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HYPOGLYCEMIC AND ANTIDIABETIC ACTIVITY OF AERIAL PARTS OF *CORALLOCARPUS EPIGAEUS* IN NORMAL AND STREPTOZOTOCIN INDUCED DIABETIC RATS

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ABSTRACT

Alcoholic and aqueous extract of aerial parts of *Corallocarpus epigaeus* (CE) were prepared and given orally at different doses to different groups of rats fasted for 18 h (both normal and streptozotocin (STZ) induced diabetic rats). The serum glucose levels were measured initially at 0 h and at 0.5,1,2,3,4,6,8,12,16,20 and 24 h after the treatment. The alcoholic extract of aerial parts of *C.epigaeus* (AEACE) at medium dose (200 mg/kg) and higher dose (400 mg/kg) produced maximal serum glucose lowering effect in both normal and STZ induced diabetic rats. The aqueous extract of aerial parts of *C.epigaeus* (AQEACE) produced maximal percent reduction in serum glucose levels at higher dose (400 mg/kg) both in normal and STZ induced diabetic rats. AEACE and AQEACE produced biphasic response with peak hypoglycemic and antidiabetic activities recorded out at 4 h and 8 h intervals in a dose dependent manner, the effect was found to be better than that of standard gliclazide (2 mg/kg) an oral hypoglycemic agent.

KEYWORDS

Corallocarpus epigaeus, Hypoglycemic, Gliclazide, Streptozotocin and Antidiabetic activity.

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INTRODUCTION

Diabetes mellitus (DM) is a chronic metabolic disorder characterized by elevated blood glucose concentration known as hyperglycemia. DM involves altered metabolism of carbohydrates, fats and proteins, which is associated with absolute (or) relative deficiencies in insulin secretion and / or insulin action. The characteristics symptoms of DM are polyuria, polydipsia, pruritus and unexpected

weight loss, etc. The management of DM involves utilization of various drugs for long period of time to save life and alleviate symptoms. The usage of synthetic oral hypoglycemic agents (OHAS) and insulin (Holman and Turner, 1991[1], Prout, 1974[2], Kameswara Rao *et al.,* 1997)[3] for chronic period, as in case of treatment of diabetes, may cause severe adverse effects and are also costlier for the common man to use. This leads to increase in demand for natural products with antidiabetic activity and less side effects. Traditional/folklore medicines are only alternatives in such conditions. The traditional practitioners, folklore herbalists and local tribes of Tirumala Hills region (which lie geographically in the South-Eastern Ghats of Andhra Pradesh state, India) claims that tuberous herbs are of great use in controlling the DM. The available literature shows that there are about 248 species, listed in the Flowering Plants of Chittoor District for treating diabetes (Madhava Chetty, 2008)[4]. Though some of the plants are reputed in the indigenous systems of medicine for their activities, it requires scientific evaluation.

Corallocarpus epigaeus (Syn: Broyonia epigaea) belongs to the family *Cucurbitaceae.* Known locally as Nagadonda and Akasagaruda. It is distributed in Punjab, Sind, Gujarat, Rajputana, Andhra Pradesh and Ceylon. In Andhra Pradesh, the plant is available at lower hill slopes, especially on hedges, Nagapatla reserve forest and Talakona hills of Tirumala. The plant CE is reported to possess antidiabetic activity (Madhav Chetty, 2008)[4] and was claimed that bitter principles present in the plant parts of most species of *Cucurbitaceae* are responsible for hypoglycemic activity (Sadyojatha and Vaidya, 1996)[5]. The survey of literature revealed that, no systematic and scientific studies have been carried out on CE, hence in the present study attempts are made to investigate the hypoglycemic and antidiabetic effects of different doses of alcoholic and aqueous extracts of aerial parts of *C.epigaeus* (ACE) in normal and STZ induced diabetic rats.

MATERIAL AND METHODS

Collection of plant material

Aerial parts of CE collected from Tirumala hills and were identified by a botanist Prof. P. Jayaraman Ph.D, Director, Plant Anatomy Research Center (PARC) West Tambaram, Chennai-45, India. A voucher specimen was deposited in the herbarium of the PARC, Chennai (voucher number PARC/2008/182). This plant material was dried in shade at room temperature and ground to optimal coarse powder.

Preparation of extracts

The above powdered material was subjected to a successive solvent extraction with petroleum ether (40-60^{0}C), chloroform, alcohol (95%) and water. Extraction was carried out for 16 h with each solvent by Soxhlet extractor. The yield of extracts was as follows, petroleum ether (2.21% w/w), chloroform (2.18% w/w) alcoholic (4.15% w/w) and aqueous (5.95% w/w). The active bitter principle(s) extracted in alcohol and water was screened pharmacologically for hypoglycemic and antidiabetic activity.

