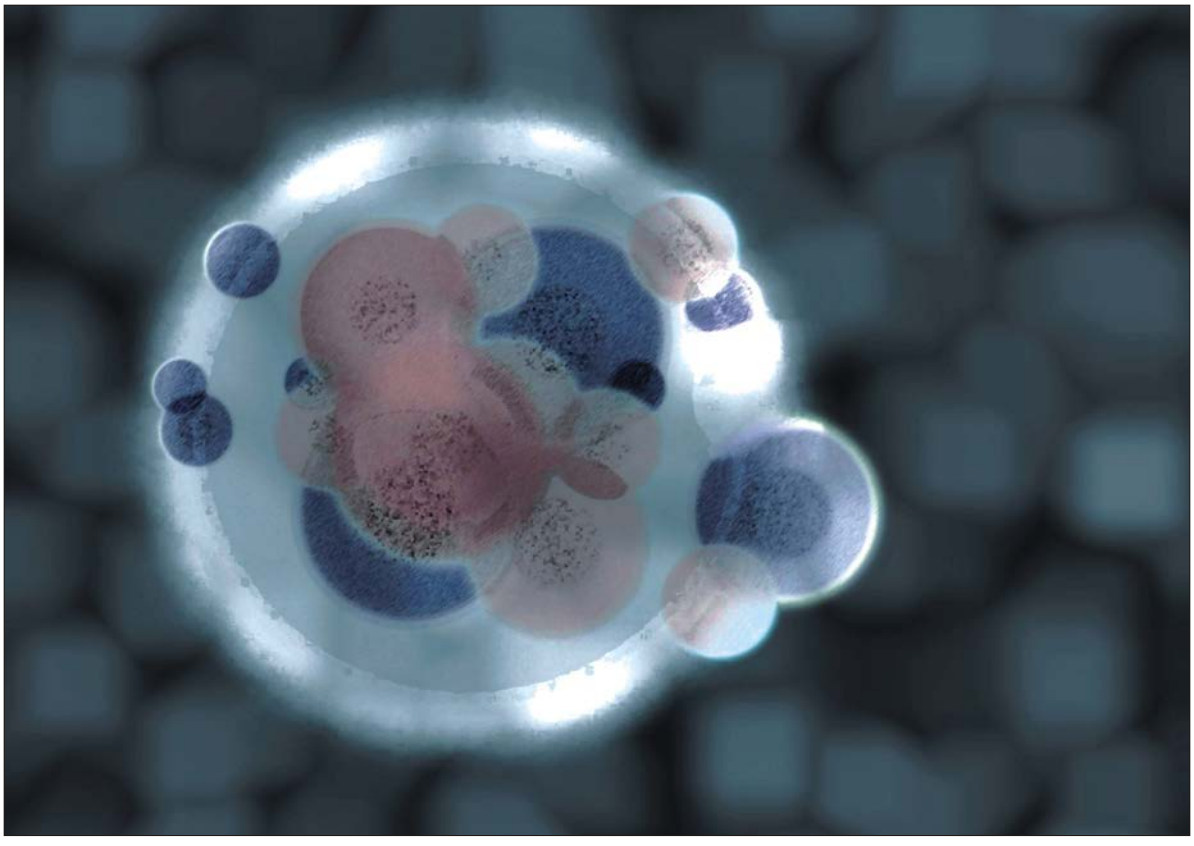

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Research Article
Blood Glucose Level and Lipid Profile of Streptozotocin-induced Diabetes Rats Treated with Sodium Alginate from *Sargassum crassifolium*

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Abstract
The objective of this study was to evaluate the potential effect of sodium alginate from *Sargassum crassifolium* on glucose level and lipid profile in streptozotocin-induced diabetes rats. Sodium alginate extract of *S. crassifolium* 200, 400 and 600 mg kg^{-1} was administered orally to streptozotocin-induced diabetes rats, once daily for 15 days. The result obtained were then compared with normal control (non-diabetic+normal saline 0.9% p.o), negative control (diabetes+CMC-Na 0.5% p.o) and positive control (diabetic+glibenclamide 5 mg kg^{-1} p.o). The glucose level, lipid profile and body weight were measured on normal condition (baseline) on 0, 5th, 10th, 15th day and pancreatic histopathological study were done on 15th day. Sodium alginate extract of *S. crassifolium* had yield 23.82% db, viscosity of 521 cps and a water content of 16.18% db. Sodium alginate 600 mg kg^{-1} significantly reduce level preprandial glucose, postprandial glucose and total cholesterol compared negative control and did not have significant difference with positive control. Levels of triglycerides and LDL-c throughout the treatment groups had significant differences with the negative control. Meanwhile, the levels of HDL-c throughout the treatment group did not have significant differences. Necrosis was found in all streptozotocin-induced rats. The higher alginate doses given, getting better lower the levels of glucose and total cholesterol.

