



ISSN:1110-0419

Original Article Vol. 61(1) (2023), 87 – 96

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DOI: 10.21608/assjm.2023.290372



Antidiabetic Activity of the Different Extracts of Some Algae on Streptozotocin-Induced Diabetic Rats

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Abstract

The algae Sargassum Petefollum (brown), Laurencia Papillose (red), and Cystoseira Myrica (brown) were used in this study to prepare extracts to improve the biological properties (for diabetic rats). Streptozotocin (STZ), 40 mg/kg rat weight was administered to raise the glucose level of rats. They were given 150 mg/kg of rat weight of the algae extracts under investigation. The injection process resulted in a significant increase in blood sugar from 87.67± 2.05 mg/dl in the control group to 331± 3.74 mg/dl in the diabetic group, Diabetic rat groups induced by STZ resulted in an increase in blood sugar level, and a significant decrease in insulin $(0.42 \pm 0.02 \mu$ U/ml). The data showed that the an increase in the lipids profile, liver and kidney functions, and a decrease in activity of antioxidant enzymes compared to the control group, and after treatment with algae extracts used, whether brown or red. The results for all types of algae extracts showed an improvement in the biological properties. The results showed that brown algae (Cystoseira Myrica) had more influence on the biological properties, and decrease in blood sugar level was 203.33±2.87 mg/dl to112.00±6.38 mg/dl in methanol extract of *Cystoseira Myrica* and a significant increase in insulin $(2.82\pm0.07 \mu \text{ U/ml})$ and beneficial cholesterol HDL, was 49.05±3.39mg/dl. Also, cleared a significant decrease in lipids profile, a significant decrease in liver and kidney functions, and a significant increase in antioxidant enzymes, compared to the diabetic group. Finally, this study demonstrates the importance of using algae as a natural source of anti-diabetic compounds. Some effective compounds can be extracted and used as diabetes medications.

Keywords: Marine algae, diabetes mellitus, biological properties

Introduction

Diabetes mellitus (D.M.) is a metabolic condition caused by a relative or absolute insulin hormone deficit associated with chronic hyperglycemia (Kooti et al., 2016). It is the third most significant cause of death in the globe. It is accompanied by severe side effects such as diabetic nephropathy and neuropathic retinopathy that can cause adult blindness and amputations brought on by diabetic foot ulcers (Bhattacharjee et al., 2014). Although there are many pathologic mechanisms associated with diabetes, the majority of cases can be divided into two kinds based on the etiology. Insulindependent diabetes is referred to as type 1, while non-insulin-dependent diabetes is referred to as type 2. Due to the autoimmune death of the pancreatic beta cells, which typically release insulin, type 1 diabetes is characterized by an utter lack of insulin, whereas type 2. As a result of the insulin resistance brought on by a poor diet, a sedentary lifestyle, and obesity, D.M. is linked to relative insulin insufficiency (Zaccardi et al., 2016). Bioactive metabolites in creating pharmaceuticals and

nutraceuticals can be found in marine algae. Diverse scientific and economic domains have paid significant interest to marine algae. According to (Navak et al. 2022). It is essential because it is a rich source of bioactive substances such as proteins, carbohydrates, lipids, and other pigments. In addition to medicinal plants, marine algae are a rich source of naturally occurring bioactive chemicals that have the potential to be used as therapeutic agents to treat type 2 diabetes mellitus (Unnikrishnan and Jayasri 2018). Therefore, it is crucial to identify the chemical components and isolate the active compounds in lessused marine algae instead of developing herbal drugs with few adverse effects and the highest possible economic value. Remarkably, most brown algae are abundant in crucial secondary metabolites like phlorotannins, which have been linked to potential anti-diabetic effects (Gupta and Abu-Ghannam 2011). This study aimed was to create several extracts from marine algae using various solvents and investigate their impact on kidney and liver functions and specific enzymes during diabetes.

May 2021, samples of *Sargassum Petefollum*, *Cystoseira Myrica*, and *Laurencia Papillose*, three

different kinds of red and brown algae, were taken from the Red Sea, Hurghada, El Zafrana, and the

Faied area of the Gulf of Suez, respectively. All algal

samples were rinsed in seawater and then constantly

Material and Methods:

Materials

Collection of macro algae samples

For the planned investigation, samples of three algal species were taken from two locations. In





with fresh water.



Sargassum Petefollum" Fig.1 A herbarium of three macro algae was used in the present

- **Solvents**: hexane, ethyl acetate, and methanol were purchased from Merck in Germany with a purity level of at least 99% each. A water purification system was used to clean the water.
- Animals: The animal house of the Food Technology Research Institute, Agricultural Research Center, Giza, Egypt, sold a male white rat weighing between 180 and 200 g. Sigma-Aldrich was used to obtain the streptozotocin (STZ) drug (St Louis, MO, USA). All biochemical assay kits were purchased from Randox Laboratories Ltd, Diamond Road Crumlin, Co. Antrim, UK, BT294QY.

Methods

Preparation of different extracts of algae

Algae samples were collected from various locations, rinsed several times in fresh water, dried away from sunlight at room temperature, and ground into a fine powder using a mechanical grinder. These samples (500g) were taken out and individually treated to the method's exhaustive continuous successive extraction. Hexane, ethyl acetate, methanol, and distilled water were used to create various extracts based on how polar they were (in ascending order). Following filtration, the filtrate was concentrated using a Rotary evaporator under reduced pressure. Each time, the leftovers were vacuum-dried before being stored at -20°C for use in biological and chemical analyses.

