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Research Article

ANTI-DIABETIC AND HYPO-LIPIDEMIC EFFECT OF *ACALYPHA INDICA* IN STREPTOZOTOCIN-NICOTINAMIDE INDUCED TYPE-II DIABETIC RATS

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ABSTRACT

Diabetes mellitus (DM) consists of a group of syndromes characterized by hyperglycemia, altered metabolism of lipids, carbohydrates and proteins. It causes an increased risk of complications from vascular disease. Streptozotocin-Nicotinamide model was used to induce Type-2 diabetes. An ethanolic extract of *Acalypha indica* was found to lower blood glucose in basal conditions and after heavy glucose load in normal rats. An ethanolic extract of *Acalypha indica* was found to lower increased blood glucose in streptozotocin-Nicotinamide induced diabetic rats (33.33% at 200mg/kg, 41.43% at 400mg/kg on 14 day when compared to standard glibenclamide (52.05%). The ethanolic extract reduces triglycerides, total cholesterol, low density lipoproteins, very low density lipoproteins (LDL, VLDL) & liver enzymes (SGPT, SGOT) effectively at 400 mg/kg extract when compared to diabetic control and it increases HDL levels. The histopathological study proved that the extract has significant β-cell regeneration and the mechanism of anti-diabetic activity of the extract was found to be through glucose uptake mechanism.

Keywords: Anti-diabetic activity, *Acalypha indica*, Streptozotocin-Nicotinamide, Diabetes.

INTRODUCTION

Diabetes mellitus (DM) consists of a group of syndromes characterized by hyperglycemia, altered metabolism of lipids, carbohydrates, and proteins. It causes an increased risk of complications from vascular disease[(1)]. Apart from currently available therapeutic options for diabetes like oral hypoglycemic agents and insulin, which have limitations of their own, many herbal medicines have been recommended for the treatment of diabetes[(2)]. A variety of ingredients present in medicinal plants are thought to act on a variety of targets by various modes and mechanisms[(3)]. They have the potential to impart therapeutic effect in complicated disorders like diabetes and its complications[(4)]. Hence the present study was carried out to evaluate the anti-diabetic activity of *Acalypha indica.*

Acalypha indica an annual erect herb found in various parts of India, Bangladesh, Srilanka, Philippines and tropical Africa. The plant is commonly known as Indian acalypha and belongs to the family Euphorbiaceae. The plant has wide uses in the traditional medicines of various countries and reported to posses diuretic, purgative and anthelmintic properties, also used in bronchitis, asthma, pneumonia, scabies and other cutaneous diseases[(5)].

Acalypha indica whole plant contain acalphine which is used in the treatment of sore gums and have post anti-fertility effect[(6)], anti-venum properties[(7)], wound healing effects[(8)], anti-oxidant effects[(9)], analgesic activity and anti-inflammatory effects[(10)], anti ulcer activity[(11)], acardial effects[(12)], diuretic effects[(13)], anti-bacterial activites[(14)], anti-helminitic[(15)]. Ayurvedic knowledge supported by modern science was necessary to isolate characterize and standardize the active constituents from herbal sources for anti-diabetic activity. The present investigation was carried out to expose the chemical and therapeutically potential by evaluating phyto-chemical and anti-diabetic activity of the whole plant of *Acalypha indica* (L.) which is presented in the article. Since, all parts of investigated plant were being used for various human ailments and very less scientific work has been performed.

MATERIALS AND METHODS

Chemicals

Streptozotocin and Nicotinamide was purchased from Sigma Aldrich Company (USA). Glibenclamide procured from Suzikem Drugs Private LTD (Hyderabad), as a gift sample. All analytical enzymatic kits were obtained from Coral clinical systems.

Plant material and Preparation of plant extract

The plant *Acalypha indica* was collected from waste lands of Kakatiya University during the month of March 2011 and authenticated by an expert taxonomist Dr. V.S.Raju department of botany, Kakatiya University, Warangal, Andhra Pradesh. Plant was shade dried and powdered in a grinder to obtain a coarse powder and then passed through 40 mesh sieve. About 80 gm of powdered drug was extracted with ethanol by soxhlet apparatus.

Experimental animals

Male Albino wistar rats weighing 160-200 g were purchased from Mahaveer Enterprises, Hyderabad. The animals were maintained at temperature of 25±5^{0C} and humidity 45±5^{0C} with 12 hr day and night cycle. The animals were fed with Pellet chew feed standard diet and water *ad libitum*. The experimental protocol was approved by the Institutional Animal Ethical Committee (IAEC).

Acute toxicity studies

Acute toxicity studies for ethanolic extract of *Acalypha indica* was carried out in mice at different doses (1000 - 5000 mg/kg, orally), showed no gross evidence of any abnormalities in the mice up to 72 hr of the observation period. Hence, further pharmacological investigation was carried at dose levels of 200, 400 mg/kg. Acute toxicity study was done as per OECD Guidelines 423[(16,17)].

Oral glucose tolerance test (OGTT)

The oral glucose tolerance test was performed in overnight fasted normal rats. Twenty four rats were divided into four groups (n = 6), group-I was administered with 0.1% sodium carboxy methyl cellulose at a dose of 2ml/kg, group-II was administered with glibenclamide at a dose of 10 mg/kg, group-III & IV were administered with ethanolic extract of *Acalypha indica* (EEAl) at a dose of 200 mg/kg & 400 mg/kg respectively. Glucose (3g/kg) was fed 30 min after the administration of extracts. Blood (0.3 ml) was withdrawn from retro-orbital plexus under mild ether anesthesia at a time periods of 0, 30, 60 and 120 min after glucose loading. Plasma was separated from the collected blood samples after centrifugation at 4000 rpm for 15 min. Blood glucose level in plasma was measured using glucose oxidase and peroxidase method[(18)].

