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Original article

Effects of coconut water on carbohydrate metabolism and pancreatic pathology of alloxan induced diabetic rats

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Abstract

Introduction: Diabetes mellitus is a chronic disease characterized by hyperglycemia and insufficiency of secretion or action of endogenous insulin. In addition to a good number of known antidiabetic drugs in the market, remedies from natural source are used with success to manage this disease because it has fewer adverse effects, potential cost effectiveness and it is easily available. Coconut water (*Cocos nucifera* L.) has many medicinal applications to treat metabolic syndromes including hyperlipidemia, hyperglycemia, hypertension, *etc.* The present study was aimed to evaluate the effects of mature coconut water (MCW) on carbohydrate metabolism in experimentally induced diabetes.

Methodology: Diabetes was induced in rats by injecting them with alloxan (150 mg/kg body weight) intraperitoneally. After inducing diabetes with alloxan, MCW was given (4 ml/100 g body weight) to rats orally for 45 days. Effects of MCW on blood glucose, glycated hemoglobin, liver glycogen, various carbohydrate metabolizing enzymes and pancreas were evaluated in normal and experimental rats.

Results: Oral administration of MCW in diabetic rats showed a significant reduction in blood glucose and glycated hemoglobin levels with improvement in plasma insulin levels. Activities of carbohydrate metabolizing enzymes were higher in MCW treated diabetic rats along with increased concentration of liver glycogen. Histopathological analysis of pancreas revealed that treatment with MCW reduced the pancreatic damage induced by alloxan and stimulated β-cell regeneration in diabetic rats.

Conclusion: The overall results show that MCW exert significant antihyperglycemic potential and could be developed as a potent drug candidate or nutraceutical for the management of diabetes and associated complications.

Keywords: Glycolytic enzymes; Glycogen phosphorylase; Insulin; Oral glucose tolerance test; Glycated hemoglobin; β-Cell regeneration

Introduction

Diabetes mellitus is a common metabolic disorder characterized by abnormal high blood glucose levels and insufficiency of secretion or action of endogenous insulin, which is considered to be one of the leading causes of mortality world wide [1]. It is estimated that the number of diabetes cases will increase to 439 million by 2030 with prevalence of 7.7% [2]. Number of deaths in adult due to diabetes is estimated to be 3.96 million per year and mortality rate of diabetes in all ages is 6.8%, at global level [3]. Hyperglycemia, a condition characterized by an abnormal postprandial increase in the blood glucose level, has been linked to the onset of type 2 diabetes and associated with oxidative dysfunction and failure of various organs, especially the eyes, kidneys, nerves, heart, and blood vessels, and has been shown to be also linked to hypertension [4]. Lifestyle and nutritional status can also influence the prevalence of glucose intolerance and other complications associated with diabetes [5]. In diabetes mellitus, alteration in carbohydrate metabolism plays a key role in the severity and progression of this disease. In experimental diabetes, enzymes of glucose metabolism are markedly altered and produce hyperglycemia, which leads to pathogenesis of diabetic complications [1]. Though there are modern drugs available to reduce hyperglycemia, patients are still suffer from

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many side effects of these modern drugs and therefore the search for new pharmacological approaches is prevalent and concerted efforts are being made to develop suitable alternative effective remedies against diabetes.

Herbal drugs have been used since ancient times as medicines for the treatment of diabetes and associated complications. Evaluation of plant products to treat diabetes mellitus is of growing interest as they contain many bioactive substances with therapeutic potential. In this regard, traditionally used medicinal plants might act as a useful source of new hypoglycemic agent. Coconut water (CW), a natural drink exorbitantly available in many tropical countries being used as an isotonic beverage as CW contains electrolyte level similar to human blood. The richness of macro and micro nutrients in CW is reported to possess many medicinal properties including hypolipidemic, cardioprotective, antihypertensive and hepatoprotective effects [6–9]. Our previous studies revealed that mature coconut water reduces blood glucose and exerts antioxidant activity in alloxan induced diabetic rats [10]. Therefore the present study aims to investigate the effects of mature coconut water (MCW) on carbohydrate metabolism in alloxan induced diabetic rats.