Animals

Albino rats (Wistar strain) of either sex weighing between 150-200 g were procured from Sainath Agencies, Hyderabad-48. These animals were housed in standard environmental conditions in polyethylene cages (20x25x35cm) maintained at controlled room temperature (27±2^{0}c), relative humidity (45-55%) and light/dark cycle (12 : 12 h) and fed with standard commercial rat pellet diet (Amrut Laboratories, Pranav Agro industries Ltd. Sangli, India) and water *ad libitum.* The animals were acclimatized to the laboratory conditions. All the experimental procedures were performed according to the committee for the purpose of control and supervision of experiments on animals (Reg. number 557/02/c/CPCSEA) and approved by the Institutional Animal Ethical Committee (IAEC) of V.L. College of Pharmacy, Raichur, Karnataka, India.

Toxicity studies

The oral acute toxicity of the extracts was performed by using Albino mice of either sex

weighing between 16-25 g as per the OECD guidelines No. 425 by fixed dose method. The LD_{50} of AEACE and AQEACE was found to be 2000 mg/kg. Therefore $1/20^{th}$ (100 mg/kg), $1/10^{th}$ (200 mg/kg) and $1/5^{th}$ (400 mg/kg) doses were selected for the present study.

Induction of diabetes

Streptozotocin (STZ) Biomol International, U.S.A., was freshly prepared by dissolving in distilled water just before use. Diabetes was induced in 18 h fasted Albino rats of Wistar strain of either sex (150-200 g) by intraperitoneal injection of STZ 60 mg/kg (Gerhard vogel, 1997,[6] Gupta, 2004,[7] Ghosh, 2005)[8]. The rats were then given 5% w/v glucose solution in feeding bottles for the next 24 h to prevent hypoglycemia. After 72 h, rats with marked hyperglycemic fasting blood glucose > 250 mg/dl were selected and were used for the study. All the animals were allowed free access to water and pellet diet and maintained at standard husbandry conditions.

Experimental design

Different groups of rats were used for studying the hypoglycemic and antidiabetic effects of AEACE and AQEACE. The rats were divided into 16 groups each consisting of 6 rats.

Group1: Normal rats treated with vehicle control (0.5 ml), p.o.
Group2: Normal rats treated with gliclazide (2 mg/kg), p.o.
Group3: Normal rats treated with 100 mg/kg of AEACE, p.o.
Group4: Normal rats treated with 200 mg/kg AEACE, p.o.
Group5: Normal rats treated with 400 mg/kg AEACE, p.o.
Group6: Normal rats treated with 100 mg/kg of AQEACE, p.o.
Group7: Normal rats treated with 200 mg/kg of AQEACE, p.o.
Group8: Normal rats treated with 400 mg/kg of AQEACE, p.o.
Group9: Diabetic rats treated with vehicle control (0.5 ml), p.o.
Group10: Diabetic rats treated with gliclazide (2 mg/kg), p.o.
Group11: Diabetic rats treated with 100 mg/kg of AEACE, p.o.
Group12: Diabetic rats treated with 200 mg/kg of AEACE, p.o.
Group13: Diabetic rats treated with 400 mg/kg of AEACE, p.o.
Group14: Diabetic rats treated with 100 mg/kg of AQEACE, p.o.
Group15: Diabetic rats treated with 200 mg/kg of AQEACE, p.o.
Group16: Diabetic rats treated with 400 mg/kg of AQEACE, p.o.

All the animals were subjected to fasting for 18 h prior to experimentation and during the course of time the animals had free access to water. Different doses of both the extracts were suspended in distilled water and administered orally by gastric intubation, using a force feeding needle to the above mentioned groups of rats respectively. Groups 1 and 9 were served as normal and diabetic controls and received 0.5 ml vehicle (distilled water with few drops of 0.1N NaOH). Groups 2 and 10 received gliclazide 2 mg/kg orally. Blood samples were withdrawn from the tail vein initially at 0 h (before the treatment) and once again at 0.5, 1, 2, 3, 4, 6, 8, 12, 16, 20 and 24 h time intervals after the treatment. The collected blood samples were centrifuged (3000 rpm for 20 min) to get clear serum. The separated serum was used for estimation of glucose levels by GOD/POD method (Trinder, 1969)[9] using commercial glucose kit (Span Diagnostics Ltd., Surat, India) by semi-auto analyzer (ERBA Mannheim, CHEM-5 plus v2 Germany).

Statistical analysis

Results were expressed as mean ± SD (n=6) and data were analyzed by one way ANOVA followed by Dunnett's test. The level of significance was setup at $p < 0.05$*, 0.01** and 0.001*** respectively.

RESULTS

The AEACE and AQEACE at different dose levels produced a biphasic response with maximum percentage reduction in serum glucose levels at 4 h and 8 h time intervals in normal and STZ induced diabetic Albino rats. Whereas the standard drug gliclazide (2 mg/kg) produced a biphasic response at 2 h and 8 h.

