WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 8.084
Volume 11, Issue 3, 1677-1692. Research Article ISSN 2277– 7105

PHARMACOLOGICAL ACTIVITY OF SELECTED MARINE SOURCE FROM COASTAL ANDHRA PRADESH

K. Swathi Priya*[1] and Dr. S. Rajasekaran[2]

[1]Department of Pharmacy, Bhagwant University, Sikar rd, Ajmer, Rajasthan.

[2]Department of Pharmacology, Bhagwant University, Sikar rd, Ajmer, Rajasthan.

Article Received on
10 January 2022,

Revised on 30 January 2022,
Accepted on 20 Feb. 2022

DOI: 10.20959/wjpr20223-23331

***Corresponding Author**
K. Swathipriya
Department of Pharmacy,
Bhagwant University,
Sikar rd, Ajmer, Rajasthan.

ABSTRACT

Aim and Objective: The present study is to assess the acute toxicity, anti diabetic activity of hydro alcoholic extract of selected marine macro algae *Spongomorpha indica* (HASI). **Material and Methods:** The *Spongomorpha indica* (green macroalgae) was collected from coastal area of Visakhapatnam Andhra Pradesh. Hydro alcoholic extract of *Spongomorpha indica* was prepared and it was screened for acute toxicity, anti diabetic. In acute toxicity study, wistar mice were grouped into 4 and dosed wit 5,50,200,2000..mg/kg of HASI and observed at 0, 30,24hrs up to 14days. Antidiabetic activity was analyzed using two models i.e., Streptozocin induced and Dexamethasone induced. The rats were grouped into five groups each named as control, diabetic control, standard (5mg /kg Glibenclamide) and remaining two as tests with 200 and 400 mg/kg HASI were administered and results were observed. **Results & Discussion:** acute toxicity study showed no significant behavioral changes and LD_{50} was determined as 200mg/kg. In Streptozocin induced diabetic study the body weight of the normal and treated groups significantly differs from diabetic control on 14th day. Also the same urine glucose level of normal and treated groups also significantly differs from diabetic control on 14th day shown in Table 1&2 and figure 1&2. The standard (Glibenclamide (5mg/kg), hydro-alcoholic extract 200 & 400 mg/kg treated groups significantly decrease in blood glucose level on 14thday compared to negative control (Table5 and Figure4). Group II animals exhibited decreased levels of protective antioxidant enzymes such as SOD and CAT, suggesting a possible free radicals generation. Treatment with standard, HASI 200 & 400 mg/kg showed significantly ($p<0.01$) increased levels of protective enzymes such as SOD and CAT, suggesting its possible antioxidant action. Whereas group III revealed less significant changes

when observed compared to extract treated group(Table 7 and Figure 6). In Dexamethasone induced study the same results were obtained when observed for 21days (Tabale 8&9 and Figure 7&8). The standard Glibenclamide (5mg/kg), HASI (200 mg/kg) treated groups revealed significant decrease in blood glucose level from 3rd day to 21st day (Table10 and Figure 10). Thus, the extracts was found to be more significant ($p<0.001$) as standard drug in lowering blood glucose level compare to negative control. HASI 400mg/kg extract shows almost equal effect compared to positive control on 21st day. **Conclusion:** Hence by the above study it was seen that HASI exhibited antidiabetic effect by lowering the urine glucose and blood glucose levels. It was also seen that it has anti oxidant activity which was studied in Streptozocin model. Further studies are continued to know the exact mechanism of action involved and also to know whether HASI has wound healing property in delayed diabetic infections.

KEYWORDS: HASI (Hydro alcoholic *Spongomorpha indica*), anti diabetic, Streptozocin, Dexamethasone, Glibenclamide.

INTRODUCTION

Spongomorpha indica is a macroalgae commonly used as a seaweed for animals belong to the family ulotrichaceae.[1] Traditional reports suggest that *Spongomorpha indica* is shown to posses antibacterial, antifungal, antiviral, anti-inflammatory activities. However, the literature indicates that there is no scientific evidence to support the antidiabetic effect of *Spongomorpha indica*. The present study investigates the action of hydroalcoholic *Spongomorpha indica* (HASI) extract in different models of rats to ascertain the scientific basis for the use of the algae in the treatment of diabetes on rats.

MATERIAL AND METHODS

Collection and Preparation of extract

The collected seaweed was washed with ocean sea water at the site of collection and then it was shade dried, extraneous matter was removed by sieving. The dried product was coarsely powdered and was extracted with hydro-alcohol 70:30(70% v/v methanol) using maceration chambers by three successive extractions followed by vacuum filtration to remove any fine particles, wastes and dust etc. After completion of extraction the filtrates were concentrated by using distillation unit, dried and stored in desiccator.

Experimental animals

All the experiments were carried out using Swiss Albino mice (25-30 g) and Wistar rats (150-200 g). The animals were placed at random and allocated to treatment groups in polypropylene cages with paddy husk as bedding. Animals were housed at a temperature of 24 ± 2^0C and relative humidity of 30–70%. A 12 hrs day: 12 hrs night cycle was followed. All animals were allowed free access to water and fed. Ethical clearance was obtained from Institutional Animal Ethical Committee with Registration No: 527/PO/ReBi-S/07/IAEC

Acute toxicity study

The acute toxicity study was carried out with hydro-alcoholic extract of *Spongomorpha indica* as per OECD 423 Guidelines. Wistar albino mice with weight ranging (25-30g) were taken for the experiment. The animals were made into a group of 3 each, dose of *Spongomorpha indica* hydro-alcoholic extract were given according to the body weight (mg/kg), starting dose of 5 mg /kg was given to the first individual animal, no death was occurred and higher doses were given to next group of animals. The animals were observed for a further 14 days for any signs for delayed toxicity.[2]

Glucose tolerance test[3]

Fasted rats were divided into five groups of six rats in each. Group I- Served as control, received 2ml distilled water, Group II- received only glucose, Group III- received standard drug glibenclamide at a dose of 5mg/kg b. wt, Groups IV-received the hydro-alcoholic extract of *Spongomorpha indica* (HASI) extract at a dose of 200 mg/kg b. wt and Groups V-received the hydro-alcoholic extract of *Spongomorpha indica* (HASI) extract at a dose of 400 mg/kg b. wt.

