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ANTI-DIABETIC, ANTI-OXIDANT ACTIVITIES OF ETHANOLIC PLANT EXTRACT OF SALICORNIA BRACHIATA ROXB. IN STREPTOZOTOCIN INDUCED DIABETIC RATS.

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ABSTRACT

Salicornia species traditionally used as food material commonly called as glasswort. The aim of the present investigation was to evaluate the antidiabetic, Antioxidant activity of ethanolic extract taken from *salicornia brachiata* Roxb (Chenopodiaceae). Acute toxicity study and oral glucose test of the extract was performed. Diabetes was induced in rat by single intra-peritoneal injection of streptozotocin (55 mg/kg).The rats were divided into following groups: Group I – normal control,Group II (Vehicle) – diabetic control, Group III (STZ-toxic) – salicornia extract I (100 mg/kg, p.o.), Group IV – salicornia extract II (250 mg/kg, p.o.), Group V – salicornia extract III (500 mg/kg, p.o.), Group VI – glibenclamide (10 mg/kg, p.o.). Body weight of each rat in the different groups was recorded daily. Biochemical and antioxidant parameters were determined on day 28.Ethanolic extract of *salicornia brachiata* did not show any acute toxicity up-to the dose of 2000 mg/kg and shown better glucose utilization in oral glucose tolerance test. orally treatment of different doses of extractdecreased the level of serum glucose, glycated hemoglobin, glucose-6-phosphatase, fructose-1-6-bis phosphate andincreased the level of plasma insulin, hexokinase,decreased liver malondialdehyde but increased thelevel of superoxide dismutase, catalase and glutathione peroxidase. In oral glucose tolerance test observed increased utilization of glucose. Streptozotocin induced diabetes group rats treated with different doses of *salicornia brachiata* plant extract and glibenclamide significantly increased the body weight.

KEY WORDS: *salicornia brachiata*, Streptozotocin, Antidiabetic, Antioxidant, Glibenclamide.

1. INTRODUCTION

Diabetes mellitus (DM) is a chronic complication of derangementof protein carbohydrate and lipid metabolism characterized by increased blood glucose level resulting from the defects in insulin secretion insulin action or both [1]. DM is the worldwide problem to leading micro vascular and macrovascular complications [2]. DM is a chronic complication that affected an estimated 135 million people in 1995, 285 million people worldwide in2010 and data reached approx 500 million people in2025 mainly increasing in rural and poor population throughout the world [3].In hyperglycemic condition continuous generation of reactive oxygen species (ROS) occurred. Reactive oxygen species increased the oxidative stress mainly due to over production of oxygen free radicals, as oxidative stressplay an important role in development of diabetes. Oxidative stress effect the endogenous antioxidant, which enzyme is responsible for the detoxification of deleterious oxygen radicals [4]. Antioxidant play an important role in scavenging the free radical, damage the reactive oxygen species and protect the human body from oxidative stress [5]. Hence, drug with both antioxidant and antidiabetic property would be useful for the treatment of the diabetic patient [6]. Medicinal plant is the rich source of various chemical constituents which act by a variety of mechanism to cure the diabetes. Despite long traditional use of salicornia species in diabetes, no systematic pharmacological work has been carried out on this potential medicinal plant. Therefore the present study focuses on screening the plant for anti oxidant and antidiabetic activity.

S. brachiata is a highly salt tolerant plant [7] that can grow in marshy lands.It belongs to the family chenopodiaceae one of the more advanced eleven families within the order Caryophyllales. This halophytic shrub of coastal mud lands is a potentially high biomass producing marine ecosystem, recently innovated as a source of high valued vegetable salt known as saloni, making it suitable for patients with high blood pressure, besides the usage of its oil in industries [8]. Several species of *Salicornia* possess antibacterial and antihypertensive properties and are quoted in folk medicine for relief of toothache and chronic rheumatism [9], constipation, obesity, diabetes and cancer [10-11].

2. MATERIALS AND METHODS

2.1 Collection of Plant Material

The halophytic plant, *S. brachiata* of Chenopodiaceae family was collected from the marine watershores of Bay of Bengal, Bapatla,Guntur district, India in the month of June, 2013. and authenticated by Department of Botany,Acharya Nagarjuna University.