Key words: Sodium alginate, *Sargassum crassifolium*, antihyperglycemia, lipid profile, streptozotocin

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Competing Interest: The authors have declared that no competing interest exists.

Data Availability: All relevant data are within the paper and its supporting information files.

INTRODUCTION

The term diabetes mellitus describes a metabolic disorder of multiple aetiology characterized by cronic hyperglycaemia with disturbances of carbohydrate, fat and protein metabolism resulting from defect in insulin secretion, insulin action or both (WHO., 1999). Insulin is required for cells to absorb glucose from blood for use as fuel or for storage. In the patients of diabetes mellitus, this glucose metabolism is altered due to either low level of insulin secretion (type 1 diabetes) or abnormal resistance to insulin's effects (type 2 diabetes) (WHO., 1985). Diabetes is a leading cause of morbidity and mortality for the world's growing population. The International Diabetes Federation has predicted a worldwide increas from 8.3-9.9% by the year 2030 (IDF., 2012).

Diabetes is associated with major abnormalities in fatty acid metabolism (Tomkin, 2008). The most common lipid pattern in type 2 diabetes consists of hypertriglyceridemia, low High Density Lipoprotein cholesterol (HDL-c) and normal plasma concentrations of Low Density Liprotein choleserol (LDL-c) (Leiter *et al*., 2006). It is one of primary threats to human health due to increas prevalence and associated disabling complication. At present, the treatment mainly involves a sustained reduction in hyperglycemia using oral hypoglycemic agents besides injectable insulin. However, prominent side-effects of such drugs are the main reason for an increasing number of people seeking alternative therapies that may have less severe or no side-effects, hence the demand has arisen for using a more benign drugs (Moller, 2001).

A number of plants originating from different parts of the world possessing antidiabetic and related beneficial effects have been documented (Kavishankar *et al*., 2011). *Sargassum* sp. is a type of seaweed that is included in the class Phaeophyta (Noiraksar and Ajisaka, 2008). Brown seaweed *Sargassum crassifolium* is a species commonly found and abundant in the world. Seaweeds have content such as polysaccharides, proteins, peptides, amino acids, lipids, minerals and some vitamins. Seaweed also has a high content of antioxidants that can be used to ward off free radicals that increase due to the condition of hyperglycemia in patients with diabetes mellitus (Firdaus *et al*., 2010). Several seaweeds, such as *Petalonia binghamiae, Padina gymnospora, Sargassum cystoseria* (Phaeophyceae) and *Spyridia fusiformis* (a red sea weed) have hypoglycemic effects in diabetic mammals (Mohamed *et al*., 2012). Bioactive compounds in *Sargassum* sp. potential as an antioxidant, antitumor, antifungal, antiviral, antihypertensive and antidiabetic (El Gamal, 2010; Husni *et al*., 2014). Marine algae and algal polysaccharides also have hypocholesterolaemic effects in mammals (Matanjun *et al*., 2010). Until now, research information on the antidiabetic activity of sea weed *Sargassum crassifolium* has not been found. The purpose of this study was to determine the effect of sodium alginate extract of sea weed *S. crassifolium* on glucose and lipid profile in wistar rats induced by streptozotocin.

MATERIALS AND METHODS

Materials: Male albino wistar rats, weighting 136.6-223.2 g were used (3 month of age), *Sargassum crassifolium* from Drini seashore, Gunungkidul, Yogyakarta, HCl (Merck KGaA), streptozotocin (Merck 572201), Na_2CO_3, $CaCl_2$ (Merck KGaA), H_2O_2, 96% ethanol (MEDISS), aquadest, aquabidest, TFA (CF_3CO_2H), isoprophanol, ethyl acetate, *glibenclamide*, CMCNa 0.5%, NaCl (Merck KGaA), glucose reagent GOD FS, triglyceride reagent GPO FS, cholesterol reagent CHOD-PAP FS, HDL-c precipitant, LDL-c precipitant, glucose standard 100 mg dL^{-1}, triglyceride standard 200 mg dL^{-1}, cholesterol standard 200 mg dL^{-1} (Diasys Diagnostic System GmbH), alginate, citrate buffer pH 4.5, picric acid, acetic acid glacial (Merck KGaA), 37% formalin, Ketamil and chloroform.

