



ANTIDIABETIC EFFECT OF COMBINED METHANOL EXTRACT OF *Ceiba pentandra* AND *Acorus calamus* IN NORMAL AND DIABETIC RATS

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ABSTRACT

The study evaluated the effect of combined extracts of root barks of *C. pentandra* and rhizomes of *A. calamus* on the streptozotocin (STZ) induced diabetic wistar rats. Study was conducted in two phases consists of 5 groups/6 rats in each phase. Phase-1 conducted in normal rats, Phase-2 was carried out in diabetic rats. In both the phases Group-2 received extract of *A. calamus* (100mpk, p.o.), Group-3 received *C. pentandra* extract (100mpk, p.o.), Group-4 received combined extract of *A. calamus* + *C. pentandra* (100mpk, p.o.) and Group-5 received Glibenclamide (5mpk, p.o.); whereas Group-1 in phase -1 is normal control and in Phase-2 is Diabetic control. Treatment carried out for three days. Blood was collected before and after treatment duration and analysed for glucose. % reduction in glucose was estimated as the final step. Combined extract of *A. calamus* + *C. pentandra* showed ($26.90 \pm 8.23^{***}$) significant % of high reduction value compared to individual *A. calamus* ($11.44 \pm 3.21^{**}$) and *C. pentandra* ($6.98 \pm 2.68^*$) treatment in diabetic rats. Whereas hypoglycemic activity produced in to normal rats by all the treatments was found to be not prominent.

Keywords: *A. Calamus*, *C. Pentandra*, Diabetes, Combinational, Hypoglycaemia, streptozotocin (STZ).

INTRODUCTION

Diabetes mellitus (DM) is a chronic metabolic disorder characterized by rise in blood glucose level known as hyperglycemia. DM is mainly of two types, Type I and Type II. Type I or Insulin dependent diabetes mellitus (IDDM) is due to lack of synthesis of insulin in the β cells of islets of Langerhans of pancreas, whereas Type II or noninsulin dependent diabetes mellitus (NIDDM) is due to lack of release of insulin from the β cells of islets of Langerhans of pancreas however Type II is common than Type I. According to review estimations, approximately 215 million people all over the world suffer from diabetes among which 80-90% belongs to Type-II diabetes [1].

A number of Type II diabetic people are expected to increase because of modern life styles with high caloric diet and low energy expenditure leading to obesity and also due to medical advances that extend life span [2, 3].

Innumerable therapies are available such as hypoglycemic drugs, insulin and recently cellular therapy, but these therapies have their own limitations [4]. Hence, alternative approaches and formulations are obligatory to encounter this problem. Medicinal plants using as traditional medicines have been one of the solutions effective against various diseases and disorders. One such plant is *Acorus calamus* (AC) and *Ceiba pentandra* which (CP) has been widely described in Indian and Chinese medicines.

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Acorus calamus (*A. calamus*) belongs to the family of Acoraceae and is generally known as sweet flag; whereas *Ceiba pentandra* (*C. pentandra*) which belongs to Bombacaceae known as silk cotton tree. Literature reflecting that combinational therapy is most advantageous than individual therapies carried by using traditional medicinal plant extract treatments. In many of the case combinational therapy produce synergistic activity which leads to the enhancement of the required biological activity than estimated theoretically. For example antidiabetic activities of *Azadirachta indica* (AI), *Vernonia amygdalina* (VA) and *Gongronema latifolium* (GL) have been reported. In a recent report, the chemical components thought to exert the antidiabetic action were compared [5]. Although extracts from these plants have individually demonstrated antidiabetic action, recent evidences showed that antidiabetic efficacy of the extracts is enhanced when given in combination [6]. It therefore became absolutely necessary to investigate the combinational mechanism(s) of the combination of extracts for enhanced desired pharmacological action.

Results indicatating that the root barks of *C. pentandra* and rhizomes of *A. calamus* was effective in decreasing the blood glucose level in normal and induced diabetic animals [7-8]. Accordingly, the present study was set up to investigate the effect of combined extracts of *Acorus calamus* (AC) and *Ceiba pentandra* (CP) on blood glucose reduction levels in both normal and diabetic induced rats.