Hypoglycemic activity

Test was performed in overnight fasted normal animals. Twenty four rats were divided into four groups (n = 6), group-I was administered with 0.1% sodium carboxy methyl cellulose at a dose of 2ml/kg, group-II was administered with glibenclamide at a dose

of 10 mg/kg, group-III & IV were administered with ethanolic extract of *Acalypha indica* (EEAI) at a dose of 200 mg/kg & 400 mg/kg respectively. Blood (0.3 ml) was withdrawn from retro orbital plexus under mild ether anesthesia at a time periods of 0, 2, 4, and 6 hour after drug administration[19,20].

Streptozotocin –Nicotinamide induced diabetic rats

Streptozotocin (STZ) was dissolved in citrate buffer (pH 4.5) and nicotinamide in normal physiological saline solution (0.9% NaCl). Diabetes was induced in overnight fasted animals by single intraperitonial(i.p) injection of 65 mg/kg of STZ, 15 min after the i.p administration of 110 mg/kg of nicotinamide[21].

Expermental protocol for anti-diabetic activity

Thirty rats were divided into five groups, (n=6). Test and standard samples were suspended in 0.1% sodium carboxy methyl cellulose SCMC) and administered orally by intragastric (i.g) route by using an i.g tube. Rats were divided into following groups.

Group I : Normal control. Recieved only 0.1% SCMC 2ml/kg per oral.

Group II : Disease control. Recived Streptozotocin 65 mg/kg (i.p) + Nicotinamide 110 mg/kg (i.p) + 0.1% SCMC 2ml/kg per oral.

Group III : Standard. Streptozotocin 65 mg/kg (i.p) + Nicotinamide 110 mg/kg (i.p) + Glibenclamide 10 mg/kg per oral.

Group IV : Test 1. Streptozotocin 65 mg/kg (i.p) + Nicotinamide 110 mg/kg(i.p) + EEAI(200 mg/kg) per oral.

Group V : Test 2. Streptozotocin 65 mg/kg (i.p) + Nicotinamide 110 mg/kg(i.p)

+ EEAI(400 mg/kg) per oral.

Acute experimental model of anti-diabetic activity

At first day blood samples were collected from all groups at 0, 2, 4, 6 and 8 hr after the drug administration. Plasma samples were analysed for the glucose levels as stated above.

Sub acute experimental model of anti-diabetic activity

The vehicle, test (200 mg/kg & 400mg/kg) and glibenclamide were administered upto 14 days. Blood glucose levels were determined at 1, 7 and 14 day. Body weights were measured on 1 and 14 day. Lipid profile, serum glutamate oxalloacetate transaminase (SGOT) and serum glutamate pyruvate transaminase (SGPT) were determined on 14 day.

Biochemical analysis

Glucose levels measured by glucose enzymatic kit. The lipid profile such as total cholesterol (TC), triglycerides (TG), high density lipoprotein (HDL) were determined by using enzymatic kits[22]. And low density lipoproteins (LDL), very low density lipoprotein (VLDL) values were calucated by Friedewalds formula as given below[23].

$$VLDL=TG/5$$

$$LDL=TC-(HDL+VLDL)$$

Histopathological studies

After the end of the study the animals were sacrificed by cervical dislocation under mild ether anesthesia and pancreas were isolated, washed with cold saline and preserved in 10% formalin solution in buffered form. Blocks from tissues were routinely processed and embedded in paraffin. Thin sections were cut by using rotary microtone and stained with hematoxylin and eosin for histomorphology evaluation.

Determination of peripheral consumption of glucose *in vitro*

The peripheral consumption of glucose *in vitro* was performed as per chattopadhyay *et al.,*[24] Pheripheral glucose consumption was studied in rat diaphragm preparation from animals fasted for 18 hours prior to experiment. The animals were sacrificed by cervical dislocation and the diaphragms were quickly taken out and divide each diaphragm into 4 pieces. The piceces of diaphragms were incubated in the nutrient solution with constant oxygenation and shaking (90 cycles/min) at 37 ^{0}c for 6 hours in accordance with procedure. The nutrient solution with diaphragms was aerated for 10 min and used immediately. Glucose was added to final concentration (2%). Then each piece of diaphragm is incubated in 2.5 ml of glucose nutrient mixture. The results were expressed as glucose consumption per 10 mg of dry diaphragm (by subtracting glucose concentration after incubation from before incubation).

Statistical Analysis

All data are expressed as mean ± SD (n=6) and evaluated by one way analysis of variance (ANOVA), employing Tukey's post hoc test and values of $P<0.05$ were considered as statistically significant.

RESULTS AND DISCUSSION

Oral glucose tolerance test

By administration of glucose (3 g/kg) produced significant change in blood glucose level of normal rats. The treatment groups with EEAI (200 mg/kg, p.o.), EEAI (400 mg/kg, p.o.) glibenclamide (10 mg/kg, p.o.) showed significant reduction ($P<0.05$) in plasma glucose level at 60 minute when compared to normal control group (Table-1).

Hypoglycemic effect of ethanolic extract of *Acalypha indica*

The results from the study clearly indicated that the ethanolic extract 200 & 400 mg exhibited significant hypoglycemic activity at 4 hour in streptozotocin-Nicotinamide induced diabetic rats. The hypoglycemic activity of EEAI was found to be dose dependent. Standard drug glibenclamide indicated a significant decrease of blood glucose levels (Table-2).

