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Effect of *Cyperus squarrosus* plant extracts on diabetic neuropathy in Streptozotocin (STZ)–induced diabetic rats

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ABSTRACT

The present study was designed to evaluate the effects of *Cyperus squarrosus* plant extracts in streptozotocin-induced diabetic neuropathy. Diabetes was induced by a single administration of streptozotocin (65 mg/kg/intraperitoneally). After 72 hours to measure the fasting blood glucose levels, blood glucose levels more than 220 mg/dl, consider diabetic rats. Animals were divided into six groups, animals untreated with STZ were kept in a normal control group. STZ-induced diabetic rats orally administered with ethanolic and aqueous plant extracts (EECS & AECS) dose 200 & 400 mg/kg, p.o. for eight weeks, Rats were subjected to evaluate serum glucose, biochemical parameters, and test were performed on the initial day, 2^{n}, 4^{th} 6^{th} and 8^{th} week in all groups to evaluate the neuropathy by Eddy's hot plate and tail immersion test respectively. Diabetic animals were treated with Glibenclamide (5 mg/kg) and plant extracts (200 & 400 mg/kg) for 8 weeks. Groups treated with Glibenclamide (5 mg/kg) and *Cyperus squarrosus* extracts (200 and 400 mg/kg) significantly reduced elevated serum glucose level & lipid profiles and restored the reduced body weight. After completion of work, we observe the changes in fasting serum glucose, triglysaroids LDL, cholesterol levels are significantly reduced in animals treated with aqueous extract 400mg/kg. Other side animals treated with extracts decrease in the severity of diabetic neuropathy compare with untreated diabetic rats. Finally concluded that *Cyperus squarrosus* plant exhibit anti-diabetic property and beneficial protection against neuropathy in STZ induced diabetic rats.

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INTRODUCTION

Diabetes mellitus (DM) is a significant endocrine issue, and the worldwide yearly expense of management of diabetes & its complications could contact US $ trillion (King *et al.*, 1998). Self-management of diabetes mellitus is a foundation to accomplishing great glucose control and decreasing the danger to creating diabetic complications like microvascular (neuropathy, nephropathy & retinopathy) and macrovascular (cardiovascular & cerebrovascular) difficulties (Stopford *et al.*, 2013). Peripheral neuropathy is one of the major well-known long term complication of diabetes mellitus, which

influences every peripheral nerves, including pain fibers. Practically 12% of every single diabetic patient is influenced with symptomatic difficult diabetic neuropathy (Said, 2007). Neuropathy is a metabolic disorders produced by microvascular damages, deficit neurotrophic support, abnormalities in neuro immune interactions, apoptosis of glial and neural cells and inflammation (van Dam, 2002; Zychowska *et al.*, 2013). As of now, the primary and effective treatment for diabetes is the utilization of insulin and hypoglycemic medications. However, these medications additionally have numerous unfavorable effects. Nowadays, Herbal preparations have been used in the management of diabetes mellitus and its releated complications because of they are safe, less toxic and readily available (Raafat *et al.*, 2008). A number of plant species are utilized in people medication for their anti hyperglycemic properties and, along these lines, conceivably utilized for the treatment of DM (Singh *et al.*, 2013). *Cyperus squarrosus* is a little sedge of family cyperaceae, genus cyperus, it reaching a maximum height in between 12-16 centimeters. The plant have 1 to 3 short, thin leaves around the base of the plant of the Cyperaceae family. Traditionally, mentioned this plant used in the treatment of hyperglycemia. Taking all this into consideration, the aim of the present study was to assess the protective effect of *Cyprus squarrosus* (CS) against streptozotocin (STZ)-induced diabetic neuropathy.

MATERIALS AND METHODS

Plant Material and Authentication

The plant was collected from Tirumala hills, authenticated by Professor Dr. K Madhava Chetty, HOD, department of botany, S V University, Tirupathi. AP. and a voucher specimen (V. No 2296) was prepared and deposited at the S V university. The collected plant was cleaned and washed well with water. The plant was dried under shade drying and grinded well to a coarse powder. Corse powder was stored in air tight container with labelling, and it is used for further experimentation.

Preparation of Aqueous Extract

The coarse powder was boiled in a predetermined volume of distilling Water (1: 5) up to volume was reduced to 1/4th the first, it is then cooled and filtered. The extract was evaporated to dryness under vacuum and dried in vacuum desiccators. The percentage yield was determined.

