3. RESULTS

*Euphorbia neriifolia* Ethanolic extract (ENEE) were determined above 4000mg/kg and one tenth of LD_{50} dose (400 mg/kg) was selected as higher dose to treat antidiabetic and antihyperlipidemic activity. One twentieth of LD_{50} dose (200 mg/kg) was selected as lower dose to evaluate antidiabetic and antihyperlipidemic activity in animal models.

3.1 Effect of *Euphorbia neriifolia* Ethanolic extract (ENEE) in sub acute toxicity study

3.1.1 Effect of *Euphorbia neriifolia* Ethanolic extract (ENEE) on relative organ weight of animals.

<table>
<thead>
<tr>
<th>Relative organ weight</th>
<th>Normal control</th>
<th>Treated Groups</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>ENEE 200 mg/kg</td>
</tr>
<tr>
<td>Heart (g)</td>
<td>1.75 ± 0.03</td>
<td>1.77 ± 0.04</td>
</tr>
<tr>
<td>Liver(g)</td>
<td>8.27 ± 0.03</td>
<td>8.29 ± 0.03</td>
</tr>
<tr>
<td>Brain(g)</td>
<td>1.85 ± 0.01</td>
<td>1.85 ± 0.02</td>
</tr>
</tbody>
</table>

Each value shown in mean±S.D. Where, n (number of animals in each group) = 10. ENEE: *Euphorbia neriifolia* Ethanolic extract. Analysis of data were analyzed by one way analysis of variance (ANOVA) followed by Dunnet’s test. Treated groups were compared with normal control group.

**Table 3.2** Effect of *Euphorbia neriifolia* Ethanolic extract (ENEE) on hematological parameters of rats in sub acute toxicity study.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Normal control</th>
<th>Treated Groups</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>ENEE 200mg/kg</td>
</tr>
<tr>
<td>WBC(×10^3/µL)</td>
<td>7.20±1.40</td>
<td>7.60±1.37</td>
</tr>
<tr>
<td>RBC(×10^6/µL)</td>
<td>8.14±0.45</td>
<td>8.94±0.85</td>
</tr>
<tr>
<td>Hb(g/dl)</td>
<td>15.13±0.35</td>
<td>15.83±0.95</td>
</tr>
<tr>
<td>Hct(%)</td>
<td>48.13±2.35</td>
<td>52.03±3.35</td>
</tr>
<tr>
<td>MCV(FL)</td>
<td>52.13±5.35</td>
<td>51.03±2.35</td>
</tr>
<tr>
<td>MCH(pg)</td>
<td>18.13±1.33</td>
<td>19.23±2.29</td>
</tr>
<tr>
<td>MCHC(g/dl)</td>
<td>38.78±3.55</td>
<td>34.44±4.80</td>
</tr>
<tr>
<td>Platelets(×10^3/µL)</td>
<td>808.13±82.75</td>
<td>838.45±89.67</td>
</tr>
</tbody>
</table>
### Results and discussion

Each value shown in mean ± S.D. n (number of animals in each group) = 10.

**Euphorbia nerifolia** ethanolic extract. Analysis of data were analyzed by one way analysis of variance (ANOVA) followed by Dunnet’s test. Treated groups were compared with normal control group.

**Table 3.3** Effect of *Euphorbia nerifolia* ethanolic extract (ENEE) in sub acute toxicity study on biochemical parameters.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Normal control</th>
<th>Treated Groups</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>ENEE 200 mg/kg</td>
</tr>
<tr>
<td><strong>Glucose(mg/dl)</strong></td>
<td>73.43±6.32</td>
<td>69.54±7.45</td>
</tr>
<tr>
<td><strong>Direct Bilirubin(mg/dl)</strong></td>
<td>0.00±0.00</td>
<td>0.00±0.00</td>
</tr>
<tr>
<td><strong>SGOT(U/L)</strong></td>
<td>134.6±7.54</td>
<td>123.6±6.37</td>
</tr>
<tr>
<td><strong>SGPT(U/L)</strong></td>
<td>39.01±3.65</td>
<td>32.22±2.54</td>
</tr>
<tr>
<td><strong>ALP(U/L)</strong></td>
<td>78.53±4.34</td>
<td>71.55±3.99</td>
</tr>
<tr>
<td><strong>Urea(mg/dl)</strong></td>
<td>5.55 ± 0.05</td>
<td>5.78 ± 0.15</td>
</tr>
</tbody>
</table>

Each value shown in mean ± S.D. n (number of animals in each group) = 10.

**Euphorbia nerifolia** ethanolic extract. Analysis of data were analyzed by one way analysis of variance (ANOVA) followed by Dunnet’s test. Treated groups were compared with normal control group.
Figure 3.1 Effect of *Euphorbia nerifolia* Ethanolic extract (ENEE) on Glucose in sub acute toxicity study of rats. Each value shown in mean ± S.D. n (number of animals in each group) = 10. ENEE: *Euphorbia nerifolia* ethanolic extract. Data were analyzed using one-way analysis of variance (ANOVA) followed by Dunnet’s test. Treated groups were compared with normal control group.
Figure 3.2 Effect of *Euphorbia nerifolia* Ethanolic extract (ENEE) on Creatinine in sub acute toxicity study of rats. Values shown in mean±S.D. where, n (number of animals in each group) = 10. ENEE: *Euphorbia nerifolia* ethanolic extract. Data were analyzed using one-way analysis of variance (ANOVA) followed by Dunnet’s test. Treated groups were compared with normal control group.
Figure 3.3 Effect of *Euphorbia nerifolia* Ethanol extract (ENEE) on Total Bilirubin in sub acute toxicity study of rats. Values shown in mean±S.D. where, n (number of animals in each group) = 10. ENEE: *Euphorbia nerifolia* ethanolic extract. Data were analyzed using one-way analysis of variance (ANOVA) followed by Dunnet’s test. Treated groups were compared with normal control group.
Figure 3.4 Effect of *Euphorbia neriifolia* Ethanolic extract (ENEE) on Total Protein in sub acute toxicity study of rats. Values shown in mean±S.D. where, n (number of animals in each group) = 10. ENEE: *Euphorbia neriifolia* ethanolic extract. Data were analyzed using one-way analysis of variance (ANOVA) followed by Dunnet’s test. Treated groups were compared with normal control group.
Figure 3.5 Effect of *Euphorbia neriifolia* Ethanol extract (ENEE) on SGOT in sub acute toxicity study of rats. Values shown in mean±S.D. where, n (number of animals in each group) = 10. ENEE: *Euphorbia neriifolia* ethanol extract. Data were analyzed using one-way analysis of variance (ANOVA) followed by Dunnet’s test. Treated groups were compared with normal control group.
Figure 3.6 Effect of *Euphorbia nerifolia* Ethanolic extract (ENEE) on SGPT in sub acute toxicity study of rats. Values shown in mean±S.D. where, n (number of animals in each group) = 10. ENEE: *Euphorbia nerifolia* ethanolic extract. Data were analyzed using one-way analysis of variance (ANOVA) followed by Dunnet’s test. Treated groups were compared with normal control group.
Figure 3.7 Effect of *Euphorbia nerifolia* Ethanolic extract (ENEE) on ALP (alkaline phosphatases) in sub acute toxicity study of rats. Values shown in mean±S.D. where, n (number of animals in each group) = 10. ENEE: *Euphorbia nerifolia* ethanolic extract. Data were analyzed using one-way analysis of variance (ANOVA) followed by Dunnet's test. Treated groups were compared with normal control group.
Figure 3.8 Effect of \textit{Euphorbia neriifolia} Ethanol extract (ENEE) on ALP (alkaline phosphatases) in sub acute toxicity study of rats. Values shown in mean±S.D. where, n (number of animals in each group) = 10. ENEE: \textit{Euphorbia neriifolia} ethanolic extract. Data were analyzed using one-way analysis of variance (ANOVA) followed by Dunnet’s test. Treated groups were compared with normal control group.