Acute and Sub acute anti-diabetic activity in Streptozotocin - Nicotinamide induced diabetes

In diabetic rats, acute i.g, administration of EEAI (200& 400 mg/kg) and glibenclamide induced a significant reduction plasma glucose level at 4 hr after administration when compared with control group ($p<0.05$) (Table 5), Sub acute administration (Table-3) of the doses produced significant reduction in plasma glucose levels in STZ-Nicotinamide diabetic rats after 1 day of administration and during all period of experimentation ($p<0.05$).

Effect of EEAI on lipid profile

After administration of STZ-Nicotinamide, alteration of lipid profile was observed in diabetic rats, both the doses of EEAI showed significant ($p<0.001$) reduction in elevated TG, TC, LDL, and VLDL levels and increased HDL levels (Table-4). The dose of 200 & 400 mg/kg of EEAI showed significant ($p<0.001$), higher reduction in elevated TC, TG, LDL and VLDL levels when compared to glibenclamide. The HDL level at the dose of 200 & 400 mg/kg was significantly increased when compared to glibenclamide.

Effect of EEAI on liver enzymes

In diabetic control rats there was gradual increase in SGOT and SGPT parameters, the groups treated with EEAI (200 & 400 mg/kg) showed a significant ($p<0.001$) reduction in these parameters when compared to diabetic control group, the reduction of these parameters by group treated with EEAI at 400 mg/kg was comparable with that of the glibenclamide treated group (Table-5).

Effect of EEAI on body weight

In diabetic control rats there was decrease in body weight, the groups treated with EEAI (200 & 400 mg/kg) showed a significant ($p<0.001$) increase in body weight when compared to diabetic control group, the increase in body weight by group treated with EEAI at 400 mg/kg was comparable with that of the glibenclamide treated group (Table-6).

Histopathological studies of pancreas.

Histopathological examination of pancreas showed the destruction of β-cells in the diabetic control group, and by the treatment with EEAI (200 &400 mg/kg) and glibenclamide showed recovery of damaged tissues when section of treated groups compared with diabetic control. (Fig. 8)

Table 1: Oral Glucose Tolerance Test (OGTT) in glucose loaded normal rats

Group	Dose	Blood glucose level (mg/dl)			
		Pretreatment	Post treatment		
		0 min	30 min	60 min	120 min
Control (0.1%CMC)	2ml/kg/bw	78.39 ± 8.25	108.64 ± 5.57	140.74 ± 7.02	92.59 ± 3.31
Glibenclamide	10mg/kg/bw	78.39 ± 2.78	87.0± 3.88***	124.69±5.57**	79.01±6.89***
EEAI 1	200mg/kg/bw	77.77 ± 5.73	96.29±5.23**	113.95±6.79^{NS}	86.41±3.02^{NS}
EEAI 2	400mg/kg/bw	79.63 ± 6.93	90.12±7.28**	128.39± 9.95*	80.86 ± 4.32**

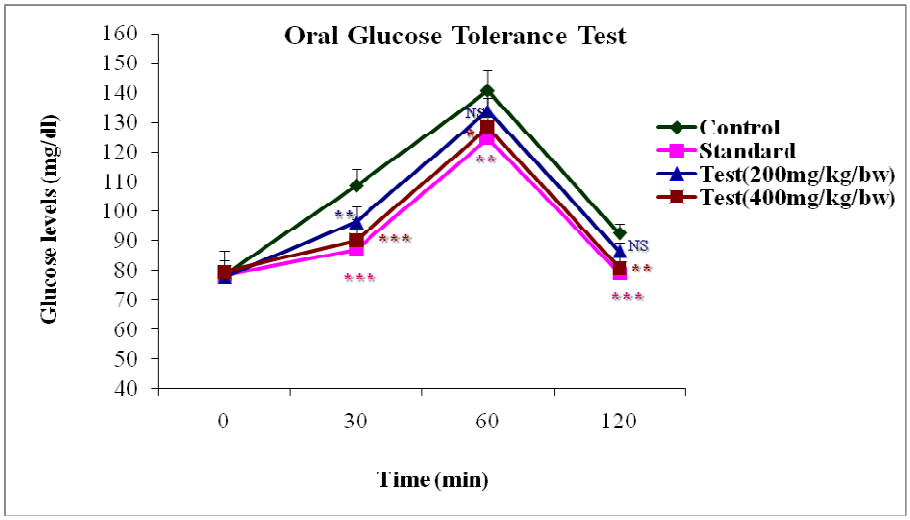


Fig. 1: Oral Glucose Tolerance Test in glucose loaded normal rats.

*Values were expressed as Mean±SD for (n=6). One way ANOVA with Tukey's post hoc test was applied .***P<0.001,**P<0.01,**P<0.01,*P<0.05 significant & NS=non significant when compared to control.*

Table 2: Hypoglycemic activity of EEAI in normal rats

Group	Dose	Blood glucose level (mg/dl)			
		Pretreatment	Post treatment		
		0	2	4	6
Control (0.1%CMC)	2ml/kg/bw	76.19±5.83	76.78±4.37	74.4±5.72	74.41±4.17
Glibenclamide	10 mg/kg/bw	73.81±1.84	66.66±2.91** (9.64±4.21)	57.14±3.19*** (22.5±5.47)	61.31±2.68*** (16.82±5.59)
EEAI 1	200mg/kg/bw	75.59±6.15	72.02±5.25^{NS} (4.25±2.62)	64.88±5.27** (13.93±7.03)	67.26±5.25* (1024±7.44)
EEAI 2	400mg/kg/bw	73.80±4.87	69.04±2.91* (6.01±2.13)	60.11±2.68*** (18.24±6.69)	63.69±2.68*** (13.38±6.99)