The experimental design:-

For the experimental study, 45 mature male albino rats weighing 180–200 g were used. The Crops Technology Department, Animal House, and Food Technology Research Institute housed animals (FTRI). Rats were fed a base meal that contained Cystoseira Myrica,

15% casein, 10% corn oil, 5% cellulose, 4% salt combination, and 1% vitamin before and during the trial, and the diet was completed to 100% with corn starch (65%). (AOAC, 2019). The rats were acclimated for seven days under standard ambient conditions of temperature, relative humidity (55%), and dark/light cycle after being randomly assigned to separate groups and before the start of the experiment. A single intraperitoneal dose of streptozotocin (STZ. 40 mg/kg rat weight) made rats diabetic. Ganda et al. (1976) recommended dissolving in 0.01 M citrate buffer (1 ml, pH 4.5) just before use. After injection, animals were given free access to food and water and a 5% glucose solution to consume overnight to prevent hypoglycemia shock. All algal extracts (in methanol and water) were given orally for 45 days at 150 mg/kg body weight. For this investigation, 45 male albino rats were chosen and divided into nine groups, each containing five rats. The groups were: C, a standard group fed on a basal diet; D, a diabetic group fed on a basal diet; G, a diabetic group given 10 mg/kg of glybenclamide. Diabetes rats were divided into the following groups: MEC (the diabetic group receiving a methanolic extract of Cystoseira Myrica 150 mg/kg), WC (the diabetic group receiving water extract of Cystoseira Myrica 150 mg/kg), MES (the diabetic group receiving methanol extract of Sargassum Petefollum 150 mg/kg), WS (the diabetic group receiving water extract of Sargassum Petefollum 150 mg/kg), MEL (the diabetic group receiving 150 mg/kg of Laurencia Papillose extract in methanol) and WL (the diabetic group receiving 150mg/kg of Laurencia Papillose extract in water). Rats were housed separately throughout the trial in airtight cages.

Analysis of biochemical parameters:-

Diethyl ether was used to put the rats to sleep for the duration of the experiment (45 days),

and the method, according to Schermer (1967), was used to collect blood samples from the eye plexuses using fine capillary glass tubes. Each sample was taken in two tubes, one with an anticoagulant to separate the serum from the plasma and the other without an anticoagulant. The tubes were then centrifuged (HERMLE Z 206 A, Germany) for 10 min at 3000 rpm to separate the plasma and serum. They were then stored in sterile, dry tubes and frozen at -20°C. Using Trinder's (1969) approach, serum glucose was measured at the start of the trial and 45 days afterward. According to Marschner et al. (1974), radioimmunoassay kits manufactured by D.P.C (Diagnostic Products Corporation, Los Angeles, USA) were used to measure serum insulin in the Radioactive Isotopes Unit of the Central Department of Scientific Analysis and Test at the National Research Center (Dokki, Giza). The method used by Allain et al. (1974) to determine total cholesterol was used. Serum triglycerides were measured using the Fassati and Prencipe(1982) method. Determination of HDL- Cholesterol was carried out according to the method of Lopez-Virella et al. (1977). Determination of LDL- Cholesterol was carried out according to the method of Wieland and Seidel (1983). Total serum lipids were determined using the method of Kinght et al. (1972). Serum alanine transaminase (ALT) and aspartate transaminase (AST) of serum activities were calorimetrically measured according to the method described by Reitman and Frankel (1957). The total protein content was determined using the method of Gornall et al. (1949). The Doumes (1971) method was used to determine the albumin content. Rats' serum urea was measured using a colorimetric kinetic technique, according to Orsonneau et al. (1992) by urease Berthelot. According to Bartels et al. (1972). the creatinine in the serum of rats was determined using a colorimetric kinetic technique. The procedure provided by Aebi (1984) was followed while determining catalase activity colorimetrically. The Nishikimi et al. (1972) method was used to determine the superoxide dismutase (SOD). Koracevic et al. (2001) used the method to determine total antioxidant capacity. The method was used by Van Der Vies (1954) to determine the glycogen 200 mg of the liver was homogenized in 4 mL of 5% trichloroacetic acid and kept at 4°C overnight before being centrifuged at 3000 rpm for 10 min. The liver, spleen, pancreas, kidney, lung, and heart were separated from the body parts, and their respective weights were recorded.

Statistical analysis

Convenient statistical analysis techniques were used on the data to compute the mean and standard error, **Snedecore and Chochran's (1980)** two-way classifications ANOVA was used to analyze the data, and Duncan's multiple comparison tests were used to determine whether there was a statistical significant difference between the untreated and treated samples. According to **Waller and Duncan** (1969), mean separation was determined by the Least Significant Differences (LSD 5%) in Duncan's multiple ring tests.

Results and Discussion:

Effect of the tested extracts algae on blood glucose and insulin hormone of nondiabetic and diabetic rats. It is well recognized that marine algae have an abundance of bioactive substances with excellent pharmacological and biological potential. Streptozotocin (STZ) was injected into rats at a rate of 40 mg/kg of body weight, and the results are shown in Table (1). The injection process significantly increased blood sugar levels, from 87.67 \pm 2.05 mg/dl in the standard group to 331 ± 3.74 mg/dl in the diabetic group and from 203.33± 2.87 mg/dl to 112.00± 6.38 mg/dlin in(MEC)groups receiving methanol extract and from 215.67± 7.85 mg/dl to 115.00 ±8.83 mg/dl in(WC)groups receiving water extract of the study algae. When rats were given water or methanolic algae extracts at the study's conclusion, their serum sugar levels significantly decreased compared to the diabetic group that did not get the extract. The sugar percentage in the group consuming the methanolic extract of the algae type Cystoseira sp (MEC) was 112.00 ± 6.38 mg/dl lower than the group consuming the aqueous extract of the same type of algae, according to the results of Table(1). In comparison to the diabetic group, which had the least significant increase in insulin hormone and took no extracts, the groups that took the extract of the type Cystoseira sp algae, followed by the groups that took the water extracts of algae Laurencia sp and Sargussium sp, had a significant increase in insulin hormone (µU/ml). In the dosed group rat recorded with glybenclamide (commercial medication), the value of the hormone insulinin the diabetic group was $0.42\pm 0.02\mu$ U/ml They have a wide range of bioactive qualities, such as potent antioxidants against oxidative stress, anticancer, antiinflammatory, and Phlorotannins found in brown algae may aid in the treatment of type 2 diabetes, according to Lee and Jeon (2013), due to the properties of phlorotannins from brown algae. According to Shakambari et al. (2015), further research on brown algae has shown that the phlorotannins present in the methanol extract of brown algae like Padina pavonica, Sargassum polycystum, and Turbinaria ornata inhibit glucose-induced protein glycation and the development of protein-bound fluorescent advanced glycation. The results showed that the phlorotannins in *P. pavonica* have a strong inhibitory effect on the development of advanced glycation. According to El-Alfy et al. (2005), pancreatotrophic activity, or enhanced insulin secretion from the pancreas' beta cells, may cause a hypoglycemic impact. The primary hormone responsible for regulating glucose metabolism is insulin. It is created in the islets of Langerhans' -cells as proinsulin, the precursor that is then converted into insulin. According to Kelman et al. (2012), many algae include natural antioxidants. These vital bioactive molecules play a significant role in preventing of many diseases and the effects of aging by shielding cells from oxidative damage.

Moreover, **Firdaus** *et al.* (2010) explained that seawee contain lipids, minerals, vitamins, proteins, peptide polysaccharides, and amino acids. Additionally, seawee are rich in antioxidants that can combat free radicals the develop in patients with diabetes mellitus due to t

hyperglycemia state. Additionally, (**Gunathilaka** *et al.*,2020) found that *Choonospora minima's* polyphenolicrich extract had strong antidiabetic effects by inhibiting the enzymes -amylase and –glucosidase.

Croups	Glucose mg/dl		- Insulin Hormone µU/ml	
Groups	Zero time	End experimental	— Insum Hormone μ0/m	
С	$87.67^{i} \pm 2.05$	$87.33^{g} \pm 5.25$	$3.60^{a} \pm 0.09$	
D	$331.00^{a} \pm 3.74$	$340.67^{a} \pm 5.79$	$0.42^{\rm f}\pm 0.02$	
G	$255.67^{d} \pm 4.19$	$110.00^{ m f} \pm 4.08$	$2.63^{e} \pm 0.09$	
MEC	$203.33^{h} \pm 2.87$	$112.00^{\circ} \pm 6.38$	$2.82^{ m b} \pm 0.07$	
WC	$215.67^{f} \pm 7.85$	$115.00^{\circ} \pm 8.83$	$2.21^{\circ} \pm 0.07$	
MES	$271.00^{b} \pm 4.55$	$116.67^{\circ} \pm 4.11$	$1.76^{\circ} \pm 0.10$	
WS	$213.33^{g} \pm 4.71$	$119.00^{\mathrm{b}} \pm 6.16$	$2.39^{\circ} \pm 0.07$	
MEL	262.33 ± 8.96	$114.33^{d} \pm 6.34$	$1.96^{d} \pm 0.08$	
WL	$241.33^{e} \pm 7.36$	$116.33^{\circ} \pm 4.78$	$2.50^{ m bc} \pm 0.08$	
LSD 0.05	28.51	11.56	0.16	

Each value is the mean of three replicates \pm SD., number in the same column followed by the same letter is not much different at p < 0.05. C: Normal Control, D: Diabetic Control, G: Glybenclamide, MEC: Methanol Extract of *Cystoseira Myrica* 150 mg/kg, WC: Water Extract of *Cystoseira Myrica* 150 mg/kg, MES: Methanol Extract of *Sargassum Petefollum* 150 mg/kg, WS: Water Extract of *Sargassum Petefollum* 150 mg/kg, MEL: Methanol Extract of *Laurencia Papillose* 150 mg/kg. WL: Water Extract of *Laurencia Papillose* 150 mg/kg.

Effect of the tested extracts algae on the lipids profile of non-diabetic and diabetic rats

Rats from the treatments and control groups had their lipid profiles estimated (Table 2). There was a significant decrease in these values following the individual administration of *Cystoseira sp, Sargussium sp,* and *Laurencia sp* at 150 mg/kg. As the dose was increased, there was a linear decrease in total cholesterol, LDL cholesterol, triglycerides (TG), and total lipids. The treatment with the methanol extract groups showed increased in HDL cholesterol

levels. Methanol Extract of Laurencia Papillose W..L: Water Extract of Laurencia 150mg/kg. Papillose 150mg/kg, methanol extracts of Sargussium sp. 150 mg/kg, and Cystoseira sp. 150 mg/kg stimulate lipid breakdown and raise levels of good cholesterol, which lower the risk of Table (2) hypercholesterolemia. shows that, compared to the diabetic groups who took the study extracts, there was a substantial rise in all of the previous tests in the drug-taking diabetic group.