2.2 Preparation of Extracts

The collected plants of *S.brachiata* were washed thoroughly with water to remove the extraporeneous matter. After washing the plants were dried in shade and grounded, 1 kg of powder was extracted with ethanol in a Soxhlet apparatus for 3 days. The extract was filtered and the filtrate wasconcentrated under reduced pressure using a rotatory evaporator at 40°C until the extra solvent completely dried. The yield of ethanolic extract was 40%.The extract was stored in the cooling condition in refrigeratorat 4°C until further use. The extract was dissolved in 1% carboxyl- methyl cellulose distilled water was used forthe animal studies.

2.3 Preliminary Phytochemical Screening of Plant Extract

The ethanolic extract of plant was subjected to preliminary screening for presence of various bioactive pharmaceutical constituents such as glycosides, alkaloids, steroids, proteins, flavonoids, phenolic compounds and terpenes.

Table.1.Qualitative Phytochemical Screening of Ethanolic Plant Extract of Salicornia Brachiate.

Test name	Ethanol Extract
Carbohydrates	-
Proteins & Amino acids	+
Steroids	+
Saponins	-
Alkaloids	+
Tannins	-
Flavonoids	+
Glycosides	+
Phenolics	+
Terpenes	+

2.4 Animals Study

Healthy albino rats (Wistar strain) weight about 170-200 g were kept in individual polyethylene cages and maintained standard condition (12 h dark and 12 h light circle; 25 ± 5°C; 40-60% humidity), and the animals were fed *ad libitum* with normal laboratory chow

standard pellet diet, purchased from the Hindustan Liver Limited, Mumbai, India. The animals were allowed to acclimatize for 5 days before commencing the experiments. All the studies were conducted in accordance with the Animal Ethical Committee of Sims college of pharmacy, Guntur IAEC/SIMS 2013/004.

2.5 Acute Toxicity Studies

For determination of acute toxicity studies the animals were famished overnight and divided into five groups (n = 5). All groups' animals were fed with different doses of the extract in increasing dose level 100, 250, 500, 1000, 2000 mg/kg body weight. The animals were continuously observed for 2 h for the following parameters: [12].

1. Behavioral profile: restlessness, irritability, alertness and fearfulness.
2. Neurological profile: spontaneous activity, touch response, reactivity, pain response and gait.
3. Autonomic profile: urination and defecation.

If any contraindication and death occur after 24 h and 72 h was recorded. oral glucose tolerance test (OGTT)

Oral glucose tolerance test was performed in overnight (16 h) starved normal albino wistar rat. The rats were randomly divided into five groups (n = 6) [13].

Group I rats treated with vehicle only

Group II rats treated with *S.brachiata* extract 100 mg/kg bodyweight

Group III rats treated with *S.brachiata* extract 250 mg/kg body weight

Group IV rats treated with *S.brachiata* extract 500 mg/kg body weight

Group V rats treated with Glibenclamide 10 mg/kg body weight

Glucose 2 g/kg was fed 30 min after the administration of different doses of *S.brachiata* extract and glibenclamide.Blood was withdrawn from the tail vein at 0, 30, 60, 90 and 120 min, blood glucose level were appraised by theGOD-POD kit (Span diagnostic).

2.6 Induction of Diabetes

Diabetes was induced in the overnight fasted male albino wistar rats by a single intra peritoneal injection (i.p.) of streptozotocin (55 mg/kg body weight) dissolved in 0.1 M citrate buffer (pH = 4.5), Normal control rats received citrate buffer only as vehicle. After 3 days induction of diabetes injection of STZ blood sample was collected from the retro-orbital of

the rat eyes and plasma, glucose level were determined. The animals confirmed diabetic by the elevated plasma glucose levels(200 mg/dl) were used for the study [14].

2.7 Experiment Design

After induction of diabetes animals were divided into six groups of six rats each.

Group I: normal control rats administered vehicle only

Group II: diabetic control rats administered tap water only

Group III: tested rats administered plant extract 100 mg/kg body weight

Group IV: tested rats administered plant extract 250 mg/kg body weight

Group V: tested rats administered plant extract 500 mg/kg body weight

Group VI: tested rats administered glibenclamide 10 mg/kg body weight

All group rats received different doses of salicornia extract and glibenclamide using intragastric tube once daily for 28 days, continuously [15]. According to the acute toxicity testing of the salicornia extract, the different dosesi. e. 100 mg/kg, 250 mg/kg, 500 mg/kg were selected.