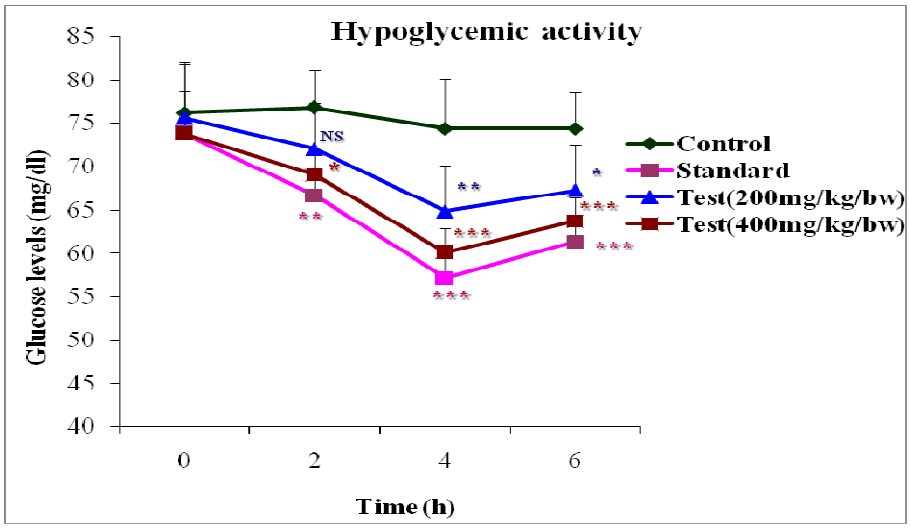


Fig. 2: Hypoglycemic activity of EEAI in normal rats

*Values were expressed as Mean ± SD for (n=6). One way ANOVA with Tukey's post hoc test was applied.***P<0.001,**P<0.01,**P<0.01,*P<0.05 significant & NS=non significant when compared to control.*

Table 3: Acute anti - diabetic activity in diabetic rats

Group	Blood glucose levels (mg/dl)				
	Pretreatment	Post treatment			
	0 h	2 h	4 h	6 h	8 h
Control (0.1%CMC)	77.78 ±3.31	77.77±5.23	78.39±6.37	77.16±5.93	78.39±5.45
Diabeticcontrol (0.1%CMC)	294.44 ±3.88	292.59 ±4.68	295.06 ±8.65	292.59±6.19	293.21±4.92
Glibenclamide	294.44 ±3.88	250.61±6.89*** (14.86±2.6)	209.87±6.48*** (28.71±2.4)	228.39±5.06*** (22.4 ±1.41)	254.32±3.02*** (13.61±1.69)
EEAI 1	293.21 ±6.37	288.27±10.1 NS (1.62 ±4.61)	277.16±7.91** (5.42±3.6)	279.01±6.48* (4.79 ±3.22)	282.09±8.58* (3.72±4.3)
EEAI 2	292.5±2.34	277.16±9.19* (5.25±3.56)	230.24±9.19*** (21.3±3.21)	274.07±5.23*** (6.32 ±1.2)	277.77±6.62** (5.05±2.5)

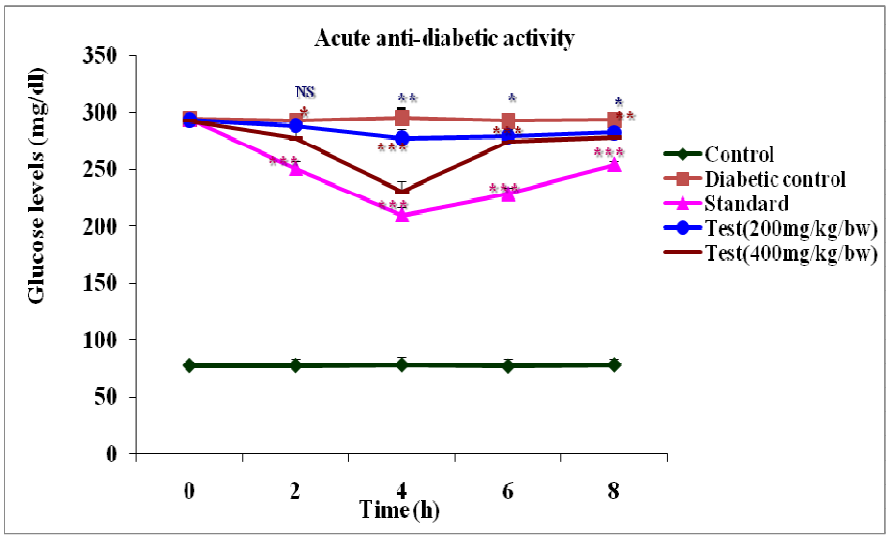


Fig. 3: Acute anti-diabetic activity in diabetic rats

*Values were expressed as Mean±SD (n=6). One way ANOVA with Tukey's post hoc test was applied .***P<0.001,**P<0.01,*P<0.05 significant & NS=non significant when compared to diabetic control.*

Table 4: Sub acute experimental model in diabetic rats

Group	Dose	1 st day	7 th day	14th day
Control (0.1%CMC)	2 ml/kg/bw	78.39±4.32***	80.24± 3.02***	81.48± 3.31***
Diabetic control (0.1%CMC)	2ml/kg/bw	295.06 ± 8.65	292.59 ± 4.54	300.92 ± 4.64
Glibenclamide	10 mg/kg/bw	209.87±6.48***	175.56±2.03*** (16.35 ± 4.22)	100.61±2.78*** (52.05 ± 6.12)
EEAI 1	200mg/kg/bw	277.16 ±7.91**	222.22±6.92*** (11.76 ± 5.34)	167.91±1.91** (33.33 ± 4.45)
EEAI 2	400mg/kg/bw	230.24±9.19***	203.70±3.70*** (8.83 ± 4.86)	130.86±3.02*** (41.43 ± 6.34)