Table 2. Total cholesterol, LDL, HDL, triglycerides and total lipids (mg/dl) in rat groups fed on the tested

CXI	liacis algae				
Groups	Total cholesterol (mg/dl)	LDL (mg/dl)	HDL (mg/dl)	Triglycerides (mg/dl)	T. lipid (mg/dl)
С	$83.33^{i} \pm 2.63$	$29.82^{g} \pm 2.55$	$53.13^{a} \pm 3.35$	$75.26^{h} \pm 3.53$	$221.11^{h} \pm 4.64$
D	$176.52^{a} \pm 5.48$	$60.47^{a} \pm 1.39$	$28.08^{g} \pm 2.19$	$171.20^{a} \pm 2.67$	$462.38^{a} \pm 7.81$
G	$120.85^{b} \pm 5.10$	$48.01^{b} \pm 3.49$	$36.95^{f} \pm 2.04$	$121.75^{g} \pm 4.44$	$235.87^{e} \pm 6.15$
MEC	$104.05^{ m f} \pm 2.68$	$31.99^{f} \pm 3.39$	$49.05^{b} \pm 3.39$	$131.31^{d} \pm 4.92$	$228.48^{f} \pm 9.23$
WC	$99.16^{h} \pm 3.60$	$33.26^{e} \pm 3.72$	$42.46^{e} \pm 2.22$	$125.43^{\rm f} \pm 3.91$	$224.44^{g} \pm 6.92$
MES	$112.06^{d} \pm 5.11$	$34.26^{d} \pm 1.90$	$45.49^{d} \pm 1.07$	$133.54^{\circ} \pm 2.47$	$236.38^{e} \pm 3.83$
WS	$100.79^{\text{g}}{\pm}~6.38$	$35.53^{\circ} \pm 3.67$	$41.54^{e} \pm 3.04$	$128.92^{e} \pm 3.79$	$255.71^{\circ} \pm 4.04$
MEL	$114.07^{\circ} \pm 5.19$	$32.05^{ m f} \pm 3.03$	$47.83^{\circ} \pm 3.57$	$134.27^{b} \pm 1.57$	$260.00^{b} \pm 6.49$
WL	$110.58^{\circ} \pm 5.63$	$34.86^{d} \pm 4.97$	$42.16^{\circ} \pm 1.96$	$129.86^{e} \pm 8.28$	$250.78^{d} \pm 6.85$
LSD 0.05	11.24	6.70	6.16	8.05	13.03

Each value is the mean of three replicates \pm SD., number in the same column followed by the same letter is not much different at p < 0.05. C: Normal Control, D: Diabetic Control, G: Glybenclamide, MEC: Methanol Extract of *Cystoseira Myrica* 150mg/kg, WC:Water Extract of *Cystoseira Myrica* 150 mg/kg ,MES: Methanol Extract of *Sargassum Petefollum* 150mg/kg,WE: Water Extract of *Sargassum Petefollum* 150mg/kg,MEL:

These findings concur with those made by Selvaraj and Palanisamy (2014) who noted that the reduction in TC., TG., and LDL cholesterol levels brought about by the administration of the ethanolic (*Sargassum longiotom*) suggests a potential defense against hypercholesterolemia. Yu et el. (2019) reported that chemicals like phlorotannin in the *Ecklonia stolonifera* species are utilized for the plant's anti-hypolipidemic effects. These compounds can aid in lowering triglyceride and LDL cholesterol levels while raising HDL cholesterol.

Effect of the tested extracts algae on albumin, total protein, ALT., and AST of nondiabetic and diabetic rats.

Table (3) indicates the liver functions in the diabetic groups using the studied algae extracts and the group receiving the commercial medicine dose (albumin as g/dl, total protein as g/dl, ALT as U/l, and AST as U/l).The data in Table(3) demonstrated that there were no significant differences in the level of albumin in the serum of rats taking the tested red algae, whether methanol or water extracts, and that a significant decrease in the level of albumin was observed in comparison to the diabetic group that did not take any extract as well as the group taking the medicinal drug, but the normal group was recorded as having the highest value in albumin. In contrast to the diabetic group and the group taking the medication, a significant rise in the total serum protein of rats' blood serum was also seen in the research groups taking algal extracts. There were no appreciable differences between the groups, even though the normal group had the highest total protein value. Slightly significant differences in the total protein percentage were seen in the groups receiving extracts of the Laurencia Papillose algae, whether they were methanolic or water extracts, and the methanolic extract of the Sargassum Petefollum algae, as well as

the groups receiving extracts of the Cystoseira Myrica. Their results in Liver enzymes (ALT. and AST) are shown in Table three, where there were significant differences between groups in ALT enzyme. There was a significant decrease between groups of rats taking algae extracts compared to the diabetic group that did not take any extracts and the group that took the medicinal drug. The group taking methanolic extract or water from type Laurencia Papillose algae had the lowest value, followed by the intake of algae extract Cystoseira Myrica and then Sargassum Petefollum. The standard group recorded the lowest value in the enzyme (ALT), and the group taking a medicinal drug was recorded at 50.33 \pm 2.62U/l The infected group recorded the highest value of 66.00 ± 1.63 U/l AST. The results showed in Table (3) a significant difference between the groups that took water and methanolic extracts of the tested algae and between the other groups, whether diabetic (negative) or the positive group and the normal group. On the opposite side, no significant differences were recorded between the groups taking water extracts of the three algae types, and those taking methanol extract from type Laurencia Papillose and Cystoseira Myrica algae, However, the Sargassum Petefollum algae methanol extract recorded significant differences between them. The previous results with the scientist Lee et al. (2015) who found that the liver functions (ALT and AST) are indicators of hepatic damage. Levels were significantly (p<0.05) lower in the diabetic group rat compared to levels in the control group and diabetic (db-rosiglitazone) group rat. The increased activities of transaminases, which are active in the absence of insulin due to the availability of amino acids in the blood of Diabetes mellitus (DM) are also responsible for increased gluconeogenesis and ketogenesis (Batran et al ... 2006).

