.C 200mg/kg | 271.83±1.07 | 267.71±1.01[b] (2.97%) | 260.38±1.60[b] (5.38%) | 253.61±4.3[b] (7.81%) |
| Ethanolic extract of C.C 300mg/kg | 273.45±0.60 | 263.81±0.92[b] (4.17%) | 254.63±1.24[b] (7.47%) | 242.43±1.49[b] (11.86%) |
| Glibanclamide 10mg/kg | 273.75±0.70 | 257.9±1.54[b] (6.32%) | 247.15±0.154[b] (10.19%) | 228±2.07[b] (17.11%) |

Each value represent mean±SEM (n=6)
Number in parenthesis denotes % reduction of plasma glucose [a]p<0.01, [b]p<0.001 Vs control saline.

**Figure I-**Effect of single dose of ethanolic extract of whole plant of *Cressa cretica* in alloxan induced hyperglycemia.

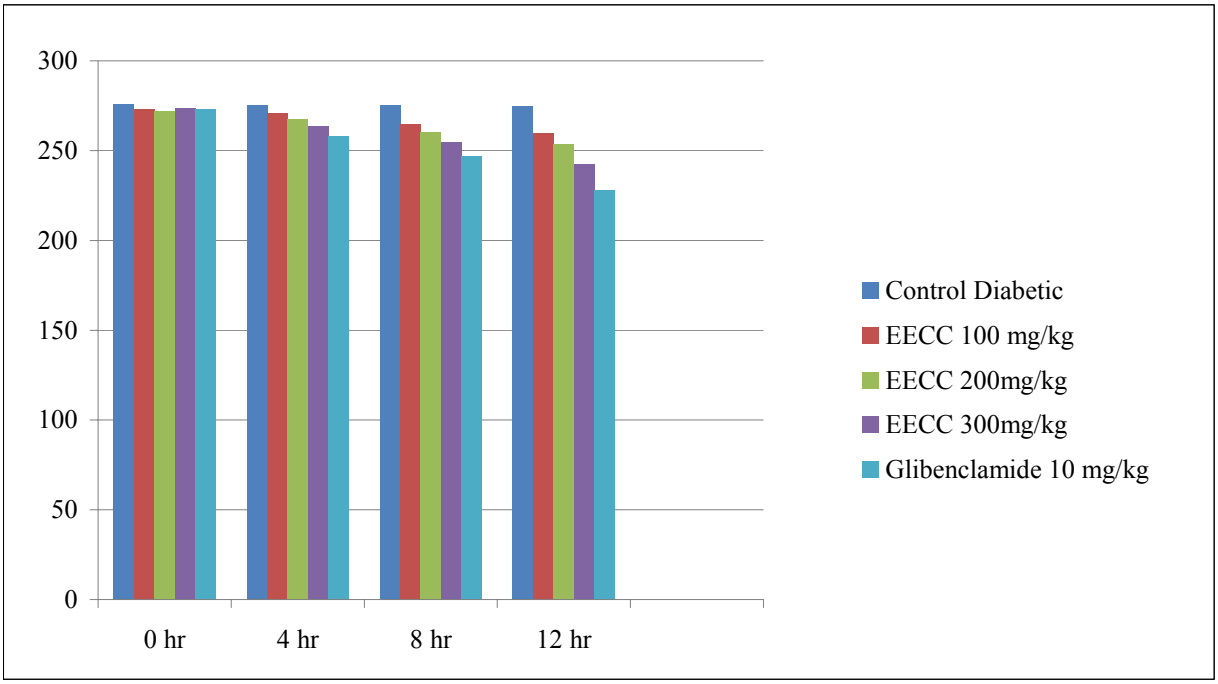
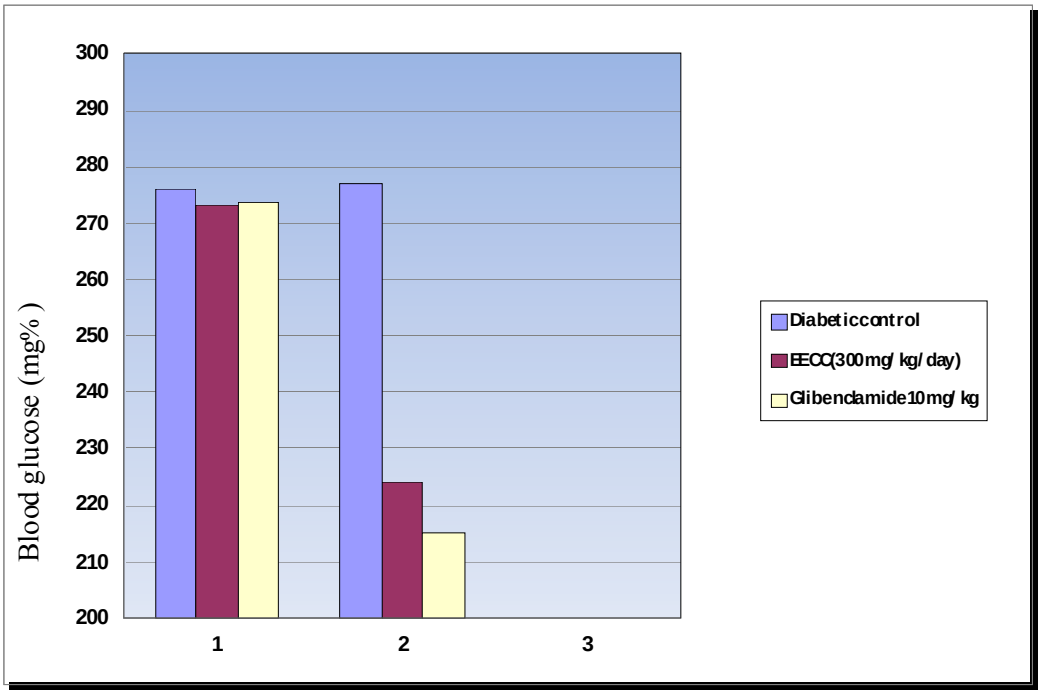