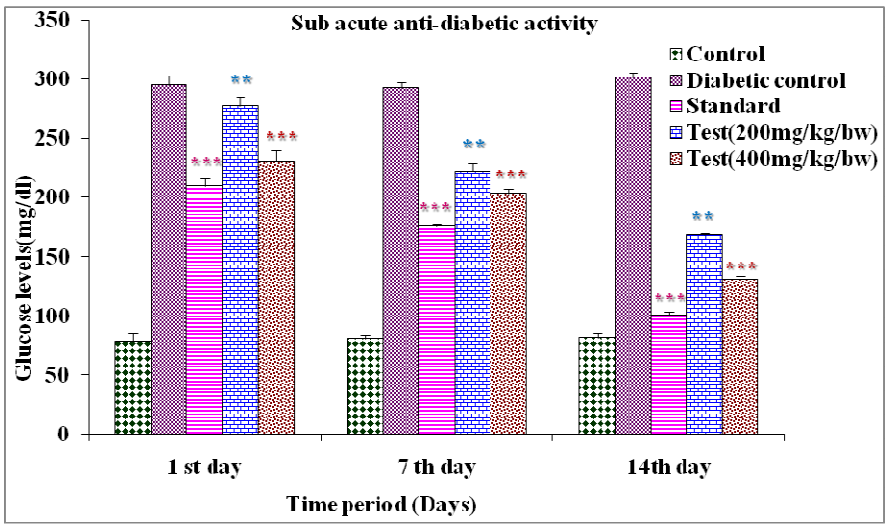


Fig. 4: Sub acute anti-diabetic activity in diabetic rats

*Values were expressed as Glucose levels in Mean±SD, percentage reduction in glucose levels (Mean±SD) for (n=6). One way ANOVA with Tukey's post hoc test was applied .***P<0.001 &,**P<0.01 significant when compared to diabetic control.*

Table 5: Lipid profile level estimation at 14 th day

Group	Triglycerides (mg/dl)	Total cholesterol (mg/dl)	HDL (mg/dl)	LDL (mg/dl)	VLDL (mg/dl)
Control (0.1%CMC)	101.4±9.90	112.28±7.8	51.1± 6.59	40.88±8.3	20.28±1.98
Diabeticcontrol (0.1%CMC)	183.66 ±6.14	180.12±6.8	33.21±4.54	110.06 ± 8.04	36.72±1.22
Glibenclamide	90.33±5.14***	132.6±4.76***	45.76±5.08*	65.08±7.55***	18.06±1.02***
EEAI (200mg)	164.5±10.94**	164.17±7.98**	49.42±8.38**	78.71 ± 6***	32.9±21.18**
EEAI (400mg)	97.46±5.42***	140.3±3.73***	57.75±5.86***	63.05±5.15***	19.49±1.08***

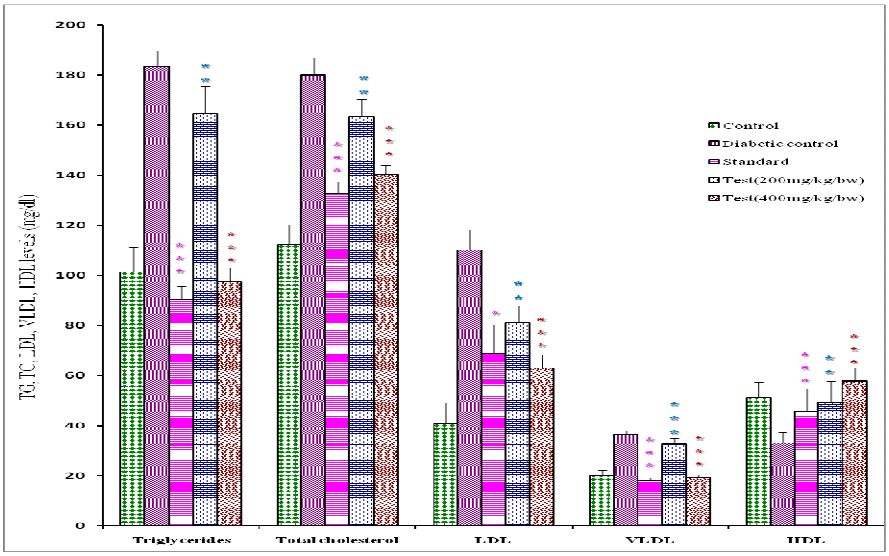


Fig. 5: Lipid profile level estimation at 14 th day

*Values were expressed as Mean±SD (n=6). One way ANOVA with Tukey's post hoc test was applied .***P<0.001,**P<0.01,*P<0.05 significant & NS=non significant when compared to diabetic control.*

Table 6: Liver enzyme levels level estimation at 14 th day

Group	Dose	SGPT(IU/ml)	SG0T(IU/ml)
Control(0.1%CMC)	2ml/kg/bw	45.37 ± 5.37	37.01 ± 3.93
Diabetic control(0.1%CMC)	2ml/kg/bw	100.05 ± 4.73	86.71 ± 6.59
Glibenclamide	10 mg/kg/bw	51.75 ± 3.52***	52.36 ± 8.06***
EEAI 1	200mg/kg/bw	86.84 ± 6.94**	71.42± 5.14**
EEAI 2	400mg/kg/bw	66.98 ± 4.25***	60.28 ± 6.9***

