ABSTRACT

The ethanol extract of Cynoglossum zeylanicum whole plant (ECZW) (Family: Boraginaceae) was investigated for its antioxidant, antihyperlipidaemic and antidiabetic effect in Wistar Albino rats. Diabetes was induced in Albino rats by administration of alloxan monohydrate (150mg/kg, i.p.). The ethanol extracts of C. zeylanicum at a dose of 150 and 300mg/kg of body weight were administered at single dose per day to diabetes induced rats for a period of 14 days. The effect of ethanol extract of C. zeylanicum whole plant (ECZW) extract on blood glucose, plasma insulin, creatinine, glycosylated haemoglobin, urea serum lipid profile [total cholesterol (TR), triglycerides (TG), low density lipoprotein – cholesterol (LDL-C), very low density lipoprotein – cholesterol (VLDL-C), high density lipoprotein – cholesterol (HDL-C) and phospholipid (PL) serum protein, albumin, globulin, serum enzymes [serum glutamate pyruvate transaminases] (SGPT), and serum glutamate oxaloacetate transaminases (SGOT), and alkaline phosphatase (ALP), lipoprotein peroxidase (LPO) antioxidant enzymes (catalase (CAT), superoxide dismutase (SOD), reduced glutathione (GSH) and glutathione peroxidase (Gpx) were measured in the diabetic rats. The ethanol extract of Cynoglossum zeylanicum whole plant (ECZW) elicited significant reductions of blood glucose (p<0.05), lipid parameters except HDL-C, serum enzymes and significantly increased HDL-C and antioxidant enzymes. The extracts also caused significant increase in plasma insulin (p<0.05) in the diabetic rats. From the above results, it is concluded that ethanol extract of Cynoglossum zeylanicum possesses significant antidiabetic, antihyperlipidaemic and antioxidant effects in alloxan induced diabetic rats.

Keywords: Antioxidant, Antihyperlipidaemic, Antidiabetic, C. zeylanicum, Alloxan.

INTRODUCTION

Diabetes mellitus is a syndrome, initially characterized by loss of glucose homeostasis resulting from defects in insulin secretion, insulin action both resulting impaired metabolism of glucose and other energy-yielding fuels such as lipids and proteins1. Diabetes is a chronic disorder of carbohydrate, fat and protein metabolism characterized by elevation of both fasting and postprandial blood sugar levels. The peroxidation of cellular membrane lipids can lead to cell necrosis and is purportedly associated with various chronic disorders including carcinogenesis and hyperglycaemia2. This pathological condition occurs as a result of the loss of insulin producing pancreatic beta-cells by an environmentally triggered autoimmune reaction. Currently available oral antidiabetic agents have a number of serious adverse effects. Treatment with sulphonylureas and biguanides are also associated with side effects3. Hence, search for a new drug with low cost, more potential, without adverse effects is being pursued in several laboratories all around the world. Since time immemorial, patients with non-insulin requiring diabetes have been created orally in folk medicine with a variety of plant extracts. Plant drugs and herbal formulations are frequently considered to be less toxic and free from side effects than synthetic one4. Recently, some medicinal plants have been reported to be useful in diabetes worldwide and have been used empirically in antidiabetic and antihyperlipidaemic remedies. The antihyperglycemic effect of these plants are of their ability to restore the function of pancreatic beta-cells and increasing insulin output or inhibit the intestinal absorption of glucose or to be the facilitation of metabolites in insulin dependent processes5.

More than 400 plant species having hypoglycemic activity have been available in literature, however, searching for new antidiabetic drugs from natural plants is still attractive because they contain substances which demonstrate alternate and safe effects on diabetes mellitus.

Cynoglossum zeylanicum (Vahl ex Hornem) Thurnb ex Lehn belongs to Boraginaceae family. It is commonly known as "Jathakkal". Decoction prepared from the whole plant is used to arrest vomiting by Badaga community in Nilgiri Biosphere Reserve, Tamil Nadu. However, inspite of traditional use, pharmacology of its whole plant has not yet been explored scientifically. So far no reports are available in antidiabetic activity of this plant. The present investigation was carried out to evaluate the antidiabetic, antihyperlipidaemic and antioxidant activity of the ethanol extracts of whole plant of Cynoglossum zeylanicum against alloxan induced diabetic rats.