Seaweed extractions: *Sargassum crassifolium* was collected from Drini seashore, Gunungkidul, Yogyakarta. Collection of sample was done by cutting the thallus near the rizoid. Algae were washed with freshwater before sun-drying at ambient temperature and stored in aerated bags in a shaded and ventilated site. Alginates were extracted according to the procedure of Rasyid (2010). One hundred and fifteen grams of dried algae were added to 0.1 N HCl (1500 mL) and left for 24 h. After this time, the sample were washed with aquadest before extraction with 0.5 N sodium carbonate during 2 h at 60°C. The alginate dissolves as sodium alginate to give a very thick slurry. The solution is too thick (viscous) to be filtered and must be diluted with a very large quantity of water. The solution were bleached with 5 NH_2O_2 (1/4; v/v). The bleached solution were added 0.5M $CaCl_2$ and was stirred 0.5 h then added a solution of 0.5 N HCl to a pH = 2. The mixture was stirred for 0.5 h at room temperature. So, the soluble fraction was collected by centrifugation (3500 rpm, 5 min) plus Na_2CO_3 and polysaccharides were precipitated by 96% ethanol and dried at 60°C. Sodium alginate extract of *S. crassifolium* have yield 23.82% db, viscosity of 521 cps and a water content of 16.18% db.

Experimental animals and induction of diabetes: Male albino wistar rats, weighting 136.6-223.2 g were obtained

from the animal house, LPPT Universitas Gadjah Mada. Animal were maintained at 24±2°C with 12 h light and dark cycle, humidity (40±5%) and provide with a standard pellet diet. Animal had free access to standard pellets as a basal diet and water *ad libitum*. All animal studies conducted were approved by the Institutional Animal Ethics Committee, Universitas Gadjah Mada (Approval No. 152/KEC-LPPT/VI/2014), Yogyakarta.

Animal were fasted overnight before injecting with streptozotocin. Diabetes mellitus was induced by single intraperitoneal injection of freshly prepared solution of STZ (60 mg kg^{-1} b.wt.) in 0.1 M citrate buffer of pH 4.5 after overnight fasting for 18 h. Animal were treated with 5% glucose solution orally to combat the early phase of drug-induced hypoglycemia. The blood glucose levels of animals were measured after 48 h STZ administration (Moree *et al*., 2013). Those rats showing fasting blood glucose levels of above 200 mg dL^{-1} with the indication of glycosuria were considered diabetic and included in the study. Each group consisted of 5 rats. The glucose levels, lipid profile and body weight were measured on normal condition (baseline) on 0, 5th, 10th and 15th day and pancreatic histopathological study were done on 15th day.

A total of 30 rats were devided into six groups as follow:

Group I: Normal rats treated with normal saline for 15 days
Group II: Diabetic rats treated with 0.5% CMC-Na for 15 days
Group III: Diabetic rats treated with 5 mg glibenclamide/kg b.wt./ day for 15 days
Group IV: Diabetic rats treated with 200 mg alginate/kg b.wt./day for 15 days
Group V: Diabetic rats treated with 400 mg alginate/kg b.wt./day for 15 days
Group VI: Diabetic rats treated with 600 mg alginate/kg b.wt./day for 15 days

Biocemical assays: Blood from the experimental rats was withdrawn by retro orbital plexus technique using capillary glass tubes. The collected blood was placed in eppendorff tubes (1.5 mL). The serum was separated by centrifugation using eppendorf centrifuge 5810 R run at speed of 10000 rpm for 20 min. Blood glucose level and lipid profiles (triglyceride, total cholesterol, HDL-c and LDL-c) were determined using diagnosis reagent kit (DiaSys Diagnostic Systems GmbH, Germany).

Hispathological procedure for pancreas: Pancreatic tissues were obtained from rats after alginate treatment for 2 week. The tissues fragments were fixed in Bouin's solution. After fixing, the tissues were dehydrated and embedded in paraffin. The paraffin blocks were sectioned at 5 μm and then stained with Hematoxylin and Eosin (H and E) for observing any histological changes.

