ANITDIABETIC, ANTIHYPERLIPIDAEMIC AND ANTIOXIDANT ACTIVITY OF ETHANOL EXTRACT OF FERONIA ELEPHANTUM CORREA LEAF AND BARK IN NORMAL AND ALLOXAN INDUCED DIABETIC RATS

Muthulakshmi A1, Jothibai Margret R2 and Mohan V.R,*

1Department of Chemistry, V.O. Chidambaram College, Tuticorin-628002, Tamil Nadu, India
2Department of Chemistry, Pope’s College, Sawayerpuram-628251, Tamil Nadu, India
3Ethnopharmacology Unit, Research Department of Botany, V.O. Chidambaram College, Tuticorin, Tamil Nadu, India

Article Received on: 04/11/12 Revised on: 09/12/12 Approved for publication: 29/12/12

ABSTRACT

The aim of the present study was to evaluate the antidiabetic Potential of ethanol extract of Feronia elephantum Correa leaf and bark in normal and alloxan induced diabetic rats. Diabetes was induced in Albino rats by administration of alloxan monohydrate (150 mg/kg). The ethanol extract of F. elephantum leaf and bark at a dose of 400mg/kg of body weight was administered separately at a single dose per day to diabetes induced rats for a period of 14 days. The effect of ethanol extract of F. elephantum leaf and bark on blood glucose, serum lipid profile, the levels of lipid peroxides and antioxidant enzymes, such as catalase, superoxide dismutase, glutathione peroxidase and reduced glutathione were examined. Oral administration of F. elephantum leaf and bark extract to diabetic rats for 14 days significantly reduced the levels of blood glucose, lipid parameters except HDL-C and lipid peroxidation, but increased the activities of plasma insulin and antioxidant enzymes. Ethanol extract of F. elephantum supplementation is useful in controlling the blood glucose level, improves the plasma insulin and lipid metabolism. It is beneficial in preventing diabetic complication from lipid peroxidation and antioxidant system in experimental diabetic rats therefore, it could be useful for prevention or early treatment of diabetes mellitus.

Keywords: Feronia elephantum, antihyperlipidaemic, antioxidant, blood glucose, diabetes mellitus, alloxan induced diabetic rats

INTRODUCTION

Diabetes mellitus, a chronic metabolic disorder, has now become an epidemic, with a worldwide incidence of 5% in general population. The number of people suffering from diabetes has soared to 246 million and the disease now kills more people than AIDS1. It is a chronic disorder caused by partial or complete insulin deficiency, resulting in hyperglycemia leading to acute and chronic complications2. Synthetic drugs are likely to give serious side effect in addition they are not suitable for intake during condition like pregnancy3-5. Hence, search for new drugs with low cost, more potential, without adverse effect is being pursued in several laboratories all around the world. However, for a number of reasons, complementary medicine has grown in popularity in recent years. Dietary measures and traditional plant therapies as prescribed by Ayurvedic and other indigenous system of medicine were used commonly in India. Many indigenous Indian medicinal plants have been found to be useful to successfully manage diabetes and some of them have been tested and their active ingredients isolated6-7. The World Health Organization (WHO) has also recommended the evaluation of the plants effectiveness and condition where we lack safe modern drugs8. In recent years, much attention has been focused on the rate of oxidative stress, and it has been reported that, oxidative stress may constitute the key and common events in the pathogenesis of secondary diabetic complications8. Free radicals are continuously produced in the body as a result of normal metabolic processes and interaction with environmental stimuli. Oxidative stress results from an imbalance between radical-generating and radical scavenging systems that has increased free radical production or reduced activity of antioxidant defenses or both. Implication of oxidative stress in the pathogenesis of diabetes mellitus is suggested not only by oxygen free radical generation; but also due to non-enzymatic protein glycosylation, auto-oxidation of glucose, impaired glutathione metabolism, alteration in antioxidant enzymes and formation of lipid peroxides10-13. In addition to reduced glutathione (GSH), there are other defense mechanisms against free radicals, such as the enzymes superoxide dismutase (SOD), glutathione peroxidase (GPx) and catalase (CAT), whose activities contribute to eliminate superoxide, hydrogen peroxide and hydroxyl radicals14. Many of the complications of diabetes mellitus, including retinopathy and atherosclerotic vascular disease, the leading cause of mortality in diabetes mellitus, have been linked to oxidative stress, and antioxidants have been considered as treatments15. Plants often contain substantial amounts of antioxidants, flavonoids and tannins. The present study suggests that antioxidant action may be an important property of plant medicines associated with the hypoglycemic effect of diabetes mellitus16. Feronia elephantum is one of the medicinally important plants belonging to Rutaceae, commonly known as wood apple. It is a large tree growing to 9 meters (30 ft) tall, with rough, spiny bark grown throughout India. The leaves are pinnate, with 5-7 leaflets each leaflet 25-35mm long and 10-20mm broad, with citrus-scent when crushed. Its fruit are, woody, rough and used as substitute for bael in diarrhea and dysentery while the bark and leaves are used for initiated conditions of vata and pitta17. Leaves are used as an astringent and carminative, good for vomiting, indigestions, hiccup and dysentery. The bark is occasionally prescribed for biliousness and useful in liver diseases18. The present study deals with antidiabetic effect of ethanol extracts of the leaf and bark of F. elephantum on alloxan induced diabetic rats and also to examine the antioxidant potential, lipid profile, protein metabolite and liver enzymes levels changes in alloxan induced diabetic rats. The effect produced by this drug on different parameters was compared with those of glibenclamide, a reference drug.
MATERIALS AND METHODS