MATERIALS AND METHODS

Plant Material

The whole plant of Cynoglossum zeylanicum were freshly collected from the well grown healthy plants inhabiting the natural forests of Kothagiri, Nilgiri Biosphere Reserve, Western Ghats, Tamil Nadu. The plant were identified and authenticated in Botanical Survey of India, Kothagiri, Nilgiri Biosphere Reserve, Western Ghats, Tamil Nadu. The voucher specimen was deposited in Ethnopharmacology Unit, Research Department of Botany, V.O.Chidambaram College, Tuticorin, Tamil Nadu.

Preparation of plant extract for phytochemical screening and antidiabetic studies

The C. zeylanicum whole plant (ECZW) was shade dried at room temperature and the dried leaves were powdered in a Wiley mill. Hundred grams of powdered C. zeylanicum whole plant (ECZW) was packed in a Soxhlet apparatus and extracted with ethanol. The extract was subjected to qualitative test for the identification of various phytochemical constituents as per the standard procedures5.

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. 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 intubations 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 observed in one animal, then the same dose was repeated again to confirm the 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 Experimental Diabetes

Rats were induced diabetes by the administration of simple intraperitoneal dose of alloxan monohydrate (150 mg/kg). 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.

Group I: Normal untreated rats
Group II: Diabetic control rats
Group III: Diabetic rats given ethanol extract of C. zeylanicum whole plant (100mg/kg body weight)
Group IV: Diabetic rats given ethanol extract of C. zeylanicum whole plant (150mg/kg body weight)
Group V: Diabetic rats given standard drug glibenclamide (600µg/kg body weight).

Biochemical analysis

The animals were sacrificed at the end of experimental period of 30 days by decapitation. Blood was collected, sera separated by centrifugation at 3000g for 10 minutes. Serum glucose was measured by the O-toluidine method. Administration of whole plant extract of C. zeylanicum induced diabetic rats (Group II) when compared with normal rats (Group I). Administration of whole plant extract of C. zeylanicum (Group III & IV) and glibenclamide (Group V) tends to bring the parameters significantly (p<0.05, p<0.01) towards the normal. It has been reported that using medicinal plant extract to treat alloxan induced diabetic rats result in activation of β-cells and insulinoenic effects. C. zeylanicum (ECZW) may also have brought about hypoglycemiac action through stimulation of surviving β-cells islets of langerhans to release more insulin. This was clearly evidenced by the increased levels of plasma insulin in diabetic rats treated with C. zeylanicum (ECZW). A number of other plants have also been observed to exert hypoglycemic activity through insulin release stimulatory effects.

### Table 1: Effect of ethanol extract of *Cynoglossum zeylanicum* whole plant on blood glucose level of normal, diabetic induced, and drug treated rats at different time intervals.

<table>
<thead>
<tr>
<th>Groups</th>
<th>Blood glucose level in mgs/dl</th>
<th>0 day</th>
<th>1 week</th>
<th>2 week</th>
<th>3 week</th>
<th>4 week</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group I</td>
<td>69.3±2.17</td>
<td>78.2±0.67</td>
<td>88.17±1.24</td>
<td>78.2±1.94</td>
<td>73.17±2.16</td>
<td></td>
</tr>
<tr>
<td>Group II</td>
<td>204.3±2.27***</td>
<td>213.6±1.7***</td>
<td>236.36±3.84***</td>
<td>209.17±5.31***</td>
<td>216.16±5.32***</td>
<td></td>
</tr>
<tr>
<td>Group III</td>
<td>216.7±6.17***</td>
<td>209.17±5.54***</td>
<td>184.27±5.54ns</td>
<td>162.16±4.84**</td>
<td>142.23±4.94**</td>
<td></td>
</tr>
<tr>
<td>Group IV</td>
<td>209.16±2.62***</td>
<td>184.21±5.23***</td>
<td>148.19±3.92</td>
<td>121.32±4.08</td>
<td>104.3±3.98**</td>
<td></td>
</tr>
<tr>
<td>Group V</td>
<td>219.32±6.34***</td>
<td>131.16±6.21**</td>
<td>124.16±4.08**</td>
<td>99.32±1.61</td>
<td>91.68±1.36**</td>
<td></td>
</tr>
</tbody>
</table>

Each Value is SEM of 6 animals (*p < 0.05; **p < 0.01 ***p<0.001 Significance between normal control vs diabetic induced control , drug treated group; *p < 0.05; **p < 0.01 Significance between diabetic induced control control vs drug treated group ns: not significant).