Ethanolic extract

Coarse powdered and solvent was taken 1:5 ratio was extracted continuously with ethanol at $60.^0$C using soxhlet apparatus for about clear solution was obtained. The filter solvent was concentrated under reduced pressure on a rotary vacuum evaporator to a constant mass and to yield a solid (12.01% w/w). The extract was stored in a screw cap glass bottle.

Phytochemical screening

The ethanol and aqueous extract of the samples was analyzed to assess for the presence or absence of secondary metabolites such as flavonoids, polyphenols, tannins, alkaloids, carbohydrates, amino acids, volatile oils and saponins glycosides by the standard methods (Akinmoladun *et al.*, 2007; Kokate *et al.*, 2002; K R Khandelwal, 2002; Bakırel *et al.*, 2008).

Acute toxicity studies

Acute toxicity was performed to find out the toxicity of plant extract, whether extracts are produced any toxic signs and dose selection on normal rats. Thirty wister healthy rats were selected and starved for 12hr. Animals were randomly divided into ten groups. Each group contains 3 animals and administered orally with AECS and EECS beginning with a fixed dose of 500, 1000, 1500, 2000and 5000 mg/kg body weight of each extract. Animas was observed for 24 hours continuously for 24 hours thereafter for 14 days individually Observed for sign (behavioral and neurological parameters). Dose 0f 2000mg/kg was assessed according to OECD 423 guidelines. All groups of rats were allowed to a normal diet, and a mortality rate also observed within this period of time.

Experimental Animals

The animal experimental protocol was approved by the IAEC (1305/Po/Re/S/09/CPCEA) of CES college of pharmacy, Kurnool, AP. Male Wistar rats weighing 180–200 g, procured from Suresh agency, Hyderabad. Animals were acclimated at local animal house conditions for one week.

Induction of diabetes in rats

Diabetes was induced by a single injection of freshly prepared STZ Solution(65 mg/kg b.w) in 0.1 M citrate buffer (pH 4.5). Animals were allowed to drink 5 % glucose solution to protect them against the diabetogenic action of STZ. After 72 hours of injection, fasting blood glucose levels are measured, blood glucose levels more than 220mg/dl were considered as a diabetic animals (Ravi *et al.*, 2004).

Experimental design

Diabetic animals were divided into 6 groups. Each group contain 8 animals(n=8). Animals untreated with STZ were kept in the normal control group. Treatment was continued for 8 weeks as per the following plan for various groups.

Table 1: Effect of *Cyperus squarrosus* on serum glucose levels

Group	Treatment	Serum glucose levels (mg/dl) (Mean ±SEM)				
		Initial day	2^{nd} week	4^{th} week	6^{th} week	8^{th} week
I	Normal	83.40±4.79	89.52±3.01	88.34±4.11	85.26±5.85	89.13±4.19
II	Control	231.82±6.12	266.99±7.84	321.69±8.39^{a}	346.68±11.95^{a}	353.12±10.26^{a}
III	Standard	228.56±11.65	198.76±10.15	140.21±10.54^{b}	118.65±9.61^{b}	92.16±7.58^{b}
IV	*AECS200mg/kg*	226.20±10.14	252.93±9.18^{C}	200.86±9.94	161.81±8.65^{b}	130.11±8.45^{b}
V	*AECS400mg/kg*	234.80±9.25	217.52±10.62^{b}	163.61±8.85^{b}	132.34±8.11^{b}	107.90±6.18^{b}
VI	*EECS200mg/kg*	227.20±10.14	239.93±9.18^{C}	180.86±8.94^{b}	155.81±7.65^{b}	122.11±7.45^{b}
VII	*EECS400mg/kg*	230.80±9.25	207.52±10.62^{b}	157.61±9.85^{b}	124.34±8.11^{b}	98.90±8.18^{b}

a= p < 0.05 & b = p < 0.01, Disease control Vs normal.
c = p< 0.01 & d = p < 0.001, Glibenclamide and extracts treated groups Vs disease control.

