International Journal of Pharmacy and Biological Sciences
ISSN: 2321-3272 (Print), ISSN: 2230-7605 (Online)
IJPBS™ | Volume 8 | Issue 4 | OCT-DEC | 2018 | 836-840
Research Article | Biological Sciences | Open Access | MCI Approved| ज्ञान-विज्ञान विमुक्तये
|UGC Approved Journal |

RENAL HYPOLIPIDEMIC EFFICACY OF SEAWEED, *Padina gymnospora* (KUTZING) ON STREPTOZOTOCIN INDUCED DIABETICS IN MALE ALBINO WISTAR RATS

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ABSTRACT

Plants have been considered as sources of medicinal agents for the treatment of many diseases. The renal hypolipidemic efficacy of seaweed, Padina gymnospora was evaluated by streptozotocin induced diabetics in rats. Male albino wistar rats were orally treated with seaweed, Padina gymnospora methanolic extracts (50, 100 and 200 mg/kg body weight) or glibenclamide (600 µg/kg) daily with administration of streptozotocin (45 gm/kg body weight- ip) only one day. Streptozotocin induced diabetics and significantly increased the levels of total cholesterol, free fatty acids, triglycerides and phospholipids in kidney as compared with control group. Treatment with seaweed, Padina gymnospora methanolic extracts or glibenclamide consecutively for forty-five days could significantly decrease the levels of renal lipid profiles when compared with streptozotocin alone treated rats.

KEY WORDS

Cholesterol, free fatty acid, Padina gymnospora, streptozotocin

INTRODUCTION

Diabetes mellitus is a chronic disease characterized by hyperglycemia resulting in insulin resistance and/or insulin secondary deficiency caused by the failure of beta- (β-) pancreatic cells (1). Streptozotocin is a natural product that selectively kills insulin-secreting β cells and is widely used to generate mouse models of diabetes (2). Diabetes mellitus often simply referred to as Diabetes. Diabetes is a group of metabolic diseases in which a person has high blood sugar, either because the body does not produce enough insulin or because cells do not respond to the insulin that is produced. This high blood sugar produces the classical symptoms of polyuria, polydipsia and polyphagia. Diabetes mellitus is often called 'The silent killer', because it causes serious complications without serious symptoms and can affect many of major organs in the body (3). It is a chronic disorder that affects the metabolism of carbohydrates, fats, proteins and electrolytes in the body, leading to severe complications (4). Diabetics have significantly accelerated levels of oxidative stress and this contributes massively to most neurological, cardiovascular, retinal, renal diabetic complications (5). Kidneys are the organs that have numerous biological roles. Their primary role is to maintain the homeostatic balance of body fluids by filtering and secreting and minerals from the blood and excreting the nitrogenous wastes along with water, as urine. Because the kidneys are poised to sense plasma concentrations of ions such as sodium, potassium, hydrogen, and compounds such as amino acids, creatinine, bicarbonate and glucose, they are important regulators of blood pressure, glucose metabolism, and erythropoiesis. Kidney disease not only has a significant morbidity, but a high mortality as well. Besides, the high costs and complexity of the treatments, very few patients are able to obtain adequate treatment and kidney disorders place a heavy financial burden on society. Nephrotoxicity is an inherent adverse effect of certain antibiotics, anticancer drugs and other synthetic molecules. A number of

extracts of natural products and dietary antioxidants have been reported to show protective effects against nephrotoxicity (6).

The management of diabetes involves both the non-pharmacological and pharmacological approaches. The non-pharmacological approach includes exercise and diet control. The pharmacological approach includes the use of drugs such as insulin and oral hypoglycemic agents. The present conventional drugs are not only costly but also associated with enormous adverse effects. Numbers of herbal medicines recommended for the treatment of diabetes. Different varieties of ingredients present in the herbal plants are thought to act on a variety of targets by various modes and mechanisms. They have the potential to impart therapeutic role in complicated disorders like diabetes and its complications (4).

Seaweeds have been used in traditional medicine for many centuries and are an object of interest for the pharmaceutical and food industries (7). Several studies reported the great potential of seaweed and their isolated compounds for their anti-inflammatory, anti-noceptive effects (8,9) or antimicrobial activity (10). In addition, seaweeds are rich source of bioactive compounds producing a great variety of secondary metabolites with broad biological activities (11). Nowadays many efforts for new natural therapies have pointed marine algae as a prominent source of active biochemically compounds (12). The present investigation involves in the renal hypolipidemic efficacy of methanolic extracts of seaweed, *Padina gymnospora* on streptozotocin induced diabetics in male albino wistar rats.