After 30 min of extract& Standard drug administration to Group III, IV & V, the rats of all groups were orally treated with 2 g/kg of glucose except Group I. All groups of rat blood samples were collected from the tail vein just prior to glucose administration and at 30, 60, 90 and 120 min after glucose loading. Blood glucose level was measured immediately by using digital glucometer (one touch select, Johnson & Johnson, USA).

Streptozotocin induced anti-diabetic activity

Induction of diabetes

STZ was freshly prepared by dissolving in citrate buffer (0.01M, PH-4.5) and kept on ice prior to practice. The overnight fasted rats were made diabetes with a single intraperitoneal

injection of STZ (60 mg/kg). After 4hrs STZ administration 5% glucose was administered orally in drinking water for a day to overcome the early hypoglycemic phase. Rats were allowed to stabilize for three days. On the third day (72hrs) blood samples were drawn to estimate the blood glucose concentration to confirm the development of diabetes. Rats with plasma glucose estimated by using digital glucometer (accu-chek, Roche Diabetes Care India) and above 250 mg/dl were considered as diabetic and used in the study. The animal confirmed diabetes was only used for anti-diabetic activity.[3]

The animals divided into five groups of six rats group 1- control, group 2- diabetic control, group 3- standard(glibenclemide 5mg/kg), group 4- 200mg HASI administered orally for 14 days and 400mg HASI administered for 14days. The body weights, blood glucose levels, urine glucose levels, biochemical parameters like and anti oxidant property using SOD model and Catalase models were determined.[4,5]

Dexamethasone induced diabetic model[6]

A total of 30 overnight fasted rats were used. The 24 rats were rendered diabetic by Dexamethasone (10mg/kg, s.c) once daily. Group I - Normal control received distilled water, Group II - Served as Diabetic control, Group III - Served as standard treated with 5 mg/kg of Glibenclamide for 21 days Orally, Group IV -Treated with 200 mg/kg of hydro-alcoholic extract of *Spongomorpha indica* (HASI) *for* 21 days orally, Group V -Treated with 400 mg/kg of hydro-alcoholic extract of *Spongomorpha indica (*HASI) for 21 days orally. The body weights, blood glucose levels, urine glucose levels, biochemical parameters were determined.

Statistical analysis

One-way analysis of variance (ANOVA) followed by Dunnett's method of multiple comparisons was employed using Graph pad Instat 5.0 software. $p<0.05$, $p<0.01$ & $p<0.001$ was considered to be statistically significant.

RESULTS

Acute oral toxicity study

Table 1: Acute oral toxicity study of hydro-alcoholic extract of *Spongomorpha indica* L *in* mice.

S. no.	Extracts	LD_{50} mg/kg	ED_{50} mg/kg
1	Hasi	2000	200

Table 2: Observation parameters in acute toxicities of hydro-alcoholic extract *Spongomorpha indica* L.

Parameters	Observation
Tremors	Not observed
Convulsions	Not observed
Salivation	Normal
Sleep	Normal
Diarrhoea	Feces normal
Lethargy	Observed laziness
Skin and fur	Normal
Eyes and mucous membrane	Normal
Respiratory	Normal
Circulatory	Normal
Autonomic and central nervous system	No observed changes
Somatomotor activity	Normal motor activity

There was no mortality and toxicity was observed up to 2000mg/kg and study was carried out with $1/10^{th}$ of LD_{50} of extract as 200 mg/kg Therapeutic dose (TD) and double the TD as 400 mg/kg.

Table 3: Effects of *Hydro-Alcoholic extract Spongomorpha indica* L on oral glucose tolerance in rats.

Groups	0 min	30 min	60 min	90 min	120 min
Group I	80.22± 0.85	79.23± 1.25***	83.57± 0.94	82.21±1. 29***	80.56±3. 12***
Group II	86.58± 0.19	168.74± 2.37	215.08± 1.83	196.25± 2.46	185.43± 2.57
Group III	75.16± 0.57	139.57± 4.25***	150.28± 0.84	129.68± 1.43***	101.28± 1.45***
Group IV	78.23± 0.83	145.64± 2.61***	158.29± 1.85***	140.51± 1.28***	129.54± 2.17**
Group V	80.84± 0.43	143.28± 3.16***	156.53± 2.57***	138.43± 2.31***	101.61± 1.84***

Values are expressed as Mean±SEM, n=6. Significant (*** p <0.001) compared with treated groups Vs diabetic control.

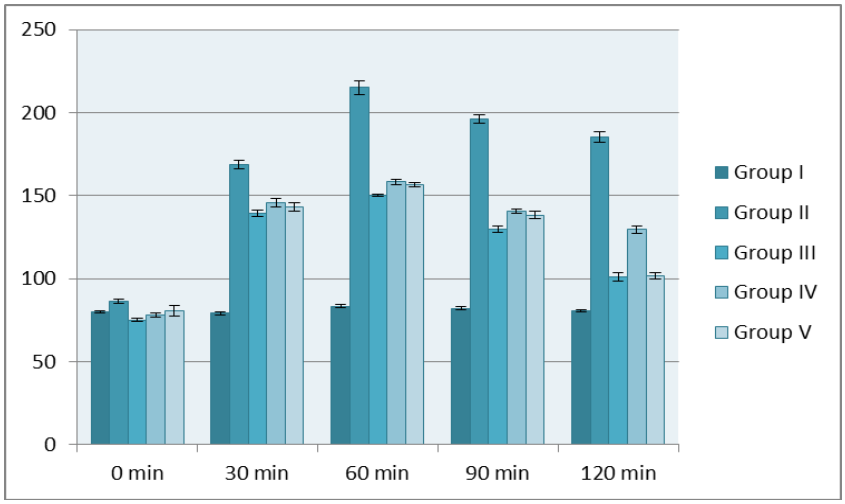


Figure 1: Effects of *Hydro-Alcoholic Extract Spongomorpha indica* L on oral glucose tolerance in rats.