Table 2: Effect of *Cyperus squarrosus* on serum triglyceride levels

Group	Treatment	Serum triglyceride levels (mg /dl) (Mean ±SEM)				
		Initial day	2^{nd} week	4^{th} week	6^{th} week	8^{th}week
I	Normal	144.21±5.05	150.64±6.06	151.56±6.16	150.36±5.53	146.37±6.22
II	Control	169.15±7.45	206.11±10.4	238.54±9.21^{a}	266.53±8.69^{a}	308.91±11.33^{b}
III	Standard	177.57±6.55	171.29±8.21	162.28±6.76^{c}	153.92±6.16^{d}	151.99±5.43^{d}
IV	*AECS200mg/kg*	179.69±7.63	185.35±8.91	181.42±8.78^{c}	177.56±9.29^{c}	169.15±7.41^{d}
V	*AECS400mg/kg*	171.51±6.64	180.10±8.23	168.38±6.53^{c}	159.67±8.37^{c}	153.22±8.13^{d}
VI	*EECS200mg/kg*	179.69±7.63	183.35±6.91	171.42±6.73^{c}	167.56±9.23^{c}	163.15±5.56^{d}
VII	*EECS400mg/kg*	179.69±5.63	182.10±8.23	168.38±6.82^{c}	164.67±6.37^{c}	151.22±7.13^{d}

a= p < 0.05, b = p < 0.01 & c = p < 0.001, Disease control Vs normal.
d= p < 0.001, Glibenclamide and extracts treated groups Vs disease control.

Table 3: Effect of *Cyperus Squarrosus* on serum cholesterol levels.

Group	Treatment	Serum cholesterol levels (mg/dl) (Mean ±SEM)				
		Initial day	2^{nd} week	4^{th} week	6^{th} week	8^{th} week
I	Normal	67.91±4.61	59.32±5.23	61.89.00±6.21	58.67±4.29	63.43±4.67
II	Control	86.81±7.71	121.31±8.61	143.31±8.84^{a}	171.91±8.54^{a}	187.68±9.18^{a}
III	Standard	95.18±5.37	114.61±7.84	101.91±8.57^{b}	86.37±5.74^{b}	72.14±5.73^{b}
IV	*AECS200mg/kg*	90.01±7.18	130.14±7.44	122.19±6.03^{b}	109.45±7.23^{b}	97.00±6.34^{b}
V	*AECS400mg/kg*	92.37±6.72	127.12±6.32	103.56±5.28^{b}	85.18±5.31^{b}	79.61±5.43^{b}
VI	*EECS200mg/kg*	89.01±6.18	129.14±6.34	118.19±6.81^{b}	102.45±6.23^{b}	88.00±7.21^{b}
VII	*EECS400mg/kg*	94.37±7.32	122.12±5.36	98.56±5.28^{b}	85.18±6.31^{b}	78.61±5.25^{b}

a= p < 0.05, b = p < 0.01 & c= p < 0.001, Disease control Vs normal.
d = p < 0.01 & e = p < 0.001, Glibenclamide and extracts treated groups Vs disease control.

Group I: Normal Control (NC): Blank acacia suspension, 1ml, orally

Group II: Diabetic Control (DC): Blank acacia suspension, 1ml, orally

Group III: Standard treatment (Std): Glibenclamide (5 mg/kg b.w.), orally

Group IV: Test 1 (AECS 200): Plant aqueous extract suspended in water using acacia as a suspending agent, 200 mg/kg bw, orally

Group V: Test 2 (AECS 400): plant aqueous extract suspended in water using acacia as a suspending agent, 400 mg/kg bw, orally

Group VI: Test 3 (EECS 200): plant ethanolic extract suspended in water using acacia as a suspending agent, 200 mg/kg bw, orally

GroupVII: Test 4 (EECS 400): plant ethanolic extract suspended in water using acacia as a suspending agent, 400 mg/kg bw, orally

The major symptoms of diabetic complications are observed chronic stage (over a period of one

Table 4: Effect of *Cyperus squarrosus* on serum HDL levels

Group	Treatment	Serum HDL levels (mg/dl) (Mean ±SEM)				
		Initial day	2nd week	4th week	6th week	8th week
I	Normal	61.57±4.32	56.94±4.87	59.35±3.60	54.64±3.31	61.99±4.32
II	Control	68.34±5.59	59.37±5.01	41.40±4.48^a	35.18±3.32^a	31.08±3.91^b
III	Standard	69.34±5.03	61.03±6.09	62.37±4.36^c	67.30±4.03^d	69.08±5.31^d
IV	*AECS200mg/kg*	67.08±4.74	51.53±5.69	50.30±5.05^c	53.63±4.69^d	55.30±5.64^d
V	*AECS400mg/kg*	71.15±6.32	65.71±6.48	63.51±5.00^c	65.91±5.37^c	67.18±5.51^c
VI	*EECS400mg/kg*	65.18±4.54	55.54±4.09	52.27±5.11^c	54.43±4.09^d	57.28±5.34^d
VII	*EECS400mg/kg*	68.26±4.32	65.32±5.48	62.31±5.00^c	66.56±4.31^c	68.28±4.26^c

a= p < 0.05 & b = p < 0.001, Disease control Vs normal.
c = p< 0.05 & d = p < 0.001, Glibenclamide and extracts treated groups Vs disease control.

