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Research Article

ANTIDIABETIC AND HYPOLIPIDEMIC POTENTIAL OF *TRAGIA INVOLUCRATA* LINN. IN STREPTOZOTOCIN-NICOTINAMIDE INDUCED TYPE II DIABETIC RATS

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ABSTRACT

Tragia involucrata Linn. (Euphorbiaceae) is traditionally used in the Indian ayurvedic system of medicine for the treatment of bronchitis, asthma, veneral disease, skin infection and diabetes. The present study was to evaluate the effect of aqueous ethanolic extract of tragia involucrata (Whole plant) using streptozotocin-nicotinamide-induced type 2 diabetes mellitus in rats. Oral administration of aqueous ethanolic extract of Tragia involucrata (AEETI) at doses of 250 and 500 mg/kg for 28 days significantly decreased blood glucose, glycosylated haemoglobin (HbA1C), total cholesterol (TC), triglyceride (TG), low density lipoprotein (LDL), very low density lipoprotein (VLDL) and significantly increased the high density lipoprotein (HDL) levels and body weight. The significant anti-hyperglycemic activity was found to be comparable with oral synthetic hypoglycemic drug, glibenclamide (0.5 mg/kg). Oral glucose tolerance test also indicated that both the doses of AEETI and standard significantly lowered glucose levels. These results clearly indicated that AEETI possess promising anti hyperglycemic and hypolipidemic effect, which might be due to peripheral glucose utilization and the observed hypolipidemic effect which may lowers the diabetes associated cardiovascular complications.

Keywords: Anti hyperglycemic, Lipid profile, Glycosylated haemoglobin, *Tragia involucrata*

INTRODUCTION

Diabetes mellitus has become foremost non communicable disorder globally which affect more than 100 million of world's population. Diabetes is considered as one of the major leading causes of death in the world. The world health organisation reports that 300 million peoples may suffer with diabetes by the year of 2025, in that India is the leading country with more number of peoples suffer with diabetes. It has been reported that approximately 58 million people would suffer with diabetes by the year of 2025 in India. Diabetes mellitus is a disorder with increased concentration blood glucose level because of derangement in carbohydrate metabolism due to defective secretion or defective action of insulin. This metabolic disorder results in various diabetic related complications, which plays a major role in the premature death and disabilities.[1]

WHO has recommended evaluation of plants effective in different diseases, Many Indian medicinal plants have been found to be useful in successfully managing diabetes and from some of them active principles have been isolated[2]. Thus it will be useful to look for new and if possible more efficacious drug and the vast reserves of phytotherapy may be an ideal target. [3]

Tragia involucrata Linn (Euphorbiaceae) is a perennial evergreen, climbing hispid herb or shrub with scattered stinging hairs. Widely distributed in the Indian subcontinent, it is locally known as senthoty or poonaikanch chedi in Tamil nadu.[4,5] The traditional Ayurvedic practitioners of kerala use all parts of this herb both externally and internally in the treatment of many common as well as complicated diseases. They also use this herb in treatment of bronchitis, asthma, veneral disease, skin infections and diabetes.[6] The objective of this investigation was to ascertain the scientific basis of its use in the treatment of diabetes. The present investigation reports the antihyperglycemic and hypolipidemic activity of the aqueous ethanolic extract of tragia involucrata (AEETI) on which there is no previous data available.

MATERIALS AND METHODS

Collection and authentication of plant material

The whole plant of *Tragia involucrata* Linn was collected from the waste lands of Padur and Kelambakkam, Kanchipuram dist, Tamil nadu. The plant material was identified and authenticated by, prof.Dr.D.Narasimhan, Centre for floristic research, Madras Christian College, Chennai. A voucher specimen was submitted at C.L. Baid Metha College of Pharmacy, Chennai.

Preparation of aqueous-ethanolic extract of *Tragia involucrata* (AEETI)

The plant was chopped to small pieces and shed dried. The dried parts were powdered mechanically and weighed quantity of the powder (850 g) was passed through sieve number 40. This powder was packed into soxhlet apparatus and extracted with aqueous-ethanol (80:20) at a temperature of 60°-70°c. The extract was concentrated to dryness at 40°c under reduced pressure in a rotary vacuum evaporator (yield 16.0g) and the semisolid residue was stored in a refrigerator at 2-8°c for use in subsequent experiments.