	Albumin	Total protein	ALT	AST
Groups	(g/dl)	(g/dl)	(U/l)	(U/I)
С	$4.11^{a} \pm 0.29$	$7.08^{a} \pm 0.31$	$31.67^{ m f} \pm 1.25$	$83.67^{\rm h} \pm 1.70$
D	$2.28^{d} \pm 0.15$	$4.86^{f} \pm 0.26$	$66.00^{a} \pm 1.63$	$118.67^{a} \pm 3.09$
G	$2.68^{\circ} \pm 0.18$	$5.76^{\circ} \pm 0.16$	$50.33^{b} \pm 2.62$	$102.33^{b} \pm 4.11$
MEC	$3.95^{ab}\pm0.11$	$6.81^{b} \pm 0.66$	$36.00^{d} \pm 1.41$	$86.33^{g} \pm 2.49$
WC	$3.77^{b} \pm 0.16$	$6.40^{ m bc} \pm 0.37$	$36.67^{d} \pm 3.30$	$91.33^{d} \pm 3.30$
MES	$3.73^{b} \pm 0.19$	$6.28^{\circ} \pm 0.58$	$40.33^{\circ} \pm 1.89$	$88.67^{e} \pm 2.87$
WS	$3.46^{b} \pm 0.27$	$5.99^{d} \pm 0.15$	$40.00^{\circ} \pm 2.83$	$93.00^{\circ} \pm 4.97$
MEL	$3.63^{b} \pm 0.25$	$6.14^{\circ} \pm 0.46$	$34.33^{\circ} \pm 3.30$	$87.00^{t} \pm 3.56$
WL	$3.64^{b} \pm 0.18$	$6.17^{\circ} \pm 0.44$	$33.00^{e} \pm 2.16$	$93.33^{\circ} \pm 4.50$
LSD 0.05	0.37	0.79	4.96	6.61

Table 3. Albumin, total protein, ALT and AST concentration of the nondiabetic and diabetic rats

Each value is the mean of three replicates \pm SD., number in the same column followed by the same letter is not much different at p < 0.05. C: Normal Control, D: Diabetic Control, G: Glybenclamide, MEC: Methanol Extract of *Cystoseira Myrica* 150mg/kg, WC:Water Extract of *Cystoseira Myrica* 150 mg/kg, MES: Methanol Extract of *Sargassum Petefollum* 150mg/kg, MEL: Methanol Extract of *Laurencia Papillose* 150mg/kg. WL: Water Extract of *Laurencia Papillose* 150mg/kg.

Effect of the tested extracts algae on kidney function of nondiabetic and diabetic rats

Kidney function (urea and creatinine as mg/dl) in diabetic and normal groups were analyzed in Table 4. By statistical analysis of the obtained results, it was found that there was a significant decrease in urea for the groups of rats that took methanolic and water extracts of algae of types *Laurencia Papillose* and *Cystoseira Myrica*, followed by the decrease of type *Sargassum Petefollum* The most significant decrease was in the groups taking the water extract of algae *Laurencia Papillose* and *Sargassum Petefollum*. In contrast, the groups taking methanolic extracts were slightly higher in the percentage of urea than those that took methanol extract of type *Cystoseira Myrica* (it was the lowest). As for the creatinine in Table (4) it was found that there was a significant decrease in the blood serum of rats taking methanol extract for all types of tested algae, followed by a decrease in the groups taking the water extract of the same types of algae, compared to the diabetic group and the group taking the medicinal drug (Glybenclamide) used $(1.19\pm 0.04 \text{ mg/dl})$. In contrast, the standard group recorded a decrease in urea and creatinine at 60.22 \pm 2.77mg/dl and 0.85 ±. 0.04mg/dl respectively. The results agreed with Santamaria et al. (2008) revealed that enhanced protein catabolism and accelerated amino acid deamination for gluconeogenesis is probably an acceptable postulate to interpret the elevated levels of urea and creatinine. Furthermore, ST.Z. Increased the production of reactive Oxygen species enhanced lipid peroxidation and protein carbonylation associated with decreased intracellular antioxidant defense in the kidney tissue.

Table 4. Urea (mg/dl) and creatinine (mg/dl) in rats groups fed on the tested extracts algae

Groups	Urea (mg/dl)	Creatinine (mg/dl)
C	$60.22^{h} \pm 2.77$	$0.85^{\circ} \pm 0.04$
D	$95.59^{a} \pm 1.86$	$1.83^{a} \pm 0.05$
G	$63.52^{g} \pm 2.08$	$1.19^{b} \pm 0.04$
MEC	$65.62^{f} \pm 2.40$	$0.91^{d} \pm 0.06$
WC	$70.00^{\circ} \pm 1.39$	$1.09^{\circ} \pm 0.03$
MES	$69.45^{d} \pm 3.46$	$0.92^{d} \pm 0.06$
WS	$66.04^{e} \pm 4.47$	$1.03^{\circ} \pm 0.04$
MEL	$77.24^{b} \pm 1.95$	$0.93^{d} \pm 0.07$
WL	$65.62^{f} \pm 4.32$	$1.02^{\circ} \pm 0.03$
LSD 0.05	5.85	0.11

Each value is the mean of three replicates \pm SD., number in the same column followed by the same letter is not much different at p < 0.05. C: Normal Control, D: Diabetic Control, G: Glybenclamide, MEC: Methanol Extract of *Cystoseira Myrica* 150 mg/kg, WC:Water Extract of *Cystoseira Myrica* 150 mg/kg, MES: Methanol Extract of *Sargassum Petefollum* 150mg/kg, WS: Water Extract of *Sargassum Petefollum*150mg/kg, MEL: Methanol Extract of *Laurencia Papillose* 150mg/kg. WL: Water Extract of *Laurencia Papillose* 150mg/kg.