Streptozotocin induced diabetic rats

Table 4: Effect of *Spongomorpha indica* L on body Weight & Urine glucose.

Groups	Treatment	Body weight		Urine Glucose	
		0th day	14th day	0th day	14th day
Group I	2 ml of Distilled water	176.48± 2.07	212.35± 2.59**	81.39± 2.34	79.48±1. 09***
Group II	Streptozotocin 60 mg/kg	161.66± 1.47	178.83± 1.24	87.24± 1.96	375.46± 0.83
Group III	glibenclamide (5mg/kg)	173.33± 2.07	215.64± 2.00**	78.15± 2.74	128.91±1. 37***
Group IV	200 mg/kg	180.83± 1.38	227.73± 1.77*	80.26± 2.12	174.62± 1.52**
Group V	400 mg/kg	174.16± 1.74	216.61± 1.07**	83.12± 1.94	132.83± 1.09***

The values are mean±SEM, n=6 when treated group compared with diabetic control $p<0.05^{*}$, **p<0.01, ***p<0.001.

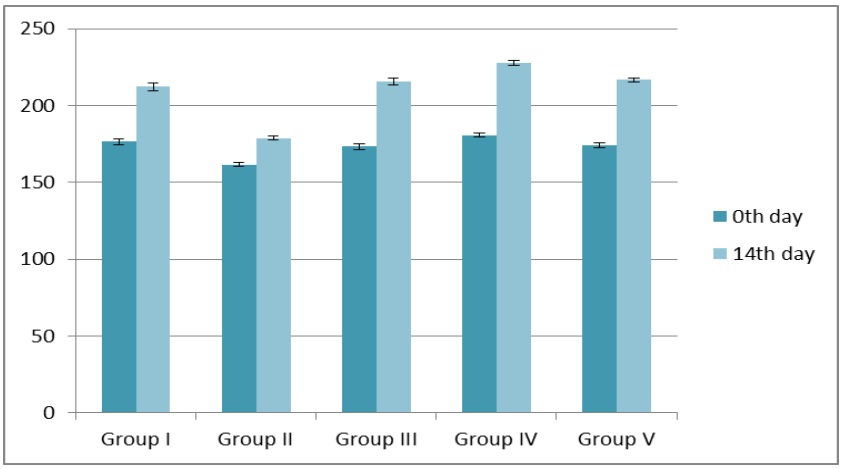


Figure 2: Effect of *Spongomorpha indica* L on body weight.

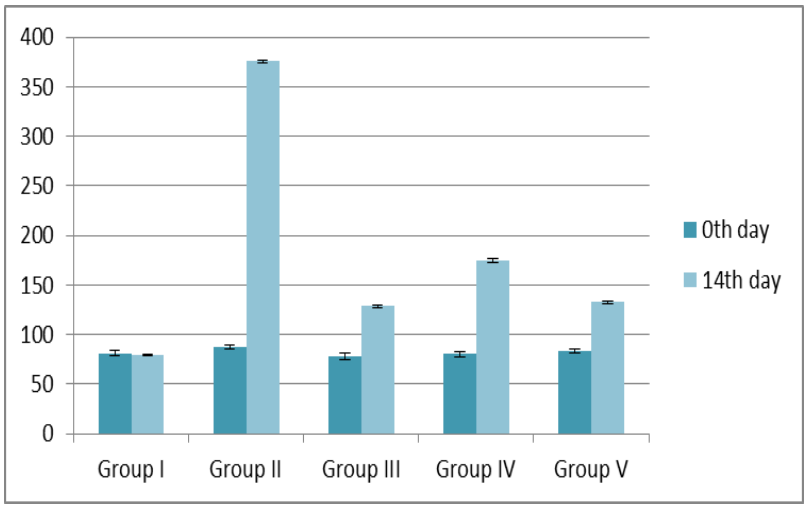


Figure 3: Effect of *Spongomorpha indica* L on urine glucose.

Table 5: Effect of *Spongomorpha indica* L on blood glucose level on streptozotocin induced diabetic rats.

Groups	Blood glucose level in mg/dl					
	0th day	3rd day	6th day	9th day	11th day	14th day
Group I	83.05± 1.83	83.8±2. 32***	76.63±1. 52***	79.83±1. 39***	80.60±1. 79***[a]	82.84±1. 05***[a]
Group II	85.5± 1.1	382.16± 2.9[c]	424.33± 1.65[c]	451.66± 1.5[c]	486.32± 1.82[c]	500.00± 1.50[c]
Group III	80.50± 1.01	271.88±3. 35**	235.0± 1.9**	171.7 ± 2.38**	142.0±1. 39***[b]	110.0±1. 42***[a]
Group IV	82.20± 1.8	357.88± 4.32*	315.0± 2.32**	300.7 ± 2.6**	220.0±1. 12***[d]	174.10±1. 02**[d]
Group V	81.24± 1.21	278.92± 3.45**	232.0±1. 80***	187.8 ± 1.88**	158.20± 1.87***[b]	130.20±1. 15***[b]

The values are mean±SEM, n=6 when compared with diabetic control *p<0.05, **p<0.01, ***p<0.001. Mean bearing different superscripted differ significantly.