The AEACE at different doses (100, 200, 400 mg/kg) has reduced the serum glucose levels in normal healthy Albino rats by (29.31±0.16%) at 4 h, (23.52±0.43%) at 8 h / 100 mg/kg, (41.63±0.32%) at 4 h, (36.15±0.48%) at 8 h / 200 mg/kg and (44.90±0.98%) at 4 h, (40.29±0.25%) at 8 h / 400 mg/kg respectively. Similarly AQEACE at 100, 200 and 400 mg/kg has reduced the serum glucose levels by (24.96±0.07%) at 4 h, (23.81±0.27%) at 8 h and (34.43±0.34%) at 4 h, (31.65±0.36%) at 8 h and (43.45±0.50%) at 4 h, (37.64±0.05) at 8 h respectively. Gliclazide (2 mg/kg) has produced percentage reduction in serum glucose levels (40.41 ± 0.30) at 2 h and (35.57 ± 0.23) at 8 h intervals in normal healthy Albino rats.

The detailed results of the percentage reduction in serum glucose levels of AEACE and AQEACE in normal rats are compiled in table 1 and figures 1 and 2 respectively.

The antidiabetic activity of AEACE with different dose levels (100, 200, 400 mg/kg) has produced reduction in serum glucose levels in STZ induced diabetic rats by (31.76±0.11%) at 4 h, (28.53±0.15%) at 8 h/(100 mg/kg), (45.25±0.81%) at 4 h, (40.47±0.46%) at 8 h/(200 mg/kg) and (48.44±0.35%) at 4 h, (42.12±0.40%) at 8 h/(400 mg/kg) respectively. Similarly AQEACE has produced reductions in serum glucose levels by (27.68±0.06%) at 4 h, (25.12±0.16%) at 8 h/(100 mg/kg), (36.38±0.07%) at 4 h, (35.33±0.40%) at 8 h/(200 mg/kg) and (47.50±0.06%) at 4 h, (41.14±0.38%) at 8 h/(400 mg/kg) respectively. In STZ induced diabetic Albino rats gliclazide (2 mg/kg) has produced percentage reduction in serum glucose levels (45.34 ± 0.41) at 2 h and (38.91 ± 0.20) at 8 h intervals.

The detailed results of the percentage reduction in serum glucose levels of AEACE and AQEACE in STZ induced diabetic rats are compiled in table 2 and figures 3 and 4 respectively.

The hypoglycemic and antidiabetic activity produced by different doses of AEACE at 200 mg/kg and 400 mg/kg was comparable and better than that of the standard gliclazide (2 mg/kg). Whereas the hypoglycemic and antidiabetic activity of AQEACE at higher dose (400 mg/kg) was comparable and even more than the effect of standard gliclazide (2 mg/kg).

DISCUSSION

In the present study, the hypoglycemic and antidiabetic activity of vehicle, gliclazide, different doses of AEACE and AQEACE were evaluated in normal and STZ induced diabetic rats. The oral administration of gliclazide (2 mg/kg), different doses of AEACE, AQEACE (100, 200, and 400 mg/kg) doses have produced a significant reduction in serum glucose levels both in normal and STZ induced diabetic rats, but the vehicle has no effect on serum glucose levels.

STZ [2-deoxy-2-(3-methyl-3-nitrosourea) 1-D-glucopyranose], a broad spectrum antibiotic, produced from *Streptomyces achromogens*. The diabetogenic property of STZ was first described by Rakieten *et al.,* (1963)[10] and is well known for its selective cytotoxicity of pancreatic islet of β-cells and has been extensively used to induce diabetes mellitus in animals. It interferes with cellular metabolic oxidative mechanisms. STZ has shows a triphasic response on serum glucose levels. Initially, serum glucose is increased after 3 h, reaching values of 150 - 200 mg%. 6-8 h after STZ induction, the serum insulin values are increased up to 4 times, resulting in a hypoglycemic phase which is followed by persistent hyperglycemia by 24-48 h after STZ administration (Papaccio *et al.,* 2000,[11] koneri raju *et al.,* 2008,[12] Ghosh, M.N., 2005,[8] Gerhard Vogel, H., 1997,[6] Gupta, S.K., 2004)[7].

In normal and STZ induced diabetic Albino rats, single dose treatment of gliclazide a sulphonylurea drug produced biphasic (maximum reduction in

serum glucose levels at 2 different time intervals) response on serum glucose levels at 2 h and 8 h. The biphasic response of gliclazide in rat model may be due to its entrohepatic circulation in rats (Miyazaki *et al.,* 1983,[13] Benakis *et al.,* 1980)[14]. Gliclazide acts by both pancreatic (Insulin release by K^+ channel inhibition in the β-cells) and extra pancreatic (tissue uptake of glucose) mechanisms. The target for sulphonylurea activity is ATP sensitive K^+ channel (K^+ ATP channel). The sulphonylureas and related drugs used in type II diabetes stimulate insulin by closing K^+ ATP channels in pancreatic β-cells. The sulphonylureas target the sulphonylurea receptor (SUR) subunit of K^+ ATP channels, which exists in several isoforms expressed in different tissues, SUR 1 in pancreatic β-cells, SUR 2A in cardiac muscle and SUR 2B in vascular smooth muscle (Gribble, F.M., Reimann, F, 2003)[15]. The pancreatic β-cells ATP increase when plasma glucose level rises resulting in the closure of K^+ ATP channel in plasma membrane, allows the cells to depolarize, triggering Ca^{2+} entry and insulin release (Eswar kumar *et al.,* 2008,[16] Gopalakrishna Muthy and Mayuren, 2008)[17].

