EFFECT OF MIMUSOPS ELENGI LINN. BARK EXTRACT ON ALLOXAN INDUCED HYPERGLYCEMIA IN ALBINO RATS

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Abstract: The present study evaluates the effect of aqueous bark extract of Mimusops elengi Linn. in alloxan induced diabetic rats. Diabetes was induced in rats by administering alloxan monohydrate (150 mg/kg bw) intraperitonially (ip). Animals were divided into five groups (n=6) receiving different treatments: Group I: vehicle (Control), Group II: diabetic (control), Groups III and IV: aqueous bark extract treated (250 mg and 500 mg/kg bw, orally respectively), and Group V: standard antidiabetic drug glibenclamide (1 mg/kg bw, orally). Blood samples and liver tissues were collected and analyzed for blood glucose, serum insulin, glycosylated haemoglobin (HbA1C) and liver glycogen, glucokinase, glucose-6-phosphatase and glucose-6-phosphate dehydrogenase after 45 days of the treatment. The aqueous bark extract of Mimusops elengi Linn. at the dose level of 500 mg/kg bw, produced significant alteration in biochemical and enzymatic parameters studied. The present investigation thereby reveals the anti-hyperglycemic potential of bark extract of Mimusops elengi Linn.

Key words: Mimusops elengi Linn., Alloxan, Hyperglycemia

INTRODUCTION

Diabetes mellitus is a chronic disease caused by inherited and/or acquired deficiency of insulin that leads to hyperglycemia, which over a period of time develops diabetic complications such as nephropathy, retinopathy, neuropathy and cardiac problems [1]. Prevalence of diabetes mellitus is increasing rapidly in both developing and developed countries. It was estimated to be 2.8% (171 million) in 2000 and it would be 4.4% (366 million) in 2030 [2]. Despite insulin and other different types of anti-hyperglycemic agents available in the pharmaceutical market, diabetes and its related complications continue to be a major health problem. Ethnopharmacological surveys indicate that more than 1200 plants are used world wide in traditional medicine for their hypoglycemic property. The investigation of antidiabetic agents of plant origin is thus of great significance because of their effectiveness, minimal side effects and relatively low cost [3].

Mimusops elengi Linn. (Sapotaceae) is commonly known as Spanish cherry or bullet wood is a small to large tree found in all parts of India. The various extracts of the plant (bark, fruit, leaves, seed, and flowers) have been reported to be cardiotonic, alexipharmic and stomachic [4], hypotensive [5], antibacterial [6], anthelmintic [7], anti-gastric ulcers [8], teeth cleaner [9] and renewable sources of energy [10]. Phytochemical review shows the presence of taraxerol, taraxerone, urosolic acid, betulinic acid, α-spinosterol, β-sitosterol, lupeol, and mixture of triterpenoid saponins in the bark of Mimusops elengi Linn. [11-14]. The aim of the present study is to investigate the anti-hyperglycemic property of Mimusops elengi Linn. in alloxan induced diabetic rats.

MATERIALS AND METHODS

Animals: Wistar strains of albino rats of either sex weighing 150-200 g were used as the experimental
models. The animals were kept in well ventilated cages and were fed with the commercial pelleted rat chow and water ad-libitum. Animals were maintained in standard animal house (CPCSEA Approval No: 790/03/ac/CPCSEA).

**Preparation of the extract:** Fresh bark of *Mimusops elengi* Linn. was obtained from places in and around Tiruchirappalli, and was authenticated by RAPINAT herbarium, St. Joseph’s College, Tiruchirappalli.

The bark was shade dried and coarsely powdered. 200 g of plant powder was taken and extracted with water. To one part of the material six parts of water was added, boiled and reduced to one third and filtrate was evaporated to dryness. The paste form of the extract was subjected to pre-clinical screening.

**Induction of experimental diabetes:** Animals were allowed to fast for 24 hours prior to the injection of a single dose (150 mg/ kg bw ip) of alloxan monohydrate dissolved in sterile normal saline. After 4 days of alloxan induction, the urine sugar and blood sugar were estimated. Animals with blood glucose level above 250 mg were chosen for further studies.

**Drug administration:** The quantities of the individual drug to be administered were calculated and administered daily for 45 days orally using an infant feeding tube. The results were compared with that of the standard drug glibenclamide, which was also given daily for 45 days.