Experimental animals

Inbred adult wistar rats (200-250g) of either sex were obtained from the animal house in C.L.Baid Metha College of Pharmacy, Chennai. The animals were maintained in a well-ventilated room with 12:12 hour light/dark cycle in polypropylene cages. Standard pellet feed (Hindustan Lever Limited., Bangalore) and drinking water was provided *ad libitum* throughout experimentation period. Animals were acclimatized to laboratory conditions one week prior to initiation of experiments. Ethical committee clearance was obtained from IAEC (Institutional Animal Ethics Committee) of CPCSEA (Committee for the Purpose of Control and Supervision of Experiments on Animals).

Ref No: IAEC/XXX/07/CLBMCP/2010.

Preliminary phytochemical screening[7,8]

Preliminary phytochemical screening revealed the presence of alkaloids, carbohydrates, protein, phenols, tannins, flavonoids, terpenes, sterols and saponins in the extract.

Acute oral toxicity studies[9,]

The procedure was followed by using OECD guidelines (organization of economic corporation and development) 423(acute toxic class method).

Three male rats weighing 180-200 gm were used for the study, since the herbal extracts are relatively non toxic, the starting dose level of Aqueous-ethanolic extract of *Tragia involucrata* (AEETI) was selected as 2000mg/kg p.o. and the extract was administered orally to rats which were fasted over night with water *ad libitum*. Body weights of the rats before and after treatment were noted. Any changes in skin and eyes and mucous membrane and also respiratory, circulatory, autonomic, CNS, motor activity, behavior pattern were observed and also sign of tremors, convulsion,

salivation, diarrhoea, lethargy, sleep and coma were noted. The onset of toxicity and signs of toxicity also noted for 14 days.

Oral glucose tolerance test (OGTT) [10,11]

Overnight fasted (16hr) normal rats were randomly divided into 4groups, of 6 rats in each. Glibenclamide (0.5 mg/kg) was used as the reference standard and the control group animals received only vehicle. Remaining groups were treated with 250 mg/kg and 500 mg/kg of AEETI suspended in 0.5% SCMC. After 30min of the drug treatment animals fed with glucose (2g/kg) and blood glucose was determined at 30 min, 60 min, 90 min and 120 min of the glucose load. Blood glucose concentration was estimated by the glucose oxidase enzymatic method using a commercial glucometer and test-strips (Onetouch horizon test meter).

Induction of diabetes mellitus in experimental animals[12,13,14]

Diabetes was induced in overnight fasted healthy inbred wistar Albino rats (200-250g) of either sex by a single intraperitoneal (i.p) injection of Streptozotocin (STZ) 45 mg/kg, 15 min after the single intraperitoneal (i.p.) injection of Nicotinamide (NA) 110 mg/kg Streptozotocin (STZ) was dissolved in 0.1 M cold citrate buffer, pH 4.5 and Nicotinamide (NA) was dissolved in normal physiological saline. After injections the animals were free access to food and water. After 4 hours the animals were given with 5% glucose in their drinking water for the first 24 hours to counter any initial hypoglycemia. The development of diabetes is confirmed after 72 hours of the streptozotocin injection and on 7th day after the injections. The animals with fasting blood glucose level more than 200 mg/dl are select for the experimentation.

Effect of sub-acute treatment of AEETI on blood glucose level in STZ-NA induced diabetic rats[15,16]

The animals were divided into 5 groups. Group I consisted of normoglycaemic rats. The remaining 4 groups consisted of 6 STZ-NA induced diabetic rats. The test samples were administered orally by using a gastric lavage.

Group I - Normal rats (Normal control) received 0.5 % SCMC 5 ml/kg p.o.

Group II - STZ-NA induced diabetic rats (Diabetic control) received 0.5 % SCMC 5 ml/kg p.o.

Group III -STZ-NA induced diabetic rats received AEETI 250 mg/kg p.o.

Group IV - STZ-NA induced diabetic rats received AEETI 500 mg/kg p.o.

Group V- STZ-NA induced diabetic rats received Glibenclamide 0.5 mg/kg p.o.

The above mentioned treatment schedule was followed for the respective group of animals for 28 days. Blood samples were collect from Tail vein in overnight fasted animals on 0th, 7th, 14th, 21st and 28th day to estimate blood glucose levels using a commercial glucometer and test-strips. (Onetouch Horizon glucometer). And the body weight was also measured gravimetrically on 0th, 7th, 14th, 21st and 28th day of treatment.