The AEACE at 200 and 400 mg/kg exhibited good biphasic response with peak hypoglycemic and antidiabetic activity at 4 and 8 h time intervals in normal and STZ induced diabetic rats when compared with gliclazide (2 mg/kg). However at 100 mg/kg of AEACE produced moderate reduction in serum glucose levels at 4 and 8 h.

The AQEACE at 400 mg/kg showed promising biphasic response with peak hypoglycemic and antidiabetic activity at 4 and 8 h time intervals with respect to gliclazide. Whereas the medium dose (200 mg/kg) of AQEACE produced moderate hypoglycemic and antidiabetic activity. At low dose levels (100 mg/kg) the AQEACE produced marginal reduction in serum glucose levels at 4 and 8 h.

It may be noted that the AEACE and AQEACE showed hypoglycemia in a dose dependent manner. The AEACE has higher and better hypoglycemic and antidiabetic activity for a prolonged period than that of AQEACE.

It is evident from the literature that voluminous amount of research has been done on various species and has established the high usefulness of it in controlling diabetes. Though there are more than 90 genera in *Cucurbitaceae*, extensive research was carried out on *Momordica* genus. *M.charantia* and *M.foetida* have been reported to have hypoglycemic effects (Akhtar *et al.,* 1981,[18] Liaquat *et al.,* 1994)[19], Iclal cakici *et al.,* 1994[20] have shown that aqueous extract of *M.Charantia* fruit reduced the fasting glucose levels of both hyperglycemic and normoglycemic in mice. *M.Charantia* aqueous extract (2.5 g/kg b.w.) produced 45% of hypoglycemic activity in normal rats after 4 h of treatment (Karunanayake *et al.,* 1984)[21]. Higashino *et al.* (1992)[22] showed 34% of hypoglycemic activity of water soluble fraction of *M.Charantia* after 3 h in streptozotocin induced diabetic rats. Welihinda *et al* (1982)[23] demonstrated that an aqueous extract from the *M.Charantia was* a potent stimulator of insulin release from β-cells rich pancreatic islets isolated from obese-hyperglycemic mice. The aqueous extract of *M.cymbalaria* at a dosage of 0.5 g/kg is showing maximum blood glucose lowering effect in diabetic rats (Kameswara Rao *et al.,* 2001)[24]. Some of the plants reported for their antidiabetic activity by increasing serum insulin levels significantly, those includes *Gymnema sylvestre* increases insulin secretion probably by regeneration of pancreatic β-cells (Baskaran *et al.,* 1990)[25], *Aegle marmelos* (Kamalakaran *et al.,* 2006)[26], *Ephedra sinica Stapf*., and *E.ditachya* (Xiu *et al.,* 2001)[27] are reported to regenerate atrophied pancreatic islets, restore the secretion of insulin and thus corrected hyperglycemia. *M.Charantia* fruit is reported to have insulin secretagogue and Insulinomimetic activity (Raman *et al.,* 1996)[28]. *Trigonella foenumgraecum* and *Allium satium* L (Augusti *et al.,* 1996)[29] are reported to act by stimulating insulin secretion. One of the main constituent of *M.Charantia* is a steroidal saponins, charantin and is responsible for the antidiabetic effect of the fruit; it is also contains momordicine and insulin like steroidal saponin (Manomoodally *et al.,* 2007)[30].

Koneri Raju and Balaraman, R., (2008)[12] studied the antidiabetic mechanisms of saponins of *M. cymbalaria* in STZ induced diabetic rats.

In view of the above, the hypoglycemic and antidiabetic activity of CE may be due to its stimulating effect on the remnant β-cells or improvement in insulin action at cellular level or it could also be due to the insulin like effect of the active principle(s) present in the extract. Steroidal saponins are reported for the antidiabetic activity. The preliminary phytochemical investigation of the above two extracts also revealed the presence of steroidal saponins, hence these can be accounted for hypoglycemic and antidiabetic activities.