2.8 Biological Assays

All rats were anesthetized by diethyl ether. The blood samples of each animal were collected from the puncturing retro-orbital plexus and preserved with anticoagulating agents, estimations done spectrophotometric ally using standard kits which include serum insulin (Span Diagnostic, India).

2.9 Estimation of Antioxidant Enzymes

Antioxidant enzyme was estimated by liver homogenate, prepared in ice chilled 10% potassium chloride solution, was used to measure the levels and activities of superoxide dismutase (SOD), catalase (CAT) glutathione peroxidase (GPx) and Malondialdehyde (MDA) by the method [16-18].

3. Statistical Analysis

All the data were expressed as the mean ± SEM and analysis of variance (ANOVA) was used for the statistical analysis using Graph Pad Prism version 5.0 . The values were considered to be significant when the P value was $p < 0.05$.

4. RESULTS

4.1 Preliminary Phytochemical Screening

Preliminary phytochemical screening of the ethanolic extract of *Salicornia brachiata* showed terpenoids, flavonoids, phenolic compound and steroids. But the content of flavonoids and phenolic compound were found to be more prominent in the extract.

4.2 Acute Toxicity Study

An acute toxicity study of the *Salicornia brachiata* plant extract was publicized the non-toxic nature of the drug. The different doses of the *Salicornia brachiata* plant extract were not showing any toxic reaction or lethality at any of the doses selected until the end of the study period. Acute toxicity of the ethanolic extract revealed the non-toxic nature of the different doses. There were no lethality or toxic reactions found in the selected group which received the different doses of the extract until the end of the experimental period.

4.3 Effect of Extract on Oral Glucose Tolerance Test

The acute effect of different doses of plant extract, when administered 30 min, prior to glucose loading produced significant reduction ($P < 0.001$) in the rise in blood glucose levels, after glucose administration (Table 1). The different doses of plant extract (100, 250 and 500 mg/kg) produced 11.76%, 19.06% and 31.84% reduction in blood glucose level at 120 min when compared to the vehicle control. Glibenclamide drug was excursion blood glucose level at 26.57% as compared to the vehicle control groups (Figure 1)

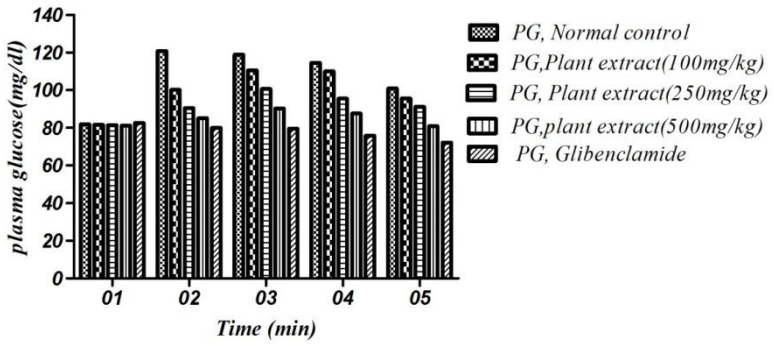

*Figure 1 Effect of salicornia brachiata on fasting plasma glucose on oral glucose tolerance test at different concentrations on STZ induced diabetic rats,compared to standard drug Glibenclamide;values are mean±SEM;n=6;*P<0.05;**P<0.01;***P<0.05 is considered as non significant(ns)*

4.4 Effect of Plant Extract on Blood Glucose Level

The antidiabetic effect of *salicornia brachiata* plant extract with repeated oral administration on STZ (streptozotocin) induced diabetic rats was presented in (Table 2). The administrationof different doses (100, 250 and 500 mg/kg) to STZ(streptozotocin) induced

diabetic rats caused significantly($P < 0.001$) decline the blood glucose level,which was showing that the different doses of extractwas showing effect at dose dependent manner.Maximum decline rate of blood glucose was observed on day 28 (52.13%, 60.93% and 68.88% respectively). On the other hand glibenclamide showing the 67.26% excursion blood glucose level at compared to the diabetic control groups (Figure 2).500 mg/kg exhibited maximum glucose lowering effect in STZ(streptozotocin) induced diabetic rats compared to the other groups rat received different doses of extract and glibenclamide.