Table 2 shows the levels of blood glucose, plasma insulin, urea, creatinine and glycosylated haemoglobin of normal, diabetic control and drug treated rats. There was a significant (p<0.001) in alloxan induced diabetic rats (Group II) when compared with normal rats (Group I). Administration of whole plant extract of C. zeylanicum (Group III & IV) and glibenclamide (Group V) tends to bring the parameters significantly (p<0.05, p<0.01) towards the normal. It has been reported that using medicinal plant extract to treat alloxan induced diabetic rats result in activation of β-cells and insulinoenic effects. C. zeylanicum (ECZW) may also have brought about hypoglycemiac action through stimulation of surviving β-cells islets of langerhans to release more insulin. This was clearly evidenced by the increased levels of plasma insulin in diabetic rats treated with C. zeylanicum (ECZW). A number of other plants have also been observed to exert hypoglycemic activity through insulin release stimulatory effects.
A significant (p<0.01, p<0.05) elevation in urea and creatinine were observed in alloxan induced diabetic rats (Group II), when compared to control rats. The C. zeylanicum (ECZW) were administrated orally (Group III & IV) to rats for thirty days, reversed the urea and creatinine level to near normal.

The level of total protein, albumin, globulin and liver marker enzymes such as SGPT, SGOT and ALP in the serum of diabetic rats are presented in the Table 3. 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 extract C. zeylanicum (ECZW) whole plant 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 Eugenia floccosa leaf in diabetic rats. The increased level of serum protein, albumin and globulin in alloxan induced diabetic rats are presumed and glucosoneogenesis during diabetes. The animals treated with alloxan developed hepatic damage which was evident from the increase in the enzyme activities. Pretreatment with ethanol extract of C. zeylanicum whole plant (ECZW) and glibenclamide resulted in a decrease of transaminase activities in alloxan treated rats. The SGPT and SGOT levels increases as a result of metabolic changes in the liver, such as administration of toxin, cirrhosis of the liver, hepatitis and liver cancer including diabetes.

The elevated levels of SGPT and SGOT in alloxan induced diabetic rats may be due to leaking out of enzymes from the tissues and migrating into the circulation by the adverse effect of alloxan. Elevation of serum biomarker enzymes such as SGPT, SGOT and ALP was observed in diabetic rats indicating impaired liver function, which is obviously due to hepatocellular necrosis. In this study, the ethanol extract of C. zeylanicum whole plant (ECZW) 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 study.

### Table 2: Effect of ethanol extract of Cynoglossum zeylanicum whole plant on the Insulin, blood glucose, urea, creatinine and HbA$_1$c level of normal, diabetic induced and drugs treated rats.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Insulin (Miu/ml)</th>
<th>Glucose (mg/dl)</th>
<th>Urea (mg/dl)</th>
<th>Creatinine (mg/dl)</th>
<th>HbA$_1$c (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group I</td>
<td>18.56±0.72</td>
<td>82.16±1.16</td>
<td>16.32±0.74</td>
<td>0.73±0.17</td>
<td>3.94±0.11</td>
</tr>
<tr>
<td>Group II</td>
<td>8.91±0.26**</td>
<td>202.14±9.16***</td>
<td>36.16±1.19**</td>
<td>1.84±0.84*</td>
<td>12.22±0.34**</td>
</tr>
<tr>
<td>Group III</td>
<td>11.56±0.91*</td>
<td>131.23±6.71**</td>
<td>31.68±1.24*</td>
<td>1.68±0.17ns</td>
<td>8.21±0.26*</td>
</tr>
<tr>
<td>Group IV</td>
<td>16.31±0.54*</td>
<td>118.17±5.27*</td>
<td>33.94±1.84*</td>
<td>1.74±0.24*</td>
<td>10.54±0.17*</td>
</tr>
<tr>
<td>Group V</td>
<td>19.26±1.64**</td>
<td>81.16±5.111</td>
<td>17.33±0.91*</td>
<td>0.70±0.21**</td>
<td>5.27±0.84**</td>
</tr>
</tbody>
</table>