3.1.2 Histopathological slides
Figure 3.9 Histological slides of liver
Figure 3.10 Histological slides of kidney

Figure 3.11 Histological slides of Heart
3.1.3 Effect of *Euphorbia neriifolia* Ethanolic extract (ENEE) in normal rats on Oral Glucose Tolerance Test (OGTT) and in streptozotocin (STZ)-nicotinamide induced Type-II diabetic rats on body weight, Fasting blood glucose level, Lipid profile, serum insulin, liver glycogen, Glycated heamoglobin and pancreas.

Table 3.4 Effect of *Euphorbia neriifolia* Ethanolic extract ENEE on Fasting blood Glucose (FBG) during Oral Glucose Tolerance Test (OGTT) in normal rats.

<table>
<thead>
<tr>
<th>Group (n=6)</th>
<th>Treatment</th>
<th>Fasting plasma glucose concentrations mg/dl</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>0 min</td>
</tr>
<tr>
<td>I</td>
<td>Normal control</td>
<td>78.34±3.05</td>
</tr>
<tr>
<td>II</td>
<td>Glibenclamide (2.5mg/kg)</td>
<td>75.52±0.84</td>
</tr>
<tr>
<td>III</td>
<td>Normal+ENEE (200mg/kg)</td>
<td>74.28±1.50</td>
</tr>
<tr>
<td>IV</td>
<td>Normal+ENEE (400mg/kg)</td>
<td>74.43±0.99</td>
</tr>
</tbody>
</table>

Each value shown in mean ± S.D. n (number of animals in each group) = 6. ENEE: *Euphorbia neriifolia* ethanolic extract. Data were analyzed using one-way analysis of variance (ANOVA) followed by Dunnet’s test. Groups II, III and IV (Glibenclamide 2.5 mg/kg, ENEE 200 mg/kg and ENEE 400 mg/kg respectively) were compared with Group I (Normal control)

*p < 0.05 vs. normal control,

**p < 0.01 vs. normal control.
Figure 3.12 Effect of *Euphorbia neriifolia* ethanolic extract ENEE on Fasting blood Glucose (FBG) during Oral Glucose Tolerance Test (OGTT) in normal rats at 0 minute. Values shown in mean±S.D. n (number of animals in each group) = 6. ENEE: *Euphorbia neriifolia* ethanolic extract. Data were analyzed using one-way analysis of variance (ANOVA) followed by Dunnet’s test. Groups II, III and IV (Glibenclamide 2.5 mg/kg, ENEE 200 mg/kg and ENEE 400 mg/kg respectively) were compared with Group I (Normal control).
Figure 3.13 Effect of *Euphorbia neriifolia* ethanolic extract ENEE on Fasting blood Glucose (FBG) during Oral Glucose Tolerance Test (OGTT) in normal rats at 30 minute. Values shown in mean±S.D. n (number of animals in each group) = 6. ENEE: *Euphorbia neriifolia* ethanolic extract. Data were analyzed using one-way analysis of variance (ANOVA) followed by Dunnet’s test. Groups II, III and IV (Glibenclamide 2.5 mg/kg, ENEE 200 mg/kg and ENEE 400 mg/kg respectively) were compared with Group I (Normal control).

*p < 0.05 vs. normal control.*

**p < 0.01 vs. normal control.*
Figure 3.14 Effect of *Euphorbia neriifolia* ethanolic extract ENEE on Fasting blood glucose (FBG) during Oral Glucose Tolerance Test (OGTT) in normal rats at 60 minute. Values shown in mean±S.D. n (number of animals in each group) = 6. ENEE: *Euphorbia neriifolia* ethanolic extract. Data were analyzed using one-way analysis of variance (ANOVA) followed by Dunnet’s test. Groups II, III and IV (Glibenclamide 2.5 mg/kg, ENEE 200 mg/kg and ENEE 400 mg/kg respectively) were compared with Group I (Normal control).

**p < 0.01 vs. normal control.
3.1.4 Effects of ENEE ON body weights

<table>
<thead>
<tr>
<th>Groups (n=6)</th>
<th>Treatment</th>
<th>Body Weight (g)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Before treatment</td>
</tr>
<tr>
<td>I</td>
<td>Normal control</td>
<td>190.43±7.65</td>
</tr>
</tbody>
</table>

Figure 3.15 Effect of Euphorbia neriifolia ethanolic extract ENEE on Fasting blood Glucose (FBG) during Oral Glucose Tolerance Test (OGTT) in normal rats at 120 minute. Values shown in mean±S.D. n (number of animals in each group) = 6. ENEE: Euphorbia neriifolia ethanolic extract. Data were analyzed using one-way analysis of variance (ANOVA) followed by Dunnet’s test. Groups II, III and IV (Glibenclamide 2.5 mg/kg, ENEE 200 mg/kg and ENEE 400 mg/kg respectively) were compared with Group I (Normal control).

**p < 0.01 vs. normal control.
### Results and discussion

<table>
<thead>
<tr>
<th>GROUP</th>
<th>Treatment</th>
<th>Body Weight before treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>II</td>
<td>Diabetic control</td>
<td>180.56±9.23</td>
</tr>
<tr>
<td>III</td>
<td>Diabetic+Glibenclamide 2.5mg/kg</td>
<td>178.45±6.10</td>
</tr>
<tr>
<td>IV</td>
<td>Diabetic+ENEE 200mg/kg</td>
<td>175.94±7.06</td>
</tr>
<tr>
<td>V</td>
<td>Diabetic+ENEE 400mg/kg</td>
<td>170.54±7.39</td>
</tr>
</tbody>
</table>

Values shown in mean±S.D. Where, n (number of animals in each group) = 6. ENEE: *Euphorbia neriifolia* ethanolic extract. Data were analyzed using one-way analysis of variance (ANOVA) followed by Dunnet’s test. Group II (Diabetic control) was compared with Group I (Normal control). Group III, IV and V (Diabetic+glibenclamide 2.5 mg/kg, Diabetic+ENEE 200 mg/kg and Diabetic+ENEE 400 mg/kg respectively) were compared with Group II (Diabetic control).

*p < 0.05 vs. normal control.

**Figure 3.16** Effect of *Euphorbia neriifolia* Ethanolic extract (ENEE) on Body weight (BW) before treatment in streptozotocin-nicotinamide induced Type-II diabetic rats. Values shown in mean±S.D. Where, n (number of animals in each group) = 6. ENEE: *Euphorbia neriifolia* ethanolic extract. Data were analyzed using one-way analysis of variance (ANOVA) followed by Dunnet’s test. Group II (Diabetic control) was compared with Group I (Normal control). Group III, IV and V (Diabetic+glibenclamide 2.5 mg/kg, Diabetic+ENEE 200 mg/kg and Diabetic+ENEE 400 mg/kg respectively) were compared with Group II (Diabetic control).
**Figure 3.17** Effect of *Euphorbia neriifolia* Ethanolic extract (ENEE) on Body weight (BW) after treatment in streptozotocin-nicotinamide induced Type-II diabetic rats. Values shown in mean±S.D. Where, n (number of animals in each group) = 6. ENEE: *Euphorbia neriifolia* ethanolic extract. Data were analyzed using one-way analysis of variance (ANOVA) followed by Dunnet’s test. Group II (Diabetic control) was compared with Group I (Normal control). Group III, IV and V (Diabetic+glibenclamide 2.5 mg/kg, Diabetic+ENEE 200 mg/kg and Diabetic+ENEE 400 mg/kg respectively) were compared with Group II (Diabetic control).