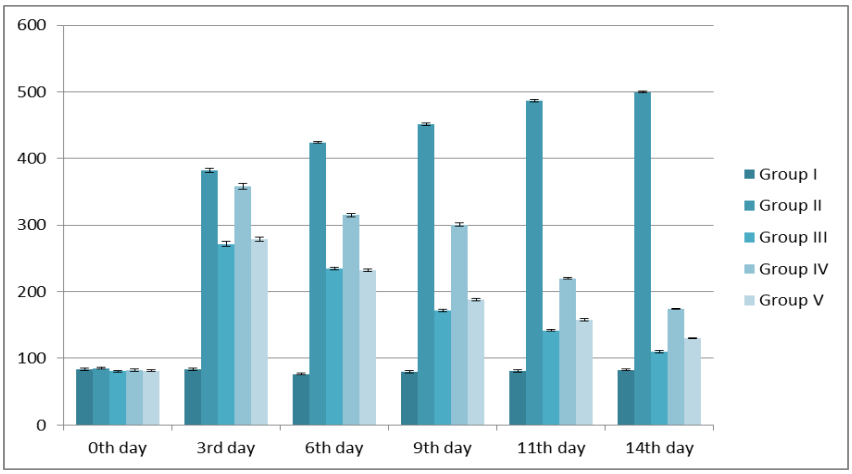


Figure 4: Effect of *Spongomorpha indica* L on blood glucose level on streptozotocin induced diabetic rats.

Table 6: Effect of *Spongomorpha indica* L on lipid parameters by streptozotocin induced diabetic rats.

Groups	TG (mg/dl)	TC (mg/dl)	HDL (mg/dl)	LDL (mg/dl)	VLDL (mg/dl)
Group I	137.47±1.76***	104.25±2.42***	37.83±1.72**	47.00±2.80***	12.65±1.27***
Group II	284.41±1.16	169.81±2.11	21.5±1.4	109.30±1.83	30.33±1.22
Group III	146.88±2.93***	118.86±1.42*	38.33±2.72**	48.67±1.28***	13.98±1.12***
Group IV	179.00±2.33**	152.56±1.33^{ns}	36.67±1.26**	75.25±1.52***	19.10±1.42**
Group V	142.64±1.05**	134.87±1.51*	34.83±1.94*	48.33±1.37***	12.35±1.15***

The values are mean±SEM, n=6 when treated groups compared with diabetic control *p<0.05, **p<0.01 & ***p<0.001.

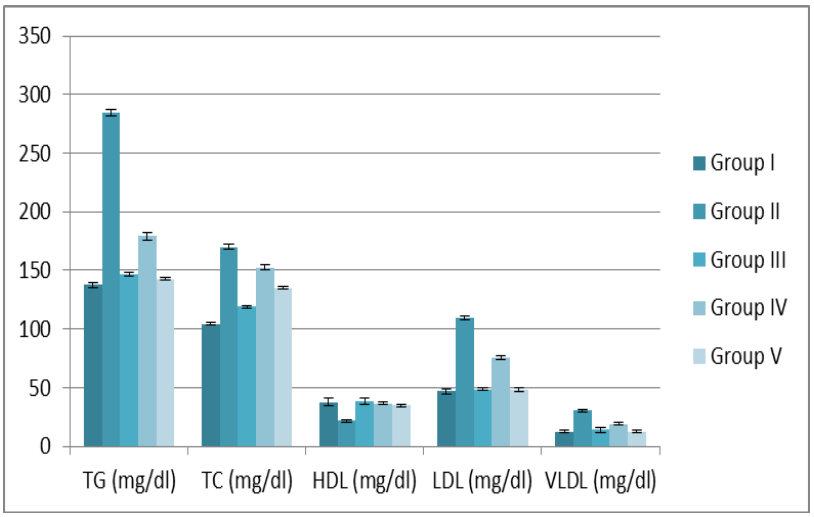


Figure 5: Effect of *Spongomorpha indica* L on lipid parameters by streptozotocin induced diabetic rats.

Anti-oxidant study

Group II animals exhibited decreased levels of protective antioxidant enzymes such as SOD and CAT, suggesting a possible free radicals generation. Treatment with standard, HASI 200 & 400 mg/kg showed significantly (p<0.01) increased levels of protective enzymes such as SOD and CAT, suggesting its possible antioxidant action. Whereas group III revealed less significant changes was observed compared to extract treated group.

Table 7: Effect of *Spongomorpha indica* L extract on Anti-oxidant enzyme in Streptozotocin induced diabetic rats.

Groups	Treatment	SOD (U/mg of tissue)	CAT (U/mg of tissue)
Group I	Normal Control	6.15±0.02	10.50±0.4
Group II	Streptozotocin	1.50±0.04	3.52±0.20
Group III	Standard	3.1±0.05*	6.01±0.46*
Group IV	HASI 200 mg/kg	4.54±0.01**	7.82±0.29**
Group V	HASI 400 mg/kg	5.84±0.06**	9.65±0.55**

The values are mean±SEM, n=6 when treated group compared with diabetic control *p<0.05, **p<0.01.