Each Value is SEM of 6 animals (* p<0.05 ; ** p<0.01 *** p<0.001 Significance between normal control vs diabetic induced control, drug treated group ; p<0.05 ; ns p>0.01 Significance between diabetic induced control vs drug treated group ns: Not significant).

### Table 3: Effect of ethanol extract of Cynoglossum zeylanicum whole plant on the protein, albumin, globulin, SGPT, SGOT and ALP level of normal, diabetic induced, and drug treated rats.

<table>
<thead>
<tr>
<th>Groups</th>
<th>Parameters 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>8.64±0.84</td>
<td>4.72±0.11</td>
<td>3.92±0.15</td>
<td>21.22±3.54</td>
<td>19.33±1.74</td>
<td>154.1±1.66</td>
</tr>
<tr>
<td>Group II</td>
<td>6.04±0.13*</td>
<td>3.74±0.10</td>
<td>2.30±0.17*</td>
<td>169.24±5.39***</td>
<td>183.74±2.84***</td>
<td>208.6±5.23***</td>
</tr>
<tr>
<td>Group III</td>
<td>6.84±0.21*</td>
<td>3.94±0.11</td>
<td>2.90±0.21*</td>
<td>119.86±3.16**</td>
<td>161.17±1.57**</td>
<td>165.2±5.34**</td>
</tr>
<tr>
<td>Group IV</td>
<td>7.27±0.17</td>
<td>4.08±0.13</td>
<td>3.19±0.14</td>
<td>57.91±2.64**</td>
<td>43.87±2.17**</td>
<td>186.3±2.81**</td>
</tr>
<tr>
<td>Group V</td>
<td>8.49±0.36</td>
<td>4.58±0.21</td>
<td>3.91±0.16*</td>
<td>24.13±3.14</td>
<td>20.18±1.94</td>
<td>142.1±1.84</td>
</tr>
</tbody>
</table>

Each Value is SEM of 6 animals ( * p<0.05 ; ** p<0.01 *** p<0.001 Significance between normal control vs diabetic induced control, drug treated group ; p<0.05 ; ns p<0.01 Significance between diabetic induced control vs drug treated group).

Table 4 shows the levels of TG, TC, LDL-C, VLDL-C, HDL-C and PL in the serum of diabetic rats showed significantly (p=0.01; p<0.001) increased serum lipid profiles except HDL-C when compared with normal rats. The ethanol extract of C. zeylanicum whole plant (ECZW) treated rats showed a significant (p<0.05) decrease in the content of lipid profiles when compared with diabetic induced rats. Similarly HDL-C level decreased in alloxan induced diabetic rats when compared with normal rats. Administration of ethanol extract of C. zeylanicum whole plant (ECZW) and glibenclamide to the diabetic rats, HDL-C level was found to be restored to normal. The level of serum lipid profiles are usually raised in diabetic rats in the present study and such elevation represents a risk factor for coronary heart diseases.

### Table 4: Effect of ethanol extract of Cynoglossum zeylanicum whole plant on the TC, TG, LDL-C and PL in the plasma of normal, diabetic induced, and drug treated rats