Table No.1: Hypoglycemic activity of AEACE and AQEACE in normal Albino rats

% Reduction in serum glucose levels at different time intervals								
Groups →	**Control (0.1N NaOH)**	**Gliclazide**	**Alcoholic extract of aerial parts of *C.epigaeus***			**Aqueous extract of aerial parts of *C.epigaeus***		
Dose (mg/kg) →	**0.5 (ml)**	**2**	**100**	**200**	**400**	**100**	**200**	**400**
Time (h)↓	**mean ± SD**	**mean ± SD**	**mean ± SD**	**mean ± SD**	**mean ± SD**	**mean ± SD**	**mean ± SD**	**mean ± SD**
0	-	-	-	-	-	-	-	-
0.5	0.79 ± 0.30	11.02±0.15**	1.73 ± 0.54**	3.57±0.87**	5.58±0.44**	0.88±0.10	1.24±0.34	3.73±0.15**
1	0.30 ± 0.66	23.24±0.19**	8.09±0.69**	10.95±1.52**	12.01±0.44*	4.17±0.13**	5.83±0.28**	6.69±0.49**
2	0.01 ± 0.19	40.41±0.30**	14.86±0.54**	18.99±0.33**	19.95±0.40*	7.74±0.21**	9.21±0.43**	10.09±0.40**
3	1.11 ± 0.87	26.04±0.27**	18.60±0.29**	24.05±0.46**	28.28±0.47*	12.35±0.14**	19.86±0.30**	22.29±0.55**
4	-0.07 ± 0.89	7.52 ± 0.16**	29.31±0.16**	41.63±0.32**	44.90±0.98*	24.96±0.07**	34.43±0.34**	43.45±0.50**
6	0.06 ± 0.46	19.86±0.31**	19.42±0.31**	27.26±0.58**	32.59±0.27*	17.26±0.16**	26.70±0.27**	31.82±0.03**
8	1.55 ± 0.87	35.57±0.23**	23.52±0.43**	36.15±0.48**	40.29±0.25*	23.81±0.27**	31.65±0.36**	37.64±0.05**
12	0.18 ± 0.96	19.86±0.39**	20.68±1.95**	28.02±2.78**	38.69±2.45*	17.24±0.02**	25.94±1.60**	33.40±2.93**
16	-0.07 ± 0.48	10.45±0.28**	16.18±2.91**	20.67±2.71**	36.95±1.59*	13.43±2.61**	20.22±1.82**	25.87±2.71**
20	2.37 ± 0.28	4.39 ± 0.25	12.73±2.77**	16.75±2.44**	25.92±2.92*	9.14±2.90**	14.52±2.78**	20.00±2.74**
24	1.03 ± 0.08	1.90 ± 0.19**	7.49±2.71**	9.78±2.78**	18.10±1.74*	4.97±1.94	8.41±2.56	14.12±2.76**

n=6 significant at $p<0.05$*, 0.01** and 0.001***.

Table No.2: Antidiabetic activity of AEACE and AQEACE in streptozotocin induced diabetic albino rats

% Reduction in serum glucose levels at different time intervals								
Groups →	**Control (0.1N NaOH)**	**Gliclazide**	**Alcoholic extract of aerial parts of *C.epigaeus***			**Aqueous extract of aerial parts of *C.epigaeus***		
Dose (mg/kg) →	**0.5 (ml)**	**2**	**100**	**200**	**400**	**100**	**200**	**400**
Time (h)↓	**mean ± SD**	**mean ± SD**	**mean ± SD**	**mean ± SD**	**mean ± SD**	**mean ± SD**	**mean ± SD**	**mean ± SD**
0	-	-	-	-	-	-	-	-
0.5	0.64 ± 0.15	15.81±0.15**	1.83 ± 0.15*	4.53 ± 0.80**	6.81 ± 0.83**	1.86 ± 0.65*	4.8 ± 0.21**	6.58 ± 0.35**
1	0.13 ± 0.39	30.25±0.91**	12.51 ± 0.98**	15.44 ± 0.22**	18.03 ± 0.74**	11.15 ± 0.34**	13.01 ± 0.35**	16.06 ± 0.45**
2	0.29 ± 0.40	45.34±0.41**	18.89 ± 0.83**	25.37 ± 1.14**	27.28 ± 0.30**	16.57 ± 0.49**	21.09 ± 0.49**	25.90 ± 0.50**
3	0.62 ± 0.54	32.34±0.53**	25.53 ± 0.73**	33.49 ± 0.33**	39.25 ± 0.62**	21.85 ± 0.12**	27.92 ± 0.11**	37.13 ± 0.11**
4	0.18 ± 0.51	16.08±0.50**	31.76 ± 0.11**	45.25 ± 0.81**	48.44 ± 0.35**	27.68 ± 0.06**	36.38 ± 0.07**	47.50 ± 0.06**
6	0.40 ± 0.03	22.85±0.03**	19.54 ± 0.06**	23.24 ± 0.55**	28.69 ± 0.40**	14.45 ± 0.15**	17.95 ± 0.15**	21.86 ± 0.19**
8	-0.14 ± 0.96	38.91±0.20**	28.53 ± 0.15**	40.47 ± 0.46**	42.12 ± 0.40**	25.12 ± 0.16**	35.33 ± 0.40**	41.14 ± 0.38**
12	0.04 ± 0.74	23.82±0.34**	24.04 ± 1.72**	33.44 ± 2.26**	40.80 ± 0.02**	20.77 ± 2.72**	29.07 ± 0.03**	37.00 ± 0.04**
16	0.41 ± 0.60	16.78±0.49**	19.52 ± 2.73**	26.30 ± 2.74**	39.07 ± 0.14**	16.42 ± 2.49**	22.81 ± 0.06**	30.21 ± 0.01**
20	0.07 ± 1.01	7.30 ± 0.12**	15.03 ± 1.84**	19.16 ± 2.90**	26.16 ± 0.03**	12.11 ± 2.88**	16.55 ± 0.04**	22.56 ± 0.12**
24	0.28 ± 0.28	0.96 ± 0.06**	10.60 ± 1.86**	11.99 ± 2.49**	20.78 ± 0.01**	7.66 ± 0.13**	10.26 ± 1.72**	16.42 ± 0.06**

n=6 significant at p<0.05*, 0.01** and 0.001***.

