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Original Article

Liver protective effects of aqueous extract of *Syzygium cumini* in Swiss albino mice on alloxan induced diabetes mellitus

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ARTICLE INFO

Article history:
Received 11 July 2013
Accepted 26 July 2013
Available online 24 August 2013

Keywords:
Syzygium cumini
Diabetes mellitus
SGOT
SGPT
Bilirubin

ABSTRACT

Background: Diabetes mellitus is one of the most common endocrine disorders accompanied with many metabolic syndromes. Use of herbal medicines has always been an option to treat a great number of diseases such as diabetes and its complications. The aim of the present study is to investigate the liver protective effects of *Syzygium cumini* seed extract in alloxan induced diabetic Swiss albino mice.

Methods: Eighteen Swiss albino mice (weighing 28–32 g) were randomly divided into control, alloxan treated and *S. cumini* treated mice group. Diabetes was induced in mice by injecting intraperitoneally alloxan monohydrate at dose of 150 mg/kg body weight. Aqueous extracts of *S. cumini* seed at dose of 250 mg/kg body weight were given orally in diabetic mice daily for three weeks after established LD_{50} value.

Results: In diabetic mice, the SGOT, SGPT, Bilirubin and serum glucose levels were significantly increased in comparison with the control groups. Statistical analysis ($p < 0.05$) of the data indicated that aqueous extract of *S. cumini* were significantly decrease serum contents of liver enzymes (SGOT, SGPT and Bilirubin) as well as serum glucose in treated groups.

Conclusion: The results suggested that aqueous extracts of *S. cumini* seed possesses liver protective effect against alloxan induced diabetic mice.

1. Introduction

Diabetes mellitus (DM) is a chronic disease caused by inherited or acquired deficiency in insulin secretion and by decreased responsiveness of the organs to secreted insulin.[1] Diabetes mellitus is a syndrome, initially characterized by a loss of glucose homeostasis resulting from defects in insulin secretion, insulin action both resulting impaired

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0974-6943/$ – see front matter
http://dx.doi.org/10.1016/j.jopr.2013.07.020

metabolism of glucose and other energy yielding fuels such as lipids and proteins.[2] DM is a leading cause of end stage kidney disease, cardiomyopathy and heart attacks, strokes, retinal degeneration leading to blindness and non-traumatic amputations.[3] Dyslipidemia, quite common in diabetic patients, is the main risk factor for cardiovascular and cerebrovascular diseases. DM is currently one of the most costly and burdensome chronic disease and is a condition that is increasing in epidemic proportions throughout the world. Diabetes is a serious illness with multiple complications and premature mortality, accounting for at least 10% of total health care expenditure in many countries.[4] The prevalence of diabetes of all age groups worldwide is projected to rise from 171 million in 2000 to 366 million in 2030.[5] Reason of this rise includes increase in sedentary life style, consumption of energy rich diet, obesity, higher life span, etc.[6] DM is a major and growing health problem in most countries. It causes considerable amount of disability, premature mortality, and loss of productivity as well as increased demands on health care facilities. As diabetes aggravates and β-cell function deteriorates, the insulin level begins to fall below the body's requirements and causes prolonged and more severe hyperglycemia.[7] Hyperglycemia induces long term complications of diabetes such as cardiovascular complications and micro vascular complications such as retinopathy, nephropathy and neuropathy and foot ulcer.[8]

Based on the WHO recommendations hypoglycemic agents of plant origin used in traditional medicine are important.[9] The attributed antihyperglycemic effects of these plants is due to their ability to restore the function of pancreatic tissues by causing an increase in insulin output or inhibit the intestinal absorption of glucose or to the facilitation of metabolites in insulin dependent processes. Hence treatment with herbal drugs has an effect on protecting β-cells and smoothing out fluctuation in glucose levels. Most of these plants have been found to contain substances like glycosides, alkaloids, terpenoids, flavonoids etc. that are frequently implicated as having antidiabetic effects.[10]

Alloxan was one of the most widely used chemical diabetogen during initial research work on experimental diabetes. It is a cyclic urea analogue of chemical composition 2,4,5,6-tetraoxo-hexa hydropyrimidine.[11] Alloxan induces diabetes in animals and impairs glucose induced insulin secretion from b cells of Islets of Langerhans of Pancreas. It has been reported that alloxan rapidly and selectively accumulates in β-cells in comparison with non-b cells. Several reports directly or indirectly indicate that alloxan affects the membrane potential and ion channels in β-cells.[12]

Syzygium cumini also called *Eugenia jambolana* (EJ) has been reported to have hypoglycemic effects both in experimental models and clinical studies. *S. cumini* seed apart from hypoglycemic activity has been reported to have anti-inflammatory,[13] neuro psychopharmacological, antibacterial,[14]antioxidant[15] and ant diarrhoeal effects.[16] In the present investigation, aqueous extract of seeds of *S. cumini* was used to evaluate the antidiabetic activity and liver protective effect in alloxan induced diabetic Swiss albino mice.

2. Matarials and methods

2.1. Animals

Healthy Swiss albino mice of both sexes, weighing approximately (28–32 g) were used in the pharmacological studies. Before and during the experiment the animals were maintained in well-ventilated room at room temperature with natural day–night cycle in polypropylene cages lined with husk in standard environmental conditions (temperature (22 ± 2) °C, relative humidity (55 ± 10) % and 12:12 (light:dark cycle). The mice was fed on a standard pellet diet *ad libitum* and had free access to water. The experiments were performed after approval of the protocol by the (CPCSEA Regd. No. 1129/bc/07/CPCSEA, dated 13/02/2008).

2.2. Preparation of plant material

The seed of *S. cumini* were procured from local market (Allahabad, U.P). The identity of the seeds of *S. cumini* was confirmed by Botanist, Department of Botany, Sam Higginbottom Institute of Agriculture, Technology & Sciences, Allahabad, UP (India). The seeds were washed with distilled water and dried completely under the mild sun and crushed with electrical grinder coarse powder. Aqueous extract was made by dissolving it in distilled water using by mortar and pestle. The dose was finally made to 250 mg/kg body weight for oral administration after the LD_{50} estimation.

2.3. Chemicals

All chemicals were obtained from the following sources: alloxan was purchased from the Loba chemie (Batch no-G204207), Mumbai. Commercially available kits for chemical analyses such as glucose, SGOT, SGPT, bilirubin was purchased from Crest Coral Clinical Systems, Goa, India. Analytical grade ethanol was purchased from Merck Company (India).

2.4. Induction of hyperglycemia with alloxan

The selected mice were weighed, marked for individual identification and fast for overnight. The alloxan monohydrate at the rate of 150 mg/kg body weight[17] were administered intraperitoneal (i.p) for making the alloxan induced diabetic mice model. Blood glucose level of these mice were estimated 72 h after alloxan administration, diabetes was confirmed by blood samples collected from the tip of the tail using a blood glucometer (Accu Sure, Taiwan). Animals with blood glucose level equal or more than 200 mg/dl were declared diabetic and were used in entire experimental group.[18]

2.5. Experimental design

Mice were divided into three groups, with six mice in each group, as follows:

(i) group I – control mice, (ii) group II – alloxan-induced diabetic control mice, (iii) group III –diabetic mice given *S. cumini* seed extract (250 mg/kg) in aqueous solution daily for 21 days through Gavage's method.