Table 5: Effect of *Cyperus Squarrosus* on serum LDL levels

Group	Treatment	Serum LDL levels (mg/dl),(Mean ± SEM)				
		Initial day	2^{nd} week	4^{th} week	6^{th} week	8^{th} week
I	Normal	63.54±5.15	68.27±4.43	54.27±4.17	67.57±5.06	59.47± 4.41
II	Disease control	86.17±7.43	115.11±4.65	138.11±5.43^a	161.61±6.47^a	185.04±7.25^a
III	Standard	91.81±5.16	100.11±6.47	93.67±6.46^b	81.21±5.85^c	68.12±5.12^c
IV	*AECS200mg/kg*	87.40±6.26	112.32±6.24	103.67±8.10^b	99.04±6.51^b	91.37±6.45^c
V	*AECS400mg/kg*	85.54±5.19	108.67±6.49	96.32±6.45^c	84.38±5.93^c	79.76±5.58^c
VI	*EECS200mg/kg*	84.40±6.45	110.32±7.37	99.67±8.18^b	94.04±6.50^b	89.37±6.45^c
VII	*EECS400mg/kg*	89.54±5.63	103.67±6.19	92.32±6.23^c	80.38±5.13^c	74.76±5.58^c

a= p < 0.05, b = p < 0.01 & c = p < 0.001, Disease control Vs normal.
d = p < 0.01 & e = p < 0.001, Glibenclamide and extracts treated groups Vs disease control.

Table 6: Effect of *Cyperus squarrosus* on body weight

Group	Treatment	Body weight (gm) (Mean ±SEM)				
		Initial day	2^{nd} week	4^{th} week	6^{th}week	8^{th} week
I	Normal	180±1.76	184.80±1.58	185.41±0.92	189.47±0.77	192.61±1.66
II	Disease control	181.2 ±1.81	169.9±0.56^a	157.23±1.68^a	142.41±1.43^a	138.47±1.28^a
III	Standard	177.46±2.67	173.68±0.50^c	179.23±0.37^b	184.2±1.06^b	190.42±1.40^b
IV	AECS200mg/kg	180.2±0.96	169.0±0.70	162.6±0.89	167±0.54^c	170.8±0.58^c
V	AECS400mg/kg	181.5±0.92	175.8±0.86^c	178.8± 0.96	182.6±1.20	188.6±1.03^b
VI	EECS200mg/kg	179.2±1.08	168.0±1.71	164.6±0.87	169±0.79^c	173.8±1.18^c
VII	EECS400mg/kg	178.5±0.91	176.8±1.08	180.8±0.98^b	184.6±1.01	192.6±1.23^b

a= p < 0.001, Disease control Vs normal, b = p < 0.01 & c = p < 0.001, Glibenclamide and extracts treated groups Vs disease control.

month).

Blood samples were collected on the initial, 2^{nd}, 4^{th}, 6^{th} and 8^{th} week from the retro-orbital under ether anesthesia after a overnight fasting. Blood was centrifuged (3000 rpm /15 min) to get a clear superintend liquid (serum).

Serum was used for estimation of glucose, triglycerides, cholesterol, HDL and LDL levels *and* before collection of a blood sample that day, we carried out the eddy's hot plate method and tail immersion method for diabetic neuropathy.

Neuropathy

Eddy's hot plate method

Animals were placed on an Eddy's hot plate. The plate was maintained at 55± 0.5^{o}C temperature. The latency to flick the hind paw or lick or jump from the hot plate was the reaction time, and the reaction time was measured.

Tail immersion method

About 5cm of the tail was dipped into a water bath containing hot water (55 ± 0.5^{o}C). The time taken

Table 7: Effect of Cyperus squarrosus on Diabetic neuropathy by Eddy's hot plate method