*p < 0.05 vs. diabetic control*
Figure 3.18 Effect of *Euphorbia neriifolia* ethanolic extract ENEE on Fasting blood Glucose (FBG) in streptozotocin-nicotinamide induced type II diabetic rats on day 0.

Values shown in mean±S.D. Where, n (number of animals in each group) = 6. ENEE: *Euphorbia neriifolia* ethanolic extract. Data were analyzed using one-way analysis of variance (ANOVA) followed by Dunnet's test. Group II (Diabetic control) was compared with Group I (Normal control). Group III, IV and V (Diabetic+glibenclamide 2.5 mg/kg, Diabetic+ENEE 200 mg/kg and Diabetic+ENEE 400 mg/kg respectively) were compared with Group II (Diabetic control).

**p < 0.01 vs Normal control**
Figure 3.19 Effect of *Euphorbia neriifolia* Ethanolic extract ENEE on Fasting blood Glucose (FBG) in streptozotocin-nicotinamide induced type II diabetic rats on day 5. Values shown in mean±S.D. Where, n (number of animals in each group) = 6. ENEE: *Euphorbia neriifolia* Ethanolic extract. Data were analyzed using one-way analysis of variance (ANOVA) followed by Dunnet’s test. Group II (Diabetic control) was compared with Group I (Normal control). Group III, IV and V (Diabetic+glibenclamide 2.5 mg/kg, Diabetic+ENEE 200 mg/kg and Diabetic+ENEE 400 mg/kg respectively) were compared with Group II (Diabetic control)

*p < 0.05 vs. diabetic control

**p < 0.01 vs. diabetic control

***p < 0.01 vs Normal control
Figure 3.20 Effect of *Euphorbia neriifolia* ethanolic extract ENEE on Fasting blood Glucose (FBG) in streptozotocin-nicotinamide induced type II diabetic rats on day 10. Values shown in mean±S.D. Where, n (number of animals in each group) = 6. ENEE: *Euphorbia neriifolia* ethanolic extract. Data were analyzed using one-way analysis of variance (ANOVA) followed by Dunnet's test. Group II (Diabetic control) was compared with Group I (Normal control). Group III, IV and V (Diabetic+glibenclamide 2.5 mg/kg, Diabetic+ENEE 200 mg/kg and Diabetic+ENEE 400 mg/kg respectively) were compared with Group II (Diabetic control).

* *p* < 0.05 vs. diabetic control

** ** *p* < 0.01 vs. diabetic control

### *p* < 0.01 vs Normal control
Figure 3.21 Effect of *Euphorbia neriifolia* ethanolic extract ENEE on Fasting blood Glucose (FBG) in streptozotocin-nicotinamide induced type II diabetic rats on day 15. Values shown in mean±S.D. Where, n (number of animals in each group) = 6. ENEE: *Euphorbia neriifolia* ethanolic extract. Data were analyzed using one-way analysis of variance (ANOVA) followed by Dunnet’s test. Group II (Diabetic control) was compared with Group I (Normal control). Group III, IV and V (Diabetic+glibenclamide 2.5 mg/kg, Diabetic+ENEE 200 mg/kg and Diabetic+ENEE 400 mg/kg respectively) were compared with Group II (Diabetic control)

*p < 0.05 vs. diabetic control

**p < 0.01 vs. diabetic control

***p < 0.01 vs Normal control
Table 3.7 Effect of *Euphorbia neriifolia* Ethanol extract (ENEE) on lipid profile in streptozotocin-nicotinamide induced Type-II diabetic rats.

<table>
<thead>
<tr>
<th>Group (n=6)</th>
<th>Treatment</th>
<th>SERUM LIPID PROFILE mg/dl</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>TG</td>
</tr>
<tr>
<td>I</td>
<td>Normal control</td>
<td>89.88±1.05</td>
</tr>
<tr>
<td>II</td>
<td>Diabetic control</td>
<td>137.5±1.55&quot;&quot;</td>
</tr>
<tr>
<td>III</td>
<td>Glibenclamide 2.5mg/kg</td>
<td>100.5±1.06&quot;&quot;</td>
</tr>
<tr>
<td>IV</td>
<td>Diabetic+ENEE 200mg/kg</td>
<td>115.8±1.17&quot;&quot;</td>
</tr>
<tr>
<td>V</td>
<td>Diabetic+ENEE 400mg/kg</td>
<td>106.0±1.05&quot;&quot;</td>
</tr>
</tbody>
</table>

Values shown in mean±S.D. Where, n (number of animals in each group) = 6. ENEE: *Euphorbia neriifolia* ethanolic extract. Data were analyzed using one-way analysis of variance (ANOVA) followed by Dunnet’s test. Group II (Diabetic control) was compared with Group I (Normal control). Group III, IV and V (Diabetic+glibenclamide 2.5 mg/kg, Diabetic+ENEE 200 mg/kg and Diabetic+ENEE 400 mg/kg respectively) were compared with Group II (Diabetic control).

*p < 0.05 vs. diabetic control,

**p < 0.01 vs. diabetic control

***p < 0.001 vs. diabetic control

## p < 0.01 vs Normal control

### p < 0.001 vs Normal control
Figure 3.22 Effect of *Euphorbia nerifolia* ethanolic extract ENEE on Triglycerides-TG in streptozotocin-nicotinamide induced type II diabetic rats. Values shown in mean±S.D. Where, n (number of animals in each group) = 6. ENEE: *Euphorbia nerifolia* ethanolic extract. Data were analyzed using one-way analysis of variance (ANOVA) followed by Dunnet’s test. Group II (Diabetic control) was compared with Group I (Normal control). Group III, IV and V (Diabetic+glibenclamide 2.5 mg/kg, Diabetic+ENEE 200 mg/kg and Diabetic+ENEE 400 mg/kg respectively) were compared with Group II (Diabetic control)

*p < 0.05 vs. diabetic control

**p < 0.01 vs. diabetic control

***p < 0.01 vs Normal control
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Figure 3.23 Effect of *Euphorbia nerifolia* ethanolic extract ENEE on Total Cholesterol-TC in streptozotocin-nicotinamide induced type II diabetic rats. Values shown in mean±S.D. Where, n (number of animals in each group) = 6. ENEE: *Euphorbia nerifolia* ethanolic extract. Data were analyzed using one-way analysis of variance (ANOVA) followed by Dunnet’s test. Group II (Diabetic control) was compared with Group I (Normal control). Group III, IV and V (Diabetic+glibenclamide 2.5 mg/kg, Diabetic+ENEE 200 mg/kg and Diabetic+ENEE 400 mg/kg respectively) were compared with Group II (Diabetic control).

*p < 0.05 vs. diabetic control

**p < 0.01 vs. diabetic control

#p < 0.01 vs Normal control
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Figure 3.24 Effect of *Euphorbia neriifolia* ethanolic extract ENEE on High Density Lipoprotein-HDL in streptozotocin-nicotinamide induced type II diabetic rats. Values shown in mean±S.D. Where, n (number of animals in each group) = 6. ENEE: *Euphorbia neriifolia* ethanolic extract. Data were analyzed using one-way analysis of variance (ANOVA) followed by Dunnet’s test. Group II (Diabetic control) was compared with Group I (Normal control). Group III, IV and V (Diabetic+glibenclamide 2.5 mg/kg, Diabetic+ENEE 200 mg/kg and Diabetic+ENEE 400 mg/kg respectively) were compared with Group II (Diabetic control).

