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HEPATICHYPOLIPIDEMIC POTENTIAL OF SEAWEED, *Padina gymnospora* (KUTZING) ON STREPTOZOTOCIN INDUCED DIABETICS IN MALE ALBINO WISTAR RATS

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ABSTRACT

Diabetes mellitus is a multisystem endocrine disorder characterized by persistent hyperglycemia resulting from the defects in insulin secretion, action or both. In the traditional system of Indian medicine, formulation with extracts of plant parts is used as the drug of choice as antidiabetic, antiulcerative, hepatoprotective and lipid-lowering agents. Herbal medicines are popular remedies for a number of diseases and used by a vast majority of the world's population. Since pre-historic times, herbs were the basis for nearly all medicinal therapy until synthetic drugs were developed in the nineteenth century. Seaweeds contain polysaccharides, proteins, amino acids, lipids, peptides, minerals and some vitamins. Polyphenols of seaweed are used as cosmetics and pharmacologicalsas antioxidants, protection from radiation, antibiotics and anti–inflammatory, hypo–allergenic, antibacterial and antidiabetic activity. The present study was undertaken to investigate the effect of methanolic extracts of Padina gymnospora on streptozotocin induced diabetics in male albino Wistar rats. Streptozotocin induced diabetic rats were treated with methanolic extracts of Padina gymnospora at the doses of 50, 100 and 200 mg/kg, p.o. and its influence on total cholesterol, phospholipids, triglycerides and free fatty acids in liver were observed. Oral administration of methanolic extract of Padina gymnospora at the doses of 50, 100 and 200 mg/kg, p.o. to streptozotocin treated rats showed significantly decreased in total cholesterol, phospholipids, triglycerides and free fatty acids in liver near normal. Hence, it can be concluded that methanolic extract of Padina gymnospora effectively reduce the lipid profiles in diabetic rats.

KEY WORDS

Cholesterol, free fatty acids, phospholipids, streptozotocin, seaweed

INTRODUCTION

Diabetes mellitus, a leading world-wide metabolic disorder, is characterized by hyperglycemia associated with impairment in insulin secretion and/or insulin action as well as alteration in intermediary metabolism of carbohydrate, protein and lipids. Several reports indicate that annual incidence rate of diabetes mellitus will increase in future worldwide, especially in the developing countries (1). In developing and developed countries cardiovascular disease is a major cause of morbidity and mortality in recent scenario. Throughout the world high blood cholesterol is one of the primary risk factors, with the global burden of diseases estimating that high blood cholesterol alone accounted for 4.0 million deaths (2-4).

The plant kingdom is a treasure house of potential drugs and in the recent years there has been an increasing awareness about the importance of medicinal plants [5]. According to World Health Organization, medicinal plants would be the best source to obtain variety of drugs. However, such plants should be investigated to better understand their properties, safety, and efficiency (6). Plant products have been part of phytomedicines since time immemorial. This can be derived from barks, leaves, flowers, roots, fruits, seeds (7). Knowledge of the chemical constituents of plants is desirable because such information will be value for synthesis of complex chemical (8-10).

Seaweeds are the most abundant resources in the ocean. Seaweeds contain polysaccharides, proteins, amino acids, lipids, peptides, minerals and some vitamins. Polyphenols of seaweed was used as cosmetics and pharmacological as antioxidants, protection from radiation, antibiotics, anti-inflammatory, hypoallergenic, antibacterial and antidiabetic (11). Polyphenol extracts from seaweed, for example, Alaria, Ascophyllum, Padina and Palmaria, are able to inhibit the activity of α-amylase and α-glucosidase that can lower blood glucose levels (12, 13). On the other hand, seaweed also has a high content of antioxidants that have beneficial value for diabetes mellitus (14).

Seaweeds are of high nutritious value due to their high contents of fibers, minerals and polyunsaturated fatty acids (15). In addition, seaweeds contain a variety of bioactive compounds such as phlorotannins and polysaccharides not found in terrestrial plants, which may play a role in modulating chronic diseases. Epidemiological studies have shown that there is an association between dietary intake of seaweeds and a reduced prevalence of chronic diseases including cardiovascular disease, hyperlipidemia and cancer (16). Bioactive molecules such as polyunsaturated fatty acids and polyphenolic compounds in seaweeds have the potential health benefits of preventing and managing type 2 diabetes (17). Extracts from brown seaweeds have been shown to inhibit α-glucosidase and dipeptidyl-peptidase-4 (DPP-4) and have the ability to stimulate incretin hormone secretion (18). There have also been many reports on the potential therapeutic benefits of seaweed consumption in the management of body weight and obesity (19, 20). Most seaweed has more ash contents than terrestrial plants and animal products. Some of the trace elements in seaweeds are rare or absent in terrestrial plants (21). Thus, seaweeds are important sources of elements vital for the metabolic reactions in the human and animal health, such as enzymatic regulation of lipid, carbohydrate and protein metabolism (22-24).