Plant Material
Fresh and disease free leaf and bark of *Feronia elephantum* Correa were collected in the month of February and March-2011 from the Agasthiarmalai Biosphere Reserve, Western Ghats, Tirunelveli. The plant was identified with the help of local flora and voucher specimen preserved in Ethnopharmacology Unit, Research Department of Botany, V.O.Chidambaram College, Tuticorin, Tamil Nadu, India.

Preparation of plant extract for phytochemical screening and antidiabetic studies
The *F. elephantum* leaf and bark were shade dried separately at room temperature and the dried leaf and bark were powdered in a wiley mill. Hundred grams of powdered *F. elephantum* leaf and bark was packed in a soxhlet apparatus separately and extracted with ethanol. The ethanol extracts were subjected to qualitative test for the identification of various phytochemical constituents as per the standard procedures\(^{19,20}\). The ethanol extracts were concentrated in a rotary evaporator. The concentrated ethanol extract were used for antidiabetic studies.

Animals
Normal healthy male Wistar albino rats (180-240g) were housed under standard environmental conditions at temperature (25±2°C) and light and dark (12:12 h). Rats were fed with standard pellet diet (Goldmohur brand, MS Hindustan lever Ltd., Mumbai, India) and water ad libitum.

Acute Toxicity Study
Acute oral toxicity study was performed as per OECD – 423 guidelines (acute toxic class method), albino rats (n=6) of either sex selected by random sampling were used for acute toxicity study\(^{21}\). The animals were kept fasting for overnight and provided only with water, after which the extracts were administered orally at 5mg/kg body weight by gastric incubations and observed for 14 days. If mortality was observed in two out of three animals, then the dose administered was assigned as toxic dose. If mortality was not observed, the procedure was repeated for higher doses such as 50,100, and 2000 mg/kg body weight.

Induction of Diabetes in Experimental animal
Rats were induced diabetes by the administration of simple intraperitoneal dose of alloxan monohydrate (150 mg/kg)\(^{22}\). Two days after alloxan injection, rats screened for diabetes having glycosuria and hypoglycemia with blood glucose level of 200-260 mg/100 ml were taken for the study. All animals were allowed free access to water and pellet diet and maintained at room temperature in plastic cages.

Experimental Design
In the present investigation, a total of 30 rats (24 diabetic surviving rats and 6 normal rats) were taken and divided into five groups of 6 rats each.

