The current study was carried out to investigate the effect of oral administration of methanolic extract of whole plant of *A. bracteolata* on blood glucose levels and lipid profile in dexamethasone-induced diabetic rats.

**MATERIALS AND METHODS**

**Materials**

Dexamethasone was purchased from SVR Chemicals Ltd., (Hyderabad). Glucose kit and lipid profile kits were purchased from K. K. Diagnostics (Hyderabad). All other chemicals were obtained from the Dwarakamai Enterprises (Hyderabad).

**Animals**

Adult Wistar albino rats (150-200 g) were used for the present study. They were kept in polypropylene cages at 25±2°C, with relative humidity 45-55% under 12 hrs light and dark cycles. All the animals were acclimatized to the laboratory conditions for a week before use. They were fed with standard animal feed and water ad libitum. All the pharmacological experimental protocols were approved by the Institutional Animal Ethics Committee (IAEC) (Reg. No. 1175/PO/OR/E/08/CPCSEA), Gokaraju Rangaraju College of Pharmacy.

**Preparation of extract**

The plant *A. bracteolata* was collected in January 2016 from the Nallamala Forest region, Velugodu, Kurnool district. The procured plant materials were authenticated by a botanist. The whole plant was washed, dried at room temperature in the dark and then finely grind to a powder. Then, the powder was extracted with the methanol in the ratio of 1:6 by simple distillation technique. The solvent was completely removed under reducing pressure, and a semisolid mass (yield: 9.4%, w/w) was obtained and stored for further study.

**Preliminary phytochemical analysis**

The preliminary phytochemical studies were performed for testing different chemical groups present in MEAB. Phytochemical screening
Acute toxicity study
The acute oral toxicity [12] study was carried out as per the guidelines set by the Organization for Economic Co-operation and Development, the study was approved by the IAEC. No mortality and no signs of toxicity were found even after administration of a limit dose of 2000 mg/kg body weight of extract; hence, 1/10th of the dose was taken as effective dose. Two doses, 200 and 400 mg/kg were selected for the present study to evaluate antihyperglycemic and antihyperlipidemic activity.

Dexamethasone-induced diabetic rat model
Diabetes was induced in healthy Wistar albino rats using dexamethasone at a dose of 10 mg/kg, body weight subcutaneous (s.c) for 10 days. Treatment was continued for 10 consecutive days with dexamethasone. The animals were randomly divided into five groups of six animals in each group. Group - I received saline (normal control), Group - II received dexamethasone 10 mg/kg, s.c (diabetic control), Group - III received dexamethasone 10 mg/kg, s.c and MEAB (200 mg/kg body weight), Group - IV received dexamethasone 10 mg/kg, s.c and MEAB (400 mg/kg body weight), and Group - V received dexamethasone 10 mg/kg, s.c and glibenclamide (0.5 mg/kg). On the 11th day, blood was withdrawn from the animals and subjected for the analysis of blood glucose and all biochemical parameters such as total cholesterol (TC), TG, LDL, and VLDL and high-density lipoprotein (HDL) levels. The levels of the biochemical parameters in the treated groups were compared with that of diabetic control group [13].

Statistical analysis
All results were expressed as the mean±standard error mean. The results were analyzed for statistical significance by one-way ANOVA followed by Dunnett’s test using GraphPad Prism version 5.0 (GraphPad Software, USA).

RESULTS

Phytochemical screening
The preliminary phytochemical screening of the A. bracteolata showed the presence of phenolic compounds, flavonoids, triterpenoids, alkaloids, steroids, cardiac glycosides, and saponins [11].

Dexamethasone-induced diabetic rat model
The parameters such as body weight, blood glucose level, and lipid profile parameters of normal control group; diabetic control group, standard group (glibenclamide 0.5 mg/kg), and MEAB were summarized in Tables 1-3.