*Values were expressed as Mean±SD (n=6). One way ANOVA with Tukey's post hoc test was applied .***P<0.001,**P<0.01 significant when compared to diabetic control.*

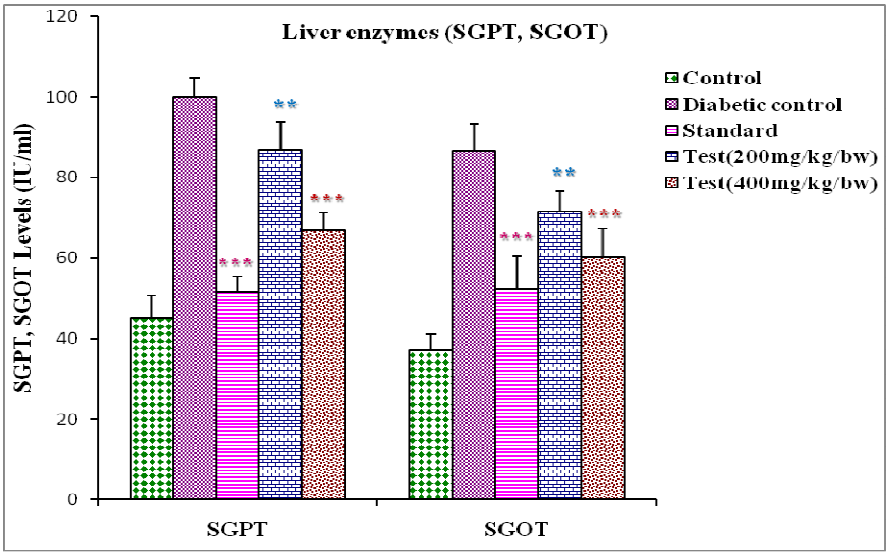


Fig. 6: Liver enzymes (SGPT, SGOT) level estimation at 14 th day

*Values were expressed as Mean±SD (n=6). One way ANOVA with Tukey's post hoc test was applied .***P<0.001,**P<0.01 significant when compared to diabetic control.*

Table 7: Effect of EEAI on body weight at 1 st & 14 th days

Group	Dose	Intial bodyweight	Final bodyweight
Control (0.1%CMC)	2 ml/kg/bw	180 ± 6.32	214.16 ± 4.91
Diabetic control (0.1%CMC)	2 ml/kg/bw	178.33± 5.16	148.33 ± 5.16
Glibenclamide	10 mg/kg/bw	175.83 ± 4.91	195.1 ± 7.07***
EEAI 1	200mg/kg/bw	176.66 ± 4.08	165.83 ± 9.73**
EEAI 2	400mg/kg/bw	175.83± 4.91	190.83 ± 8.61***

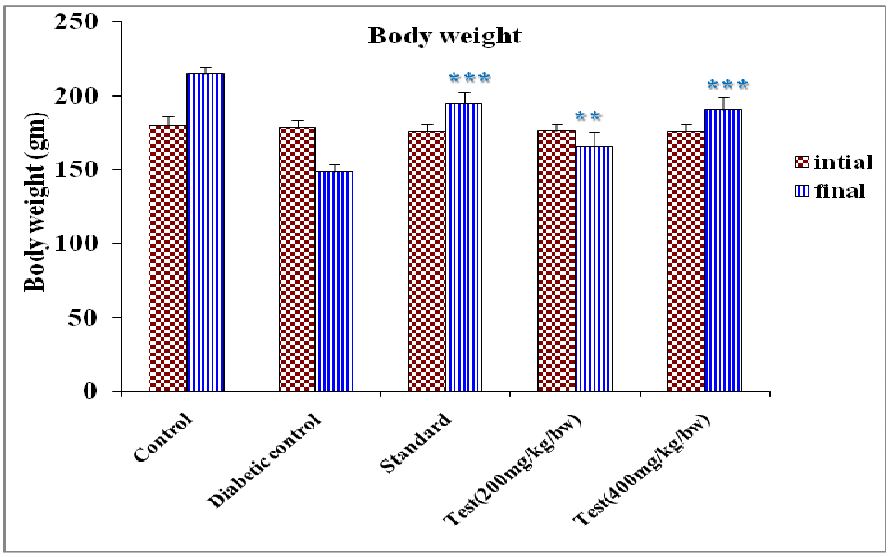
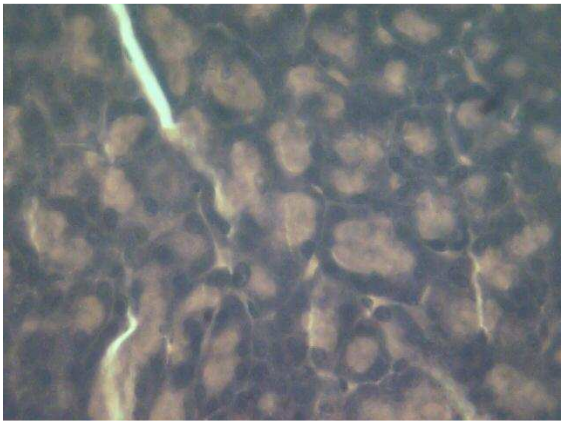
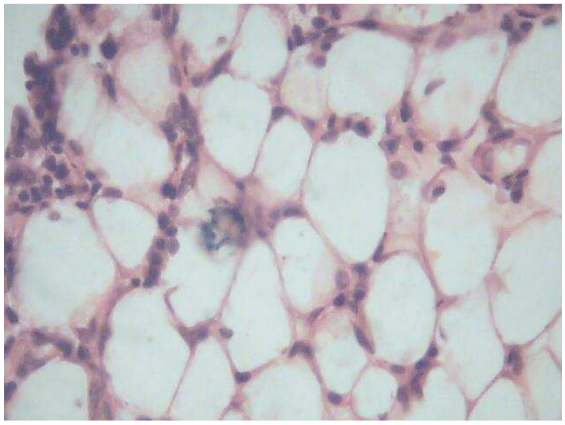