**Table 2.** Effect of repeated dose treatment of ethanolic extract of whole plant of *Cressa cretica* on alloxan induced diabetic rat.

| Treatment | Plasma glucose concentration (mg%) | |
|---|---|---|
| | Before treatment | After treatment |
| Control diabetic Saline 10 ml/kg | 275.86±1.0 | 277±1.4 |
| Ethanolic extract of C.C 300mg/kg | 273.45±0.60 | 224.22±3.4[a] (18%) |
| Glibanclamide 10mg/kg | 273.75±0.70 | 214.89±4.3[a] (21.5%) |

Each value represents mean±SEM (n=6)
[a]p<0.01compared to initial value (0 hr) (Student's paired t-test)
Number in parenthesis denotes % reduction of plasma glucose

**Figure II-.** Effect of repeated dose treatment of ethanolic extract of whole plant of *Cressa cretica* on alloxane induced diabetic rat.




TableIII report the effect on biochemical parameters such serum cholesterol, HDL-cholesterol, total protein, albumin, triglycerides and alkaline phosphate on diabetic rats treated with of EECC once a day for 2weeks. The serum cholesterol, triglycerides and alkaline phosphatase were significantly higher while serum HDL-cholesterol , total protein level were significantly decreased in diabetic group as compared to normal rats.EECC significantly reduced serum cholesterol(13.7%) and increased HDL-cholesterol(12.4%), and albumin (24.28%) compared to diabetic group.

**Table3.** Effect of repeated dose treatment of Ethanolic extract of cressa cretica (EECC) on some blood parameters in alloxane- induced diabetic rats.

| S.No | Treatment | Cholesterol (mg/dl) | HDL-cholestrol (mg/d)l | Total Protein g/dl | Albumin (g/dl) | Triglycerides (mg/dl) | ALP (IU/I) |
|---|---|---|---|---|---|---|---|
| 1 | Normal control | 117.22±5.4 | 39.94±1.39 | 8.11±0.24 | 6.13±0.49 | 154.58±5.65 | 106.45±7.50 |
| 2 | Diabetic control | 162.95±2.34[a] | 34.2±0.6 [a] | 7.30±0.15 [a] | 4.57±0.39 [a] | 186.46±4.46 [a] | 141.34±9.58 [a] |
| 3 | Diabetic+EECC (300mg/day) | 140.47 ±4.56[b] | 38.45±0.45 [b] | 7.45±0.46 | 5.68±0.04 [b] | 169.89±4.56 | 125.64±6.78 |
| 4 | Diabetic+Glibenclamide 10mg/kg/day | 122.56±6.42 [b] | 38.01±0.22 | 7.57±0.34 | 5.66±0.34 [b] | 162.56±5.68 [b] | 114.42±8.78 |

n=6 in each group, values are mean±SEM

[b] $p<0.05$compared to diabetic control(ANOVA followed by Dunnett's test)

[a] $p<0.05$ compared to diabetic control(ANOVA followed by Dunnett's test)

## Discussion

Diabetes mellitus is a chronic disorder caused by partial or complete insulin deficiency which produces inadequate glucose control and leads to acute and chronic complications. The global cost of treating diabetes and its complication could reach US$1trillion annually. Nowadays herbal drugs are gaining popularity in the treatment of diabetes and its complications due to their efficacy, less incidence of side effects and low costs.[15] There for investigation of such agents from traditionlal medicinal plant has become more important.

The finding of this study indicates that the ethanolic extract of *Cressa Cretica* has significant hypoglycemic effects 4hr after oral administration and the effect lasted up to 12 hr. The maximum glucose lowering effect (11.86%) is observed at a dose of 300 mg/Kg at 12 hr after single dose administration of ethanolic extract of *Cressa cretica.*
Repeated dose administration for 2 weeks caused dose dependent reduction in blood glucose to 224.22±3.4 which was 18% less than the diabetic group.
Administration of EECC (300mg/kg once a day for 2 weeks) significantly reduced serum cholesterol(13.7%) and increased HDL-cholesterol(12.4%), and albumin (24.28%) compared to diabetic group.
A preliminary phytochemical analysis of alcoholic extract showed flavonoids, glycosides and alkaloids. Many plant extracts and some of their active principles including flavonoids are known to be used for the treatment of diabetes due to their hypoglycemic and antioxidant properties.[16-17]. The extracts should be investigated further for lead compounds through bioactivity guided drug discovery responsible for hypoglycemic action.

## Conclusion

Ethanolic extract of *Cassia cretica* showed significant hypoglycemic effect in Alloxane induced diabetic rat. It also reduced serum cholesterol and increased HDL-cholesterol and albumin. Further studies are required to find out the active principle responsible for this action .

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