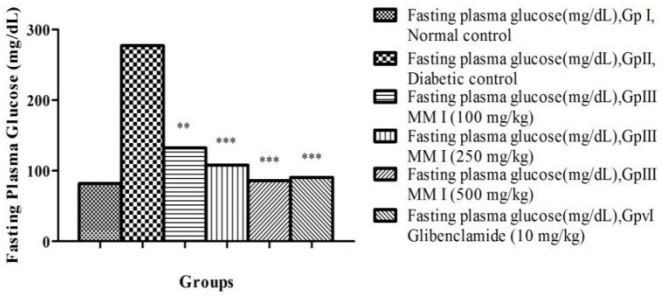

Figure 2 Effect of salicornia brachiata on fasting plasma glucose at different concentrations on STZ induced diabetic rats,compared to standard drug Glibenclamide;values are mean±SEM;n=6;*P<0.05;P<0.01;***P<0.001;P>0.05 is considered as nonsignificant (ns)**

4.5 Effect of *Salicornia* Extract on Plasma Insulin

The effect of different doses of *salicornia* extract on plasma insulin was presented in (Table 3). In STZ (streptozotocin) induced diabetic rats there is a significant decline in the level of plasma insulin as compared to the normal rat group (rats receiving the vehicle only). oral administration of different doses of *salicornia* extract, significantly ($P < 0.001$) increased the level of plasma insulin. Amongst all the doses of *salicornia* extract 500 mg/kg was more effective in increasing the level of plasma insulin as compared to other doses and glibenclamide (Figure 3).

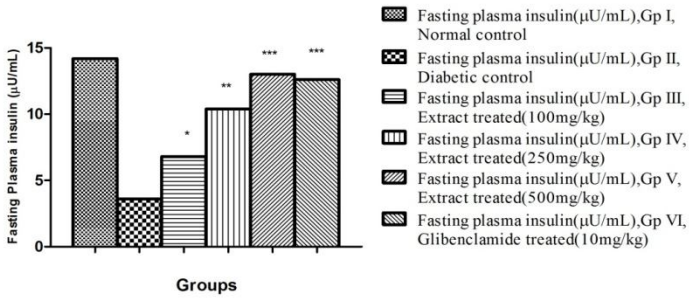

Figure 3 Effect of salicornia brachiata plant extraxt on levels of plasma insulin at different concentrations on STZ induced diabetic rats,compared to standard drug Glibenclamide;values are mean ±SEM;n=6;*P<0.05;P<0.01;***P<0.001;P>0.05 is considered as non significant (ns).**

Table 3 Effect of salicorniabrachiata extract on blood glucose levels in STZ-induced diabetic rats

S.n.	Biochemical Parameter	Normal ontrol	STZ-diabetic control[a]	STZ-diabetes+ extract I[b] (100 mg/kg)	STZ-diabetes+ extract II[b] (250 mg/kg)	STZ-diabetes+ xtract III[b] (500 mg/kg)	STZ-diabetes+ Glibenclamide (10 mg/kg)
1	Fasting Plasma Glucose (mg/dL)	81.8 ± 0.969	277 ± 2.608**	132.6 ± 1.965*	108.2 ± 2.922**	86.2 ± 1.428***	90.6 ± 0.509***
2	Fasting Plasma Insulin (µU/mL)	14.2 ± 0.583	3.6 ± 0.509***	6.8 ± 0.58	10.4 ± 0.601**	13 ± 0.316***	12.6 ± 0.411***
3	Glycated Haemoglobin (A1c) (%)	1.32 ± 0.73	4.86 ± 0.151***	3.72 ± 0.081*	2.96 ± 0.678**	2.04 ± 0.129***	2.16 ± 0.107***
4	Hexokinase (µg/mg of tissue)	147.8 ± 3.484	90.4 ± 3.203***	115.6 ± 1.631*	131 ± 1.871**	142.6 ± 2.015***	140.4 ± 2.182***
5	Glucose-6-Phosphatase (unit/mg of tissue)	9 ± 0.707	14.2 ± 0.583***	13.4 ± 0.509*	11.6 ± 0.611**	8.6 ± 0.712***	9.8 ± 0.567***
6	Fructose-1-6-biphosphatase (unit/mg of tissue)	28.8 ± 0.861	55 ± 1.012***	43.8 ± 1.158*	38.2 ± 1.068**	30 ± 0.707***	31.8 ± 0.861***
7	Weight Variation (g)	192.6 ± 0.872	157.8 ± 1.625***	189.4 ± 1.032***	186.4 ± 1.749***	197 ± 1.304***	194.2 ± 1.393***

All values represent mean ± SEM *P < 0.05; **P < 0.01; ***P < 0.001; ANOVA, Followed by

Dunnett's multiple comparison test.