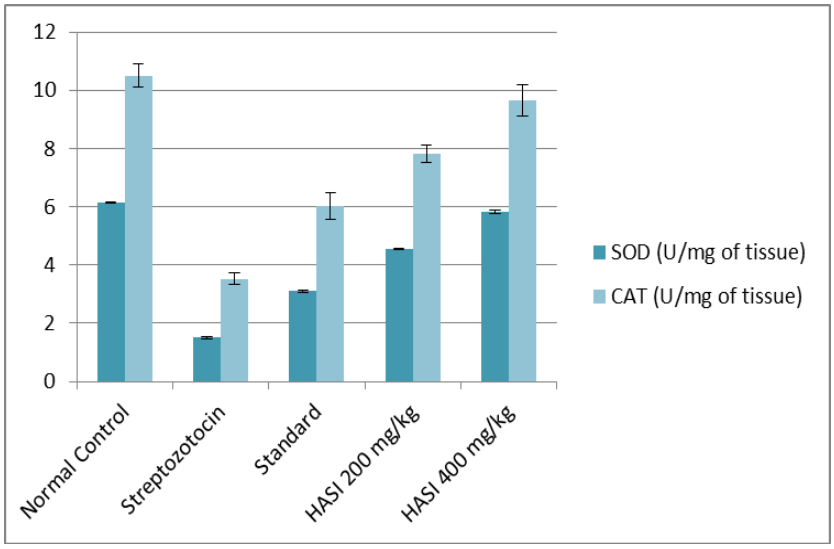
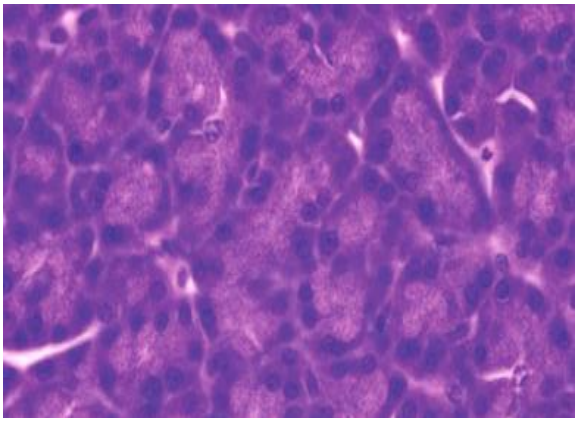


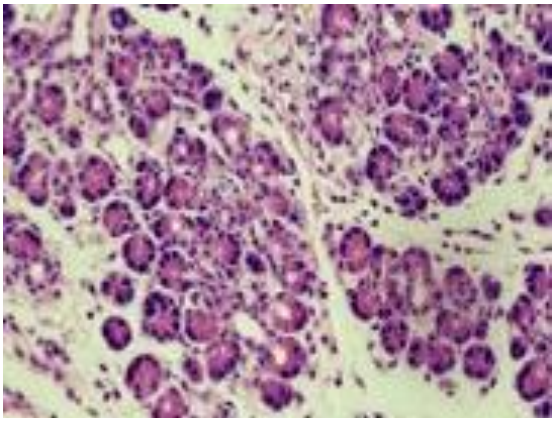
Figure 6: Effect of *Spongomorpha indica* L extract on Anti-oxidant enzyme in Streptozotocin induced diabetic rats.

Histopathology of pancreas in streptozotocin induced diabetic rats

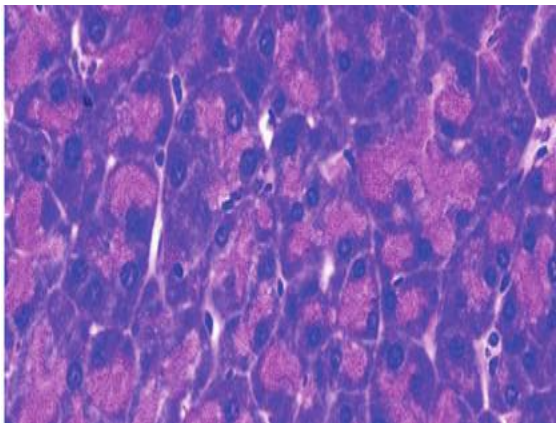
Normal control rat pancreas showing normal islets of Langerhans with pale rounded and ovoid β-cells in the center, embedded in exocrine portion of pancreas. Diabetic control rat pancreas showing shrinkage of islets of Langerhans with degeneration and necrosis of components cells where its nucleus appeared densely basophilic and karyolysis is evident. Pancreas of diabetic rat treated with glibenclamide and HASI 200mg/kg showing normal islets of Langerhans with its normal pale large round to ovoid shaped containing cells that embedded in exocrine portion of pancreas. Pancreas of diabetic rat treated with HASI 400mg/kg showing normal sized islets of Langerhans but some degeneration of the β cell in the center were noticed.



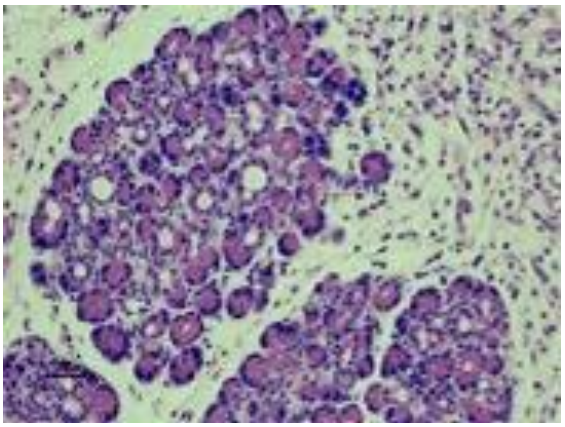
Normal control



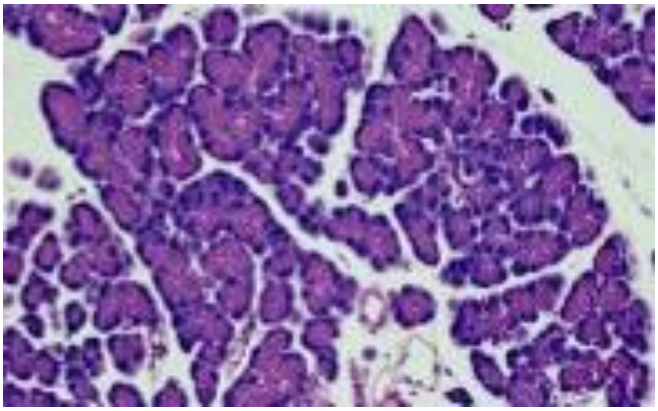
Negative control (Streptozotocin)



Standard (Glibenclamide 5 mg/kg)



HASI 200mg/kg



HASI 400mg/kg

Dexamethasone induced diabetic rats

Table 8: Effect of *Spongomorpha indica* L on body Weight and Urine glucose in dexamethasone induced diabetic rats.