Statistical analysis: All the data were expressed as Mean±Standar Deviation (SD) of three determinations. Statistical comparison was performed via one-way analysis of variance (ANOVA) followed by Duncan's multiple range test (DMRT) using 8 version of SPSS computer softwere. The values were considered significant when $p<0.05$.

RESULTS AND DISCUSSION

Body weight of rats: The STZ induced diabetic rats are one of the animal models of type 1 diabetes mellitus. It is well known for its selective pancreatic islet beta cell cytotoxicity and has been extensively used to induce type 1 diabetes in experimental rat model. Glibenclamide was often used as a standard antidiabetic drug in STZ induced diabetes to compare the efficacy of variety of hypoglycemic drugs (Gandhi and Sasikumar, 2012).

Throughout the experiments, all the rats were monitored daily and/or weekly for the symptoms of type diabetes mellitus, including polydipsia, polyuria, polyphagia, hyperglycemia and muscle wasting leading to weight loss and insulin deficiency. Figure 1 shows the observations of body weight of treated rats during the whole period of experiments. The body weight was continuously increased in group I (normal rats) and decreased in all diabetes groups. The STZ induced diabetes is characterized by a severe loss in body weight. Due to absolute or relative deficiency of insulin and decreased production of ATP and protein synthesis decreases in all tissues.

This insulin deficiency cause hyperglycemia and when blood glucose level exceeds the renal threshold, glucose

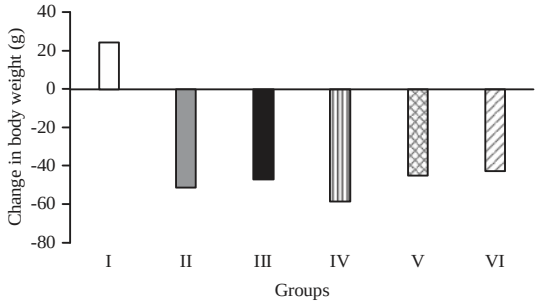

Fig. 1: Effect of STZon change in body weight (g) of normal and experimental diabetic rats

Table 1: Effect of sodium alginate from *S. crassifolium* on the preprandial blood glucose levels in normal and diabetic rats

	Blood glucose level (mg dL^{-1})				
Groups	Baseline	Day 0	Day 5	Day 10	Day 15
Group I	69.311±1.9^{ns}	128.346±10.8^{a}	127.355±29.2^{a}	116.847±10.7^{a}	126.305±0.5^{a}
Group II	71.456±2.6^{ns}	473.884±46.8^{b}	553.021±51.2^{c}	535.936±32.8^{d}	568.823±46.4^{c}
Group III	76.115±12.6^{ns}	472.519±142^{b}	399.463±33.6^{b}	234.166±21.8^{c}	316.357±20.9^{b}
Group IV	74.115±11.8^{ns}	453.987±29.5^{b}	424.172±39.4^{b}	108.208±37.3^{a}	279.454±92.5^{b}
Group V	88.029±11.7^{ns}	520.987±66.2^{b}	450.935±16.7^{b}	175.903±40.5^{b}	336.639±66.32^{b}
Group VI	70.500±14.3^{ns}	474.794±30.5^{b}	533.021±63.0^{c}	91.416±18.07^{a}	257.667±34.61^{b}

Each value represent Mean±SD, n = 3, mean values with different superscripts are significantly different ($p<0.05$), ns: Non significant

excretes in urine. Water accompanies glucose due to osmotic effect and to compensate for this loss of water, thirst center was activated and more water is taken. The loss and ineffective utilization of glucose leads to breakdown of fat and protein. Structural proteins are known to contribute to body weight, the loss or degradation of these structural proteins reflects the reduction in body weight (Kavishankar and Lakshmidevi, 2014).

Glucose level: The present study measures series of biochemical indicators including preprandial glucose and posprandial glucose. Administration of STZ (60 mg kg^{-1} b.wt. I.P.) induced hyperglycemia (blood glucose level ≥200 mg dL^{-1}) in almost all treated rats. The blood glucose level was monitored for 48 h. Fasting blood glucose of untreated diabetic rats was significantly higher than those of normal control rats (Table 1). Diabetes induced by STZ was characterized by apoptosis of cells of pancreas, attenuation of gene expression of insulin and reduced synthesis of insulin. Usually, cells of pancreas normally maintain blood glucose concentrations within a narrow range by modulating their insulin secretion rate in response to the blood glucose concentration apoptosis of pancreatic cells is believed tobe the primary factor which ultimately results in hyperglycemia (Patel *et al*., 2006).