Effect of sub-acute treatment of AEETI on biochemical parameters in STZ-NA induced diabetic rats

At the end of the study the blood samples were collected from the animals under light ether anaesthesia by retro-orbitally from the inner canthus of eye using micro capillary tubes into the vials containing EDTA and serum was separated to study the biochemical parameters. The liver and muscles were dissected out and washed in ice-cold saline for estimation of glycogen levels in it. The serum parameters were estimated by Bio-chemistry auto analyzer manufactured by Aspen technologies (Star plus 21) and diagnostic kits. Liver and muscle glycogen was estimated by Nicholas anthrone reagent method.[17]

Histopathological analysis

The animals from each group under light ether anaesthesia were sacrificed by cervical dislocation, the pancreas and left kidneys were carefully dissected and washed with ice- cold saline and fixed in 10% formalin solution for histopathological studies.

Statistical analysis

The data's were expressed as mean ± standard error (S.E.M). The significance of differences among the groups was assessed using one way analysis of variance (ANOVA). The test followed by Dunnet's test p values less than 0.05 (95% confidence limit) were considered as significance.

RESULTS

Effect of AEETI on acute toxicity studies:

Acute toxicity studies revealed the non-toxic nature of the AEETI. There was no lethality or any toxic reaction found at any of the doses selected until the end of the study period.

Effect of AEETI on Oral Glucose tolerance test (OGTT) in normal rats

The blood glucose levels of control group increase when compared with glibenclamide treated group. Rats which are loaded with glucose (2 gm/kg p.o) after 30 min of AEETI administration both 250 mg/kg p.o and 500 mg/kg p.o reduced blood glucose levels which was comparable with that of glibenclamide (0.5 mg/kg p.o). AEETI 250 mg/kg p.o reduced blood glucose level less significantly (P<0.05) and 500 mg/kg p.o more significantly (P<0.01) when compared with control. Whereas, glibenclamide 0.5 mg/kg p.o treated animals also showed more significant (p<0.01), (p<0.001) reduction in blood glucose as compared to control. Results are shown in **Table 1** and **Fig 1.**

Effect of sub-acute treatment of AEETI on blood glucose level on STZ-NA induced diabetic rats

The blood glucose levels increased significantly (p<0.001) in STZ-NA treated group with compared to control group. In the sub-acute study the STZ-NA induced diabetic rats were treated with AEETI 250 mg/kg p.o and 500mg/kg p.o for the duration of 28 days. Treatment with AEETI 250 mg/kg significantly (p<0.05) decreased the blood glucose level after 14th day and (p<0.01) on 28th day. Whereas the treatment with AEETI 500mg/kg reduced blood glucose level significantly (p<0.05) on 7th day, which was further reduced significantly (p<0.01) on 14th, 21st and which was further reduced significantly (p<0.001) on 28th day when compared with glibenclamide 0.5mg/kg/p.o treated group. Treatment with glibenclamide 0.5mg/kg/p.o produced a significant (p<0.01) decrease in blood glucose level on 7th and 14th day which was further reduced significantly (p<0.001) on 21st and 28th day. Results are shown in **Table 2** and **Fig 2.**

Table 1: Effect of AEETI on blood glucose levels in glucose loaded hyperglycaemic rats (OGTT)

Groups	Test Sample (mg/kg)	Blood glucose levels (mg/dl)			
		30 min (glucose load)	60 min	90 min	120min
I	Control	73.45±2.39	113.20±4.43	104.0±3.01	98.10±2.40
II	AEETI-250	71.40±3.46	106.50±2.23^{ns}	99.43±2.33*	80.54±4.51*
III	AEETI-500	72.50±3.02	99.43±2.33*	86.10±2.21**	76.30±1.42**
IV	Standard (Glibenclamide)	73.50±2.24	80.54±4.51**	74.52±3.60**	69.45±2.33***

The values are expressed as mean ± SEM. Statistical significance test was done by ANOVA followed by Dunnet's test.The blood glucose values of group II, III and IV are compared with control rats values. ***p<0.001, **p<0.01, *p<0.05, ns-non significant