**p < 0.01 vs diabetic control

###p < 0.01 vs Normal control
Figure 3.25 Effect of *Euphorbia nerifolia* ethanolic extract ENEE on Low Density Lipoprotein-LDL in streptozotocin-nicotinamide induced type II diabetic rats. Values shown in mean±S.D. Where, n (number of animals in each group) = 6. ENEE: *Euphorbia nerifolia* ethanolic extract. Data were analyzed using one-way analysis of variance (ANOVA) followed by Dunnet’s test. Group II (Diabetic control) was compared with Group I (Normal control). Group III, IV and V (Diabetic+glibenclamide 2.5 mg/kg, Diabetic+ENEE 200 mg/kg and Diabetic+ENEE 400 mg/kg respectively) were compared with Group II (Diabetic control)

*p < 0.05 vs. diabetic control,

**p < 0.01 vs. diabetic control

***p < 0.001 vs. diabetic control

###p < 0.001 vs Normal control
**Figure 3.26** Effect of *Euphorbia nerifolia* ethanolic extract ENEE on Very Low Density Lipoprotein-VLDL in streptozotocin-nicotinamide induced type II diabetic rats. Values shown in mean±S.D. Where, n (number of animals in each group) = 6. ENEE: *Euphorbia nerifolia* ethanolic extract. Data were analyzed using one-way analysis of variance (ANOVA) followed by Dunnet’s test. Group II (Diabetic control) was compared with Group I (Normal control). Group III, IV and V (Diabetic+glibenclamide 2.5 mg/kg, Diabetic+ENEE 200 mg/kg and Diabetic+ENEE 400 mg/kg respectively) were compared with Group II (Diabetic control).

*p < 0.05 vs diabetic control

**p < 0.01 vs diabetic control

***p < 0.01 vs Normal control
Table 3.8 Effect of *Euphorbia neriifolia* Ethanolic extract (ENEE) on serum insulin level, Glycated haemoglobin and Liver glycogen in streptozotocin-nicotinamide induced Type-II diabetic rats.

<table>
<thead>
<tr>
<th>Group (n=6)</th>
<th>Treatment</th>
<th>Serum insulin (µu/ml)</th>
<th>Glycated haemoglobin (%)</th>
<th>Liver glycogen (mg/g)</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Normal control</td>
<td>125.42±1.80</td>
<td>2.73±1.44</td>
<td>12.98±2.59</td>
</tr>
<tr>
<td>II</td>
<td>Diabetic control</td>
<td>61.88±2.13**</td>
<td>7.83±2.21**</td>
<td>5.19±0.69##</td>
</tr>
<tr>
<td>III</td>
<td>Diabetic+Glibenclamide 2.5mg/kg</td>
<td>114.95±1.43**</td>
<td>3.89±1.51**</td>
<td>11.11±0.71**</td>
</tr>
<tr>
<td>IV</td>
<td>Diabetic+ENEE 200mg/kg</td>
<td>87.61±1.99*</td>
<td>5.28±1.82</td>
<td>9.03±0.53**</td>
</tr>
<tr>
<td>V</td>
<td>Diabetic+ENEE 400mg/kg</td>
<td>101.99±2.22**</td>
<td>4.13±1.55**</td>
<td>10.72±0.45**</td>
</tr>
</tbody>
</table>

Values shown in mean±S.D. Where, n (number of animals in each group) = 6. ENEE: *Euphorbia neriifolia* ethanolic extract. Data were analyzed using one-way analysis of variance (ANOVA) followed by Dunnet’s test. Group II (Diabetic control) was compared with Group I (Normal control). Group III, IV and V (Diabetic+Glibenclamide 2.5 mg/kg, Diabetic+ENEE 200 mg/kg and Diabetic+ENEE 400 mg/kg respectively) were compared with Group II (Diabetic control).

* p < 0.05 vs. diabetic control
** p < 0.01 vs. diabetic control
## p < 0.01 vs Normal control
### p < 0.001 vs Normal control
Figure 3.27 Effect of *Euphorbia neriifolia* ethanolic extract ENEE on Serum Insulin in streptozotocin-nicotinamide induced type II diabetic rats. Values shown in mean±S.D. Where, n (number of animals in each group) = 6. ENEE: *Euphorbia neriifolia* ethanolic extract. Data were analyzed using one-way analysis of variance (ANOVA) followed by Dunnet’s test. Group II (Diabetic control) was compared with Group I (Normal control). Group III, IV and V (Diabetic+glibenclamide 2.5 mg/kg, Diabetic+ENEE 200 mg/kg and Diabetic+ENEE 400 mg/kg respectively) were compared with Group II (Diabetic control).

*p < 0.05 vs diabetic control

**p < 0.01 vs diabetic control

###p < 0.001 vs Normal control
Figure 3.28 Effect of *Euphorbia nerifolia* ethanolic extract ENEE on Glycated Hemoglobin in streptozotocin-nicotinamide induced type II diabetic rats. Values shown in mean±S.D. Where, n (number of animals in each group) = 6. ENEE: *Euphorbia nerifolia* ethanolic extract. Data were analyzed using one-way analysis of variance (ANOVA) followed by Dunnet’s test. Group II (Diabetic control) was compared with Group I (Normal control).Group III, IV and V (Diabetic+glibenclamide 2.5 mg/kg, Diabetic+ENEE 200 mg/kg and Diabetic+ENEE 400 mg/kg respectively) were compared with Group II (Diabetic control)

* p < 0.05 vs diabetic control

** p < 0.01 vs diabetic control

### p < 0.001 vs Normal control
Liver Glycogen

**Figure 3.29** Effect of *Euphorbia nertifolia* ethanolic extract ENEE on Liver Glycogen in streptozotocin-nicotinamide induced type II diabetic rats. Values shown in mean±S.D. Where, n (number of animals in each group) = 6. ENEE: *Euphorbia nertifolia* ethanolic extract. Data were analyzed using one-way analysis of variance (ANOVA) followed by Dunnet’s test. Group II (Diabetic control) was compared with Group I (Normal control). Group III, IV and V (Diabetic+glibenclamide 2.5 mg/kg, Diabetic+ENEE 200 mg/kg and Diabetic+ENEE 400 mg/kg respectively) were compared with Group II (Diabetic control).

**p < 0.01 vs diabetic control**

**p < 0.01 vs Normal control**
3.1.5 Effect of *Euphorbia neriifolia* Ethanolic extract (ENEE) on islets of pancreas

**Figure 3.30** Histological slide of normal control group showing normal architecture of islets of pancreas.

**Figure 3.31** Histological slide of diabetic control group showing degeneration of islets of pancreas as compared to normal control group.

**Figure 3.32** Histological slide of Diabetic+Glibenclamide 2.5 mg/kg group showing recovered islets of pancreas close to normal control group.
Figure 3.33 Histological slide of Diabetic+ENEE 200 mg/kg group showing recovery of islets of pancreas.