Significant decrease in blood glucose levels were observed in diabetic treated rats (474.794±30.5 to 257.667±34.61 mg dL^{-1}) after treatment with alginate from *S. crassifolium* at 600 mg kg^{-1} b.wt. The treatment showed significant antihyperglycemic activity (45.7%) by bringing down the blood glucose level to near normal on day 15 in diabetic rats. At 200 mg kg^{-1} b.wt., alginate *S. crassifolium* treatment showed 38.4% fall in diabetic treated rats and at 400 mg kg^{-1} b.wt. alginate *S. crassifolium* treatment showed 35.3% fall in diabetic treated rats. No hypoglycemic effect was observed in normal treated rats. Treatment of diabetic rats with standard antidiabetic drug glibenclamide at 5 mg kg^{-1} b.wt. resulted in 33.1% fall in blood glucose level on day 15.

Alginate is a polysaccharide. Sodium alginate consists of α-l-guluronic acid residues (G blocks) and β-d-mannuronic acid residues (M blocks), as well as segments of alternating guluronic and mannuronic acids (GM blocks). The guluronate residue blocks allow alginate fibres to form gels by binding Ca^{2+} ions and stomach H^{+} ions, which cross-link the fibres into a viscous polymer matrix (Draget *et al*., 2000). Viscous dietary fibres dampen the rise in blood glucose levels following food intake by delaying gastric emptying and slowing the absorption of nutrients in the small intestine. Whether one of these mechanisms or both of them enable sodium alginate's effect on glycemic response attenuation was unclear (Yavorska, 2012).

There is a normal physiological increase in glycemia after a meal, with an increment of up to 50 mg dL^{-1}, which does not surpass 140 mg dL^{-1}. This increase depends on the amount of glucose consumed and the endogenous glucose production. Postprandial hyperglycemia is the result of an excessive glucose production associated to its reduced peripheral uptake. When the glucose uptake exceeds its production, the glycemia returns to normal levels. In individuals with carbohydrate intolerance and in those with type 2 diabetes, the postprandial glycemic excursion was higher and more prolonged, submitting these individuals to a long-term postprandial state (Geloneze *et al*., 2006).

As shown in Table 2, the plasma postprandial glucose level of control group (normal rats) showed a negligible change during the experimental period. In diabetes group (Group II), however, it continuously increased and reached as high as approximately 600 mg dL^{-1}. In contrast, 15 days of oral hypoglycemic agent treatment (5 mg glibenclamide/kg b.wt.) significantly lowered the plasma postprandial glucose level by 31.7% comparing with that of the diabetes group (Group II) treated with physiological saline alone. Significant decrease in blood postprandial glucose levels were observed in diabetic treated rats (538.513±78.8 to 381.250±11.4 mg dL^{-1}) after treatment with alginate from

Table 2: Effect of sodium alginate from *S. crassifolium* on the postprandial blood glucose levels in normal and diabetic rats

	Blood glucose level (mg dL^{-1})				
Groups	Baseline	Day 0	Day 5	Day 10	Day 15
Group I	189.485±7.4^{c}	139.940±17.2^{a}	142.148±18.5^{a}	134.598±29.6^{a}	150.416±5.1^{a}
Group II	178.282±41.5^{bc}	539.256±59.0^{b}	600.933±30.8^{d}	706.444±95.3^{c}	633.470±27.8^{c}
Group III	173.521±15.5^{abc}	488.00±72.2^{b}	436.907±41.1^{b}	432.611±38.9^{b}	333.814±64.5^{ab}
Group IV	149.601±27.0^{ab}	501.718±41.6^{b}	421.568±38.6^{b}	607.654±82.4^{c}	421.652±214^{bc}
Group V	144.036±13.7^{a}	577.205±96.0^{b}	597.006±42.5^{d}	628.888±84.6^{c}	433.333±21.8^{bc}
Group VI	162.876±8.5^{abc}	538.513±78.8^{b}	504.000±36.0^{c}	608.222±20.5^{c}	381.250±114^{ab}

Each value represent Mean±SD, n = 3, Mean values with different superscripts are significantly different (p<0.05)