Groups	Treatment	Body weight		Urine Glucose	
		0^{th} day	21^{st} day	0^{th} day	21^{st} day
Group I	Normal Control	156.48±2.07	252.35±2.59**	80.51±1.90	83.27±1.17***
Group II	Dexamethazone 10 mg/kg	151.66±1.47	169.83±1.24	79.27±1.38	305.32±1.02

Group III	Glibenclamide (5mg/kg)	163.33±2.07	252.64±2.00**	78.54±1.65	116.71±1.07***
Group IV	HASI 200 mg/kg	170.83±1.38	227.73±1.77*	81.69±1.58	184.49±1.76**
Group V	HASI 400 mg/kg	174.16±1.74	245.61±1.07**	84.38±1.47	157.62±1.41***

The values are mean±SEM, n=6 when treated group compared with diabetic control $p<0.05^{*}$, **p<0.01, ***p<0.001.

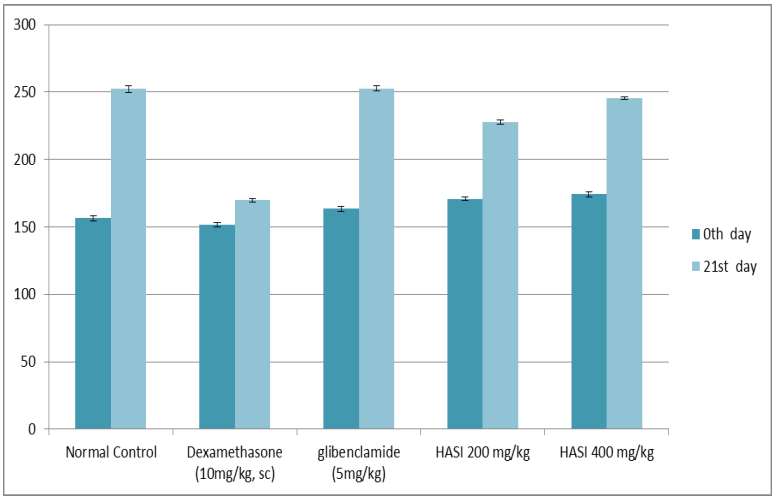


Figure 7: Effect of *Spongomorpha indica* L on body weight in dexamethasone induced diabetic rats.

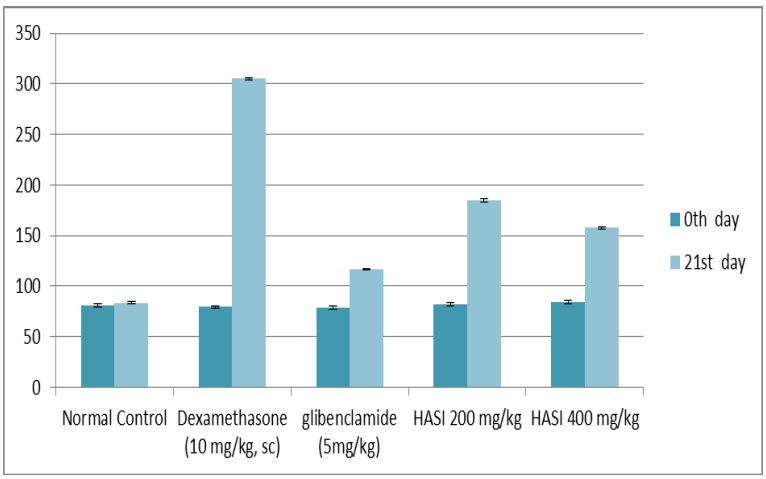


Figure 8: Effect of *Spongomorpha indica* L on urine glucose in dexamethasone induced diabetic rats.

Table 9: Theeffect of *Spongomorpha Indica* L extract on blood glucose level in dexamethasone induced hyperglycemic rats.

Groups	Blood glucose level in mg/dl							
	0 day	3 day	6 day	9 day	11 day	14 Day	17 Day	21 day
Group I	84.66± 4.88	89.33± 4.07***	80.16± 2.57***	101.7± 4.11***	97.7±1. 05***	85.45±4. 11***	82.34±2. 43***	86.5±1. 57***[a]
Group II	76.83±	248.16±	267.47±	286.33±	309.43±	345.28±	364.26±	380.54±

	5.26	4.98	5.17	2.84	3.48	5.27	3.79	2.38
Group III	82.16± 2.27	178.5±4. 00**	186.28± 4.06**	158.24±2. 51***	139.52±2. 31***	130.57±2. 51***	124.62± 2.19***	113.17± 2.81***[a]
Group IV	77.33± 3.21	195.5±3. 73*	204.64± 5.45*	195.74± 2.59***	176.70± 2.59***	152.45±3. 59***	144.91± 2.46***	122.92± 2.12***
Group V	83.83± 1.99	176.66± 2.72**	198.15± 2.90**	163.15± 3.12***	143.5±3. 04***	130.47±3. 04***	123.5±3. 04***	94.50±3 .75***[a]