MATERIALS AND METHODS

Procurement and rearing of experimental animals

Adult male albino rats (Wistar strain) were collected from Central Animal House, Rajah Muthiah Medical College, Annamalai University and were used for the present study. The rats were housed in polypropylene cages at room temperature (28 ± 2°C). The animals were randomized and separated into normal and experimental groups of body weight ranging from 160-200 g. The animals received a diet of standard pellets (Hindustan Lever Ltd., Bombay). Rats were provided free access to water *ad libitum* and food through the tenure of acclimatization to the environment for a minimum period of two weeks prior to commencement of experiment. The study was approved by the Institutional Animal Ethical Committee of Rajah Muthiah Medical College (160/1999/CPCSEA, Proposal No. 1167), Annamalai University, Annamalainagar, Chidambaram.

Preparation of methanolic extract

The collected seaweed, *Padina gymnospora* were air dried and powdered. The powdered seaweeds were kept in airtight containers in a deep freeze until the time of use. A sample containing 250 g of seaweed were mixed with 1000 mL of distilled water and stirred magnetically overnight (12h) at 37°C. This was repeated three consecutive times. The residue was removed by filtration and the extract evaporated to dryness at a lower temperature (<40 °C) under reduced pressure in a rotary evaporator. The residual extract was dissolving in normal physiological saline and used in the study. The yield of the extract was approximately 20.50 g.

Administering the methanolic extracts of seaweed, *Padina gymnospora* identified the suitable optimum dosage schedule. The suitable optimum dosage schedule was identified by administering the methanolic extracts of seaweed, *Padina gymnospora* at different dosages (50, 100, 200, 400, 800, 1000, 2000 and 4000 mg/kg body weight) in a day daily for 45 days. The optimum doses were selected as 200 mg/kg body weight of the animals for 45 days.

Experimental design

The animals were divided into 7 groups of 6 rats each.

Group 1: Control rats given physiological saline solution 10 mL/kg body wt.

Group 2: Rats injected streptozotocin (45 mg/kg ip body wt.) intraperitonially.

Group 3: Rats injected streptozotocin (45 mg/kg ip body wt.) intraperitonially + methanolic extract of *Padina gymnospora* (MEPG) (50 mg/kg body wt.) administered orally using an intragastric tube.

Group 4: Rats injected streptozotocin (45 mg/kg ip body wt.) intraperitonially + methanolic extract of *Padina gymnospora* (MEPG) (100 mg/kg body wt.) administered orally using an intragastric tube.

Group 5: Rats injected streptozotocin (45 mg/kg ip body wt.) intraperitonially+ methanolic extract of *Padina gymnospora* (MEPG) (200 mg/kg body wt.) administered orally using an intragastric tube.

Group 6: Rats injected streptozotocin (45 mg/kg ip body wt.) intraperitonially + glibenclamide (600 µg/kg body wt.) administered orally using an intragastric tube.

Group 7: Methanolic extract of *Padina gymnospora* (MEPG) alone (200 mg/kg body wt.) administered orally using an intragastric tube.

At the end of the experimental period in 24 h after last treatment the animals were killed by cervical decapitation. The kidney tissues were excised immediately and washed with chilled physiological saline for estimation of lipid profiles.

Biochemical analysis

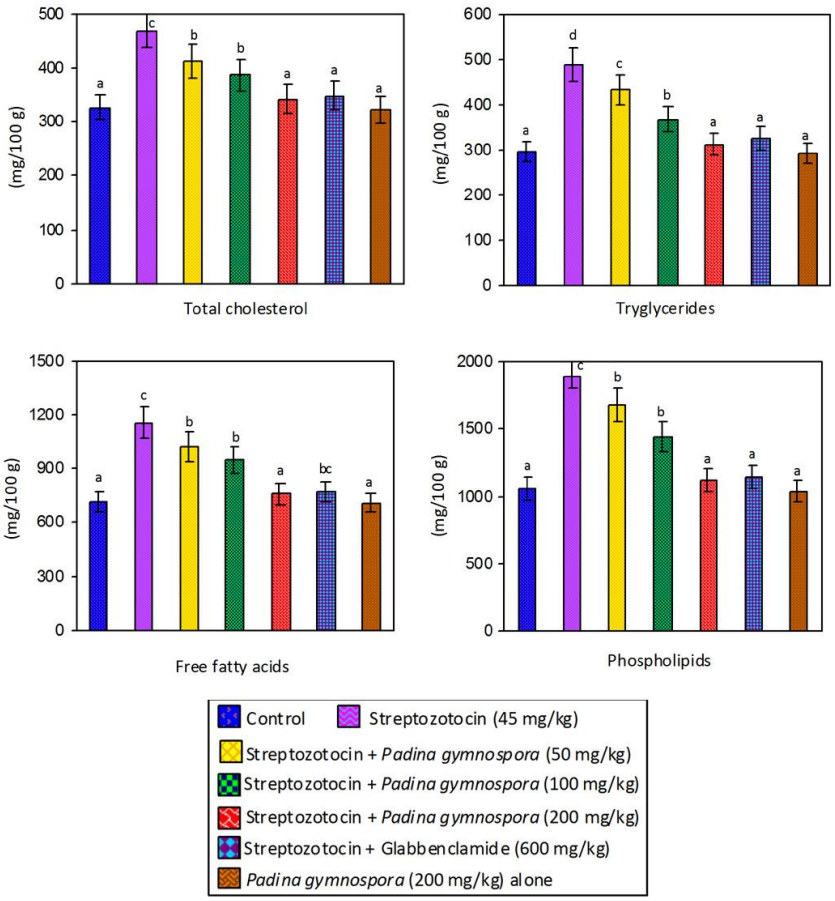
Kidney tissues were taken into centrifuge tube with rubber caps labeled and centrifuged at 3000 rpm for 15 minutes. Lipid profiles such as cholesterol, Phospholipids, triglycerides and free fatty acids (13-16) respectively.