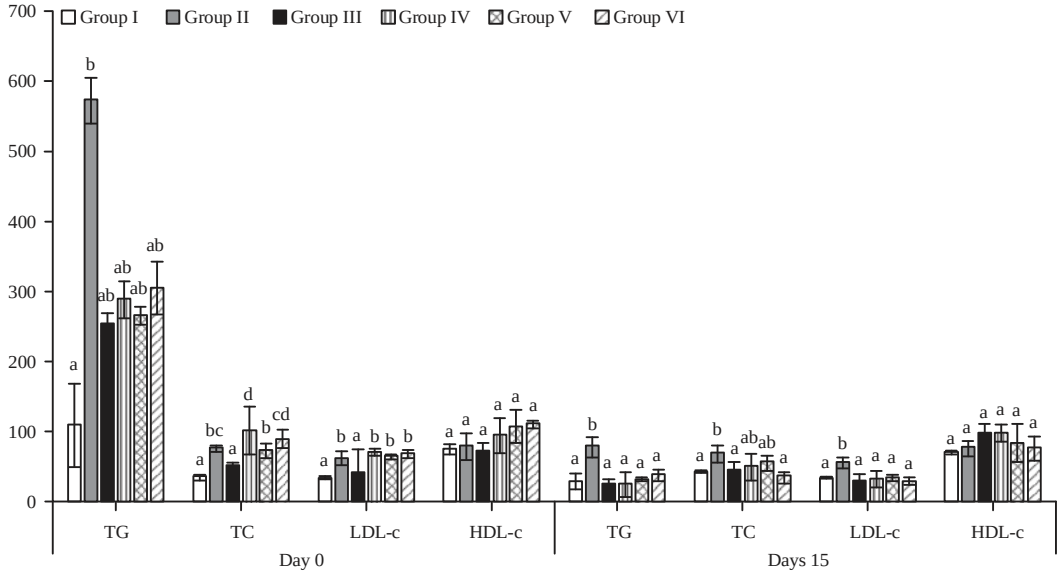

Fig. 2: Effect of oral administration alginate from *S. crassifolium* at doses of 200, 400 and 600 mg kg^{-1} b.wt. on serum lipid profiles of diabetic rats

S. crassifolium at 600 mg kg^{-1} b.wt. The treatment showed significant antihyperglycemic activity (29.2%) by bringing down the blood glucose level to near normal on day 15 in diabetic rats.

Lipid profiles: The hyperglycemia in diabetes mellitus mechanism involves overproduction (excessive hepatic glycogenolysis and gluconeogenesis) and decreased in glucose utilization by the tissues and the diabetes pathogenesis associated with disturbances in carbohydrate, fat and protein metabolism. These complex multifactorial changes of metabolic often lead to functional impairment damage of various organs in both types of diabetes and the associated disturbances are usually characterized by hyperglycemia, hypertriglyceridemia combined with low level of insulin, c-peptide and HDL-c (Moree *et al*., 2013). However, the results of the present investigation indicate that Alginate *S. crassifolium* significantly reduced (p<0.05) the triglyceride (TG), Total Cholesterol (TC) and LDL-c levels in diabetic rats and normal plasma concentrations of HDL-c (Fig. 2). The reason for the elevated triglycerides in diabetes is complex and stems from a disturbance in fatty acid metabolism (Tomkin, 2008).

Histology of pancreas: Histological examinations of the rat pancreas sections under light microscopy with (H and E) stain were presented in Fig. 3. Non-diabetic control group (Group I) showed normal size (Fig. 3a). Diabetic control group (Group II) pancreatic section showed occasional islets with severe destruction (Fig. 3b). Group III (diabetic rats+5 mg gliben clamide/kg b.wt.) pancreatic section showed moderate islet architecture and destruction was moderate (Fig. 3c). Alginate pancreatic section (200 (Fig. 3d) and 400 mg alginate/kg b.wt.) showed severe islet architecture (Fig. 3e). Group VI (400 mg alginate/kg b.wt.) showed additive improvement in mass of islets with mild destruction as compared to other alginate treatment (Fig. 3f). In the