<table>
<thead>
<tr>
<th>Group</th>
<th>Treatment</th>
<th>Blood glucose level mg/100ml (mean) ± SEM at Time (Hrs)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>0</td>
</tr>
<tr>
<td>Fasted</td>
<td>Control</td>
<td>89.56±2.12</td>
</tr>
<tr>
<td></td>
<td>FEL</td>
<td>81.45±2.78</td>
</tr>
<tr>
<td>Fed</td>
<td>Control</td>
<td>103.56±3.90</td>
</tr>
<tr>
<td></td>
<td>FEL</td>
<td>92.78±3.01</td>
</tr>
<tr>
<td>Diabetic</td>
<td>Control</td>
<td>196.34±5.78</td>
</tr>
<tr>
<td></td>
<td>FEL</td>
<td>181.57±3.23</td>
</tr>
</tbody>
</table>

Each value is SEM of 5 animals. *p=0.05; **p=0.01; ***p=0.001
<table>
<thead>
<tr>
<th>Group</th>
<th>Treatment</th>
<th>Blood glucose level mg/100ml (mean SEM) at Time (Hrs)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fasted</td>
<td>Control</td>
<td>86.2±1.34</td>
</tr>
<tr>
<td></td>
<td>FEL</td>
<td>79.5±2.01</td>
</tr>
<tr>
<td>Fed</td>
<td>Control</td>
<td>112.2±3.54</td>
</tr>
<tr>
<td></td>
<td>FEL</td>
<td>93.2±2.12</td>
</tr>
<tr>
<td>Diabetic</td>
<td>Control</td>
<td>189.5±2.91</td>
</tr>
<tr>
<td></td>
<td>FED</td>
<td>182.4±2.34</td>
</tr>
</tbody>
</table>

Each value is SEM of 5 animals. *p<0.05

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Mean initial body (g)</th>
<th>Mean final body (g)</th>
<th>Mean weight Gain (G)/loss (L) (g)</th>
<th>Fasting Blood glucose (mg/dl)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group I</td>
<td>156.45±0.23</td>
<td>184.3±10.11*</td>
<td>26.59±1.97 (G)</td>
<td>84.23±2.12</td>
</tr>
<tr>
<td>Group II</td>
<td>184.58±0.94</td>
<td>169.83±10.45*</td>
<td>14.69±2.31</td>
<td>221.56±2.45</td>
</tr>
<tr>
<td>Group III</td>
<td>182.58±0.82</td>
<td>199.3±9.56</td>
<td>15.67±1.02</td>
<td>218.54±1.79</td>
</tr>
<tr>
<td>Group IV</td>
<td>191.52±10.43</td>
<td>196.89±0.55ns</td>
<td>0.94±1.23</td>
<td>226.87±6.89</td>
</tr>
<tr>
<td>Group V</td>
<td>179.56±0.97</td>
<td>192.23±0.99</td>
<td>13.67±1.65</td>
<td>219.50±9.11</td>
</tr>
</tbody>
</table>

*p<0.05 comparison with Normal control Vs diabetic and drug treated: a=p<0.05 Diabetic control vs drug treated: b=p<0.05 comparison with initial vs final.

Table 3. Effect of ethanol extract of F. elephantum leaf and bark on the plasma glucose level in normal, diabetic induced and drug treated rats

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Insulin (M/ml)</th>
<th>Glucose (mg/dl)</th>
<th>Urea (mg/dl)</th>
<th>Creatine (mg/dl)</th>
<th>Glycolytaly Hb</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group I</td>
<td>23.56±2.12</td>
<td>72.48±0.98</td>
<td>13.45±1.9</td>
<td>0.61±0.53</td>
<td>3.9±0.12</td>
</tr>
<tr>
<td>Group II</td>
<td>08.29±1.72**</td>
<td>201±1.11*</td>
<td>31.73±3.56*</td>
<td>2.01±0.59</td>
<td>10.65±0.91*</td>
</tr>
<tr>
<td>Group III</td>
<td>20.12±2.44*</td>
<td>96.57±2.1*</td>
<td>12.35±2.67</td>
<td>0.71±0.76</td>
<td>5.29±0.67*</td>
</tr>
<tr>
<td>Group IV</td>
<td>15.32±1.19*</td>
<td>136.65±3.18a</td>
<td>19.54±3.13aa</td>
<td>0.93±0.22</td>
<td>8.13±0.32a</td>
</tr>
<tr>
<td>Group V</td>
<td>15.02±1.15a</td>
<td>101.35±2.71</td>
<td>14.33±1.93*</td>
<td>0.81±0.31</td>
<td>5.41±0.46*</td>
</tr>
</tbody>
</table>

Each value is SEM of 6 animals: *Comparison made between normal control to diabetic control and drug treated groups *p<0.05, **p<0.01 a, Comparison made between diabetic control to drug treated groups level of significance a=p<0.05 ; aa p<0.01