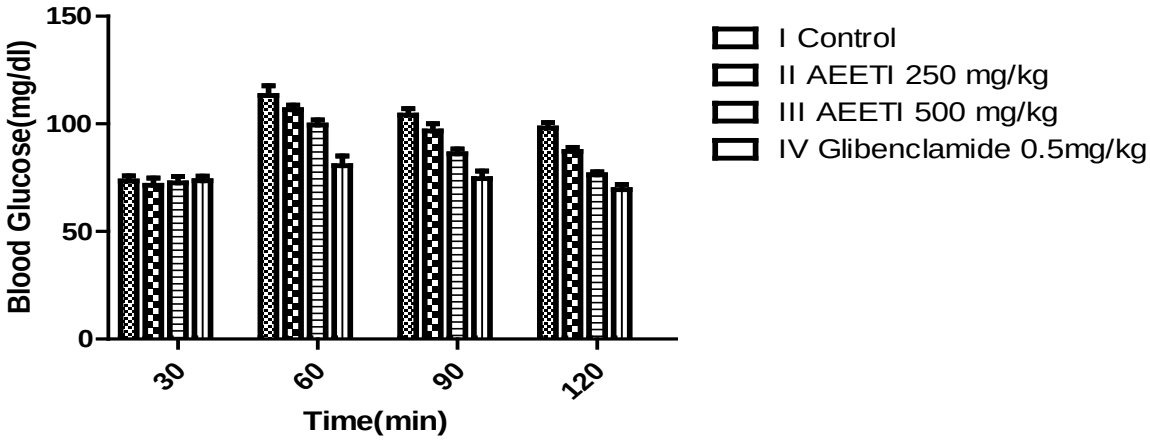

Fig. 1: Effect of AEETI on blood glucose levels in glucose loaded hyperglycaemic rats (OGTT)

Table 2: Effect of sub-acute treatment of AEETI on Blood glucose level in STZ-NA induced diabetic rats

Groups	Treatment	Fasting blood glucose level (mg/dl)				
		1st day	7th day	14th day	21st day	28th day
I	Normal (0.5 % SCMC)	73.6±2.41	72.8±3.12	73.2±2.66	73.4±3.40	72.4±2.38
II	Diabetic (0.5 % SCMC)	268.4±4.12	273.3±3.8^{a***}	278.9±3.1^{a***}	282.5±2.1^{a***}	288.5±2.3^{a***}
III	Diabetic (AEETI 250)	267.6±3.83	220.2±3.5^{bns}	192.5±2.6^{b*}	162.1±4.5^{b*}	140.3±3.0^{b**}
IV	Diabetic (AEETI 500)	269.0±5.25	198.5±4.2^{b*}	164.4±3.4^{b**}	131.3±2.3^{b***}	119.5±2.1^{b***}
V	Diabetic (Glibenclamide)	269.8±4.12	168.3±3.3^{b**}	142.6±2.4^{b**}	123.4±2.0^{b***}	110.2±1.9^{b***}

The values are expressed as mean ± SEM. Statistical significance test was done by ANOVA followed by Dunnet's t test. n= 6.a- Group II is compared with Group I. b- Groups III, IV, V are compared with group II. $^{***}p<0.001$, $^{**}p<0.01$, $^{*}p<0.05$, ns-non significant.

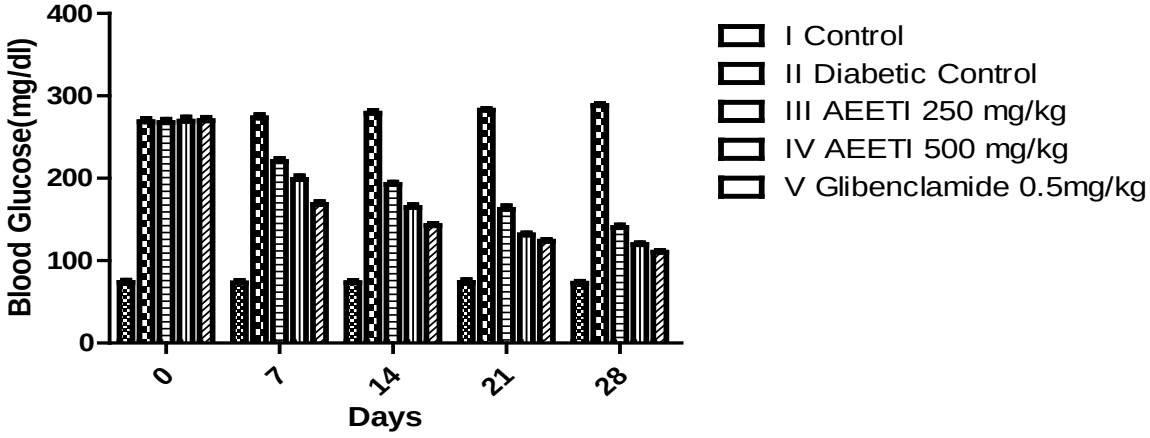

Fig. 2: Effect of sub-acute treatment of AEETI on Blood glucose level in STZ-NA induced diabetic rats