Materials and methods

Chemicals

Alloxan was purchased from SRL chemicals, India. Kit for glucose estimation was purchased from Agappe Diagnostics, India. Kit for serum insulin analysis was purchased from AVIDA Centaur ready pack, Japan by Kyowa Medex. Co. Ltd. for Bayer Corporation. All other chemicals used were of highest analytical grade.

Collection of mature coconut water (MCW)

MCW from mature coconuts (*Cocos nucifera* L.) (10–12 months of age), West Coast Tall variety grown in the university campus, dehusked, broken carefully and liquid endosperm was collected and used for the experiment which was carried out over two days.

Animals and experimental design

Male Sprague-Dawley rats weighing between 160–190 g were used for the study. The rats were kept in a laboratory animal unit with a 12 h light/dark cycle. Throughout the experiment, room temperature was maintained at 25 ± 2 °C. The rats were maintained on a standard Chow diet (Sai Feeds, Bangalore, India) and water *ad libitum* prior to dietary manipulation. The animals were maintained as per the protocol and guidelines of our Institutional Animal Ethical Committee.

After acclimatization, the rats were divided into 4 groups of 12 rats each. Duration of the experimental period was 45 days.

Group I – Normal
Group II – MCW treated group
Group III – Diabetes group
Group IV – Diabetes + MCW

Diabetes was induced in groups III and IV by injecting them with alloxan (150 mg/kg body weight) intraperitoneally after fasting the animals for 24 h. The rats were given 5% glucose solution for the next 24 h to prevent hypoglycemia. After 72 h, rats with fasting blood glucose more than 200 mg/dl were considered diabetic and included in the study. MCW was fed daily to the rats of group II and IV using an intragasric tube (4 ml/100 g body weight) for 45 days. Normal rats received same amount of distilled water. At the end of the experimental period, half of the rats in each of the four groups were fasted for 24 h and underwent OGTT, while the other half were fasted overnight and sacrificed by sodium pentothal injection. Blood and tissues were collected for various estimations.

Biochemical estimations

Estimation of serum glucose was done using a commercial kit based on glucose oxidase method [11]. Serum insulin was measured with an automated immunochemiluminometric (ICL) assay provided by Bayer Diagnostics (ADVIA Centaur insulin assay) according to the manufacture's instruction. Estimation of Glycated hemoglobin was done using Micromat 2 hemoglobin Acc test using Micromat 2 instrument (280-00016XI, Biorad). Liver glycogen content was estimated as per the method of Carrol [12]. Activities of glucose 6 phosphatase [13], glycogen phosphorylase [14], hexokinase [15], fructose-1,6-bisphosphatase [16], pyruvate kinase [17], were measured in the liver of normal and experimental rats. Protein content in tissue homogenate was determined by Lowry et al. [18].

Oral glucose tolerance test (OGTT)

OGTT in fasted animals was performed using the procedure of Young et al. [19]. Blood samples from animal tails were collected into heparinized micro-hematocrit tubes after 24 h of fasting and the baseline serum glucose levels were measured. The animals were given 1 ml of a glucose solution containing 0.6 g glucose (3 g/kg body weight) by intragastric gavage and duplicate blood samples from their tails were collected after 45, 90 and 135 min. The glucose concentration data were used to compare glucose tolerance in the various groups.

Histopathology of pancreas

After the experimental period, rats were anesthetized and the pancreas were removed and preserved in 10% neutral buffered formaldehyde. Dehydration and clearing of the tissues were performed automatically. Five micrometer thickness sections were prepared and stained with hematoxylin and eosin (H/E) [31]. Stained sections were qualitatively evaluated using a digital microscope (Labomed, iVu 3000, USA). The images were analyzed using Digipro software (Germany).