<table>
<thead>
<tr>
<th>Groups</th>
<th>Parameter TC (mg/dl)</th>
<th>TG (mg/dl)</th>
<th>HDL (mg/dl)</th>
<th>LDL (mg/dl)</th>
<th>VLDL (mg/dl)</th>
<th>PL (mg/dl)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group I</td>
<td>12.67±3.84</td>
<td>76.91±2.14</td>
<td>54.16±2.94</td>
<td>56.73±1.98</td>
<td>15.38±0.76</td>
<td>180.3±3.56</td>
</tr>
<tr>
<td>Group II</td>
<td>19.26±4.93**</td>
<td>134.6±4.16***</td>
<td>26.38±1.94**</td>
<td>138.86±3.72**</td>
<td>26.92±2.11*</td>
<td>239.0±4.37**</td>
</tr>
<tr>
<td>Group III</td>
<td>15.38±4.17*</td>
<td>86.27±2.11**</td>
<td>45.18±2.04**</td>
<td>90.56±2.43**</td>
<td>17.54±0.94ns</td>
<td>204.4±1.88**</td>
</tr>
<tr>
<td>Group IV</td>
<td>13.26±1.84</td>
<td>81.33±1.93</td>
<td>48.91±1.94*</td>
<td>66.59±2.74*</td>
<td>16.66±0.32*</td>
<td>185.6±3.55*</td>
</tr>
<tr>
<td>Group V</td>
<td>11.85±2.21**</td>
<td>75.24±2.29**</td>
<td>51.63±1.86**</td>
<td>51.92±2.12**</td>
<td>15.04±0.58*</td>
<td>173.5±4.27**</td>
</tr>
</tbody>
</table>

Each Value is SEM of 6 animals ( * p<0.05 ; ** p<0.01 *** p<0.001 Significance between normal control vs diabetic induced control, drug treated group ; p<0.05 ; ns p<0.01 Significance between diabetic induced control vs drug treated group).

During diabetes, enhanced activity of the enzyme, increased lipolysis and release more fatty acids into the circulation. The increased fatty acid concentration also increases the β-oxidation of fatty acids, producing more acetyl Co-A and cholesterol during diabetes. In normal condition, insulin increases receptor-mediator removal of LDL-cholesterol and decreased activity of insulin.
during diabetes causes hypercholesterolemia. Hypercholesterolemia and hypertriglyceridemia have been reported to occur in diabetic rats\(^1\). The increased concentration of free fatty acid may be due to lipid break-down and this may cause increased generation of NADPH-dependent microsomal lipid peroxidation. Phospholipids were increased in alloxan diabetic rats. Phospholipids are present in cell membrane and make up vast majority of the surface lipoprotein forming a lipid bilayer that acts as an interface with both polar plasma environment and non-polar lipoprotein of lipoprotein core\(^2\). Increased phospholipids levels in tissues were reported by Venkateswaran\(^3\), Pari and Sathheesh\(^4\) in streptozotocin diabetic rats. Administration of ethanol extract of \textit{Senna auriculata} leaf and glibenclamide decreased the levels of phospholipids.

The activities of LPO, SOD, CAT, GPX and GSH in the alloxan induced diabetic rats were presented in Table 5. In the present study, the alloxan induced diabetic rats had shown increased activities of LPO. The levels of SOD, CAT, GPX and GSH in the serum were significantly (\(p<0.01; p<0.001\)) reduced in alloxan induced rats. Treatment with \textit{C. zeylanicum} whole plant (ECZW) extract exhibited reversal of all these parameters to near normal levels. Hyperglycemia results in free radical formation through various biochemical reactions. Free radicals may also be formed via the auto-oxidation of unsaturated lipids in plasma and membrane lipids. The free radical produced may react with poly unsaturated fatty acids in cell membranes leading to lipid peroxidation. Lipid peroxidation will in turn results in elevated production of free radicals\(^5\). Lipid peroxide mediated tissue damage has been observed in the development of both type I and type II diabetes. It has been observed that insulin secretion is closely associated with lipoxygenase-derived peroxydes\(^6\).

In the present study, LPO was significantly lower in the \textit{C. zeylanicum} whole plant (ECZW) extract treated groups compared to the diabetic control group. The above results suggest that the ethanol extract of \textit{C. zeylanicum} may exert antioxidant activities and protect the tissues from lipid peroxidation.