Effect of the tested extracts algae on serum enzymes activity and glycogen of non diabetic and diabetic rats.

Between the examined groups of rats, there were appreciable variations in the catalase (U/L) in Table 5. The group that consumed a water extract, a methanolic extract from *Cystoseira sp* 150 mg/kg algae, and the group that consumed a methanolic extract from *Laurencia Papillose* 150 mg/kg algae had the least catalase (U/L) values, where a significant increase in the value of catalase was observed in group *Cystoseira sp* 150 mg/kg, followed by group giving glibenclamide. The results are shown in Table 5 in the superoxide dismutase (SOD). (U/ml) showed obvious differences between the groups of tested rats, with the normal group having the highest significant SOD value, followed by the group receiving the medication (glibenclamide), and the

diabetic group having the lowest significant SOD value. The diabetic group also had the lowest significant SOD value, with methanol and water extract of Laurencia Papillose, Sargussium sp, and Cystoseira sp 150 mg/kg. On the other hand, it was evident from the results of Table (5) that there were also significant differences in the antioxidant activity in the serum of the tested groups of rats, with a significant rise in this activity seen in the two groups, those taking the natural and the drug, respectively. An antioxidant activity decline was observed in the groups used for the water and methanolic extracts of the investigated algae. The data on glycogen were displayed in Table (5), where a significant increase was seen in the standard group. The groups of rats given methanol and water extracts of Laurencia Papillose, Sargussium sp, and Cystoseira sp 150 mg/kg were next, and they were the least significant in terms of the amount of glycogen in blood serum in the diabetic group and the group treated with the medication (glibenclamide). Wohaieb and Godin (1987) reported that the many antioxidant enzymes, including SOD and CAT., protect cells against damage due to Reactive oxygen species (ROS) overproduction. It has been reported that levels of these enzymes are decreased during chronic diabetic conditions, resulting in reductions in antioxidant enzyme activities. Erythrocytes are particularly susceptible to oxidative damage from high oxygen and hemoglobin concentrations. The liver is also known to undergo free radical-mediated injury in diabetes.

Table 5. Serum enzymes activity, total antioxidant capacity and glycogen of no	nondiabetic and diabetic rats
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Groups	Catalase (U/L)	superoxide dismutase (U/ml)	Total antioxidant capacity(mM/L)	Glycogen mg/g
С	$444.93^{a} \pm 3.17$	$1630.43^{a} \pm 4.55$	$2.37^{a} \pm 0.19$	34.25 ^a ± 0.73
D	$210.62^{i} \pm 3.55$	$1088.50^{ m j}\pm7.62$	$1.22^{e} \pm 0.23$	$9.78^{g} \pm 0.06$
G	$415.43^{b} \pm 3.65$	$1484.17^{b} \pm 11.57$	$2.23^{ab} \pm 0.08$	$32.74^{\text{f}} \pm 0.63$
MEC	$403.17^{d} \pm 6.56$	$1431.00^{\circ} \pm 7.12$	$2.29^{ab} \pm 0.04$	$31.27^{b} \pm 0.84$
WC	$411.03^{\circ} \pm 4.26$	$1386.00^{d} \pm 7.35$	$0.88^{f}_{i} \pm 0.07$	$31.12^{b} \pm 0.83$
MES	$384.09^{g} \pm 7.83$	$1356.30^{e} \pm 6.74$	$1.90^{b} \pm 0.11$	$30.03^{\circ} \pm 0.36$
WS	392.37 ± 7.26	$1200.67^{h} \pm 5.19$	$1.64^{d} \pm 0.03$	$28.28^{e} \pm 0.89$
MEL	$328.07^{\rm h} \pm 1.20$	$1283.33^{\text{f}} \pm 8.97$	$1.87^{\circ} \pm 0.17$	$29.34^{d} \pm 1.00$
WL	$388.77^{e} \pm 1.85$	$1249.33^{g} \pm 6.94$	$1.61^{d} \pm 0.10$	$28.26^{e} \pm 0.61$
LSD 0.05	11.68	18.21	0.29	1.51

Each value is the mean of three replicates \pm SD., number in the same column followed by the same letter is not much different at p < 0.05. C: Normal Control, D: Diabetic Control, G: Glybenclamide, MEC: Methanol Extract of *Cystoseira Myrica* 150 mg/kg, WC:Water Extract of *Cystoseira Myrica* 150 mg/kg, MES: Methanol Extract of *Sargassum Petefollum* 150mg/kg, WS: Water Extract of *Sargassum Petefollum*150mg/kg, MEL: Methanol Extract of *Laurencia Papillose* 150mg/kg. WL: Water Extract of *Laurencia Papillose* 150mg/kg

Impact of the extracts algae on the body weight (gm) of nondiabetic and diabetic rats

According to the data in Table (6), the diabetic rat groups that received injections of streptozotocin (STZ) lost weight. The nondiabetic control group, diabetic group, and diabetic group all

had dramatically different body weights throughout the investigation. Comparing diabetic rat groups fed with the tested algae extracts to positive control (D) and diabetic (glibenclamide) rat groups revealed an improvement in body weight.