MATERIALS AND METHODS

Albino rats of either sex obtained from M/s. Mahaveer Enterprises, Hyderabad. All animals were maintained on pellet diet supplied by M/s. Provimi pellet feed for rodents, Bangalore with 12h/12h light/dark cycle and water ad libitum. Animals were fasted for 18h before the experiment. Both water and food were withdrawn during the experiment.

Experimental Design:

Study in normal rats:

Group-2 and Group-3 received methanolic extracts of *A. calamus* (100mpk, *p.o.*), and *C. pentandra* extract (100mpk, *p.o.*)

simultaneously, Group-4 received combined extract of *A. calamus* + *C. pentandra* (100mpk, *p.o.*) and Group-5 received Glibenclamide (5mpk, *p.o.*); whereas Group-1 is normal control. A group of six albino rats weighing between 250-300g were administered with respective treatments for 3 days after completion of acclimatization. Blood was withdrawn before and after completion of treatment. Blood samples were analysed for blood glucose levels by GOD/POD method [9] using commercial glucose kits (Span diagnostics).

Study in diabetic rats:

Group-2 received extract of *A. calamus* (100mpk, *p.o.*), Group-3 received *C. pentandra* extract (100mpk, *p.o.*), Group-4 received combined extract of *A. calamus* + *C. pentandra* (100mpk, *p.o.*) and Group-5 received Glibenclamide (5mpk, *p.o.*); whereas Group-1 was Diabetic control. A group of six albino rats having blood glucose levels $\geq 250\text{mg/dL}$ was taken in to study and were administered with respective treatments for 3 days. Blood was withdrawn before and after completion of treatment. Blood samples were analysed for blood glucose levels by GOD/POD method [9] using commercial glucose kits (Span diagnostics).

Induction of diabetes:

Rats previously fasted for 16 h were given single intraperitoneal injection of 40 mg/kg body wt. Streptozotocin (Sigma, USA) dissolved in freshly prepared citrate buffer (0.1 M, pH 4.5). Animals with fasting blood glucose over 250mg/dL, three days after streptozotocin administration were considered as diabetic and received treatment regimen as similar to that of normal rats in phase-1.

Data and Statistical analysis:

Data was expressed as Mean \pm Standard Error Mean (SEM). The significance was determined by applying One-way ANNOVA followed by Dunnett's Test.

RESULTS AND DISCUSSION

Combined extract of *A. calamus* + *C. pentandra* showed ($26.90 \pm 8.23^{***}$) significant % of high reduction value compared to

individual *A. calamus* ($11.44 \pm 3.21^{**}$) and *C. pentandra* ($6.98 \pm 2.68^*$) treatment in diabetic rats. Whereas hypoglycemic activity produced in to normal rats by all the treatments was found to be not prominent. Synergistic/Antagonist drug actions are usually seen in clinical practice and the mechanisms of actions are evaluated usually in animal models. We studied the efficacy of *A. calamus*, *C. pentandra*, and combination of both on the pharmacodynamics (Hypoglycemic potential) in normal and diabetic. The diabetic rat model served to validate the pharmacodynamic (Hypoglycemic potential) response in the actually used condition of the drug (in Type II diabetes). Possible mechanism by which *A. calamus* and *C. pentandra* brings about their hypoglycemic action may be by potentiating the plasma insulin effects by increasing either the pancreatic secretion of insulin from the existing beta cells or by its release from the bound form.

The hypoglycemic activity of AC, CP and AC + CP extract was compared with Glibenclamide, a standard hypoglycemic drug acts on Glucose-6-phosphatase which is a crucial enzyme for the final step of gluconeogenesis or glycogenolysis in which it catalyzes the hydrolysis of glucose-6-phosphate to glucose and phosphate. Glucose is transported out of the liver to increase blood glucose concentration. Normally insulin inhibits the hepatic glucose production by suppressing Glucose-6-phosphatase and fructose-1,6-bisphosphatase enzyme activities[10].

In conclusion, our results clearly showed that the methanol extract of AC + CP possesses potent antihyperglycemic activity in STZ induced diabetic rats and further study is needed to identify the compounds responsible for its promising *in vivo* antidiabetic activity. Our study adds credence to the traditional use of AC + CP combinational therapy to treat diabetes.