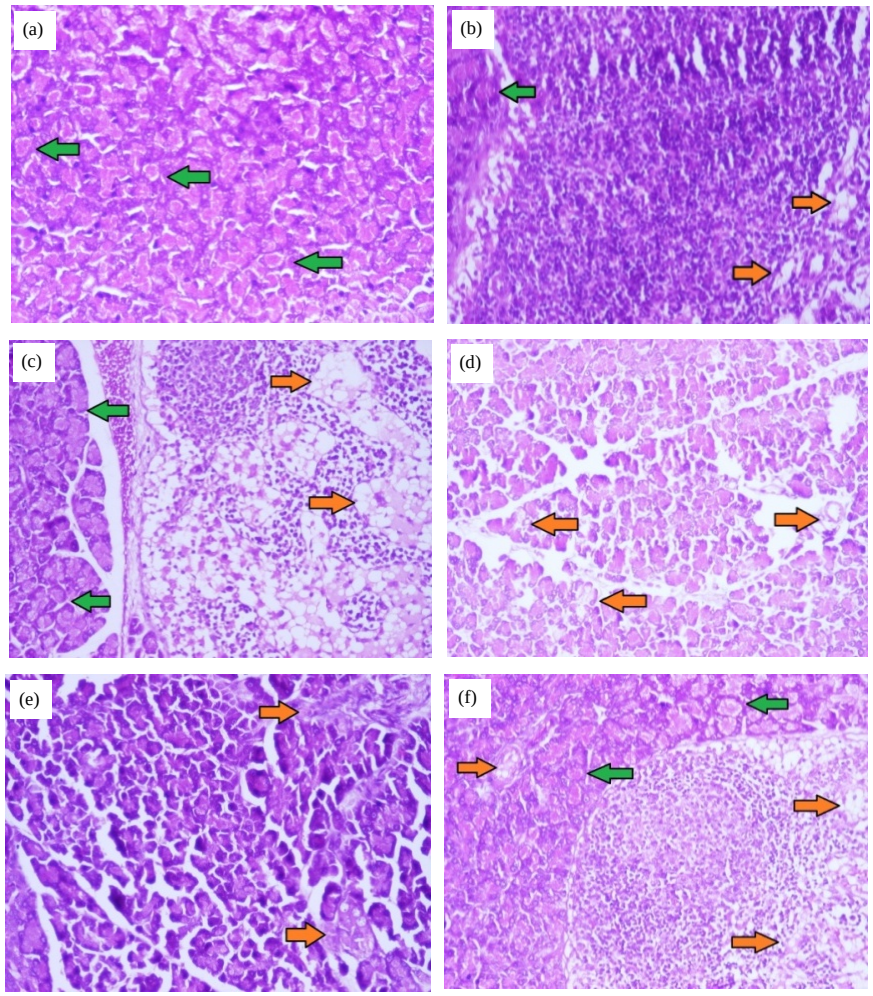

Fig. 3(a-f): Histological studies of STZ diabetic rat pancreas. Photographs of histological changes of rat pancreas of islets of Langerhans (H and E stain). (a) Group I (non-diabetic control): Pancreatic section showed normal size of islets and destruction was absent (Grade -), (b) Group II (diabetic control group): Pancreatic section showed (green arrow) occasional islets and (orange arrow) destruction was severe (Grade ++++), (c) Group III (diabetic rats+5 mg glibenclamide/kg b.wt.): Pancreatic section showed moderate islet architecture (green arrow) and destruction (orange arrow) was moderate (Grade +++), (d) Group IV diabetic rats+200 mg alginate/kg b.wt. and (e) Group V (diabetic rats 400 mg alginate/kg b.wt.): Pancreatic section showed (green arrow) occasional islets and (orange arrow) destruction was severe (Grade ++++) and (f) Group VI (diabetic rats+600 mg alginate/kg b.wt.) showed (green arrow) additive improvement in mass of islets as compared to other alginate treatment and (orange arrow) destruction was mild (Grade ++). Grade –: normal, Grade ++++: Severe destruction, Grade +++: Moderate destruction and Grade ++: Mild injury

diabetic rats, treatment with alginate *S. crassifolium* 600 mg kg^{-1} b.wt. resulted in normalizing the pancreatic histoarchitecture quite appreciably. An increase in the number of beta cells in the islets showed that they were regenerated.

CONCLUSION

In conclusion, the present study shows that the alginate *S. crassifolium* has potential antidiabetic action in STZ induced diabetic rats and the effect was found to be more similar to the reference drug glibenclamide.