Hypoglycemic activity of AEACE and AQEACE in normal Albino rats

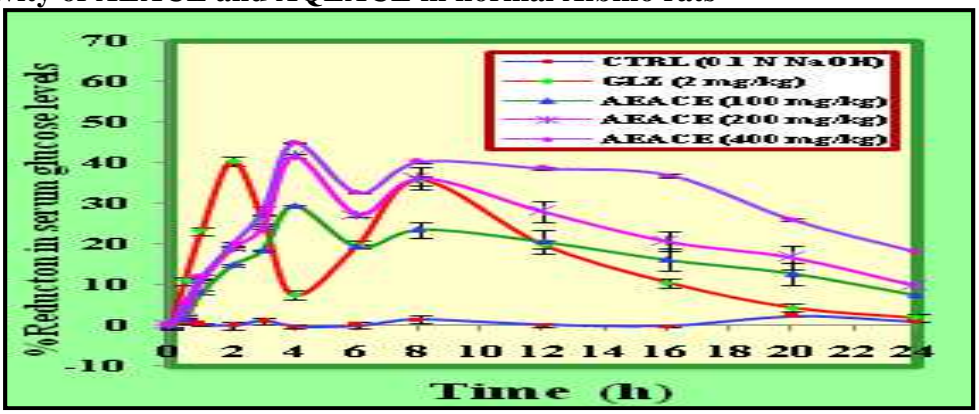

Figure No.1: % Reduction in serum glucose levels of AEACE at different time intervals

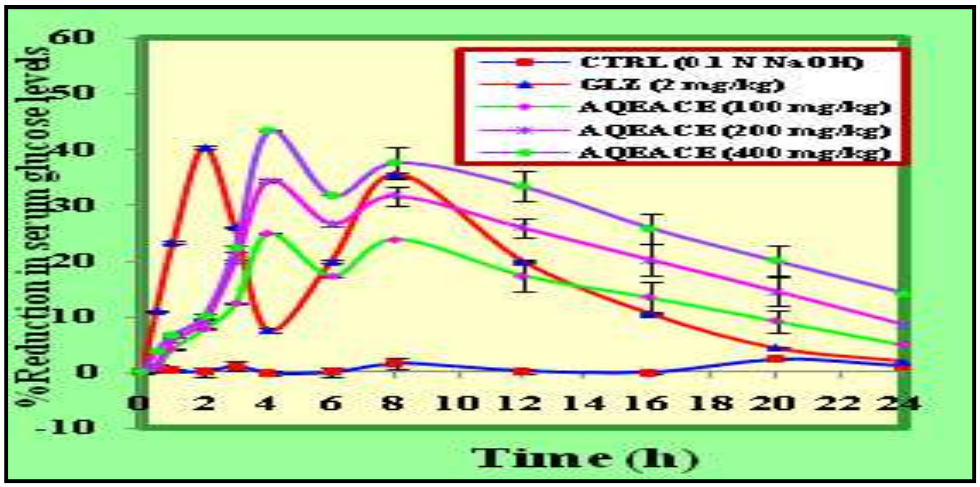

Figure No.2: % Reduction in serum glucose levels of AQEACE at different time intervals