[a]Compared to vehicle control.

[b]Compared to diabetic control.

4.6 Effect of *Salicornia* Plant Extract on Glycated Haemoglobin (A1c)

The administration of different doses of plant extract significantly (P < 0.001) increased the level of glycated haemoglobin (A1c) in STZ-induced treated diabetic rats (Table 3). Upon administration of different doses of extract (100, 250 and 500 mg/kg) and glibenclamide increased the level of glycated haemoglobin (A1c) in STZ-induced treated diabetic rats to a

good extend. The maximum lowering of glycated haemoglobin (A1c) in STZ-induced treated diabetic rats was appeared in group received plant extract of 500 mg/kg dose (Figure 4).

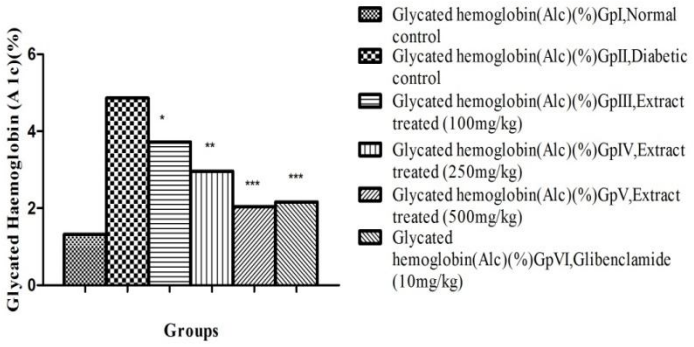

Figure 4 Effect of salicornia brachiata plant extract on levels of glycated haemoglobin (A1c)(%) at different concentrations on STZ induced diabetic rats,compared to standard drug Glibenclamide;values are mean ±SEM;n=6;*P<0.05;P<0.01;***P<0.001;P>0.005 is considered as non significant (ns).**

Table 2. Effect Of Salicornia Brachiata Plant Extract On Oral Glucose Tolerance Test

S.NO	Groups	Time (min)				
		0	30	60	90	120
1	Glucose Control	85.4 ± 2.041	115.4 ± 1.077	112.6 ± 0.0509	106.9 ± 0.872	98.6 ± 0.927
2	Glucose+extract	85.8 ± 0.663	105 ± 1.732*	101.2 ± 1.655*	98.2 ± 0.734	87± 1.378***
3	Glucose+ extract (250 mg/kg)	86.6 ± 0.871	98.2 ± 1.428*	94.6 ± 1.077**	88.6 ± 1.806***	79.8 ± 1.497***
4	Glucose+extract(500 mg/kg)	85.8 ± 1.28	189.2 ± 1.655**	80.8 ± 1.985***	73.6 ± 1.327***	67.2 ± 0.861***
5	Glucose+ Glibenclamide (10 mg/kg)	84.8 ± 0.58	394.6 ± 1.364**	88.4 ± 1.913***	81.4 ± 1.435***	72.7 ± 0.872***

All values represent mean ± SEM *P < 0.05; **P < 0.01; ***P < 0.001; ANOVA, followed by``Dunnett's multiple comparison test.

4.7 Effect of Extract on Hexokinase

The level of hexokinase was observed decrease in STZ treated group rat as compared to the normal group (Table 3). Upon oral administration of different doses of *salicornia brachiata* extract and glibenclamide was significantly (P < 0.001) boosting the level of hexokinase in

STZ-induced treated diabetic rats. STZ (streptozotocin) induced diabetic rats treated with extract doses 500 mg/kg showing the maximum increasing the level of hexokinase at compared to the other doses treated group rat (Figure 5).