Figure 3.34 Histological slide of Diabetic+ENEE 400 mg/kg group showing recovered islets of pancreas.
3.1.6 Effect of *Euphorbia neriifolia* Ethanolic extract (ENEE) in normal rats on OGTT

<table>
<thead>
<tr>
<th>Group (n=6)</th>
<th>Treatment</th>
<th>Fasting plasma glucose concentrations mg/dl</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>0 min</td>
</tr>
<tr>
<td>I</td>
<td>Normal control</td>
<td>88.6±2.531</td>
</tr>
<tr>
<td>II</td>
<td>Glibenclamide (2.5mg/kg)</td>
<td>93.2±2.706</td>
</tr>
<tr>
<td>III</td>
<td>Normal+ENEE (200mg/kg)</td>
<td>90.1±2.603</td>
</tr>
<tr>
<td>IV</td>
<td>Normal+ENEE (400mg/kg)</td>
<td>92.4±2.812</td>
</tr>
</tbody>
</table>

Table 3.9
Figure 3.35 Effect of *Euphorbia nerifolia* ethanolic extract ENEE on Fasting blood Glucose (FBG) during Oral Glucose Tolerance Test (OGTT) in normal rats at 0 minute.

Values shown in mean ± S.D. n (number of animals in each group) = 6. ENEE: *Euphorbia nerifolia* ethanolic extract. Data were analyzed using one-way analysis of variance (ANOVA) followed by Dunnet’s test. Groups II, III and IV (Glibenclamide 2.5 mg/kg, ENEE 200 mg/kg and ENEE 400 mg/kg respectively) were compared with Group I (Normal control).
Figure 3.36 Effect of *Euphorbia nerifolia* ethanolic extract ENEE on Fasting blood Glucose (FBG) during Oral Glucose Tolerance Test (OGTT) in normal rats at 30 minute. Values shown in mean ± S.D. n (number of animals in each group) = 6. ENEE: *Euphorbia nerifolia* ethanolic extract. Data were analyzed using one-way analysis of variance (ANOVA) followed by Dunnet’s test. Groups II,III and IV (Glibenclamide 2.5 mg/kg, ENEE 200 mg/kg and ENEE 400 mg/kg respectively) were compared with Group I (Normal control).
Figure 3.37 Effect of *Euphorbia neriifolia* ethanolic extract ENEE on Fasting blood Glucose (FBG) during Oral Glucose Tolerance Test (OGTT) in normal rats at 60 minute. Values shown in mean ± S.D. n (number of animals in each group) = 6. ENEE: *Euphorbia neriifolia* ethanolic extract. Data were analyzed using one-way analysis of variance (ANOVA) followed by Dunnet’s test. Groups II,III and IV (Glibenclamide 2.5 mg/kg, ENEE 200 mg/kg and ENEE 400 mg/kg respectively) were compared with Group I (Normal control)

*p < 0.05 vs. normal control*
Figure 3.38 Effect of *Euphorbia neriifolia* ethanolic extract ENEE on Fasting blood Glucose (FBG) during Oral Glucose Tolerance Test (OGTT) in normal rats at 120 minute. Values shown in mean ± S.D. n (number of animals in each group) = 6. ENEE: *Euphorbia neriifolia* ethanolic extract. Data were analyzed using one-way analysis of variance (ANOVA) followed by Dunnet’s test. Groups II,III and IV (Glibenclamide 2.5 mg/kg, ENEE 200 mg/kg and ENEE 400 mg/kg respectively) were compared with Group I (Normal control)

*p* < 0.05 vs normal control

**p** < 0.01 vs normal control

Table No:3.10 Effect of *Euphorbia neriifolia* Ethanolic extract (ENEE) on Body weight
### Groups (n=6)

<table>
<thead>
<tr>
<th>Groups</th>
<th>Treatment</th>
<th>Body Weight (g)</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Normal control</td>
<td>245.65±6.76</td>
<td>260.87±4.58</td>
<td></td>
</tr>
<tr>
<td>II</td>
<td>Diabetic control</td>
<td>361.45±7.34##</td>
<td>399.44±9.32##</td>
<td></td>
</tr>
<tr>
<td>III</td>
<td>Diabetic+Glibenclamide 2.5mg/kg</td>
<td>353.33±5.12</td>
<td>285.76±10.94**</td>
<td></td>
</tr>
<tr>
<td>IV</td>
<td>Diabetic+ENEE 200mg/kg</td>
<td>365.78±8.79</td>
<td>325.34±8.41*</td>
<td></td>
</tr>
<tr>
<td>V</td>
<td>Diabetic+ENEE 400mg/kg</td>
<td>356.38±6.67</td>
<td>297.87±7.03**</td>
<td></td>
</tr>
</tbody>
</table>

Values shown in mean±S.D. Where, n (number of animals in each group) = 6. ENEE: *Euphorbia nerifolia* ethanolic extract. Data were analyzed using one-way analysis of variance (ANOVA) followed by Dunnet’s test. Group II (Diabetic control) was compared with Group I (Normal control). Group III, IV and V (Diabetic+glibenclamide 2.5 mg/kg, Diabetic+ENEE 200 mg/kg and Diabetic+ENEE 400 mg/kg respectively) were compared with Group II (Diabetic control).

* *p < 0.05 vs diabetic control
** **p < 0.01 vs diabetic control
## n < 0.01 vs Normal control
Figure 3.39 Effect of *Euphorbia neriifolia* Ethanolic extract (ENEE) on Body weight before treatment in High Fat Diet-streptozotocin induced Type-II diabetic rats. Values shown in mean±S.D. Where, n (number of animals in each group) = 6. ENEE: *Euphorbia neriifolia* ethanolic extract. Data were analyzed using one-way analysis of variance (ANOVA) followed by Dunnet’s test. Group II (Diabetic control) was compared with Group I (Normal control). Group III, IV and V (Diabetic+glibenclamide 2.5 mg/kg, Diabetic+ENEE 200 mg/kg and Diabetic+ENEE 400 mg/kg respectively) were compared with Group II (Diabetic control).

## p < 0.01 vs Normal control
Chapter 3

Results and discussion

![Bogy Weight after treatment](image)

**Figure 3.40** Effect of *Euphorbia neriifolia* Ethanolic extract (ENEE) on Body weight after treatment in High Fat Diet-streptozotocin induced Type-II diabetic rats. Values shown in mean±S.D. Where, n (number of animals in each group) = 6. ENEE: *Euphorbia neriifolia* ethanolic extract. Data were analyzed using one-way analysis of variance (ANOVA) followed by Dunnet’s test. Group II (Diabetic control) was compared with Group I (Normal control). Group III, IV and V (Diabetic+glibenclamide 2.5 mg/kg, Diabetic+ENEE 200 mg/kg and Diabetic+ENEE 400 mg/kg respectively) were compared with Group II (Diabetic control)

*p < 0.05 vs diabetic control

**p < 0.01 vs diabetic control

###p < 0.01 vs Normal control

**Table 3.11** Effect of *Euphorbia neriifolia* Ethanolic extract (ENEE) on Fasting Blood Glucose (FBG) in High Fat Diet-streptozotocin induced Type-II diabetic rats.