Antidiabetic activity of AEACE and AQEACE in STZ induced diabetic Albino rats

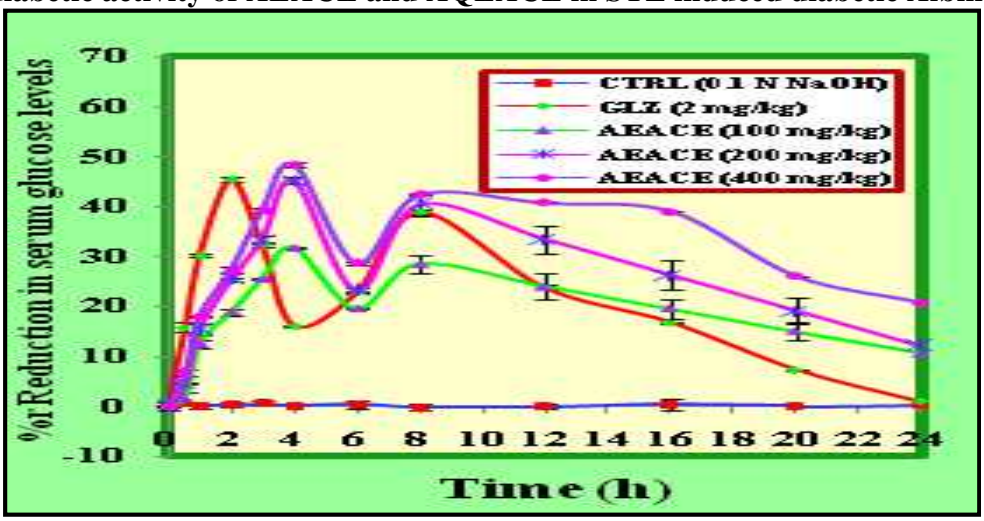

Figure No.3: % Reduction in serum glucose levels of AEACE at different time intervals

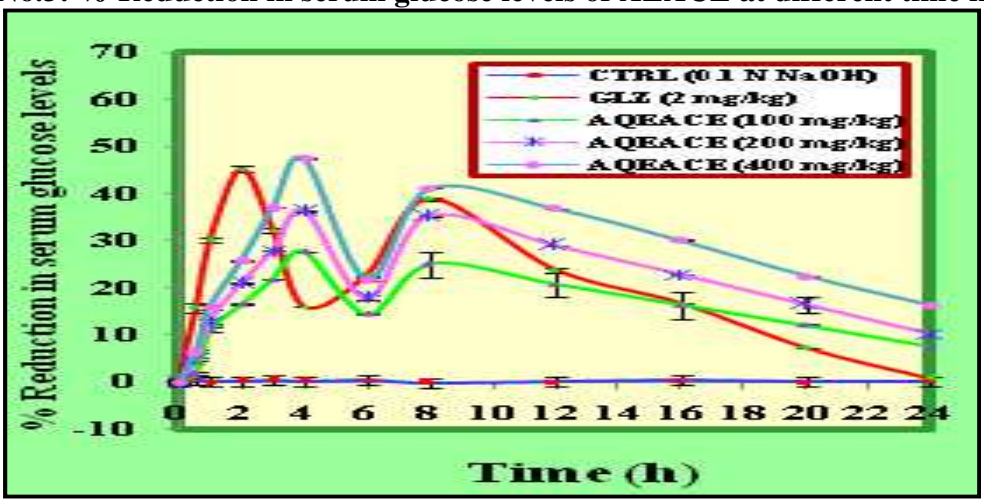

Figure No.4: % Reduction in serum glucose levels of AQEACE at different time intervals

CTRL- Control, GLZ- Gliclazide, AEACE- Alcoholic extract aerial parts of C. epigaeus

CONCLUSION

From this study it can be concluded that AEACE and AQEACE possess beneficial effects on serum glucose levels in normal and STZ induced diabetic Albino rats. Further pharmacological and biochemical investigations are under progress to elucidate the mechanism(s) of the hypoglycemic/antidiabetic effects and biphasic response of both the extracts.

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CONFLICT OF INTEREST

We declare that we have no conflict of interest.

BIBLIOGRAPHY

1. Holman R R, Turner R C. Oral agents and insulin in the treatment of NIDDM. In: Pickup, J., William, G. (Eds.), Textbook of Diabetes, *Blackwell, Oxford,* 4th Edition, 1991, 467- 469.
2. Prout T E. In: Malaisse, W J, Pirart J. (Eds.), Proceedings VIII Congress of International Diabetes Federation, *Excerpta Medica, Amstredam,* 1974, 162.
3. Kameswara Rao B, Giri R, Kesavulu M M, Apparao C H. Herbal Medicine: In the management of Diabetes mellitus, *Manphar Vaidhya Patrika,* 1(4-5), 1997, 33-35.
4. Madhava Chetty K, Sivaji K, Tulasi Rao K. Flowering plants of Chitoor District Andhra Pradesh, *India.* 256, 2008, 522-525.
5. Sadyojatha A M, Vaidya V P. Chemical constituents of the roots of *Momordica dioica, Indian Drugs,* 33(9), 1996, 473-475.
6. Gerhard Vogel H. Drug Discovery and Evaluation of Pharmacological Assays, *Springer-verlag Berlin Heidelberg publication, Germany,* 2nd Edition, 1997, 951.
7. Gupta S K. Drug Screening Methods, *Jaypee Brothers, New Delhi,* 1st Edition, 2004, 308.
8. Ghosh M N. Fundamentals of Experimental Pharmacology, *Hilton and company, Kolkata,* 3rd Edition, 2005, 242.
9. Trinder P. Determination of glucose in blood using glucose oxidase with on alternative oxygen receptor, *Ann. Clin. Biochem,* 6(1), 1969, 24-27.
10. Rakieten N, Rakieten M L, Nadkarni M V. Studies on the diabetogenic action of streptozotocin, *Cancer Chemother. Rep,* 29(105), 1963, 91-98.
11. Papaccio G, Pisanti F A, Latronico M V, Ammendola E, Galgieri M. Multiple low dose and single high dose treatments with streptozotocin do not generate nitric oxide, *J. Cell. Biochem,* 77(1), 2000, 82-91.
12. Koneri Raju, Balaraman R. Antidiabetic mechanisms of saponins of *Momordica cymbalaria, Phcog. Mag,* 4(15), 2008, 197-206.
13. Miyazaki H, Fujii T, Yoshida K, Arakawa S and Furukawa H. Disposition and metabolism of (H3) gliclazide in rats, *Eur. J. Drug. Metab. Pharmacokinet,* 8(2), 1983, 117-131.
14. Benakis A and Glasson B. Metabolic study of 14 C-labelled Gliclazide in normal rats and in rats with streptozotocin induced diabetes, *in Gliclazide and Treatment of Diabetes Academic press and the Royal Society of Medicine, London, UK,* 1980, 57-69.
15. Gribble F M, Reimann F. Differential selectivity of insulin secretogogues: mechanism, clinical implications and dug interactions, *J. Diabetes complications,* 17(2), 2003, 11-15.
16. Eswar Kumar K, Ramesh A, Satyanarayana S. Pharmacodynamic and Pharmacokinetic Drug Interaction of Gliclazide and