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REFERENCES

Draget, K.I., B. Strand, M. Hartmann, S. Valla, O. Smidsrod and G. Skjak-Braek, 2000. Ionic and acid gel formation of epimerised alginates: The effect of AlgE4. Int. J. Biol. Macromol., 27: 117-122.

El Gamal, A.A., 2010. Biological importance of marine algae. Saudi Pharmaceut. J., 18: 1-25.

Firdaus, M., M. Astawan, D. Muchtadi, T. Wresdiyati, S. Waspadji and S.S. Karyono, 2010. Prevention of endothelial dysfunction in streptozotocin-induced diabetic rats by *Sargassum echinocarpum* extract. Med. J. Indonesia, 19: 32-35.

Gandhi, G.R. and P. Sasikumar, 2012. Antidiabetic effect of *Merremia emarginata* Burm. F. in streptozotocin induced diabetic rats. Asian Pac. J. Trop. Biomed., 2: 281-286.

Geloneze, B., R.N. Lamounier and O.R. Coelho, 2006. Postprandial hyperglycemia: Treating its atherogenic potential. Arquivos Brasileiros de Cardiologia, 87: 604-613.

Husni, A., R. Wijayanti and Ustadi, 2014. Inhibitory activity of α-Amylase and α-Glucosidase by *Padina pavonica* extracts. J. Biol. Sci., 14: 515-520.

IDF., 2012. Diabetes Atlas. 5th Edn., International Diabetes Federation, China.

Kavishankar, G.B. and N. Lakshmidevi, 2014. Anti-diabetic effect of a novel N-Trisaccharide isolated from *Cucumis prophetarum* on streptozotocin-nicotinamide induced type 2 diabetic rats. Phytomedicine, 21: 624-630.

Kavishankar, G.B., N. Lakshmidevi, S.M. Murthy, H.S. Prakash and S.R. Niranjana, 2011. Diabetes and medicinal plants: A review. Int. J. Pharm. Biomed. Sci., 2: 65-80.

Leiter, L.A., J. Genest, S.B. Harris, G. Lewis and R. McPherson *et al*., 2006. Dyslipidemia in adults with diabetes. Can. J. Diabetes, 30: 230-240.

Matanjun, P., S. Mohamed, K. Muhammad and N.M. Mustapha, 2010. Comparison of cardiovascular protective effects of tropical seaweeds, *Kappaphycus alvarezii*, *Caulerpa lentillifera* and *Sargassum polycystum*, on high-cholesterol/high-fat diet in rats. J. Med. Food, 13: 792-800.

Mohamed, S., S.N. Hashim and H. Abdul Rahman, 2012. Seaweeds: A sustainable functional food for complementary and alternative therapy. Trends Food Sci. Technol., 23: 83-96.

Moller, D.E., 2001. New drug targets for type 2 diabetes and the metabolic syndrome. Nature, 414: 821-827.

Moree, S.S., G.B. Kavishankar and J. Rajesha, 2013. Antidiabetic effect of secoisolariciresinol diglucoside in streptozotocin-induced diabetic rats. Phytomedicine, 20: 237-245.

Noiraksar, T. and T. Ajisaka, 2008. Taxonomy and distribution of *Sargassum* (Phaeophyceae) in the gulf of Thailand. J. Applied Phycol., 20: 963-977.

Patel, R., A. Shervington, J.A. Pariente, M.A. Martinez-Burgos, G.M. Salido, E. Adeghate and J. Singh, 2006. Mechanism of exocrine pancreatic insufficiency in streptozotocin-induced type 1 diabetes mellitus. Ann. N. Y. Acad. Sci., 1084: 71-88.

Rasyid, A., 2010. [Extraction of sodium alginate from brown algae *Sargassum echinocarphum*]. Oseanologi dan Limnologi di Indonesia, 36: 393-400, (In Indonesian).

Tomkin, G.H., 2008. Targets for intervention in dyslipidemia in diabetes. Diabetes Care, 31: S241-S248.

WHO., 1985. Diabetes mellitus. Technical Report Series, Worl Health Organizaion, Geneva.

WHO., 1999. Definition Diagnosis and Classification of Diabetes Mellitus and its Complications. Part 1: Diagnosis and Classification of Diabetes. WHO/NCD/NCS., Geneva, pp: 1-58.

Yavorska, N., 2012. Sodium alginate-a potential tool for weight management: Effect on subjective appetite, food intake and glycemic and insulin regulation. J. Undergraduate Life Sci., 6: 66-69.