Table 6. Body weight and body gain in nondiabetic and diabetic rats

Groups	Initial body weight	Final body weight	Body weight gain	Body weight gain
	(gm)	(gm)	(gm)	(%)
С	$186.67^{g} \pm 4.71$	$257.33^{a} \pm 1.70$	70.67 ^a ± 6.02	37.96 ^a ± 4.24
D	194.00° ±5.89	$167.67^{\rm f} \pm 5.56$	-26.33°± 0.47	$-13.58^{\circ} \pm 0.30$
G	195.00° ± 8.16	$200.67^{e} \pm 7.04$	$5.67^{d} \pm 1.70$	$2.90^{d} \pm 1.43$
MEC	193.33 ^d ±5.31	$221.00^{d} \pm 5.35$	$27.67^{\circ} \pm 0.47$	$14.32^{bc} \pm 0.46$
WC	$196.67^{\rm b} \pm 4.71$	224.6° ± 8.65	$28.00^{\circ} \pm 5.72$	$14.22^{bc} \pm 2.76$
MES	191.67 ^e ± 6.94	217.33 ^e ± 6.80	$25.67^{d} \pm 1.70$	$13.41^{\circ} \pm 1.07$
WS	203.00 ^a ± 4.97	231.33 ^b ± 4.78	$28.33^{\circ} \pm 0.47$	$13.97^{\circ} \pm 0.48$
MEL	$202.33^{ab} \pm 5.56$	232.33 ^b ± 4.50	$30.00^{\rm b} \pm 1.63$	$14.85^{b} \pm 1.12$
WL	194.00° ± 4.24	223.00 ^c ± 3.56	$29.00^{\rm b} \pm 6.98$	$15.03^{b} \pm 3.86$
LSD 0.05	10.84	10.43	7.80	4.44

Each value is the mean of three replicates \pm SD., number in the same column followed by the same letter is not much different at p < 0.05. C: Normal Control, D: Diabetic Control, G: Glybenclamide, MEC: Methanol Extract of *Cystoseira Myrica* 150 mg/kg, WC:Water Extract of *Cystoseira Myrica* 150 mg/kg, MES: Methanol Extract of *Sargassum Petefollum* 150mg/kg, WS: Water Extract of *Sargassum Petefollum*150mg/kg, MEL: Methanol Extract of *Laurencia Papillose* 150mg/kg. WL: Water Extract of *Laurencia Papillose* 150mg/kg.

These results were in agreement with those of Lee et al. (2015) who discovered that after the study period, the body weight of rat in the positive control group was considerably (p<0.05) higher than that of rat in the diabetic group. There was a significant increase in body weight by 37.96% in the standard group(C), In comparison, it increased by 13.41% in the group taking methanolic extract from *Sargussium sp* 150mg/kg algae to 15.03% in the group taking an water extract from *Laurencia Papillose* 150mg/kg algae. However, a significant decrease (13.58 %) in body weight occurred in the diabetic group, and it did not take any extracts (D). There was a slight increase in body weight percentage (2.90 %) in the diabetic group taking the glibenclamide.

Impact of the algae extracts on the organ weight of nondiabetic and diabetic rats

The obtained data in Table (7) illustrate a decrease in liver weight in diabetic rats compared with normal ones. In this study, the decrease in liver weight may be due to enhanced catabolic processes such as glycogenolysis and lipolysis. These results agreed with **Yadav** *et al.* (2004), who reported that, during diabetes liver decreased in weight due to enhanced catabolic processes such as glycogenolysis, lipolysis, and proteolysis, which is the outcome of insulin lake and /or cellular glucose in liver cells.

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Table 7. (Organ weight ((gm) in rats group	s fed on the tested	algae extracts a	at the feeding pe	eriod end

Groups	Liver	Spleen	Pancreas	Kidney	Lung	Heart
	(g)	(g)	(g)	(g)	(g)	(g)
С	$6.84^{a} \pm 0.24$	$0.79^{a} \pm 0.09$	$0.53^{a} \pm 0.25$	$1.43^{a} \pm 0.21$	$1.39^{ab} \pm 0.18$	$0.65^{b} \pm 0.03$
D	$5.67^{b} \pm 1.61$	$0.72^{ab} \pm 0.16$	$0.48^{ab} \pm 0.20$	$1.81^{a} \pm 0.14$	$1.54^{a} \pm 0.20$	$0.64^{b} \pm 0.11$
G	$6.28^{ab} \pm 0.18$	$0.54^{\circ} \pm 0.03$	$0.37^{ab} \pm 0.04$	$1.51^{a} \pm 0.31$	$1.48^{ab} \pm 0.07$	$0.51^{d} \pm 0.06$
MEC	$5.99^{b} \pm 1.08$	$0.74^{ab} \pm 0.05$	$0.42^{ab} \pm 0.02$	$1.34^{a} \pm 0.25$	$1.57^{a} \pm 0.02$	$0.73^{a} \pm 0.04$
WC	$5.96^{b} \pm 0.76$	$0.52^{\circ} \pm 0.07$	$0.37^{ab} \pm 0.02$	$1.73^{a} \pm 0.17$	1.17°± 0.20	$0.58^{\circ} \pm 0.03$
MES	$4.76^{\circ} \pm 0.33$	$0.72^{ab} \pm 0.18$	$0.42^{ab} \pm 0.18$	$1.51^{a} \pm 0.63$	1.15° ±0.13	$0.56^{\circ} \pm 0.03$
WS	$5.41^{b} \pm 1.25$	$0.56^{\circ} \pm 0.19$	$0.47^{ab} \pm 0.12$	$1.65^{a} \pm 0.42$	$1.13^{\circ} \pm 0.19$	$0.69^{\rm b} \pm 0.18$
MEL	$6.04^{ab} \pm 2.16$	$0.70^{\rm ab} \pm 0.22$	$0.30^{\rm b} \pm 0.04$	$1.56^{a} \pm 0.15$	$1.40^{ab} \pm 0.07$	$0.55^{\circ} \pm 0.06$
WL	$6.02^{ab} \pm 1.44$	$0.63^{b} \pm 0.09$	$0.31^{b} \pm 0.06$	$1.54^{a} \pm 0.16$	$1.31^{b} \pm 0.14$	$0.59^{\circ} \pm 0.05$
LSD 0.05	2.02	0.36	0.25	0.58	0.24	0.13