Effect of extract on body weight
The body weight of the normal and treated groups significantly differ from diabetic control on the 11th day shown in Table 1. The treated groups of animal body weight maintained throughout the experiment compared to diabetic control.

Effect of extract on blood glucose level
Blood glucose level was found to be increased in dexamethasone-induced diabetic rats significantly when compared to control. The MEAB and standard drug treated groups had shown a significant decrease in blood glucose level when compared to diabetic control group. The results were tabulated in the Table 2, respectively.

Effect of extract on blood lipid profile
The diabetes-induced hyperlipidemia was reversed significantly when compared to diabetic control which was depicted in the Table 3. A significant percentage reduction of TC level, LDL, TG, and VLDL in extract treated group was significant when compared to diabetic group. However, HDL levels increased with treatment of extract and standard group, respectively.

Table 1: Effect of MEAB on body weight by dexamethasone-induced diabetic rats

<table>
<thead>
<tr>
<th>Group</th>
<th>Treatment</th>
<th>Body weight (g) mean±SEM</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0th day</td>
<td>11th day</td>
</tr>
<tr>
<td>I</td>
<td>Normal control</td>
<td>166.5±2.125</td>
</tr>
<tr>
<td>II</td>
<td>Diabetic control</td>
<td>165.5±2.109</td>
</tr>
<tr>
<td>III</td>
<td>MEAB200 mg/kg</td>
<td>168.6±1.926</td>
</tr>
<tr>
<td>IV</td>
<td>MEAB400 mg/kg</td>
<td>169.8±1.661</td>
</tr>
<tr>
<td>V</td>
<td>Glibenclamide 0.5 mg/kg</td>
<td>167.1±1.807</td>
</tr>
</tbody>
</table>

Values are mean±SEM, n=6 when compared with control *p<0.05, **p<0.01. SEM: Standard error mean, MEAB: Methanolic extract of Aristolochia bracteolata

Table 2: Antihyperglycemic activity of MEAB on dexamethasone-induced diabetic rats

<table>
<thead>
<tr>
<th>Group</th>
<th>Treatment</th>
<th>Blood glucose levels (mg/dL) mean±SEM</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0th day</td>
<td>11th day</td>
</tr>
<tr>
<td>I</td>
<td>Normal control</td>
<td>84.5±2.446</td>
</tr>
<tr>
<td>II</td>
<td>Diabetic control</td>
<td>84.6±2.859</td>
</tr>
<tr>
<td>III</td>
<td>MEAB200 mg/kg</td>
<td>87.6±2.548</td>
</tr>
<tr>
<td>IV</td>
<td>MEAB400 mg/kg</td>
<td>87.6±2.304</td>
</tr>
<tr>
<td>V</td>
<td>Glibenclamide (0.5 mg/kg)</td>
<td>86.3±2.639</td>
</tr>
</tbody>
</table>

Values are mean±SEM, n=6 when compared with control *p<0.05, **p<0.01. SEM: Standard error mean, MEAB: Methanolic extract of Aristolochia bracteolata

DISCUSSION
Dexamethasone is a potent glucocorticoid. Glucocorticoids are widely used therapeutic tools, particularly in treatment for anti-inflammatory and immunomodulatory purposes. Side effects of glucocorticoid treatment include steroid diabetes. Glucocorticoid-induced hyperglycemia is partially due to increased hepatic glucose production and insulin resistance of peripheral tissues. Moreover, glucocorticoids are known to inhibit insulin secretion.

Glibenclamide has been used for many years to treat diabetes to stimulate insulin secretion from pancreatic β-cells. In general diabetic rats show lower body weight, high blood glucose, and lipid levels as compared to normal rats. The present data indicated that MEAB at 200 and 400 mg/kg significantly reduced the elevated fasting blood glucose levels and increased body weight in a dose-dependent manner in diabetic animals. The possible mechanism by which MEAB reduced hypoglycemic action might be due to the presence of phenolic and flavonoids. These phytochemical constituents might be increasing either the pancreatic action might be due to the presence of phenolic compounds, flavonoids, triterpenoids, alkaloids, steroids, cardiac glycosides, and saponins.