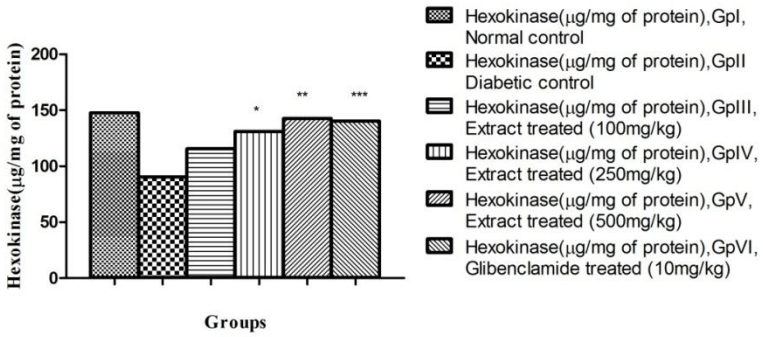

Figure 5 Effect of salicornia brachiata extract on levels of hexokinase (µg/mg of protein) at different concentrations on STZ induced diabetic rats,compared to standard drug Glibenclamide;values are mean±SEM;n=6;*(P<0.05;P<0.01;***P<0.001;P>0.05 is considered as non significant(ns).**

4.8 Effect of *Salicorniabrachiata*on Glucose-6-Phosphate

To evaluate the potency of the extract on STZ (streptozotocin) induced diabetic rats on glucose-6-phosphate on diabetic rat (Table 3). The level of glucose-6-phosphate was significantly increased in STZ (streptozotocin) induced diabetic groups rat when compared to the normal rat. Upon oral administrationof different doses of extract and glibenclamide was significantly ($P < 0.001$) decline theincreased level of glucose-6-phosphate. Different doses received groups rat significantly decreased the level of glucose-6-phosphate but the dose of plant extract 500 mg/kg was more effective to decline the increased level of glucose-6-phosphate (Figure 6).

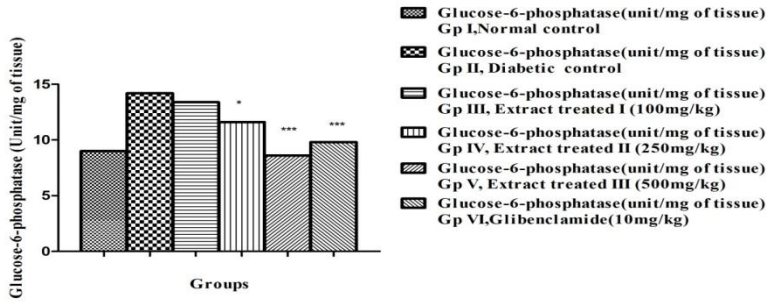

Figure 6 Effect of salicornia brachiata plant extract on levels of glucose6-phosphatase at different concentrations on STZ induced diabetic rats,compared to standard drug Glibenclamide;values are mean±SEM;n=6;*P<0.05;P<0.01;***P<0.001;P>0.05 is considerd as non significant(ns).**

4.9 Effect of Plant Extract on Fructose-1-6-Bisphosphatase

The oral administration of different doses of extract and glibenclamide were significantly ($P < 0.001$) decreased the level of fructose-1-6-bisphosphatase in STZ (streptozotocin) induced diabetic rats (Table 3). The level of fructose-1-6-bisphosphatase enhance in STZ induced

diabetes. STZ (streptozotocin) induced diabetic rats treatment with different doses of plant extract was sharp and decreased the level of fructose-1-6-bisphosphatase to normalize rat. The extract with dose 500 mg/kg shown the supreme diminish levels of fructose-1-6-bisphosphatase in comparison to other diabetic treated group rats receiving dose of 100 mg/kg, 250 mg/kg dose of extract and 10 mg/kg of Glibenclamide respectively (Figure 7).

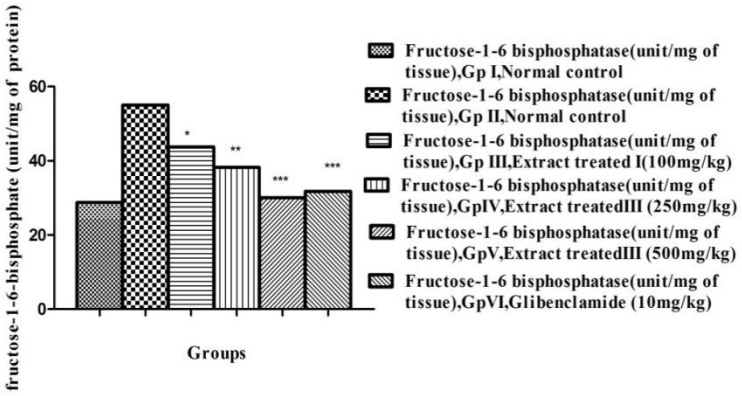

Figure 7 Effect of salicornia brachiata plant extract on levels of Fructose-1-6-bis phosphatase at different concentrations on STZ induced diabetic rats,compared to standard drug Glibenclamide;values are mean ±SEM;n=6;*P<0.05;P<0.01;***P<0.001;P>0.05 is considered as nonsignificant (ns).**