MATERIAL AND METHOD

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 extracts

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 (12 h) 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 dissolved 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 were 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 liver tissues were excised immediately and washed with chilled physiological saline for estimation of lipid profiles.

Biochemical analysis

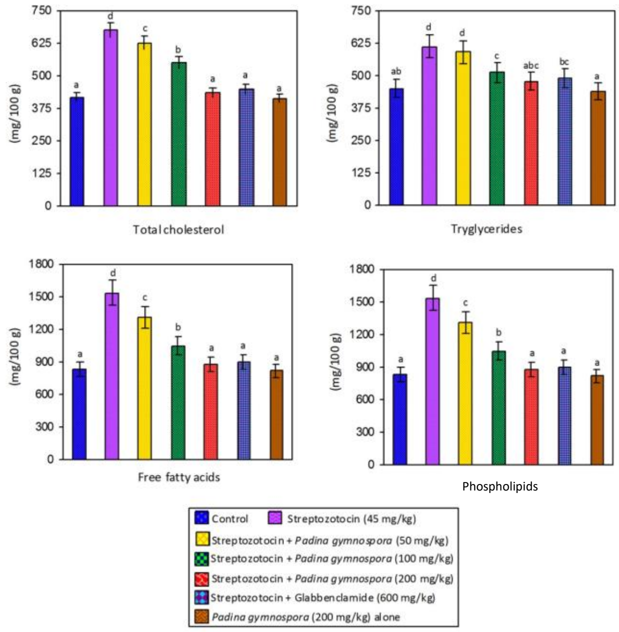
Liver tissues were taken into centrifuge tube with rupper caps labeled and centrifuged at 3000 rpm for 15 minutes. Lipid profiles such as cholesterol, Phospholipids, triglycerides and free fatty acids (25–28) respectively.

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 0.05 (29).

RESULTS

The level of lipid profiles in liver was estimated in normal and experimental rats. There was a significant elevation of the liver lipid profiles like total cholesterol, phospholipids, triglycerides 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 liver lipid profiles of total cholesterol, phospholipids, triglycerides and free fatty acids when compared with streptozotocin alone treated rats. No effects were observed on liver of lipid profiles when extract alone 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 hepatic lipid profile in control experimental group

DISCUSSION

Diabetes mellitus, as one of the most important public health concerns is a worldwide metabolic disease with fast-increasing prevalence (30). It is predicted that, by the year 2025 the incidence of diabetics will reach to the 300 million (31, 32). The term diabetes mellitus describes a metabolic disorder characterized by chronic hyperglycaemia with disturbances of carbohydrate, fat and protein metabolism resulting from defect in insulin secretion, insulin action or both (33). 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) (34). Diabetes is a leading cause of morbidity and mortality for the world's growing population. The International Diabetes Federation has predicted a worldwide increase from 8.3-9.9% by the year 2030 (35,36). The impairment of insulin secretion results in enhanced metabolism of lipids from the adipose tissue to the plasma (37- 39). In addition, leads to a variety of derangements in lipid metabolism, which inturn leads to accumulation of lipids such as total cholesterol and triglycerides in diabetic patients (40,41). However, abnormal high concentration of serum lipids in the diabetics is mainly to increase in the mobilization of free fatty acids from the peripheral fat deposits (42).

In the present investigation, oral administration of methanolic extract of seaweed, *Padina gymnospora* (50, 100 and 200 mg /kg body weight) and glibenclamide to streptozotocin induced diabetic liver showed reduced the elevated levels of total cholesterol, phospholipids, triglycerides and free fatty acids 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 (43). When the glucose levels excess in the blood, glucose will be converted to triglycerides in which triacylglycerol synthesis process is known as lipogenesis. Carbohydrate rich meals lead to increase the process of lipogenesis in the liver and adipose tissue. However, the occurrence of insulin resistance inhibits lipogenesis process making glucose and free fatty acid levels in blood plasma increased. In the liver, triglyceride accumulation can cause fatty liver (44). Diabetic dyslipidemia has long been shown to have a strong relation with coronary heart disease, which is the most dangerous and life-threatening complication of diabetes (45-47). Seaweeds are of the commercially important marine living and renewable resources in India. Algae are enriched with many trace elements, protein, vitamins, several bioactive substances and secondary metabolites Seaweeds have been used since ancient times as food, fuel, fertilizer and as source of medicine (48).

CONCLUSION

The methanolic extract of seaweed, *Padina gymnospora* effectively minimized the lipid profiles in liver of streptozotocin induced diabetics rats. The reduction of lipid profiles may be presence of secondary metabolites, minerals and vitamins are present in the seaweed, *Padina gymnospora*. Further study is required to find out which active principles responsible for minimizing the lipid profiles.

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