Fig. 7: Effect of EEAI on body weight at 1 st & 14 th days

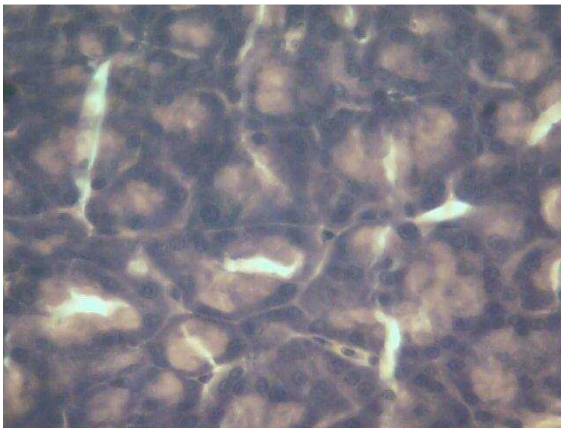
*Values were expressed as Mean±SD (n=6). One way ANOVA with Tukey's post hoc test was applied .***P<0.001,**P<0.0 when compared to diabetic control.*



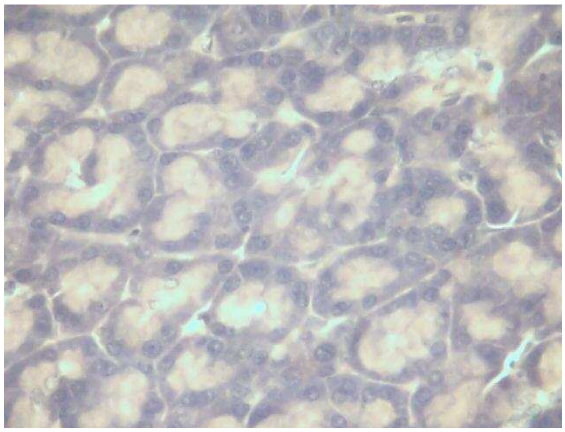
(A) Normal control



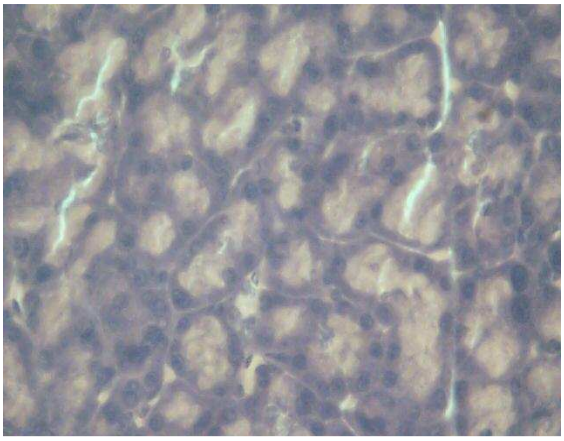
(B) Diabetic control



(C) Standard (Glibenclamide 10mg/kg)



(D) EEAI(200mg/kg)



(E) EEAI(400mg/kg)

Fig. 8: **Histopathological studies**

Rat Hemi-diaphragm method:Determination of pheripheral glucose consumption *in vitro*. EEAI showed the glucose consumption *in-vitro*. Glucose consumption is more in 400µg/ml than 200µg/ml of ethanolic extract of *Acalypha indica.*

Table 8: *In-vitro* Rat Hemi-diaphragm method in normal rats

Group	Dose	Intial glucose	Final glucose	Glucose consumption (mg/10mg of diaphragm dry weight)
Control(0.1%CMC)	2ml/kg/bw	582.75	417.24	165.51 ± 5.89
Insulin	5 U/ml	586.21	279.31	306.89 ± 7.86***
EEAI 1	200 µg/ml	586.21	379.31	206.89 ± 6.45**
EEAI 2	400 µg/ml	579.31	313.79	225.51 ± 8.85***

*Values were expressed as Mean±SD for (n=6). One way ANOVA with Tukey's post hoc test was applied .***P<0.001,**P<0.01 significant when compared to control.*

CONCLUSION

Ethanolic extract of *Acalypha indica* showed significant anti-hyperglycemic and hypo-lipidemic activity in STZ-Nicotinamide induced diabetic rats. 400mg/kg EEAI showed significant reduction in glucose and lipid profile and it increases the body weight, HDL levels. It improves regeneration of damaged pancreatic β-cells. EEAI showed the anti-diabetic activity by the glucose uptake mechanism.