Group	Treatment	Reaction time in seconds (Mean ±SEM)				
		Initial day	2^{nd} week	4^{th} week	6^{th} week	8^{th} week
I	Normal	8.6±1.51	8.5±0.68	9.38±0.54	8.59±0.63	8.61±0.65
II	Control	9.32±1.63	7.53±0.54	5.99±1.08^{a}	5.74±0.83^{a}	5.13±1.03^{a}
III	Standard	8.12±0.28	9.13±0.83	8.61±1.23^{c}	9.16±0.75^{c}	9.81±0.98^{c}
IV	*AECS200mg/kg*	9.31±1.34	6.05±0.89	6.43±0.78	6.96±1.13^{b}	8.43±1.81^{a}
V	*AECS400mg/kg*	8.61±0.83	5.65±0.81	7.99±0.75^{b}	8.81±0.91^{b}	9.72±0.75^{a}
VI	*EECS200mg/kg*	8.31±1.18	6.98±0.94	5.12±0.81	6.96±0.86^{a}	7.46±1.63^{a}
VII	*EECS400mg/kg*	8.61±0.93	7.65±0.91	7.877±0.96^{b}	8.81±0.94^{b}	9.01±0.98a

a= p < 0.05, b = p < 0.01 & c = p < 0.001, Disease control Vs normal.
d = p< 0.01 & e = p < 0.001, Glibenclamide and extracts treated groups Vs disease control.

Table 8: Effect of *Cyperus squarrosus* on Diabetic neuropathy by Tail immersion method

Group	Treatment	Latency time (in seconds) (Mean ±SEM)				
		Initial day	2^{nd} week	4^{th} week	6^{th} week	8^{th} week
I	Normal	8.12±1.23	8.18±1.62	8.01±0.93	9.24±1.13	8.91±1.32
II	Control	9.32±0.18	6.99±0.19	5.72±0.82^{a}	5.52±0.79^{b}	4.83±1.01^{b}
III	Standard	8.17±0.35	8.42±0.91	8.10±0.78^{c}	9.19±0.71^{d}	9.37±0.62^{d}
IV	*AECS200mg/kg*	8.92±0.72	5.98±0.54	6.52±0.72	6.82±0.63	7.98±0.83^{c}
V	*AECS400mg/kg*	8.71±0.92	7.54±0.71^{c}	7.99±0.81^{c}	8.21±0.58^{d}	8.35±0.61^{d}
VI	*EECS200mg/kg*	9.45±0.97	6.91±0.75	6.41±0.84	7.89±0.69^{c}	7.98±0.86^{c}
VII	*EECS400mg/kg*	9.63±0.98	7.12±0.81^{c}	7.52±0.76^{c}	7.94±0.83^{c}	8.18 ± 0.73^{d}

a= p < 0.05 & b = p < 0.001, Disease control Vs normal.
c = p < 0.05 & d = p < 0.001, Glibenclamide and extracts treated groups Vs disease control.

for the rat to flick its tail was recorded (Kushwah *et al.*, 2018; Nasikkar and Mali, 2016).

Statistical analysis

All the data were expressed as mean ± SEM. One way analysis of variance followed by tukeys multiple comparison test or by unpaired students T-test by using graph pad prism 5.0. Values are considered statistically significant when P<0.05.

RESULTS

The preliminary phytochemical screening carried out on both extracts revealed the presence of phytoconstituents such as alkaloids, glycosides, flavonoids, saponins, carbohydrates were present in both extracts. Tannins, steroids, saponins were present in only AECS and Proteins, and Terpenoids were present in the only EECS.

Acute toxicity studies

Aqueous and ethanolic extracts of *Cyperus squarrosus* did not show any mortality and toxic manifestations up to the dose of 2000 mg/kg. b.w. according to OECD 423 guidelines, the 1/10 th and 1/5 th dose as 200 mg/kg and double dose 400mg/kg has been selected as the therapeutic doses for both extracts.

Effect of ethanolic and aqueous extracts of Cyperus *squarrosus* (AECS & EECS) on serum biochemical parameters

Untreated diabetic rats (disease control) showed a significant (p<0.001) increase in serum glucose as well as cholesterol, triglycrides, LDL levels when compared with normal rats. Hyperglycemic rats treated with AECS & EECS (200 and 400 mg/kg) for eight weeks significantly decreased the elevated glucose, triglycerides, cholesterol and LDL levels when compared with non-diabetic rats. While EECS (400 mg/kg) showed a more significant decrease (P<0.001) in serum glucose levels (Table 1), triglycerides (Table 2), cholesterol (Table 3) and LDL (Table 5) compared to other test groups. Diabetic regulation significantly reduced the amount of elevated HDL(Table 4) compared to normal, while EECS (400 mg/kg) showed a substantial increase in HDL compared with other test group.

Effect of AECS & EECS extracts on body weight.