<table>
<thead>
<tr>
<th>Group (n=6)</th>
<th>Treatment</th>
<th>Fasting plasma glucose concentrations mg/dl</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Day 0</td>
</tr>
<tr>
<td>I</td>
<td>Normal control</td>
<td>77.0±1.92</td>
</tr>
<tr>
<td>II</td>
<td>Diabetic control</td>
<td>288.56±3.48###</td>
</tr>
</tbody>
</table>
### Results and discussion

<table>
<thead>
<tr>
<th>Group</th>
<th>Treatment</th>
<th>Mean ± S.D.</th>
<th>194.56 ± 2.73</th>
<th>147.5 ± 1.62</th>
<th>94.17 ± 2.99</th>
</tr>
</thead>
<tbody>
<tr>
<td>III</td>
<td>Diabetic+ Glibenclamide 2.5mg/kg</td>
<td>282.0 ± 3.69</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IV</td>
<td>Diabetic+ ENEE 200mg/kg</td>
<td>277.35 ± 2.88</td>
<td>236.79 ± 3.08</td>
<td>189.88 ± 2.20</td>
<td>137.76 ± 3.39</td>
</tr>
<tr>
<td>V</td>
<td>Diabetic+ ENEE 400mg/kg</td>
<td>278.73 ± 2.86</td>
<td>212.46 ± 2.32</td>
<td>164.06 ± 2.24</td>
<td>127.26 ± 3.03</td>
</tr>
</tbody>
</table>

Values shown in mean±S.D. Where, n (number of animals in each group) = 6. ENEE: *Euphorbia neriifolia* ethanolic extract. Data were analyzed using one-way analysis of variance (ANOVA) followed by Dunnet’s test. Group II (Diabetic control) was compared with Group I (Normal control). Group III, IV and V (Diabetic+ glibenclamide 2.5 mg/kg, Diabetic+ ENEE 200 mg/kg and Diabetic+ ENEE 400 mg/kg respectively) were compared with Group II (Diabetic control).

* p < 0.05 vs diabetic control

** p < 0.01 vs diabetic control

*** p < 0.001 vs diabetic control

**** p < 0.001 vs Normal control
Figure 3.41 Effect of *Euphorbia neriifolia* ethanolic extract ENEE on Fasting blood Glucose (FBG) in High Fat Diet-streptozotocin induced type II diabetic rats on day 0.

Values shown in mean±S.D. Where, n (number of animals in each group) = 6. ENEE: *Euphorbia neriifolia* ethanolic extract. Data were analyzed using one-way analysis of variance (ANOVA) followed by Dunnet’s test. Group II (Diabetic control) was compared with Group I (Normal control). Group III, IV and V (Diabetic+glibenclamide 2.5 mg/kg, Diabetic+ENEE 200 mg/kg and Diabetic+ENEE 400 mg/kg respectively) were compared with Group II (Diabetic control)

### p < 0.001 vs Normal control
Figure 3.42 Effect of *Euphorbia neriifolia* ethanolic extract ENEE on Fasting blood Glucose (FBG) in High Fat Diet-streptozotocin induced type II diabetic rats on day 7. Values shown in mean±S.D. Where, n (number of animals in each group) = 6. ENEE: *Euphorbia neriifolia* ethanolic extract. Data were analyzed using one-way analysis of variance (ANOVA) followed by Dunnet’s test. Group II (Diabetic control) was compared with Group I (Normal control). Group III, IV and V (Diabetic+glibenclamide 2.5 mg/kg, Diabetic+ENEE 200 mg/kg and Diabetic+ENEE 400 mg/kg respectively) were compared with Group II (Diabetic control)

* p < 0.05 vs diabetic control,

** p < 0.01 vs diabetic control

### p < 0.001 vs Normal control
Figure 3.43 Effect of *Euphorbia nerifolia* ethanolic extract ENEE on Fasting blood Glucose (FBG) in High Fat Diet-streptozotocin induced type II diabetic rats on day 14. Values shown in mean±S.D. Where, n (number of animals in each group) = 6. ENEE: *Euphorbia nerifolia* ethanolic extract. Data were analyzed using one-way analysis of variance (ANOVA) followed by Dunnet’s test. Group II (Diabetic control) was compared with Group I (Normal control). Group III, IV and V (Diabetic+glibenclamide 2.5 mg/kg, Diabetic+ENEE 200 mg/kg and Diabetic+ENEE 400 mg/kg respectively) were compared with Group II (Diabetic control).

* p < 0.05 vs diabetic control

** p < 0.01 vs diabetic control

### p < 0.001 vs Normal control
Figure 3.44 Effect of *Euphorbia neriifolia* ethanolic extract ENEE on Fasting blood Glucose (FBG) in High Fat Diet-streptozotocin induced type II diabetic rats on day 21.

Values shown in mean±S.D. Where, n (number of animals in each group) = 6. ENEE: *Euphorbia neriifolia* ethanolic extract. Data were analyzed using one-way analysis of variance (ANOVA) followed by Dunnet’s test. Group II (Diabetic control) was compared with Group I (Normal control). Group III, IV and V (Diabetic+glibenclamide 2.5 mg/kg, Diabetic+ENEE 200 mg/kg and Diabetic+ENEE 400 mg/kg respectively) were compared with Group II (Diabetic control).

**p < 0.01 vs diabetic control

***p < 0.001 vs diabetic control

###p < 0.001 vs Normal control
**Table 3.12** Effect of *Euphorbia neriifolia* ethanolic extract ENEE on lipid profile in High Fat Diet-streptozotocin induced type II diabetic rats on day 21.

<table>
<thead>
<tr>
<th>Groups (n=6)</th>
<th>Treatment</th>
<th>Serum lipid profile mg/dl</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>TG</td>
</tr>
<tr>
<td>I</td>
<td>Normal control</td>
<td>96.85±1.25</td>
</tr>
<tr>
<td>II</td>
<td>Diabetic control</td>
<td>142.33±1.54##</td>
</tr>
<tr>
<td>III</td>
<td>Diabetic+Glibenclamide 2.5mg/kg</td>
<td>105.4±1.16**</td>
</tr>
<tr>
<td>IV</td>
<td>Diabetic+ ENEE 200mg/kg</td>
<td>121.9±1.21*</td>
</tr>
<tr>
<td>V</td>
<td>Diabetic+ ENEE 400mg/kg</td>
<td>111.1±1.15**</td>
</tr>
</tbody>
</table>

Values shown in mean±S.D. Where, n (number of animals in each group) = 6. ENEE: *Euphorbia neriifolia* ethanolic extract. Data were analyzed using one-way analysis of variance (ANOVA) followed by Dunnet’s test. Group II (Diabetic control) was compared with Group I (Normal control). Group III, IV and V (Diabetic+glibenclamide 2.5 mg/kg, Diabetic+ENEE 200 mg/kg and Diabetic+ENEE 400 mg/kg respectively) were compared with Group II (Diabetic control).

*p < 0.05 vs. diabetic control

**p < 0.01 vs. diabetic control

***p < 0.001 vs. diabetic control

##p < 0.01 vs Normal control

###p < 0.001 vs Normal control
Figure 3.45 Effect of *Euphorbia neriifolia* ethanolic extract ENEE on Tryglycerides in High Fat Diet-streptozotocin induced type II diabetic rats on day 21. Values shown in mean±S.D. Where, n (number of animals in each group) = 6. ENEE: *Euphorbia neriifolia* ethanolic extract. Data were analyzed using one-way analysis of variance (ANOVA) followed by Dunnet’s test. Group II (Diabetic control) was compared with Group I (Normal control). Group III, IV and V (Diabetic+glibenclamide 2.5 mg/kg, Diabetic+ENEE 200 mg/kg and Diabetic+ENEE 400 mg/kg respectively) were compared with Group II (Diabetic control)

*p < 0.05 vs. diabetic control

**p < 0.01 vs. diabetic control

##p < 0.01 vs Normal control
Figure 3.46 Effect of *Euphorbia neriifolia* ethanolic extract ENEE on Total cholesterol in High Fat Diet-streptozotocin induced type II diabetic rats on day 21. Values shown in mean±S.D. Where, n (number of animals in each group) = 6. ENEE: *Euphorbia neriifolia* ethanolic extract. Data were analyzed using one-way analysis of variance (ANOVA) followed by Dunnet’s test. Group II (Diabetic control) was compared with Group I (Normal control). Group III, IV and V (Diabetic+glibenclamide 2.5 mg/kg, Diabetic+ENEE 200 mg/kg and Diabetic+ENEE 400 mg/kg respectively) were compared with Group II (Diabetic control).