Lacidipine in Animal Models, *Indian J. Pharm. Educ. Res,* 42(3), 2008, 277-282.
17. Gopala Krishna Murthy T E, Mayuren C. Influence of calcium channel antagonist on the pharmacodynamics of a second - generation sulfonylurea in rats and rabbits, *Asian J. Pharm,* 2(3), 2008, 163-166.
18. Akhtar M S, Athar M A, Yaqub M. Effect of *Momordica charantia* on the blood glucose level of normal and alloxan diabetic rabbits, *Planta Medica,* 42(3), 1981, 205-212.
19. Liaquat A, Khan A A, Mamun M I, Mosihuzzaman M, Nahar N, Alam M N, Rokeya B. Studies on hypoglycaemic effects of fruit pulp, seed and whole plant of *Momordica charantia* on normal and diabetic model rats, *Planta Medica,* 59(5), 1994, 408-412.
20. Iclal cakici, Canset Huragin, Bahar tunctan, Nurettin Abacioglu, Ilker Kanzik, Bilge Sever. Hypoglycaemic effect of *Momordica charantia* extracts in normoglycaemic or cyproheptadine induced hyperglycaemic mice, *J. Ethnopharmacol,* 44(2), 1994, 117-121.
21. Karunanayake E H, Welihinda J, Sirimanne S R, Sinnadorai G. Oral hypoglycemic activity of some medicinal plants of Srilanka, *J. Ethnopharmacol,* 11(2), 1984, 223-231.
22. Higashino H, Suzuk A, Tanaka Y, Pootakhan K. Hypoglycemic effects of Siamese *M. charantia* and *Phyllanthus urinaria extract* in Stz-induced diabetic rats, *Folia. Pharmacol. Jpn. (Nipponu Yakurigaku Zassi),* 100(5), 1992. 415-421.
23. Welihinda J, Arvidson G, Gylfe E, Hellman B, Karsson E. The insulin releasing activity of the tropical plant *M. charantia, Acta Biologica et Medica Germanica,* 41(12), 1982, 1229-1240.
24. Kameswara Rao B, Kesavulu M M, Apparao C H. Antihyperglycemic activity of *Momordica cymbalaria* in alloxan diabetic rats, *J. Ethnopharmacol,* 78(1), 2001, 67-71.
25. Baskaran K, Ahamath B K, Shanmugasundaram R K, Shanmugasundram E R. Antidiabetic effect of leaf extracts from *Gymnema sylvestre* in non-insulin dependent diabetes mellitus patients, *J. Ethnopharmacol,* 30(3), 1990, 295-300.
26. Kamalakaran N, Mamzen P S. The effect of *Aegle marmelos* fruit extract in Streptozotocin diabetes, A histopathological study, J. *Herb. Pharmacother,* 5(3), 2006, 87-96.
27. Xiu L, Miura A B, Yamamoto K, Kobayashi T, Song Q H, Kitamura H, Cyong J C. Pancreatic islets regeneration by ephedrine in mice with Streptozotocin induced diabetes, *Am. J. Chin. Med*, 29(3-4), 2001, 493-500.
28. Raman A, Lau C. Antidiabetic properties and phytochemistry of *Momordica charantia L (Cucurbitaceae), Phytomed,* 2(4), 1996, 349-62.
29. Augusti K T, Sheela C G. Antiperoxide effect of S. allyl cysteine sulfoxide, an insulin secretagogue, in diabetic rats, *Experientia,* 52(2), 1996, 115-20.
30. Mahomoodally M F, Gurib-Fakim A, Subratty A H. Effect of exogenous atp on Momordica charantia Linn.(cucurbitaceae) induce inhibition of d-glucose, 1-tyrosine and fluid transport across rat averted intestinal sacs *in vitro*, *J. Ethnopharmacol,* 110(2), 2007, 257-263.

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