Effect of sub-acute treatment of AEETI on body weight changes on STZ-NA induced diabetic rats

The body weight was decreased significantly ($p<0.001$) in STZ-NA treated group compared to control. The AEETI at the dose levels of 250 mg/kg p.o and 500 mg/kg p.o which increased body weight significantly when compared with diabetic control. An oral dose of 250 mg/kg produced significant increase ($p<0.05$) in bodyweight after 14th day and shows more significant ($p<0.01$) from 21st day. An oral dose of 500 mg/kg p.o produce significant ($p<0.01$) increase in body weight in STZ-NA induced diabetic rats from 14th day onwards and produce significant ($p<0.001$) increase in body weight on 21st and 28th day. Standard (glibenclamide 0.5mg/kg/p.o) produced significant ($p<0.05$) improvement on 7th day and shows more significant ($p<0.01$), ($p<0.001$) improvement from 14th day in the body weight of STZ-NA induced diabetic rats.

Results are shown in **Table 3** and **Fig 3.**

Table 3: Effect of sub-acute treatment of AAETI on body weight changes in STZ-NA induced diabetic rats

Groups	Treatment	Body weight (gms)				
		1st day	7th day	14th day	21st day	28th day
I	Normal (0.5% SCMC)	223.30±8.4	224.0±7.3	225.0±7.4	225.33±6.5	226.40±6.6
II	Diabetic (0.5% SCMC)	210.10±5.4	180.0±5.2^{a***}	166.33±4.3^{a***}	158.50±4.6^{a***}	155.30±4.2^{a***}
III	Diabetic (AEETI 250 mg)	208.60±6.3	182.40±5.6^{bns}	181.45±5.3^{b*}	184.0±4.4^{b**}	187.10±4.7^{b**}
IV	Diabetic (AEETI 500 mg)	210.20±6.4	190.0±5.5^{bns}	193.45±4.2^{b**}	197.50±4.2^{b**}	200.0±3.3^{b***}
V	Diabetic (Glibenclamide 0.5 mg)	212.45±6.4	196.40±5.5^{b*}	198.50±4.7^{b**}	210.2±5.5^{b***}	205.4±4.6^{b***}

The values are expressed as mean ± SEM. Statistical significance test was done by ANOVA followed by Dunnet's t test. n= 6.a- Group II is compared with Group I. b- Groups III, IV, V are compared with group II. $^{***}p<0.001$, $^{**}p<0.01$, $^{*}p<0.05$, ns-non significant.

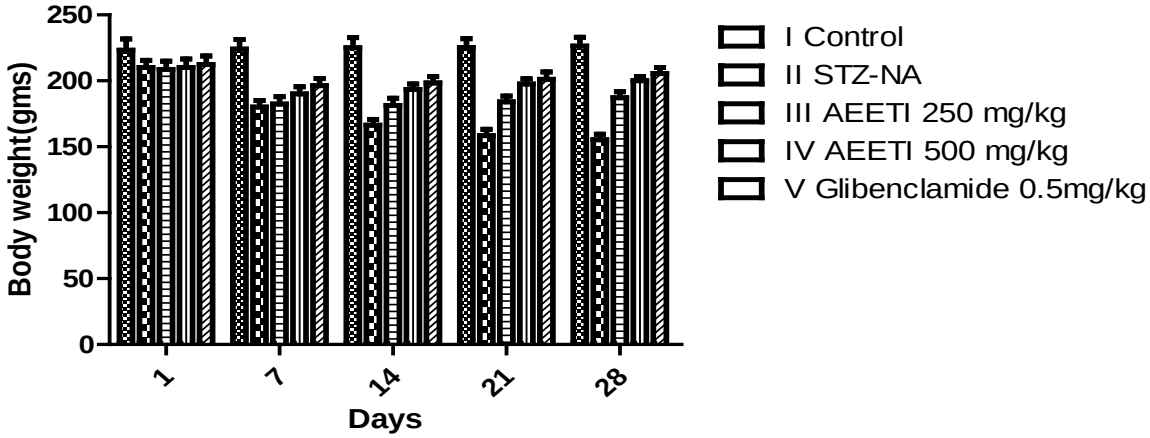

Fig 3: Effect of sub-acute treatment of AAETI on body weight changes in STZ-NA induced diabetic rats