**Biochemical analysis:** Fasting blood glucose [15], fasting serum insulin [16], glycosylated haemoglobin [17,18], liver glycogen [19,20], glucokinase [21], glucose-6-phosphatase [22] and glucose-6-phosphate dehydrogenase [23] were estimated by standard techniques.

**Statistical analysis:** All values were expressed as mean ± standard error mean (SEM). The differences were compared using one-way analysis of variance (ANOVA). p values < 0.05 were considered to be significant.

**RESULTS**

The hypoglycemic effect of aqueous bark extract of *Mimusops elengi* Linn. is shown in Table 1. The rats of diabetic control (Group II) showed a marked

<table>
<thead>
<tr>
<th>Treatment groups</th>
<th>Fasting blood glucose mg/dl</th>
<th>Serum insulin micro units/ml</th>
<th>HbA1C (%)</th>
<th>Glycogen mg/g</th>
<th>Glucokinase micromoles/ml/min</th>
<th>Glucose-6-phosphatase U/mg</th>
<th>Glucose-6-phosphate dehydrogenase IU/g Hb</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group I Vehicle (control)</td>
<td>82.4 ± 1.4</td>
<td>25.6 ± 0.9</td>
<td>2.5 ± 1.1</td>
<td>40.1 ± 1.7</td>
<td>110.4 ± 1.4</td>
<td>5.9 ± 0.9</td>
<td>12.4 ± 0.5</td>
</tr>
<tr>
<td>Group II Diabetic (control)</td>
<td>286.3 ± 1.9*</td>
<td>8.6 ± 0.6*</td>
<td>7.2 ± 1.8*</td>
<td>11.7 ± 1.5*</td>
<td>86.7 ± 1.7*</td>
<td>16.2 ± 1.5*</td>
<td>6.3 ± 0.6*</td>
</tr>
<tr>
<td>Group III <em>Mimusops elengi</em> Linn. aqueous extract (250 mg/kg bw)</td>
<td>175.6 ± 1.8*</td>
<td>18.7 ± 0.4*</td>
<td>4.1 ± 1.6*</td>
<td>26.3 ± 1.4*</td>
<td>90.4 ± 0.9*</td>
<td>11.3 ± 1.1*</td>
<td>9.3 ± 0.7*</td>
</tr>
<tr>
<td>Group IV <em>Mimusops elengi</em> Linn. aqueous extract (500 mg/kg bw)</td>
<td>80.6 ± 1.7*</td>
<td>23.5 ± 0.5*</td>
<td>3.0 ± 2.1*</td>
<td>39.8 ± 1.8*</td>
<td>106.5 ± 1.2*</td>
<td>7.3 ± 1.6*</td>
<td>11.4 ± 0.5*</td>
</tr>
<tr>
<td>Group V Glibenclamide (1 mg/kg bw)</td>
<td>80.1 ± 1.6</td>
<td>23.2 ± 0.4</td>
<td>2.8 ± 2.0</td>
<td>39.5 ± 1.6</td>
<td>105 ± 1.5</td>
<td>6.9 ± 1.4</td>
<td>11.1 ± 0.9</td>
</tr>
</tbody>
</table>
increase in fasting blood glucose (286.3 ± 0.9 mg/dl), HbA1C levels (7.2 ± 0.08 %) and glucose-6-phosphatase activity (16.2 ± 0.3 U/mg) and a fall in serum insulin (8.6 ± 0.3 micro unit/ml), liver glycogen levels (11.7 ± 1.5 mg/g), and glucokinase (86.7 ± 0.7 micromoles/ml/min) and glucose-6-phosphate dehydrogenase activity (6.3 ± 0.2 IU/g Hb) when compared to normal control group (Group I).

However, following the treatment with aqueous extract of Mimusops elengi Linn. (for 45 days), Group III (250 mg/kg bw) and Group IV (500 mg/kg bw) animals showed significant (p<0.05) reduction in the fasting blood glucose (175.6 ± 0.8 and 80.6 ± 0.7 mg/dl), HbA1C levels (4.1 ± 0.06 and 3.0 ± 0.07 %) and glucose-6-phosphatase activity (11.3 ± 0.5 and 7.3 ± 0.2 U/mg). The serum insulin (18.7 ± 0.4 and 23.5 ± 0.5 micro unit/ml), liver glycogen levels (26.3 ± 1.4 and 39.8 ± 1.8 mg/g) and glucokinase (90.4 ± 0.3 and 106.5 ± 0.6 micromoles/ml/min) and glucose-6-phosphate dehydrogenase activity (9.3 ± 0.1 and 11.4 ± 0.3 IU/ g Hb) was increased significantly (p<0.05) when compared with diabetic rats (Group II). The maximum effect of Mimusops elengi Linn. was seen at a dose level of 500 mg/kg bw and also the Group IV rats showed results comparable with the glibenclamide treated rats (Group V).