The values are mean ± SEM, n=6 when compared with diabetic control **p<0.01

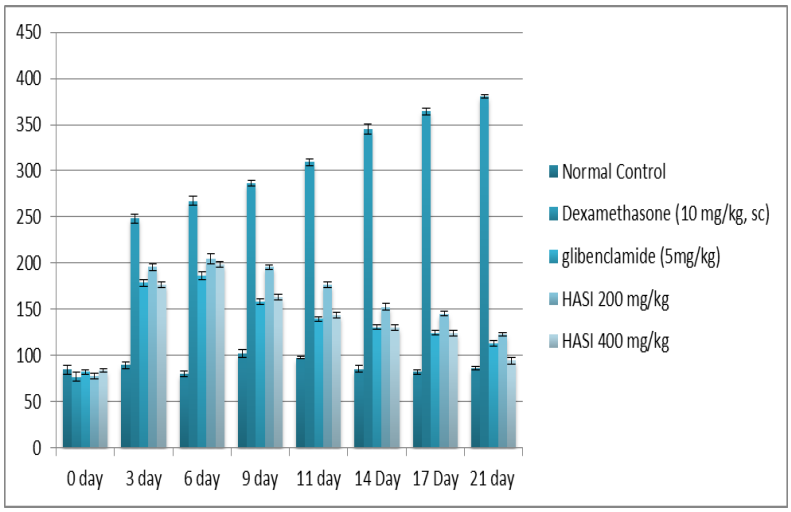


Figure 9: The effect of *Spongomorpha indica* L extract on blood glucose level in dexamethasone induced hyperglycemic rats.

Table 10: Effect of *Spongomorpha indica* L extract on lipidprofilein dexamethasone induced hyperglycemic rats.

Groups	TG (mg/dl)	TC (mg/dl)	HDL(mg/dl)	LDL(mg/dl)	VLDL(mg/dl)
Group I	118.47±3. 13***[a]	153.18±4. 27***	36.08±2. 80**	42.13±2. 24***	28.49±2. 24***
Group II	235.79±5. 25	238.27±4. 91	24.01±1. 05	68.75±3. 38	69.13±4. 25
Group III	139.50±3. 00***[b]	162±3. 52***	34.64±2. 93***	49.43±2. 36**	34.27±2. 32***
Group IV	145.18±4. 93***[c]	163.75±2. 88***	32.53±2. 14**	50.43±2. 15*	36.26±2. 62***
Group V	124.82±1. 00***[a]	158.61±4. 83***	38.59±2. 25*	43.18±3. 81***	30.46±2. 83***

The values are mean±SEM, n=6 when treated groups compared with diabetic control *p<0.05, **p<0.01 &***p<0.001. Means bearing same superscript do not differ significantly between treated groups. Means bearing different superscript differ significantly at p<0.01 & p<0.05, between treated groups.

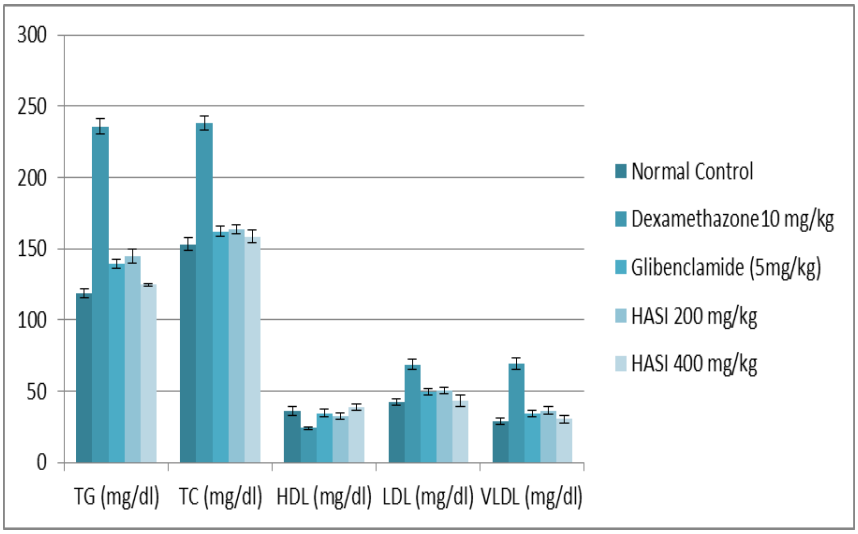


Figure 11: Effect of *Spongomorpha indica* L extract on lipidprofilein dexamethasone induced hyperglycemic rats.

DISCUSSION

The acceptance of medicinal plants into scientific medicine, it is necessary that their effectiveness and safety be evaluated and confirmed through active ingredient testing. To maximize the extractive capability of phenolic, tannin and flavonoids components from plant material is considerably depended on the type of solvent. Highest content of phenolic, flavonoids and tannin in ethanol and hydro-alcoholic extract in comparison to other solvents used, make this solvent an ideal and selective to extract a great number of bioactive phenolic compounds.[7] Collagen fibers treated with the plant flavonoid, catechin, have been found to be stable. Such stabilization effect has been shown to involve hydrogen bonding and hydrophobic interactions.[8]

Tannins are generally defined as naturally occurring polyphenol compounds of high molecular weight to form complexes with the proteins. Tannins are important source of protein in animals but unfortunately the amounts of tannins that they contain vary widely and largely unpredictably, and their effects on animals range from beneficial to toxicity and death.[9] The toxic or anti-nutritional effects tend to occur in times of stress when a very large proportion of the diet having high concentration of tannins. Thus consumption of foods naturally having antioxidant activity is the most efficient way of combating such tissue injuries, undesired transformations and preventing health risks.[10] The oxidative free radical to cause degeneration of Langerhans islets beta cells by Streptozotocin[11,12] leads to diabetes, it was reversed and protected by HASI extract confirmed through Streptozotocin model and also supported with result of increased antioxidant enzyme in pancreatic tissue SOD &

catalase. Dexamethasone is a potent and highly selective glucocorticoid used in the treatment of inflammation. Side effects of glucocorticoid treatment include steroid diabetes.[13,14]

High exposure to glucocorticoids impairs insulin sensitivity, contributing to the generation of metabolic syndrome including insulin resistance and hypertension.[15] The mechanism by which dexamethasone induces peripheral insulin resistance is by inhibiting GLUT-4 translocation.[16] The underlying mechanism involves increased α_2- adrenoceptor signaling.[210] increased Potassium channel activity[17] and impaired glucose metabolism.[18,19] Although reduced insulin secretion during glucocorticoid treatment can be overcome by blocking adrenoceptor signaling or by inhibition of potassium channel, compelling evidence suggests that the proper functioning of β-cells also depends on cell survival.[20] Accordingly, a reduction of β-cell mass in long-standing glucocorticoid therapy may contribute to the consecutive development of steroid diabetes. The decreased blood glucose level was observed with HASI extract in Streptozotocin and dexamethasone induced diabetic models.