Biochemical estimations

Glycosylated haemoglobin (HbA1c)

The diabetic control rats showed significant ($p<0.001$) increase in Glycosylated haemoglobin (HbA1c) level when compared to control rats. The Glycosylated haemoglobin (HbA1c) levels in AEETI (250 and 500 mg/kg p.o.) treated diabetic rats showed significant decrease ($p<0.05$) and ($p<0.01$) respectively. Glibenclamide 0.5 mg/kg p.o. treated diabetic rats showed significant ($p<0.001$) decrease when compared to STZ-NA induced diabetic rats. Results are shown in **Table 4.**

Glycogen level in liver and muscle:

The liver and muscle glycogen level was significantly ($p<0.001$) decreased in STZ-NA induced diabetic rats when compared to control rats. This tissue glycogen level of diabetic rats treated with AEETI (250 mg/kg p.o) and (500 mg/kg p.o) was increased significantly ($p<0.05$) and ($p<0.01$) in respective group. However glibenclamide (0.5 mg/kg) treated diabetic rats show significant ($p<0.001$) increase when compared with to STZ-NA induced diabetic rats. Results are shown in **Table 4.**

Table 4: Effect of sub-acute treatment of AAETI on Glycosylated haemoglobin (HbA1c) and Glycogen level in liver and muscle in STZ-NA induced diabetic rats:

Groups	Treatment	Glycosylated Hemoglobin (GHb%)	Liver glycogen (mg/g wet tissue)	Muscle glycogen (mg/g wet tissue)
I	Normal (0.5% SCMC)	2.87±0.21	48.50±2.01	4.33±0.21
II	Diabetic (0.5% SCMC)	7.78±0.25^{a***}	20.83±1.62^{a***}	1.50±0.23^{a***}
III	Diabetic (AEETI 250 mg)	5.67±0.32^{b*}	28.50±1.82^{b*}	2.63±0.20^{b*}
IV	Diabetic (AEETI 500 mg)	4.20±0.29^{b**}	36.51±2.12^{b**}	3.40±0.38^{b**}
V	Diabetic (Glibenclamide 0.5 mg)	3.98±0.17^{b***}	41.83±1.49^{b***}	3.95±0.37^{b***}

The values are expressed as mean ± SEM. Statistical significance test was done by ANOVA followed by Dunnet's t test. n= 6.a- Group II is compared with Group I. b- Groups III, IV, V are compared with group II. $^{***}p<0.001$, $^{**}p<0.01$, $^{*}p<0.05$.

Hypolipidemic activity of AEETI

Serum total cholesterol, triglyceride, LDL and VLDL levels were significantly elevated with a fall in HDL levels in diabetic group when compared with control group animals. Administration of AEETI at doses of 250 and 500 mg/kg p.o and standard drug glibenclamide resulted in a significant fall of these serum lipoproteins when compared to diabetic rats. After 28 days of AEETI and glibenclamide supplementation, there was a significant elevation in HDL level in serum and the results were found to be comparable to that of control rats. Results are shown in **Table 5.**

Table 5: Hypolipidemic activity of AEETI in STZ-NA induced diabetic rats

Groups	Treatment	Total cholesterol (mg/dl)	Triglyceride (mg/dl)	LDL-Cholesterol (mg/dl)	VLDL-Cholesterol (mg/dl)	HDL cholesterol (mg/dl)	VLDL-Cholesterol (mg/dl)
I	Normal (0.5% SCMC)	63.33± 4.16	57.33± 4.52	33.00± 3.18	11.47±0.904	54.50± 3.12	11.47±0.904
II	Diabetic (0.5% SCMC)	92.83± 5.31 a ***	92.50± 3.40 a ***	97.50± 4.32 a ***	18.50±0680 a***	26.83± 1.77 a ***	18.50±0680 a***
III	Diabetic (AEETI 250 mg)	84.17± 4.33 b *	69.67± 2.80 b *	65.83± 3.85 b *	16.08±0.74 b*	35.67± 2.29 b **	16.08±0.74 b*
IV	Diabetic (AEETI 500 mg)	72.83± 3.32 b **	64.33±2.82 b **	44.33± 3.46 b **	14.17±0.725 b**	49.67± 2.51 b ***	14.17±0.725 b**
V	Diabetic (Glibenclamide 0.5 mg)	68.50± 2.85 b ***	60.67±2.64 b ***	39.50± 2.64 b ***	12.12±0.375 b***	47.33± 1.89 b ***	12.12±0.375 b***

The values are expressed as mean ± SEM. Statistical significance test was done by ANOVA followed by Dunnet's t test. n= 6.a- Group II is compared with Group I. b- Groups III, IV, V are compared with group II. $^{***}p<0.001$, $^{**}p<0.01$, $^{*}p<0.05$.