Each value is the mean of three replicates \pm S.D., number in the same column followed by the same letter is not much different at p < 0.05. C: Normal Control, D: Diabetic Control, G: Glybenclamide, MEC: Methanol Extract of *Cystoseira Myrica* 150mg/kg, WC:Water Extract of *Cystoseira Myrica* 150 mg/kg, MES: Methanol Extract of *Sargassum Petefollum* 150mg/kg, WE: Water Extract of *Sargassum Petefollum* 150mg/kg, MEL: Methanol Extract of *Laurencia Papillose* 150mg/kg. WL: Water Extract of *Laurencia Papillose* 150mg/kg.

There is, however, an increase, but with an insignificant level in kidney weight due to glucose over-utilization and subsequent enhancement in glycogen synthesis, lipogenesis, and protein synthesis. The same Table shows slight changes in spleen, pancreatic, lung and heart weight among all the rats fed on the tested algae extracts and basal diet. On the other hand, there was an insignificant difference in the kidney weight of all the tested rats.

Concluded that , from this study that algae are a natural source of some natural antioxidants to reduce blood sugar and liver and kidney functions, and we single out the type of brown algae (*Cystoseira Myrica*) as it had a greater influence on the biological properties.

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النشاط المضاد لمرض السكر للمستخلصات المختلفة لبعض الطحالب التي يسببها الستربتوزوتوسين فى الفئران المصابة

بداء السكري

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تم استخدام الطحالب Cystoseira Myrica (البنية) ، Laurencia Papillose (البنية) في هذه الدراسة لإعداد المستخلصات لتحسين الخصائص البيولوجية (للفئران المصابة بداء السكري). تم إعطاء (Streptozotocin (STZ) 40 مجم / كجم من وزن الفئران لرفع مستوى السكر للفئران. تم إعطاؤهم 150 ملجم / كجم من وزن الفئران من مستخلصات الطحالب قيد الدراسة. أدت عملية كجم من وزن الفئران لرفع مستوى السكر للفئران. تم إعطاؤهم 150 ملجم / كجم من وزن الفئران من مستخلصات الطحالب قيد الدراسة. أدت عملية الحقن إلى زيادة ملحوظة في نسبة السكر في الدم من200±57.62 مجم / ديسيلتر في المجموعة الضابطة إلى3.74 ±3.01 مجم / ديسيلتر في مجموعة الصابطة إلى3.74 ±3.01 مرام ، والحقن إلى زيادة ملحوظة في نسبة السكر في الدم من200±87.62 مجم / ديسيلتر في المجموعة الضابطة إلى3.74 ±3.01 مجم / ديسيلتر في مجموعة المصابة بالسكري ، وأدت مجموعات الفئران المصابة بداء السكري الناجمة عن STZ إلى زيادة مستوى السكر في الدم ، و انخفاض كبير في الأنسولين (2.04 ± 0.02) وحدة / مل). وأظهرت النتائج زيادة في نسبة الدهون ووظائف الكبد والكلى وانخفاض في نشاط الانزيمات المضادة للكركسي في الأنسولين (2.04 ± 0.02) وحدة / مل). وأظهرت النتائج زيادة في نسبة الدهون ووظائف الكبد والكلى وانخفاض في نشاط الانزيمات المضادة للكرك للأكسدة مقارنة بمجموعة الطبيعية وبعد المعاملة بمستخلصات الطحالب المستخدمة سواء كانت بنية أو حمراء. أظهرت نتائج ان جميع أنواع مستخلصات الطحالب البنية (3.04 ± 0.350) كان لها تأثير أكبر على مستخلصات الطحالب البنية (3.34 ملكري المواحية في خلولي في الأكسدة مقارنة بمجموعة الطبيعية وبعد المعاملة بمستخلصات الطحالب الستخدمة سواء كانت بنية أو حمراء. أظهرت نتائج أن الطحالب البنية (3.34 ملكري الها تأثير أكبر على مستخلصات الطحالب تحسنًا في خواصها البيولوجية.كما أظهرت النتائج أن الطحالب البنية (3.350 ملكري عالى 3.350 ملكري المواحي المواحية في الأثير على مستخلصات الطحالب البنية (3.350 ملكري الكري على مستخلصات الطحالب البيولوجية ، و انخفاض مي مستوى الكر في الخصائص البيولوجية ، و انخفاض مستوى في ألكسائص البيولوجية ، و انخفاض مستوى في 3.350 ملكر في الدم من7.350 ملكري في مستخلصات الطحالب البنية إلى مالكري المواحي مالكري مو الخمائس مستوى مالكومي وي مالكوميي مالكومي مالكومي مالكومي وي الغولي في 3.350 ملكري م

(2.07±2.82وحدة/مللى) والكوليسترول النافع HDL كان 3.39±49.05ملجم / ديسيلتر. كما لوحظ انخفاض معنوي في مستوى دهون الدم ، وانخفاض معنوي في وظائف الكبد والكلى ، وزيادة معنوية في إنزيمات مضادات الأكسدة ، مقارنة بمجموعة المصابة بالسكري. أخيرًا ، توضح هذه الدراسة أهمية استخدام الطحالب كمصدر طبيعي للمركبات المضادة لمرض السكري. كما يمكن استخلاص بعض المركبات الفعالة واستخدامها كأدوبة لمرضى السكري.