Table 4. Effect of ethanol extract of F. elephantum leaf and bark on the serum insulin, glucose, urea, creatinine and HbAlc level of normal diabetic induced adult albino rats

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Treatment Group</th>
<th>Level (nmol/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fasting</td>
<td>Control</td>
<td>128±2.56</td>
</tr>
<tr>
<td>Fasting</td>
<td>FEL</td>
<td>137±3.56</td>
</tr>
<tr>
<td>Fasting</td>
<td>Control</td>
<td>108±4.56</td>
</tr>
<tr>
<td>Fasting</td>
<td>FEL</td>
<td>117±5.67</td>
</tr>
</tbody>
</table>

Each value is SEM of 6 animals: *Comparison made between normal control to diabetic control and drug treated groups *p<0.05, **p<0.01 a, Comparison made between diabetic control to drug treated groups level of significance a=p<0.05 ; aa p<0.01

Table 6. Effect of ethanol extract of F. elephantum leaf and bark on the serum protein, albumin, globulin, SGOT, SGPT and ALP level of normal, diabetic induced and drug treated rats

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Protein (g/dl)</th>
<th>Albumin (g/dl)</th>
<th>Globulin (g/dl)</th>
<th>SGPT (u/l)</th>
<th>SGOT (u/l)</th>
<th>ALP (u/l)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group I</td>
<td>8.06±0.56</td>
<td>4.98±0.12</td>
<td>3.08±0.19</td>
<td>39.22±3.55</td>
<td>43.25±1.54</td>
<td>163.25±6.03</td>
</tr>
<tr>
<td>Group II</td>
<td>5.88±0.21</td>
<td>3.78±0.22</td>
<td>2.11±0.21</td>
<td>132.57±4.52*</td>
<td>129.33±2.52*</td>
<td>201.58±5.39*</td>
</tr>
<tr>
<td>Group III</td>
<td>7.97±0.33a</td>
<td>4.08±0.36</td>
<td>3.89±0.46a</td>
<td>33.77±3.56a</td>
<td>40.09±1.98a</td>
<td>166.59±4.14a</td>
</tr>
<tr>
<td>Group IV</td>
<td>6.21±0.41</td>
<td>3.91±0.63</td>
<td>2.30±0.61</td>
<td>36.53±2.78a</td>
<td>43.56±1.45a</td>
<td>171.52±5.69a</td>
</tr>
<tr>
<td>Group V</td>
<td>7.89±0.24a</td>
<td>4.11±0.51</td>
<td>3.78±0.33</td>
<td>31.22±1.7a</td>
<td>39.66±1.23a</td>
<td>161.33±4.98a</td>
</tr>
</tbody>
</table>

Each value is SEM of 6 animals: *Comparison made between normal control to diabetic control and drug treated groups *p<0.05, **p<0.01 a, Comparison made between diabetic control to drug treated groups level of significance a=p<0.05 ; aa p<0.01

Table 7: Effect of ethanol extract of F. elephantum leaf and bark on lipoperoxidation (LPO), glutathione (GSH), superoxide dismutase (SOD), catalase (CAT) glutathione peroxidase (GPx) and glutathione reductase (GR) in blood and liver tissue in normal, alloxan induced diabetic and drug treated rats

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Treatment Group</th>
<th>Units</th>
</tr>
</thead>
<tbody>
<tr>
<td>LPO</td>
<td>Serum</td>
<td>1.5±0.11a</td>
</tr>
<tr>
<td>SOD</td>
<td>Serum</td>
<td>498.21±3.12b</td>
</tr>
<tr>
<td>CAT</td>
<td>Serum</td>
<td>16.51±1.24a</td>
</tr>
<tr>
<td>GPx</td>
<td>Serum</td>
<td>16.51±1.24a</td>
</tr>
<tr>
<td>GR</td>
<td>Serum</td>
<td>16.51±1.24a</td>
</tr>
</tbody>
</table>

Alphabets (a, b, c) indicate the result of ANOVA test. The alloxan treated group was compared with normal. Whereas, drug treated group (F. elephantum leaf and bark) with the alloxan treated and normal group. Significant at* p<0.05, **p<0.01 Levels.
RESULTS