Histopathology of pancreas

The histopathology of pancreas of normal control groups show normal islets and acini whereas diabetic control show damages and atrophy islets with acini. Diabetic rats treated with glibenclamide (0.5 mg/kg p.o) showed preserved normal islets in pancreas whereas AEETI 250 mg/kg p.o showed small pancreatic islets and 500 mg/kg p.o showed hyperplastic islets with acini. Results are shown in **Fig 4.**

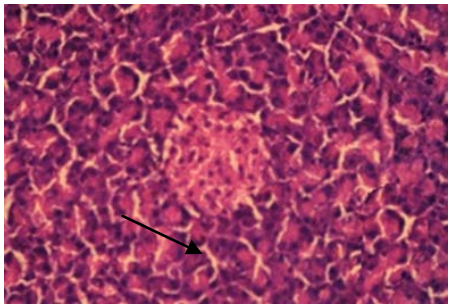

Fig 4.1 (Normal control)

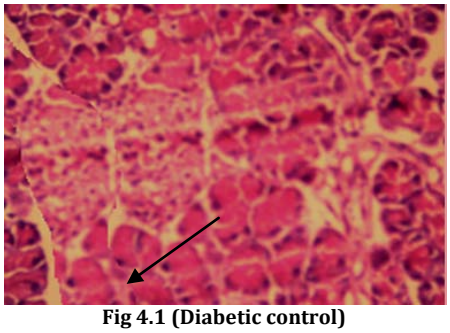

Fig 4.1 (Diabetic control)

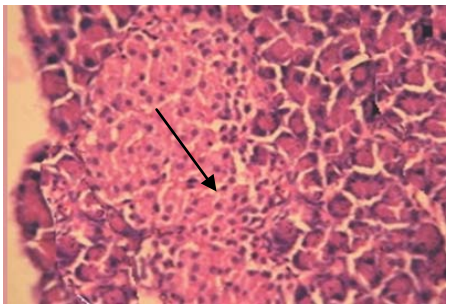

Fig 4.3 (AEETI 250 mg/kg treated)

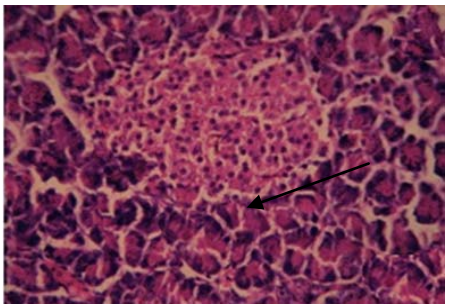

Fig 4.4 (AEETI 500 mg/kg treated)

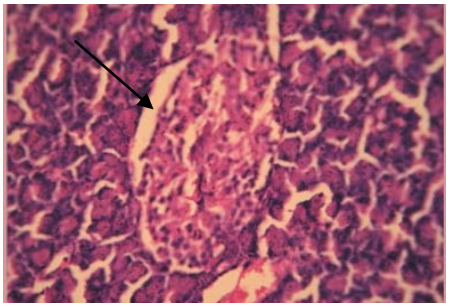

Fig 11.5 (Glibenclamide 0.5 mg/kg)

Fig. 4: Histopathology of pancreas

DISCUSSION

The AEETI showed significant improvement in glucose tolerance in glucose fed hyperglycaemic normal rats; such effect may be due the decrease in the rate of intestinal glucose absorption or due to the extra pancreatic effect including the stimulation of peripheral glucose utilization,[18] however the effect was significant when compared to standard drug glibenclamide.