Statistical analysis

Statistical analysis was done by analysis of variance (ANOVA) and the groups were compared by Duncan's multiple range test (DMRT). The level of statistical significance was set at $p \leq 0.05$ (17).

RESULTS

The level of lipid profiles in kidney was estimated in normal and experimental rats. There was a significant elevation of the kidney lipid profiles like cholesterol, triglycerides, phospholipids and free fatty acids in rats treated with streptozotocin when compared with the corresponding control rats. Administration of methanolic extracts of seaweed, *Padina gymnospora 50*, 100, 200 mg/kg body weight and glibenclamide to streptozotocin treated rats caused a significant reduction in kidney of cholesterol, triglycerides, phospholipids and free fatty acids when compared with streptozotocin alone treated rats. No effects were observed on kidney of lipid profiles when extract alone was administered rats (Fig 1).



Values not sharing a common superscript letter (a, b, c and d) differ significantly at *p*<0.05 (DMRT)

Fig. 1. Effect of methanolic extract of *Padina gymnospora* on renal lipid profiles in control experimental group

DISCUSSION

Diabetes mellitus is a severe endocrine disease that includes a group of disorders of varying etiology and pathogenesis. The management of diabetes is an escalating global predicament and a cure has yet to be discovered. Drugs such as insulin and other hypoglycemic agents control blood glucose level only when they are regularly administered. These treatments, however, have several disadvantages (18). Fortunately, natural products, among other alternative medicines, offer a similar degree of efficacy without many problematic side effects. Streptozotocin is a selectively toxic to the *β*-cells in the pancreatic islets and it eventually induces diabetes in adult rats (19). Streptozotocin induced hyperglycemia has been described as a good experimental model to study diabetes mellitus. Its administration to rats showed an increase in the blood glucose levels and a decrease in the plasma insulin levels (20,21).

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 metabolism often lead to functional impairment of different organs in diabetes and associated troubles are usually characterized by hyperglycemia, hypertriglyceridemia combined with low level of insulin (22).

Hyperlipidaemia is the greatest risk factor of coronary heart disease. Currently available hypolipidaemic drugs have been associated with number of side effects. Plant based treatment for hyperlipidaemia has no side effects, cheap and locally available. Seaweeds are frequently consumed in Asia and occasionally consumed in the rest of the world. Edible seaweeds are rich in non-starch polysaccharides, proteins, minerals and vitamins (23-25).

In the present investigation, oral administration of methanolic extract of seaweed, *Padina gymnospora* 50, 100 and 200 mg/kg body weight and also glebenclamide to streptozotocin induced diabetics rats showed reduced the increased the levels of total cholesterol, phospholipids, triglycerides and free fatty acids in kidney when compared with streptozotocin alone treated rats. Glibenclamide was often used as a standard antidiabetic drug in streptozotocin induced diabetes to compare the efficacy of variety of hypoglycemic drugs (26). The cholesterol-lowering effects of water-soluble fibers are believed to be a result of the interference with the enterohepatic circulation of bile acids (27). The reason for the elevated triglycerides in diabetes is complex and stems from a disturbance in fatty acid metabolism (28). Administration of Sodium Alginate from seaweed, *Sargassum crassifolium* to streptozotocin treated rats showed decreased the levels of lipid profiles (29). Oral administration of seaweed, *Gelidium amansii* hot-water extract to high fat diet fed hamster rats shows that ameliorates lipid profiles when compared with high-fat diet alone fed hamster rats (30).

CONCLUSION

The seaweed, *Padina gymnospora* contains plenty of secondary metabolites, vitamins and minerals. The antihyperlipidemic efficacy of methanolic extract of seaweed, *Padina gymnospora* on streptozotocin induced diabetics rats showed reduction of increased lipid profiles in kidney may be the substances which are present in the seaweed. Accordingly, such effects may reduce risk factors for cardiovascular disease in patients with diabetes. Further study is needed to find out the exact mechanism and bioactive compounds involve the antihyperlipidemic activity.

ACKNOWLEDGEMENT

The authors thankful to Professor and Head, Department of Zoology and Authorities of Annamalai University for providing facilities to carry out this work.

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Received:03.08.18, Accepted: 07.09.18, Published:01.10.2018

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