Plasma glucose level

Table 1 showed the effect ethanol of extract of *F. elephantum* leaf on the plasma glucose level in fasted, fed and alloxan induced diabetic rats. Blood glucose level to fasted control (normal) rats decreased from 89.56±2.12 at 0 min to 71.61±2.05 at 4h. Glucose loading to feed normal rats increased from 103.56±3.9 to 132.53±2.76 at 2h and returned to normal at 4h. Glucose loading to diabetic control rats increased from 196.34±5.78 to 243.2±3.21 at 2h. And returned to normal at 4h. *F. elephantum* leaf extract improved glucose tolerance significantly (p<0.05) with the dose of 400 mg/kg body wt, at 2h (Table 1). The effect of *F. elephantum* on glucose tolerance remained statistically significant (p<0.001) at 4h. with the dose 400mg/kg body wt.

Table 2 depicts the effect of ethanol extract of *F. elephantum* bark extract on the plasma glucose level in fasted, fed and alloxan induced diabetic rats. Blood glucose level to fasted normal rats decreased from 86.21±3.24 at 0 min to 68.52±2.45 at 4h. Glucose loading to feed normal rats increased from 112.21±3.54 to 137.33±2.56 at 2h and returned to normal at 4h. Glucose loading to diabetic control rats increased from 189.52±2.91 to 264.77±3.78 at 2h. and returned to normal at 4h. *F. elephantum* leaf extract improved glucose tolerance significantly (p<0.05) which is less than the glucose tolerance effect of *F. elephantum* leaf extract with the dose of 400mg/kg body wt. at 4h (Table 2).

Fasting blood glucose levels (FBG)

The fasting blood glucose levels of normal, diabetic and drug treated rats are summarized in Table 3. Alloxan produced marked hyperglycemia as evident from significant elevation in FBG level in alloxan control group as compared to normal control group. The administration of *F. elephantum* leaf and bark extract in alloxan induced diabetic rats at the dose of 400mg/kg body wt, produced significant fall in blood glucose levels when compared with the alloxan control group (Table 3). The FBG reducing effect of *F. elephantum* leaf extract at a dose of 400mg/kg was found to be comparable to that of the reference drug glibenclamide.

Effect on body weight

Diabetic rats (Group II) showed significant reduction in body weight during 14 days when compared with control animals (Group I) (Table 3). Alloxan caused body weight reduction, which was significantly reversed by *F. elephantum* extract treatment.

Blood parameter

The blood parameters such as insulin, glucose, urea, creatinine and glycosylated haemoglobin (HbA1c) are presented in Table 4. Insulin level was significantly (p<0.01) increased in group III and group IV treated with extract (20.12±2.44 and 15.32±1.91) compared to group II diabetic control diabetic control (08.29±0.81). The glucose, urea and creatinine levels of group treated with *F. elephantum* leaf and bark extracts showed a decrease in comparison with diabetic control. A significant (p<0.05) decrease in the level of glycosylated hemoglobin in group III and IV (5.29±0.67 and 8.13±0.32) compared with group II (10.65±0.91) was observed.

Effect of *F. elephantum* leaf and bark extracts on hypolipidemic profile

The effect of oral administration of *F. elephantum* leaf and bark extracts on the levels of TC, TG, HDL, LDL-C, VLDL & PL in the serum of normal and diabetic rats are shown in table 5. The diabetic rats (Group II) had elevated levels of serum TC, TG, LDL-C, VLDL, PL and decreased level of HDL as compared with normal control rats (Group I). Diabetic rats treated with *F. elephantum* leaf and bark extracts (group III & IV) and glibenclamide (Group V) reversed serum lipid profile to near normal levels.

Effect of *F. elephantum* leaf and bark extracts on serum biochemical parameters

The effect of oral administration of *F. elephantum* leaf and bark extracts on the levels of total protein, albumin, globulin and liver marker enzymes such as SGPT, SGOT and ALP in the serum of diabetic rats are shown in Table 6. The diabetic rats (Group II) had decreased levels of serum total protein, albumin, globulin and elevated level of liver marker enzymes such as SGPT, SGOT and ALP when compared with normal control rats (Group I). After treatment with *F. elephantum* leaf, bark extracts and glibenclamide, total protein, albumin, globulin and liver marker enzymes were brought back to near normal levels (Group III, IV & V).