STZ is an alkylating agent which causes DNA damage which results in the activation of Poly (ADP-ribose) synthetase that leads to the depletion of NAD and ATP virtually causes β cell necrosis in the experimental rats. It has been reported in various studies that administration of Poly-ADP-ribose synthetase inhibitor like nicotinamide protects the β cells by improving the level of NAD and Proinsulin whereby prevents the provocation of diabetes in the experimental rats by STZ.[19]

It has been reported that experimental diabetes induced by streptozotocin along with nicotinamide has a useful characteristics like constant hyperglycemia, glucose intolerance and glucose stimulated insulin secretion in experimental models.[12] Hence in the present work, STZ-NA induced diabetes in experimental rats was chosen as the rats model to evaluate the anti hyperglycaemic potential of *Tragia involucrata.*

A single dose administration of AEETI at a dose of 500 mg/Kg p.o significantly reduced the blood glucose level at 120 and 240 min. In the sub acute study glibenclamide treatment reduced the blood glucose level from 7th day to 28th day where as the treatment with AEETI at a dose of 250 mg/Kg p.o significantly ($p < 0.05$) decreased the blood glucose level only after 14th day and the dose of 500 mg/kg p.o significantly ($p < 0.05$) decreased the blood glucose level from 7th day and significantly ($p < 0.01$) decreased the blood glucose level from 14th day to 21st day and significantly ($p < 0.001$) decreased the blood glucose level on 28th day. However at the end of the study a marked anti-hyper glycaemic effect was observed in the AEETI treatment.

The possible mechanism involved with suppressing blood glucose levels may be by the following possibilities.

1. Reduced glucose transport or absorption from the gut.
2. Extra pancreatic action probably by stimulation of glucose utilisation in peripheral tissues.
3. Increase in glycogenic or glycolytic enzyme activities in peripheral tissues. Decrease in the secretion of counter-regulatory hormones like glucagon, growth hormones.[20]

In the current study the antidiabetic activity of AEETI was compared with standard drug glibenclamide which stimulate the secretion of insulin from β-cells by inhibiting ATP sensitive K+ channels in the plasma membrane. The hypoglycemic effect of oral administration of AEETI in STZ-NA may be by the mechanism similar to sulfonylureas is the another possible mechanism which should be explore by the detailed investigation.[16]

Histopathological studies showed prominent islet cell hyperplasia and regeneration of islet cells show a proof for the possible anti-hyperglycemic property of the AEETI.

The induction of DM ultimately causes decrease in the body weight gain due to alteration in protein turnover in the skeletal muscles. Hence a notable decrease in the body weight observed in the diabetic group of rats. Whereas the improvement of body weight gain in diabetic rats treated with AEETI 250 and 500 mg/Kg p.o highlights the blood glucose homeostasis which in turn promotes the body weight gain.[10]

Glycosylated haemoglobin is one of the easily measurable bio chemical marker which strongly correlates with the level of blood glucose during the period of 2 to 3 months and it is more reliable measure than FBG level[11].The treatment of AEETI at dose of 250 and 500 mg/Kg p.o over 28 days significantly ($p<0.05$, $p<0.01$) reduced the HbA1c levels in respective group compared to the diabetic control.

Insulin is the main regulator of glycogenesis in the muscle and liver. The decrease of liver glycogen level observed in diabetic rats may be due to lack of insulin in diabetic condition or oxidative stress in diabetes may inactivate the glycogen synthetase. The marked reduction in the liver and muscle glycogen level is observed in STZ-NA induced diabetic rats and the treatment with AEETI showed significant ($p<0.05$ and $p< 0.01$) increase in the glycogen level in the liver and muscle.[10]

Hyperlipidemia is pathological state observed in the DM, elevated serum total cholesterol, triglycerides, LDL- cholesterol, VLDL-cholesterol and reduced serum HDL level consequently increases the risk of diabetic complications and atherosclerosis. In the present study treatment with AEETI at the dose of 250 mg/Kg/p.o and 500 mg/Kg/p.o significantly ($p<0.05$ and $p<0.01$) reduced the total cholesterol, triglycerides, LDL- cholesterol, VLDL- cholesterol and significantly ($p<0.01$ and $p<0.001$) increased the HDL levels. This effect may not only due to better glycaemic control but also due to its action on the lipid metabolic pathway.[18]

CONCLUSION

Based on the results obtained, we can conclude that the aqueous ethanolic extract of *Tragia involucrata* Linn. At 250 and 500 mg/kg showed significant antidiabetic and hypolipidemic potential in dose dependant manner which could be used as the supportive treatment of diabetes mellitus for better glycemic control and the AEETI also offers effective hypolipidemic effect which may lowers the diabetes associated cardiovascular complications.

However, further studies are required to establish the anti diabetic and hypolipidemic potential of *Tragia involucrata* in terms of molecular mechanism(s) involved in the activity.

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