* p < 0.05 vs diabetic control

** p < 0.01 vs diabetic control

## p < 0.01 vs Normal control
Figure 3.47 Effect of *Euphorbia neriifolia* ethanolic extract ENEE on High Density Lipoprotein in High Fat Diet-streptozotocin induced type II diabetic rats on day 21. Values shown in mean±S.D. Where, n (number of animals in each group) = 6. ENEE: *Euphorbia neriifolia* ethanolic extract. Data were analyzed using one-way analysis of variance (ANOVA) followed by Dunnet's test. Group II (Diabetic control) was compared with Group I (Normal control). Group III, IV and V (Diabetic+glibenclamide 2.5 mg/kg, Diabetic+ENEE 200 mg/kg and Diabetic+ENEE 400 mg/kg respectively) were compared with Group II (Diabetic control).

*p < 0.05 vs diabetic control

**p < 0.01 vs diabetic control

##p < 0.01 vs Normal control
Figure 3.48 Effect of *Euphorbia nerifolia* ethanolic extract ENEE on Low Density Lipoprotein in High Fat Diet-streptozotocin induced type II diabetic rats on day 21. Values shown in mean±S.D. Where, n (number of animals in each group) = 6. ENEE: *Euphorbia nerifolia* ethanolic extract. Data were analyzed using one-way analysis of variance (ANOVA) followed by Dunnet’s test. Group II (Diabetic control) was compared with Group I (Normal control). Group III, IV and V (Diabetic+glibenclamide 2.5 mg/kg, Diabetic+ENEE 200 mg/kg and Diabetic+ENEE 400 mg/kg respectively) were compared with Group II (Diabetic control)

**p < 0.01 vs diabetic control

***p < 0.001 vs diabetic control

###p < 0.001 vs Normal control
**Figure 3.49** Effect of *Euphorbia nerifolia* ethanolic extract ENEE on Very Low Density Lipoprotein in High Fat Diet-streptozotocin induced type II diabetic rats on day 21. Values shown in mean±S.D. Where, n (number of animals in each group) = 6. ENEE: *Euphorbia nerifolia* ethanolic extract. Data were analyzed using one-way analysis of variance (ANOVA) followed by Dunnet’s test. Group II (Diabetic control) was compared with Group I (Normal control). Group III, IV and V (Diabetic+glibenclamide 2.5 mg/kg, Diabetic+ENEE 200 mg/kg and Diabetic+ENEE 400 mg/kg respectively) were compared with Group II (Diabetic control).

*p < 0.05 vs diabetic control

**p < 0.01 vs diabetic control

***p < 0.01 vs Normal control
Table 3.13 Effect of *Euphorbia nerifolia* ethanolic extract ENEE on Serum Insulin, Glycated Hemoglobin and liver Glycogen in High Fat Diet-streptozotocin induced type II diabetic rats.

<table>
<thead>
<tr>
<th>Group (n=6)</th>
<th>Treatment</th>
<th>Serum insulin (µu/ml)</th>
<th>Glycated hemoglobin Hb1Ac (%)</th>
<th>Liver glycogen (mg/g)</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Normal control</td>
<td>30.8±3.45</td>
<td>4.33±0.26</td>
<td>18.99±0.65</td>
</tr>
<tr>
<td>II</td>
<td>Diabetic control</td>
<td>74.76±2.09##</td>
<td>12.83±1.93###</td>
<td>7.86±1.86###</td>
</tr>
<tr>
<td>III</td>
<td>Diabetic+Glibenclamide 2.5mg/kg</td>
<td>51.54±2.75</td>
<td>5.66±0.98**</td>
<td>16.43±0.57**</td>
</tr>
<tr>
<td>IV</td>
<td>Diabetic+ ENEE 200mg/kg</td>
<td>43.23±3.94*</td>
<td>8.23±0.76*</td>
<td>10.64±0.81*</td>
</tr>
<tr>
<td>V</td>
<td>Diabetic+ ENEE 400mg/kg</td>
<td>33.65±2.45***</td>
<td>6.60±0.45**</td>
<td>12.34±0.32**</td>
</tr>
</tbody>
</table>

Values shown in mean±S.D. Where, n (number of animals in each group) = 6. ENEE: *Euphorbia nerifolia* ethanolic extract. Data were analyzed using one-way analysis of variance (ANOVA) followed by Dunnet’s test. Group II (Diabetic control) was compared with Group I (Normal control). Group III, IV and V (Diabetic+glibenclamide 2.5 mg/kg, Diabetic+ENEE 200 mg/kg and Diabetic+ENEE 400 mg/kg respectively) were compared with Group II (Diabetic control).

*p < 0.05 vs diabetic control

**p < 0.01 vs diabetic control

###p < 0.01 vs Normal control
Figure 3.50 Effect of Euphorbia nerifolia ethanolic extract ENEE on Serum Insulin in High Fat Diet-streptozotocin induced type II diabetic rats. Values shown in mean±S.D. Where, n (number of animals in each group) = 6. ENEE: Euphorbia nerifolia ethanolic extract. Data were analyzed using one-way analysis of variance (ANOVA) followed by Dunnet’s test. Group II (Diabetic control) was compared with Group I (Normal control).Group III, IV and V (Diabetic+glibenclamide 2.5 mg/kg, Diabetic+ENEE 200 mg/kg and Diabetic+ENEE 400 mg/kg respectively) were compared with Group II (Diabetic control)

*p < 0.05 vs. diabetic control
**p < 0.01 vs. diabetic control
***p < 0.01 vs Normal control
Figure 3.51 Effect of *Euphorbia neriifolia* ethanolic extract ENEE on Hb1Ac in High Fat Diet-streptozotocin induced type II diabetic rats. Values shown in mean±S.D. Where, n (number of animals in each group) = 6. ENEE: *Euphorbia neriifolia* ethanolic extract.

Data were analyzed using one-way analysis of variance (ANOVA) followed by Dunnet’s test. Group II (Diabetic control) was compared with Group I (Normal control). Group III, IV and V (Diabetic+glibenclamide 2.5 mg/kg, Diabetic+ENEE 200 mg/kg and Diabetic+ENEE 400 mg/kg respectively) were compared with Group II (Diabetic control).

*p* < 0.05 vs. diabetic control

**p** < 0.01 vs. diabetic control

###p** < 0.001 vs Normal control
**Figure 3.52** Effect of *Euphorbia neriifolia* ethanolic extract ENEE on Liver Glycogen in High Fat Diet-streptozotocin induced type II diabetic rats. Values shown in mean±S.D. Where, n (number of animals in each group) = 6. ENEE: *Euphorbia neriifolia* ethanolic extract. Data were analyzed using one-way analysis of variance (ANOVA) followed by Dunnet’s test. Group II (Diabetic control) was compared with Group I (Normal control). Group III, IV and V (Diabetic+glibenclamide 2.5 mg/kg, Diabetic+ENEE 200 mg/kg and Diabetic+ENEE 400 mg/kg respectively) were compared with Group II (Diabetic control).