Effect of *F. elephantum* leaf and bark extracts on in-vivo antioxidant parameters

Alloxan induced diabetic rats (Group II) were found to have increased LPO levels and decreased SOD, CAD, GPx and GSH levels in serum and liver as compared to control (Group I). Treatment with *F. elephantum* leaf and bark extracts and glibenclamide (group III, IV & V) produced significant (p<0.05) decrease in LPO levels and significant (p<0.01) increase in antioxidant enzyme levels.

DISCUSSION

Currently available drug regimens for management of diabetes mellitus have certain drawbacks and therefore, there is a need for safer and more effective antidiabetic drugs.

This study was undertaken to assess the antidiabetic effect of *F. elephantum* leaf and bark in alloxan induced diabetic rats. Alloxan causes diabetes through its ability to destroy the insulin producing β-cells of the pancreas. Diabetogenic effect of alloxan is due to excess production of reactive oxygen species (ROS) leading to cytotoxicity in pancreatic β-cells which reduces the synthesis and release of insulin, while affecting organs such as liver, kidney and haemopoietic system. Decreased antioxidant enzyme levels and enhanced lipid peroxidation have been well documented in alloxan induced diabetes.

Administration of alloxan increased the serum glucose levels when compared to normal animals and also induced persistent diabetes mellitus in rats. In the present investigation also indicates the efficacy of ethanol extract in decrease of blood glucose levels in normal and alloxan induced diabetic rats. Diabetic rats treated with the *F. elephantum* showed restoring of body weight as compared to the diabetic control, which may be due to its effect in controlling muscle wasting.

Glycosylated hemoglobin has been found to be increased over a long period of time in diabetes. During diabetes, the excess of glucose present in blood reacts with hemoglobin to form glycosylated hemoglobin. The rate of glycation is proportional to the concentration of blood glucose. In the present study, the diabetic rats had shown higher levels of HbA1C compared to those in normal rats. Treatment with *F. elephantum* and glibenclamide showed a significant decrease HbA1C levels in diabetic rats, that could be due to an improvement in glycemic status. The *F. elephantum* increased serum insulin level significantly (P<0.05), indicating that they might have insulin secretagogues activity, which in turn controls the hyperglycaemia state of type-2 diabetes. The reduction of blood urea and creatinine level...
indicates a normal function and nontoxic effect on the kidney. The concentration of lipids, such as cholestrol, TG, LDL-cholesterol, VLDL, PL were significantly (p<0.01) increased, where as HDL-cholesterol was decreased in the diabetic rats than normal rats. The impairment of insulin secretion results in enhanced metabolism of lipids from the adipose tissue to the plasma. A variety of derangements in metabolic and regulatory mechanisms, due to insulin deficiency, are responsible for the observed accumulation of lipids47. Further it has been reported that diabetic rats treated with insulin shows normalized lipid levels48. Diabetic rats treated with F. elephantum and glibenclamide also shows normalized lipid levels. Thus, the results indicate that F. elephantum also may possess insulin like action by virtue of the ability to lower the lipid levels. These results are similar to earlier reports observed with the other plant59.

A significant reduction in serum protein, albumin and globulin were observed in alloxan induced diabetic rats (Group II), when compared to control (Group I) and glibenclamide treated rats (Group V). On administration of ethanol extracts of F. elephantum leaf and bark to the diabetic rats, protein, albumin and globulin levels were found to be restored in normal. These results were in accordance with the effect of Wattakakla volubilis leaf in diabetic rats50. The animals treated with alloxan developed hepatic damage which was evident from the increase in the enzyme activities, Pretreatment with ethanol extracts of F. elephantum leaf and bark, glibenclamide resulted in a decrease of transaminase activities in alloxan treated rats. The serum AST and ALT levels increases as a result of metabolic changes in the liver, such as administration of toxin, cirtosis of the liver43, hepatitis and liver cancer including diabetes. Similarly in the present study, it was observed that the levels of SGPT and SGOT in alloxan induced diabetic rats were elevated. It may be due to leaking out of enzymes from the tissues and migrating into the circulation by the adverse effect of alloxan52. AST and ALT were used as markers to assess the extent of liver damage in streptozotocin induced diabetic rats53. In this study, the ethanol extracts of F. elephantum leaf and bark regulated the activity of SGPT, SGOT and ALP in liver of rats intoxicated with alloxan. The effect of glibenclamide on the recovery of hepatic enzyme activity in serum was very similar to that of the earlier study54.