Lipids play a vital role in the pathogenesis of diabetes mellitus. The levels of serum lipids are usually elevated in diabetes cases, and such an elevation represents the risk factor of coronary heart disease. High levels of TC and more importantly LDL-cholesterol in blood are major coronary risk factor [15]. The abnormal high concentration of serum lipids in the diabetic subjects is due, mainly to the increase in the mobilization of free fatty acids from the peripheral fat depots. Acute insulin deficiency initially causes an increase in free fatty acid mobilization from adipose tissue. The most common lipid abnormalities in diabetes are hypertriglyceridemia and hypercholesterolemia.
The MEAB at 200 and 400 mg/kg significantly reduced the elevated levels of TC, TGs, LDL, and VLDL and also increases the HDL levels in a dose-dependent manner in diabetic animals. The presence of phytochemical constituents such as phenolic, flavonoids, and triterpenoids may be responsible for the activity. These phytochemicals might have decreased cholesterol genesis and blood glucose levels [16].

CONCLUSION

The results of the present investigation are quite encouraging on oral administration of MEAB at a dose of 200 and 400 mg/kg body weight for 11 days in dexamethasone-induced diabetic rats. There was a significant decrease in elevated blood glucose levels when compared with diabetic control group. MEAB has also lowered the TC, TGs, LDL, and VLDL levels and increased the levels of HDL when compared to that of the diabetic control group in a dose-dependent manner. The present study revealed that MEAB possesses significant antihyperglycemic and antihyperlipidemic activity. However, further studies are required to confirm the exact mechanism of action and to isolate the phytochemical constituents responsible for these activities.

ACKNOWLEDGMENT

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REFERENCES


Table 3: Antihyperlipidemic activity of MEAB on dexamethasone-induced diabetic rats

<table>
<thead>
<tr>
<th>Group</th>
<th>Treatment</th>
<th>Lipid profile (mg/dL)</th>
<th>TC</th>
<th>TG</th>
<th>HDL</th>
<th>LDL</th>
<th>VLDL</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Normal control</td>
<td>92.5±1.394</td>
<td>74.6±1.327</td>
<td>37.50±1.945</td>
<td>40.16±2.194</td>
<td>14.83±0.265</td>
<td></td>
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<tr>
<td>II</td>
<td>Diabetic control</td>
<td>150.16±1.621</td>
<td>160.33±1.358</td>
<td>22.83±0.909</td>
<td>95.26±1.801</td>
<td>32.06±0.271</td>
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</tr>
<tr>
<td>III</td>
<td>MEAB (200 mg/kg)</td>
<td>122.16±0.792</td>
<td>101.83±0.833</td>
<td>31.83±1.621</td>
<td>69.96±1.456</td>
<td>20.36±0.160</td>
<td></td>
</tr>
<tr>
<td>IV</td>
<td>MEAB (400 mg/kg)</td>
<td>103.33±1.49*</td>
<td>86.33±1.498*</td>
<td>36.1±1.125*</td>
<td>50.06±1.757*</td>
<td>17.26±0.299*</td>
<td></td>
</tr>
<tr>
<td>V</td>
<td>Glibenclamide (0.5 mg/kg)</td>
<td>122.16±0.792</td>
<td>86.33±1.498</td>
<td>36.1±1.125</td>
<td>50.06±1.757</td>
<td>17.26±0.293</td>
<td></td>
</tr>
</tbody>
</table>

Values are mean±SEM, n=6 when compared with control *p<0.05, **p<0.01. SEM: Standard error mean, MEAB: Methanolic extract of Aristolochia bracteolute, TC: Total cholesterol, TG: Triglyceride, LDL: Low-density lipoprotein, VLDL: Very low-density lipoprotein, HDL: High-density lipoprotein.