**DISCUSSION**

Diabetes mellitus is a major health problem in the world, reaching presently to epidemic proportions, which is known to affect the activities of various enzymes involved in carbohydrate metabolic pathways. Insulin deficiency or decreased insulin action, results in decreased glucose utilization by insulin requiring tissues and an increased glucose production through an increased rate of gluconeogenesis and results in hyperglycemia, thus leads to major complications such as peripheral and cardiovascular disease and renal damage [24].

Alloxan induces “chemical diabetes” in a wide variety of animal species by damaging the insulin secreting pancreatic beta cells resulting in a decrease in endogenous insulin release [25,26], which results in various diabetic complications.

In the present study, diabetic animals treated with Mimusops elengi Linn. (500 mg/ kg bw) produced significant (p<0.05) decrease in blood glucose, HbA1C levels, and glucose-6-phosphatase activity and significant rise in serum insulin, liver glycogen levels, and glucokinase and glucose-6-phosphate dehydrogenase activity. The results were also compared with that of standard drug glibenclamide.

This study showed an increased blood glucose levels in diabetic rats and reduced levels in plant treated groups. This may be due to increased insulin secretion from beta cells of pancreas i.e., pancreotrophic action [27,28] in Mimusops elengi Linn. treated animals. This was also evident from the increased level of insulin in test drug treated animals.

In diabetic controls, marked elevations of HbA1C levels were observed. Increased glycation of haemoglobin has been found to be an important diabetic complication, which is due to the presence of hyperglycemia. Excessive glucose present in blood reacts with haemoglobin (Hb) and convert it to glycosylated haemoglobin (HbA1C) [29,30]. After 45 days of treatment with plant extract, profound reduction in the percentage of glycosylated haemoglobin was observed.

The increased activity of glucose-6-phosphatase was observed in diabetic control compared to normal control. Glucose-6-phosphatase plays a major role in the homeostatic regulation of blood glucose levels. When the blood glucose level falls, the liver is capable of rapidly releasing glucose into circulation, where it serves as a fuel for other tissues that lack the ability to make glucose. The two metabolic pathways by which liver can produce glucose are gluconeogenesis and glycogenolysis. A single enzyme glucose-6-phosphatase, catalyses the final step of these pathways and leads to increased glucose production. Increased hepatic glucose output is a major cause of the fasting hyperglycemia that characterizes diabetes [31]. The present study showed that the extract at a dose level of 500 mg/ kg bw inhibits the activity of glucose-6-phosphatase by decreasing the hepatic glucose output.

The diabetic control showed decreased level of glycogen compared to normal rats. Due to insulin deficiency in diabetes mellitus the cells utilize glycogen for energy rather than glucose [32]. The increased glycogen level is observed in the plant extract (500 mg/ kg bw) treated groups. The prevention of depletion of glycogen in the liver tissue is possibly due to the stimulation of insulin release, which activates the glycogen synthase system [33].
Multiple factors may be responsible for such a rapid improvement in insulin secretion and/or action in vivo, which helps to maintain glucose homeostasis.

During diabetes, lipogenesis is decreased while lipolysis is increased in the hepatic tissue which is the outcome of underutilization of glucose resulting in increased lipolysis and stimulation in the activities of gluconeogenic enzymes. The present study showed the increased activity of NADP-linked lipogenic enzyme glucose-6-phosphate dehydrogenase which restored the redox state of hydrogen shuttle system leading to controlled NADPH formation by feedback mechanism [24].

From above data it is concluded that the aqueous bark extract of Mimusops elengi Linn shows significant anti-hyperglycemic activity in alloxan induced diabetic rats and that their effect is comparable to that of glibenclamide. Thus it is evident that Mimusops elengi Linn. could be a potent anti-hyperglycemic drug. However, further studies are needed to isolate its active components and find out the mechanism of its protective effect against hyperglycemia.

REFERENCES