Oxidative stress has been shown to play a role in the causation of diabetes mellitus. Antioxidants have been shown to have a role in the alleviation of diabetes mellitus55. In diabetes mellitus, oxygen free radicals (OFRS) are generated by stimulating H2O2 in-vitro, as well as in vivo, in pancreatic β-cells56. OFR- scavenging enzymes can respond to conditions of oxidative stress with a compensatory mechanism that increases the enzyme activity in diabetic rats57. In our study, concentrations of lipid peroxides are increased in serum and liver of diabetic rats, indicating an increase in the generation of free radicals. Increased lipid peroxidation in diabetes mellitus can be due to increased oxidative stress in the cell as a result of depletion of antioxidant scavenger systems. The present finding indicates significantly increased lipid peroxidation of rats exposed to alloxan and its attenuation by F. elephantum treatment. This suggests that the protective role of F. elephantum leaf and bark extract could be due to the antioxidative effect of flavonoids present in the leaf, which in turn act as strong superoxide radicals and singlet oxygen quenchers. Numerous studies have revealed lowered antioxidant and enhanced peroxidative status in diabetes mellitus58. In the current study, the SOD, CAT, Gpx, GR and GSH activities were significantly reduced in blood and liver tissues of diabetic rats. These observations emphasise the critical importance of maintaining the antioxidant potential of the pancreatic β-cell in order to ensure both its survival and insulin secretion capacity during times of increased oxidative stress. The decreased activities of SOD and CAT in both blood and liver tissues during diabetes mellitus may be due to the production of reactive oxygen free radical that can themselves reduce the activity of these enzymes. Reduced glutathione is a potent –free radical scavenger (GSH) within the islet of β-cell and is an important factor against the progressive destruction of the β-cell following partial pancreatectomy59. Depletion of GSH results in enhanced lipid peroxidation. Treatment of Feronia elephantum resulted in the elevation of the GSH level, which protect the cell membrane against oxidative damage by regulating the redox status of protein in the membrane60. SOD, CAT and GPx are enzymes that destroy the peroxides and play a significant role in providing antioxidant defenses to an organism. GPx and CAT are involved in the elimination of H2O2, which is then acted upon by GPx. The functions of all three enzymes are interconnected and a lowering of their activities results in the accumulation of lipid peroxides and increased oxidative stress in diabetic rats. Treatment of F. elephantum increased the activity of these enzymes and thus may help to avoid the free radicals generated during diabetes mellitus.

CONCLUSION

It is concluded that, the medicinal plants have been reported to possess antihyperglycemic activity, F.elephantum leaf and bark is gaining much importance in diabetic control as it has been used as a traditional medicine for diabetes; since the phytochemical analysis has shown the presence of potent phytochemicals like flavonoids, glycosides, phytosteroids, tannins and phenols. Several authors reported that flavonoids, steroids, terpenoids, phenolic acids are known to be bioactive antidiabetic principles61,62. Flavonoids are known to regenerate the damaged beta cells in the alloxan induced diabetic rats and acts as insulin secretagogues63, 64. Saponin reduces the uptake of certain nutrients including glucose and cholesterol at the gut through intraluminal physicochemical reaction. Hence, it has been reported to have hypercholesterolemic effect and thus may aid a lessening metabolic burden that would have been placed in the liver65. In the present study, the phytochemical analysis of ethanol extracts of F.elephantum leaf and bark clearly pointed out the presence of above said active principles. The preliminary investigation on the antidiabetic efficacy of ethanol extracts of F. elephantum leaf and bark will be significant to proceed further in this path for the identification and isolation of active principles responsible for antidiabetic activity.

ACKNOWLEDGEMENT

The authors are thankful to Dr. R. Sampathraj, Honorary Director, Samsun Clinical Research Laboratory Tripur for helping in carrying out the animal studies.

REFERENCES


44. Chalasani N, Aljadhey H, Kesterson J, Murray MD, Hall SD. Patients with elevated liver enzymes are not at higher risk for statin hepatotoxicity. Gastroenter 2004; 1287-1292


Source of support: Nil, Conflict of interest: None Declared