5. Changes in Body Weight

Table 3 display the effect of the different doses of extract and glibenclamide on the body weight of the STZ (streptozotocin) induced diabetic rat. At the end of 28 days treatment, the body weight of normal rats, diabetic control, different doses of extract and glibenclamide treated rats were observed. Diabetic control group continued to decrease the weight till the end of the study. Glibenclamide and different doses (100, 250 and 500mg/kg) of extract treated rats significantly ($P < 0.001$) increased the weight as compared to the diabetic control rats.

6. Effect of Salicornia Extract on Antioxidant Enzymes

In STZ induced diabetes increase the level of SOD, GPx, CAT and decrease the level of MDA. The level of CAT increased due to increase production of H_2O_2 in diabetic pancreas and increase the level of SOD due to increased the production of superoxide, which has been implicated in cell dysfunction. The level of antioxidant enzyme SOD (superoxide dismutase), CAT (catalase) and GPx (Glutathione Peroxidase) were significantly ($P < 0.001$) decreased in diabetic control groups and level of MDA (Malonaldehyde) were significantly increased. Glibenclamide (5 mg/kg) and different doses of extract (100, 250 and 500mg/kg) received groups rat signification ($p < 0.001$) increase the level of SOD , CAT, GPx and decreased the

level of MDA.The result suggests that glibenclamide and all the doses of extract increase the level of SOD, CAT and GPx, but extract doses 500mg/kg was more effective in increase the level of SOD,CAT and GPx in diabetic rat as compared with different doses of extract and glibenclamide.

7. DISCUSSION

The present manuscript discuses about the antioxidant and Antidiabetic effect of ethanolic extract of *salicornia brachiata* on normal and streptozotocin (STZ) induced diabetic wistar rats.Streptozotocin (STZ) is a nitroso urea compound(cytotoxic compound) obtained from soil microbe Streptomyces achromogenes, is mediated by reactive oxygen species (ROS). Streptozotocin (STZ) specially penetrates the β-cells via glucose transporter and induce the DNA strand breakage in β-cells causing decrease the endogenous insulin release [19]. The breakage of DNA is due to nitroso urea moiety. This breakage of DNA strand leads to amendment the blood sugar level and glucose concentrations in blood.Certain changes start after the administration of Streptozotocin (STZ), two hours after Streptozotocin(STZ) administration, hyperglycemia develops with a concomitant plunge in insulin level [20]. After six hours, hyperglycemia develops with high levels of insulin. Finally, severe hyperglycemia develops with a decreasein insulin levels [21]. In the present investigation the antidiabetic effect of salicornia batrachia was reported scientifically for the first time.

Oral glucose tolerance test is used to identify the altered carbohydrate metabolism during post glucose administration.The ability of ethanolic extract of plant to lower the blood glucose level in oral glucose tolerance test suggest that rats treated with different doses of extract have better glucose utilization capacity[22]. The results suggest that increased levels of glucose tolerance in different doses of plant extract treated groups were due to insulin emission from β-cells and glucose improved glucose transport and consumption [23].In Streptozotocin (STZ) induced diabetes groups rat, there is a loss in body weight due to muscle destruction or degradation of structural proteins [24]. Diabetic rats groups received different doses of extract and glibenclamide significantly improve the body weight