**Table 5: Effect of ethanol extract of \textit{Cynoglossum zeylanicum} whole plant on serum LPO, GPX, GSH, SOD and CAT in the normal, diabetic and drug treated rats.**

<table>
<thead>
<tr>
<th>Groups</th>
<th>Parameters</th>
<th>LPO (nanomol/mg protein)</th>
<th>GPX (u/mg protein)</th>
<th>GSH (u/mg protein)</th>
<th>SOD (u/mg protein)</th>
<th>CAT (u/mg protein)</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>I</td>
<td>1.84±0.027</td>
<td>614.23±17.36</td>
<td>32.94±1.94</td>
<td>468.13±11.32</td>
<td>73.22±1.84</td>
</tr>
<tr>
<td>II</td>
<td>I</td>
<td>5.61±0.031**</td>
<td>324.56±16.24***</td>
<td>15.14±0.86**</td>
<td>234.59±16.32***</td>
<td>41.91±1.23***</td>
</tr>
<tr>
<td>III</td>
<td>I</td>
<td>3.86±0.034**</td>
<td>389.54±15.29**</td>
<td>19.66±1.04*</td>
<td>263.1±15.27**</td>
<td>53.74±1.81*</td>
</tr>
<tr>
<td>IV</td>
<td>I</td>
<td>3.28±0.05***</td>
<td>421.59±15.29**</td>
<td>23.76±1.84*</td>
<td>314.19±13.92**</td>
<td>60.06±1.24*</td>
</tr>
<tr>
<td>V</td>
<td>I</td>
<td>2.04±0.024</td>
<td>594.68±18.21</td>
<td>34.91±1.59**</td>
<td>447.27±11.46*</td>
<td>88.14±1.94**</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Each Value is SEM of 6 animals (* (p&lt;0.05); ** (p&lt;0.01); *** (p&lt;0.001) Significance between normal control vs diabetic induced control, drug treated group; (p&lt;0.05)<strong>; (p&lt;0.01)</strong>; (p&lt;0.001)** Significance between diabetic induced control vs drug treated group as; Not significant).</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Numerous studies have revealed lowered antioxidant and enhanced peroxidative status in diabetes mellitus\(^6\). In the present study, the SOD, CAT, GSH and GPX activities were significantly reduced in the serum of diabetic rats. These observations emphasize the critical importance of maintaining the antioxidant potential of the pancreatic \(\beta\)-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 serum 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 \(\beta\) cell and is an important factor against the progressive destruction of the \(\beta\) cell following partial pancreatectomy\(^6\). Depletion of GSH results in enhanced lipid peroxidation. This can cause increased GSH consumption and can be correlated to the increase in the level of oxidized glutathione (GSSG). Administration of \textit{C. zeylanicum} resulted in the elevation of GSH levels, which protect the cell membrane against oxidative damage by regulating the redox status of protein in the membrane\(^7\). 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 \(H_2O_2\) SOD acts to dismutate superoxide radical to \(H_2O\) 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\(^8\). Administration of \textit{C. zeylanicum} extract increased its activity of these enzymes and thus may help to avoid the free radicals generated during diabetes mellitus. These results reveal the protective role of plant extract in decreasing lipid peroxidation and by normalizing antioxidant system.

In the present study, the administration of \textit{Cynoglossum zeylanicum} whole plant (ECZW) extracts to alloxan induced hyperglycemic rats demonstrated prominent reduction in blood sugar level, normalization of serum biochemical profile including lipid content, as compared to alloxan control rats. Also ECZW treatment resulted in significant modulation of lipid peroxidation, endogenous non enzymatic and enzymatic antioxidant and detoxification status. The phytochemical analysis has shown the presence of potent phytochemicals like flavonoids, terpenoids, glycosides, steroids, saponin and phenols. Several authors reported that flavonoids, steroids/terpenoids, phenolic acids are known to be bioactive antidiabetic principles\(^9\),\(^10\). Flavonoids are known to regenerate the damaged beta cells in the alloxan induced diabetic rats and acts as insulin secretagogues\(^11\),\(^12\). In the present study, the phytochemical analysis of ethanol extract of \textit{C. zeylanicum} whole plant clearly prints out the presence of above said active principles. The preliminary investigation on the antihyperglycemic, antihyperlipidemic and antioxidant efficacy of ethanol extract of \textit{Cynoglossum zeylanicum} whole plant (ECZW) will be significant to proceed further in this path for the isolation of active principles responsible for the antidiabetic activity.

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