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REFERENCES

1. Joel G, Hardman and Limbard LE. Insuin oral hypoglycemic agents and the pharmacology of the endocrine pancreas. Goodman and Gilman's The pharmacology basis of Therapeutics, 10 th ed. Mcgraw Hill publishers; 2006. p. 1679 -1714.
2. Mukherjee P, Maiti K, Mukherjee K and Houghton PJ. Leads from Indian medicial plants with hypoglycemic potentials. Journal of Ethnopharmacology 2006; 106: 1-28.
3. Tende JA, Ezekiel I, Dikko AAU and Goji ADT. Effect of Ethanolic Leaves Extract of *Moringa oleifera* on Blood Glucose Levels of Streptozocin-Induced Diabetics and Normoglycemic Wistar rats. British Journal of Pharmacology and Toxicology 2011; 2 Suppl 1: 1-4.
4. Tiwari A and Rao J. Diabetes mellitus and multiple therapeutic approaches of phytochemicals: Present status and future prospects. Current Science 2002; 83: 30-38.
5. Kirtikar KR and Basu BD. Indian medicinal plant ,3rd ed. International book distributors; 1999. p.2262-2263.
6. Shivayogi PH, Rudresh K, Shrishailappa B, Saraawatti BP and Somanth RP. Post-coital antifertility activity of *Acalypha indica* L. Journal of Ethnopharmacology 1999; 67: 253-58.
7. Annie S, Rajendran K, Ramgopal B and Dinesh Kumar C. Neutralization potential of *viper russelli* venom by ethanol leaf extract of *Acalypha indica*. Journal of Ethnopharmacology 2004; 94: 267-273.
8. Sureshreddy J, Rajesara Rao P, Mada SR wound healing effects of *Heliotropium indicum & Acalypha indica* in rats Journal of Ethnopharmacology 2002; 79: 267-273.
9. Ruchi GM , Majekodunmi, Ramia, Gouri BV, Hussain A and Saud Khamis. Anti-oxidant activity of some edible and wound healing plantsin oman. Food Chemistry 2007; 101: 465-470.
10. Mohana Vamsi N, Venkata Sunil Kumar M, Kodandaram N and Padmanaba reddy Y. Evalution of anti inflammatory activity of *Acalypha indica.* Industrial Pharmacy 2008; 7: 89-91.
11. Klimuthu S, Rajesh P,Rajesh Kannan V, Balamurugan B and Chandrasekar TM. Antiulcer activity of methanolic extract of *Acalypha indica* Linn by pylorus ligature and swimm stress induced ulceration. Journal of Pharmacy Research. 2010; 3 Suppl 1: 2779-2783.
12. Singh DAP, Raman M , Saradha V, Jayabarathi P and Kumar VRS. Acardicidal property of *Acalypha indica* against natural psoroptes cuniculi infestation in broiler rabbits. Indian Journal of Animal Sciences 2005; 4:1-2.
13. Das AK, Ahmed F, Biswas NN, Dev S and Masud MM. Diuretic activity of *Acalypha indica*. Journal of Pharmaceutical Sciences 2005; 4:1-2.
14. Govindarajan M , Jeabanesean A ,Reetha D , Anisath R, Pusphananthan T and Samidurai K. Antibacterial activity of *Aaclypha indica* L. The European Review for Medicinal and Pharmacological Sciences 2008; 12 Suppl 5: 299-302.
15. Ranju G, Niranjan S, Saroj kumar P, Vishesh kumar P and Shailendr P. *In vitro* anthelmintic activity of *Acalypha indica* leaves extracts. International Journal of Research in Ayurveda and Pharmacy 2011; 2 Suppl 1: 247-249.
16. Sanjay J, Gaurav B, Rakesh B, Praveen kumar, Avinash J and Vinod kumar D. Anti-diabetic activity of *Paspalum scrobiculatum* in alloxan induced diabetic rats. Journal of Ethnopharmacology 2010; 127 Suppl 2: 325-328.
17. Sakthi Priyadarsini S, Vadivu R and Jayshree N. *In vitro* and *in vivo* antidiabetic activity of the leaves of *Ravenala madagascariensis* on

alloxan induced diabetic rats. Journal of Pharmaceutical Science and Technology 2010; 2 Suppl 9: 312-317.

18. Prakasam A, Sethupathy S and Pugalendi K. Effect of *Casearia esculenta* root extract on blood glucose and plasma antioxidant status in streptozotocin diabetic rats. Polish Journal of Pharmacology 2003; 55: 43-49.
19. Rajendran K, Kishore Gana S, Srinivasan KK and Shirwaikar A. Short term antidiabetic studies on alcoholic root extract of *Pseudarthria viscida* Linn. International Journal of Research in Pharmaceutical Sciences 2010; 1 Suppl 3: 382-385.
20. Kar D, Maharan L, Pattnaik S and Dash G. Studies on hypoglycemic activity of *Solanum xanthocarpum* Schrad. & Wendl fruit extract in rats. Journal of Ethnopharmacology 2006; 108: 251-256.
21. Masiello P, Broca C, Gross R, Manteghetti M, HillaireBuys D, Novelli M and Ribes G. Expermental NIDDM: Development of a new model in adults administered streptozotocin and nicotinamide. Diabetes 1998; 47: 224-229.
22. Islam MA, Afia Akhtar M, Khan MRI, Hossain MS, Alam MK, Rahman BM, Shaheen and Maruf Ahmed SM. Antidiabetic and Hypolipidemic Effects of Different Fractions of *Catharanthus Roseus* (Linn.) on Normal and Streptozotocin-induced Diabetic Rats. Journal of Scientific Research 2009; 1 Suppl 2: 334-344.
23. Friedwald WT, Levy RI and Fredrickson DS. Estimation of the concentration of low density lipoprotein cholesterol in plasma, without use of preparative ultracentrifuge. Clinical Chemistry 1972; 18 Suppl 6: 499-502.

24. Chattopadhyay RR, Sarkar SK, Ganguly S, Banerjee RN and Basu TK. Effect of extract of leaves of *vinca rosea* Linn on glucose utilization and glycogen deposition by isolated rat hemidiaphargm. Indian Journal of Physiology and Pharmacology 1992; 36: 137-138.