Comparison to the diabetic control group rats, all doses of extract and glibenclamide showing a protective effect in controlling muscle wasting (reversal of gluconeogenesis).The dose of extract (500 mg/kg) showed more improvement in the body weight in comparison to the diabetes control and glibenclamide tested groups.Glibenclamide persuade insulin secretion from β cell in the pancreas. The extract of salicornia decreased the serum glucose

level and increased pancreatic insulin as shown in our research exertion Therefore result suggests that extract may stimulate insulin secretion and decreased serum glucose.Streptozotocin (STZ) induced diabetes rat decrease the level of plasma insulin. Different doses of extract treated groups rat scramble the level of plasma insulin due to active constituent present in the plant extract which persuade insulin secretion or shield the intact function β-cells from further decline so they remain active and continue to produce insulin. The plant extract induces the protection to the β-cells, that result in the decline of blood glucose and diminishes the glucotoxicity to the β-cells [25]. oral administration of the extract for 28 days caused the significant decrease in the blood glucose level with increasing the level of plasma insulin. The possible mechanism of action of Plant extract treated groups animal could be potentiating the pancreatic secretion of insulin from β-cells of islets, as was evident by significantly elevating the level of insulin. The hypoglycemic activity of extract compared with glibenclamide (standard drug), the results suggest that the mechanism of action of extract and glibenclamide may be similar. Insulin is the most important medicine for the treatment of diabetes,a lot of research carried out to find the substitute, secretagogues or sensitizers from synthetic or plant source for the treatment. Some researcher claims that rich source of flavonoids containing plant showed the hypoglycemic and Antidiabetic activity [26,27] and its is reported in our research exertion that *salicornia brachiata* plant extract is the rich source of flavonoids and phenolic compound [28]. STZ induced diabetic rats' increases the level of lipid peroxidation (MDA), as an indirect evidence of production of free radical [29]. In STZ induced diabetes increase the level of lipid, which cause the development of diabetes and increase the production of free radical formation. Escalating levels of free radical play an important role in causing the hyperglycemia, followed by generation of reactive oxygen species (ROS). Continuous generation of free radicals can lead to tissue damage by attacking membranes through peroxidation of unsaturated fatty acids [30], ROS to elevate the lipid peroxidation and alter the antioxidant defense mechanism and further impair glucose metabolism in biological systems [31,32]. Lipid peroxidation eventually leads to extensive membrane damage and dysfunction [33]. Pancreatic β cell having low level of endogenous antioxidantenzyme and danger to cytotoxic action of free radical.In STZ induced diabetes the level of SOD, GPx, and CAT was increased and the level of MDA was decreased. The level of CAT increased due to increase production of H_2O_2 in diabetic pancreas and increase the level of SOD due to increased the production of superoxide, which has been implicated in cell dysfunction. Increasethe level of SOD without increasing the level of GPx, increase the peroxide level in the cells, cell face the overloading of peroxide.

Peroxide can react with transitional metals and generates the radical hydroxyl, whichis very harmful radical [34]. On other hand increase thelevel of superoxide increase the level of GPx, which is directly propositional to MDA (decrease the level of MDA). Different doses of extract treated groups significantly improved the level of endogenous antioxidant (SOD, CAT and GPx) and prevent the membrane to damage by decreasing lipid peroxidation compared to diabetic control. Decreased the level of lipid peroxidation (MDA as an indicator) and improved antioxidant status may be one of the mechanism by which drug treatment could contribute to the prevention of diabetic complications [35]. Glycogen plays an important role in the storage of glucose in the form of intracellular storable. Many tissues directly an expression of insulin activity as insulin encourage intracellular glycogen deposition by stimulating glycogen synthesis and inhibiting glycogen phosphorylase. The storage of liver glycogen was markedly reduced in Streptozotocin (STZ) induced diabetes rats, which directly affect the insulin and caused insulin deficiency [36]. Streptozotocin (STZ) induced diabetes rat treated with different doses of extract brings back the liver glycogen near the normal rat, which increases the level of insulin secretion. Streptozotocin(STZ) induced diabetes rat enhanced the level of glycated hemoglobin (A1c) due to excessive production of glucose in blood which further react with blood hemoglobin and prepared the glycated hemoglobin [37]. Three different doses of extract significantly lowerd the blood glucose, which lead to decreasing the level of glycated hemoglobin. The possible mechanism of action in decreasing the blood glucose which is directly propositional to reducing the glycated hemoglobin.

8. CONCLUSIONS

Thus, our findings demonstrate that different doses of plant extract has an antidiabetic, and antioxidant effects, which is evidenced by decreased level of blood glucose, glycated hemoglobin, glucose-6-phosphate, fructose-1-6-phosphate,SOD, CAT, GPx, MDA. Oral glucose tolerance test shown that

Plant extracts having better glucose utilization capacity.

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