CONCLUSION

In the present study it is shown that hydroalcoholic extract of *Spongomorpha indica* a macroalgae has potential effects in lowering the glucose levels in both streptozocin as well as dexamethazone induced diabetic rats and the effects were found to be more effective than glibenclamide at the heighest doses i.e., 400mg/kg. Further studies are in progress at molecular level to explicitly explain more about the mechanism of the antidiabetic activity and compounds responsible for its effects.

REFERENCE

1. Guiry, M.D & Guiry, G.M, Algae Base. World-wide electronic publication,National University of Ireland, Galway(taxonomic information republished from Algae Base with permission of M.D.Guiry), 2020.
2. OECD/OCDE, OECD Guidelines for the testing of chemicals, revised draft guidelines 423: Acute Oral toxicity- Acute toxic class method, revised document, CPCSEA, Ministry of Social Justice and Empowerment. New Delhi: Government of India, 2000.
3. Sellamuthu PS, Muniappan BP, Perumal SM & Kandasamy M: Antihyperglycemic effect of mangiferin in streptozotocin induced diabetic rats. J. Health Sci, 2009; 55: 206–14.
4. Misra H, Fridovich I. Role of superoxide anion in the autooxidation of epinephrine and a simple assay for superoxide dismutase. J Biol Chem, 1972; 247: 3170.

5. Beers R, Sizer I. A spectrophotometric method for measuring the breakdown of hydrogen peroxide by catalase. J Biol Chem, 1952; 195: 133.
6. Shalam MD, Harish MS & Farhana SA: Prevention of dexamethasone- and fructose-induced insulin resistance in rats by SH-01D, a herbal preparation. Indian J Pharmacol, 2006; 38: 419-422.
7. Mohammedi Z. Impact of solvent extraction type on total polyphenols content and biological activity from tamarixaphylla (l.) Karst. International Journal of Pharma and Bio Sciences, 2011; 2(1): 609-615.
8. Madhan B, Subramanian V, Rao JR, Nair BU, Ramasami T. Stabilization of collagen using plant polyphenol: role of catechin. International Journal of Biological Macromolecules, 2005; 37(1-2): 47-53.
9. Yang CMJ, Russell JB. Resistance of proline-containing peptides to ruminal degradation in vitro, Appl. Environ. Microbiol, 1992; 58: 3954–3958.
10. Mau JL, Lin HC, Chen CC. Antioxidant properties of several medicinal mushrooms. Journal of Agricultural andFood Chemistry, 2002; 50(21): 6072–6077.
11. Ikebukuro K, Adachi Y, Yamada Y, Fujimoto S, Seino Y, Oyaizu H: Treatment of Streptozotocin-induced diabetes mellitus by transplantation of islet cells Plus bone Marrow cells via portal vein in rats. Transplantation, 2002; 73: 512-518.
12. Smith SB, Prior RL, Mersmann HJ: Interrelationship between insulin and lipid metabolism in normal and alloxan-diabetic cattle. J Nutr, 1983; 113: 1002-1015.
13. Hoogwerf B and Danese RD. Drug selection and the management of corticosteroid-related diabetes mellitus. Rheum Dis Clin North Am, 1999; 25: 489 –505.
14. Schacke H, Docke WD and Asadullah K. Mechanisms involved in the side effects of glucocorticoids. Pharmacol Ther, 2002; 96: 23– 43.
15. Kabosova A, Kramerov AA, Aoki AM, Murphy G, Zieske JD, Ljubimov AV, Human diabetic corneas preserve wound healing, basement membrane, integrin and MMP-10 differences from normal corneas in organ culture, Exp Eye Res., 2003; 77: 211– 217.
16. Dake QI, Thomas P, Ding AN, Diabetes triggers a PARP1 mediated death pathway in the heart through participation of FoxO1, Diabetes., 2004; 53: 1790–97.
17. Hamamdzic D, Duzic E, Sherlock JD and Lanier SM: Regulation of α2-adrenergic receptor expression and signaling in pancreatic β-cells. Am J Physiol., 1995; 269: 162– 71.
18. Ullrich S, Berchtold S, Ranta F, Seebohm G, Henke G, Lupescu A, Mack AF, Chao CM, Su J, Nitschke R, Alexander D, Friedrich B, Wulff P, Kuhl D and Lang F: Serum- and

glucocorticoid-inducible kinase 1 (SGK1) mediates glucocorticoid-induced inhibition of insulin secretion. Diabetes, 2005; 54: 1090–1099.

19. Gremlich S, Roduit R and Thorens B. Dexamethasone induces posttranslational degradation of GLUT2 and inhibition of insulin secretion in isolated pancreatic β-cells: comparison with the effects of fatty acids. J Biol Chem, 1997; 272: 3216 –3222.
20. Ling ZC, Khan A, Delauny F, Davani B, Ostenson CG, Gustafsson JA, Okret S, Landau BR and Efendic S: Increased glucocorticoid sensitivity in islet β-cells: effects on glucose 6-phosphatase, glucose cycling and insulin release. Diabetologia, 1998; 41: 634–639.