Table 1: Summary of Mean percent of blood glucose levels in normal rats

Normal RAT			
Group	Blood glucose Levels (mg/dL)		
	Before Treatment	After Treatment	% Reduction
Normal	98.76 \pm 1.28	104.47 \pm 8.62	-5.78 \pm 2.41
AC Extract	94.28 \pm 1.72	92.28 \pm 9.54	2.12 \pm 142
CP Extract	97.62 \pm 2.34	94.43 \pm 8.84	3.27 \pm 2.35
AC + CP	100.04 \pm 2.38	94.24 \pm 10.21	5.80 \pm 2.74
Glibenclamide	96.27 \pm 1.34	92.62 \pm 7.68	3.79 \pm 2.64

Values are expressed as Mean \pm SEM; n=6 animals / group

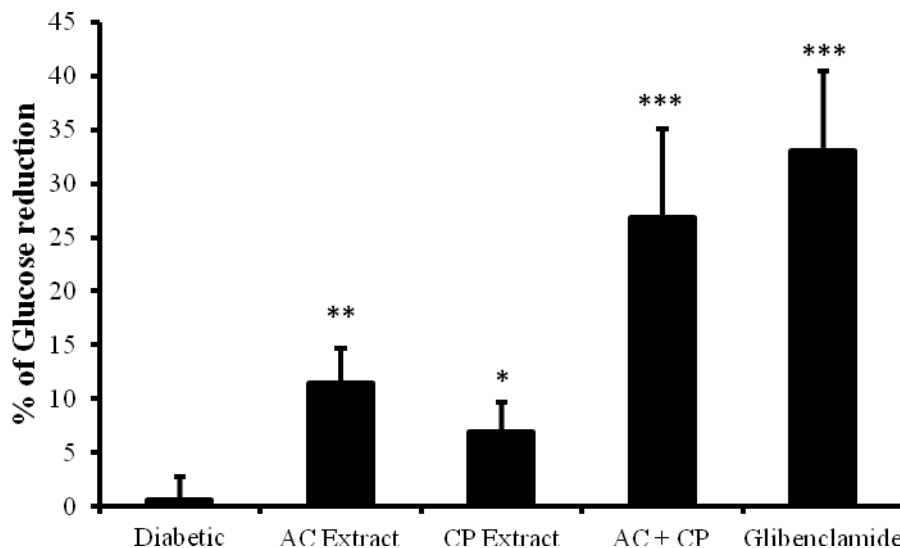
* $P \leq 0.05$, ** $P \leq 0.01$ and *** $P \leq 0.001$ as compared to Normal Control Group by One-way ANNOVA followed by Dunnett's Test

Table 2: Summary of Mean percent of blood glucose levels in Diabetic rats

Diabetic RAT			
Group	Blood glucose Levels (≥ 250 mg/dL)		
	Before Treatment	After Treatment	% Reduction
Diabetic	294.12 \pm 8.38	292.27 \pm 7.29	0.63 \pm 2.14
AC Extract	288.36 \pm 9.44	255.38 \pm 10.61*	11.44 \pm 3.21**
CP Extract	301.24 \pm 7.62	280.21 \pm 9.54*	6.98 \pm 2.68*
AC +CP	290.51 \pm 10.51	212.35 \pm 11.32***	26.90 \pm 8.23***
Glibenclamide	300.72 \pm 9.25	201.26 \pm 8.27***	33.07 \pm 7.37***

Values are expressed as Mean \pm SEM; n=6 animals / group

* $P \leq 0.05$, ** $P \leq 0.01$ and *** $P \leq 0.001$ as compared to Diabetic Control Group by One-way ANNOVA followed by Dunnett's Test

Figure 1: Effect of AC Extract, CP Extract, AC + CP and Glibenclamide on Mean percent of blood glucose reduction in Diabetic Rats

Values are expressed as Mean ± SEM; n=6 animals / group

* P<0.05, ** P<0.01 and ***P<0.001 as compared to Diabetic Control Group by One-way ANNOVA followed by Dunnett's Test

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