After 8 weeks of study, we found a decreased in body weight in diseased control when compared to non-diabetic rats. Eight weeks of treatment of AECS

& EECS (200 and 400 mg/kg) in diabetic rats was found to increase (equal to normal) in body weight when compared to diabetic control rats (Table 6).

Effect of AECS & EEC on neuropathy

The diabetic neuropathy was assessed by the hot pate method and tail immersion methods. By using these methods, measure the response of pain stimuli. The response time in diseased control rats showed significantly lower (p<0.001) than normal rats in the hot plate method. The response time increased in STZ diabetic rats treated with AECS & EECS 200 and 400 mg/kg and Glibenclamide (5mg/kg). Animals treated with AACS 400 mg/kg were a more significant (p<0.001) protective effect on neuropathic rats compare with other test groups (Table 7). Tail immersion test revealed that in a significant (p<0.01) decrease the tail withdrawal time in the disease control group during 6^{th} and 8^{th} week when compared to healthy rats. Animals AECS & EECS 200 and 400 mg/kg during 7^{th} and 8^{th} week resulted in a significant increase (P<0.01) tail withdrawal latency time (Table 8). Diabetic rats with AECS & EECS dose 200 and 400 mg/kg dose resulted in increased latency time. Completion of the study more significant effect was observed in animals treated with AECS 400mg/kg.

DISCUSSION

Long term hyperglycemia promotes macrovascular and microvascular complications associated with diabetes mellitus (Singh *et al.*, 2013). Oxidative stress is also one of the selected factors to producing the complication in diabetes. Treatment of diabetes and its complications with neutral side effects is a major challenge to medication therapy (Baynes and Thorpe, 1999). Researchers have focused that the number of natural plants has an effective hypoglycemic effect with less side 3weffects. In this study, we have chosen the *Cyperus Squarrosus* plant because, in a traditional report, it is used as an antidiabetic. The current research focused on evaluating the possible antidiabetic and antinociceptive activities of extracts from *cyperus squarrosus.* Our results showed a hyperglycemic effect in all rats at 72 h after the injection of stz to animals. It has been proved that STZ (as a glucosamine-nitroso-urea compound) can develop destruction in pancreatic beta cells. Long term hyperglycaemia has been proposed as the main contributor to begin and develop the microvascular complications of diabetes (Lehmann and Schleicher, 2000). Administration of STZ cause decreased sodium-potassium ATPase activity, as supported by previous studies (Kushwah *et al.*, 2018). This decreased activity leads to altered neuronal normal functions along with lowered antioxidant level. Eddy's hot plate, tail immersion test have been reported as a method for evaluation of peripheral hyperalgesia. Administration of STZ results into worsening of sensory-motor nerve fibres resulting decrease in withdrawal latency time in diabetic rats (Nasikkar and Mali, 2016). Significant dose-dependent amelioration were seen on the $6^{th}$and 8^{th} week in reduction of thermal hyperalgesia and increased tail-flick latency compared to the control group. Our data revealed that alkaloids, glycosides, flavonoids, steroids, saponins and Terpenoids, and tannins (only in EECS) were present in both extracts. Polyphenols, flavonoids has been found to inhibit the activity of aldose reductase (Obrosova *et al.*, 2007). It is the first enzyme of the orbital pathway and plays an impotent role in the pathogenesis of diabetic neuropathy (Obrosova *et al.*, 2002).

The number of Phytoconstituents has a different mechanism to produce anti-diabetic action. Flavonoids, saponins and tannins were already reported as their anti-diabetic and analgesic activity. However, many herbal formulations already have fewer side effects (Yu *et al.*, 2006).

In these study, *Cyperus squarrosus* extracts containing flavonoids, saponins, tannins. Based on this phytochemical studies, *cyperus squarrosus* exhibit an anti-diabetic effect and also protective against neuropathy.

The above profile which provides background for further research in the same direction (Nangle *et al.*, 2006; Aida *et al.*, 1990).

CONCLUSIONS

From this study, we proved that the aqueous extract of *Cyperus squarrosus* has beneficial effects on blood glucose levels as well as improve the hypoglycemic action and their protect against neuropathy. The diabetic neuropathy activity of *cyperus squarrosus* may be attributed by the presence of phytoconstituents present in the drug. So *Cyperus squarrosus* has shown a significant increase in pain sensitivity. The result indicates its protective role against neuron damage. Therefore, finally that *Cyperus squarrosus* exhibit antidiabetic and neuroprotective effects in STZ induced diabetic rats.

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Conflict of Interest

The authors declare that they have no conflict of interest for this study.

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