* *p < 0.05 vs. diabetic control

** *p < 0.01 vs. diabetic control

### #p < 0.001 vs Normal control
Effect of *Euphorbia neriifolia* Ethanolic extract (ENEE) on islets of pancreas

**Figure 3.53** Histological slide of normal control group showing normal architecture of islets of pancreas

**Figure 3.54** Histological slide of diabetic control group showing degeneration of islets of pancreas as compared to normal control group.
Figure 3.55 Histological slide of Diabetic+Glibenclamide 2.5 mg/kg group showing recovered islets of pancreas close to normal control group.

Figure 3.56 Histological slide of Diabetic+ENEE 200 mg/kg group showing recovery of islets of pancreas.
Figure 3.57 Histological slide of Diabetic+ENEE 400 mg/kg group showing recovered islets of pancreas as compared to diabetic control group and close to Glibenclamide treated group
3.2 DISCUSSION

The primary goal of this project work was to evaluate the antidiabetic and antihyperlipidemic activity of Euphorbia neriifolia Linn.

Type 2 diabetes mellitus is a chronic metabolic disorder that is primarily characterized by relative insulin deficiency, insulin resistance and increased serum glucose levels (hyperglycemia) which is also associated with hyperlipidemia, abdominal obesity, oxidative damage (Toledo et al., 2006) predominantly 90% peoples are suffering from Diabetes decreases the life span due to micro and macro vascular complications which are associated with morbidity and mortality. Retinopathy, nephropathy, arteriosclerosis and hypertension are some of these complications (Cooper et al., 2001).

So many allopathic antidiabetic contraindications and serious have marred their choice. Traditional medicinal plant have gain popularity Euphorbia Neriifolia is used traditionally in the treatment of diabetes in different rural areas of India. Euphorbia Neriifolia shows medicinal traditional pharmacological uses like antifungal, antibacterial, antiparasitic, antiviral, antidiabetic, antiarthritic, antioxidant anticonvulsant, radioprotective, wound healing, anticancer and spasmodic. (Sharma et al., 2011).

No reports have been found which describes the safety and toxicity profile of Euphorbia neriifolia ethanolic extract (ENEE) , hence it is extracts of leaves of Euphorbia neriifolia Linn. to expand benefits of the plant. During acute toxicity study it was found that single dose For acute toxicity study higher dose (400 mg/kg) and one twentieth of lethal dose was selected as lower dose (200 mg/kg). At selected doses ENEE did not produce any significant changes in relative organ body weight, haematological parameters (RBC, WBC, Platelet count, MCV, MCH, MCHC, Heamatocrit, granulocyte, monocytes and basophils) and biochemical parameters (TC, TB, TP, SGOT, SGPT, ALP and urea) which determines the functions of haemopoetic system and vital organs of the body like liver when treated groups compared with normal control groups. Blood parameters analysis is related to predict the study of animals (Hossain et al., 2012 & Kiran et al., 2012). Increase in levels of liver enzymes in blood is associated with functional and structural dysfunction of hepatocyte membrane damage (Burger et al., 2005).
Histopathological examinations of heart, liver and kidney showed normal architecture of cells without any fatty infiltration or necrosis in treated groups when compared with normal control group which gives sure (Figures 5.9, 5.10 & 5.11). *Euphorbia neriifolia* ethanolic extract ENEE

When ENEE (200 mg/kg and 400 mg/kg) hours. After 60 mins reduction in blood glucose levels groups and decline observed after 120 mins (Table 5.4) (Figures 5.12, 5.13, 5.14 & 5.15).

difference was observed in initial and final FBG of different groups showed significant indrease in study when compared with (Table 5.6) (Figures 5.18, 5.19, 5.20 & 5.21).

Hypoglycemic effect of ENEE might Other behind it might be from diet plays to blood.

This action is specifically beneficial to the patients of diabetes type 2. (Khan et al., 2003). Normally LPL (lipoprotein lipase enzyme) causes hydrolysis of triglycerides. In diabetes mellitus, failure of activation of LPL occurs which causes hypertriglyceridemia. TG (triglyceride) and cholesterol is lowered by content of dietary fibers (Anderson et al., 2000).Deficiency if insulin leads to various derangements in metabolic and regulatory processes. Increase in glucose in the blood itself is responsible for the higher FFAs. Higher free fatty acids level causes increase in coagulation, insulin resistance, endothelial dysfunction, lipid deposition in various organs and also affects the movement of cholesterol content. Diabetic rats showed significant elevation in TG (Triglycerides), TC group. to diabetic rats showed in TG, This effect might be due to stimulation of lipoprotein lipase enzyme and antioxidant effect of ENEE. Normalization of lipid levels gives beneficial effect on beta cells function hence, histopathological examination of pancreas was done herein.

Difference in body weights were observed in treated groups with ENEE which was less when compared with diabetic control groups. (gluconeogenesis due to proper glycemic control) (Table 5.5) (Figures 5.16 & 5.17).
Chapter 3

Results and discussion

Previous studies showed decrease in content of glycogen and the diabetes leads level were observed in treated groups, might be (Table 5.8) (Figure 5.29). Antidiabetic action of ENEE might be due to improvement in glycogenesis process (Maiti et al., 2004). Present study showed that increase in content of glycosylated hemoglobin (HbA1c) group. Increase in auto oxidative and non enzymatic is one of the possible mechanism linked with vascular complications and hyperglycemia. Treatment with the ENEE (200 mg/kg and 400 mg/kg) and Glibenclamide 2.5 mg/kg STZ produces destruction beta cells of pancreas. Histopathological micrographs of pancreas in diabetic control group showed severe destruction of beta cells of pancreas as compared to normal control group (Figures 5.30 & 5.31). Treatment with the ENEE showed starting of recovery and recovered beta cells of pancreas as compared to diabetic control group (Figures 5.32, 5.33 & 5.34).

reduction in blood glucose levels was observed after 60min in Glibenclamide 2.5 mg/kg and after 120 min in ENEE 400 mg/kg. ENEE 200 mg/kg did not produce any significant decrease in fasting blood glucose level. After 60 mins reduction in blood glucose levels were observed in treated groups when compared with normal control groups and decline observed after 120 mins (Table 5.9) Adipocity enhancement is linked which is (Bornstein et al., 2000). Leptin plays (Halaas et al., 1995 & Sandoval et al., 2003).

Body weights were recorded before and after the treatment in rats. Before treatment significant increase (Table 5.10) (Figure 5.39). After treatment significant above enzyme (in-vivo) causes decrease in blood glucose levels. (Rahman et al., 1994). Fasting blood glucose (FBG) levels were determined on day 0, 7,14 and 21 in normal control, diabetic control and treated groups . On day 0 of treatment significant elevation of FBG was observed in diabetic (HFD-STZ) rats as compared to normal control group. Administration of ENEE (200 mg/kg and 400 mg/kg) and Glibenclamide 2.5 mg/kg showed significant decrease in FBG gradually on day 7, 14 and 21 as compared to diabetic control group (Table 5.11) (Figure 5.41, 5.42, 5.43 and 5.44). consumption of
high fat or high. This may indicate the over activation of glycogen synthase in HFD-STZ diabetic rats.

Degeneration and deterioration of beta cells associated with impaired actions of the incretin hormones, which could be aiding of mass of beta cells and beta cells function. Glucagon like Peptide (GLP)-1 are high in concentration of beta cells of pancreas and have many functions like increase in beta cells proliferation, neogenesis and beta cells mass. Diabetic patients exert a shift towards an increased rate of beta cells apoptosis compared to the new proliferation of beta cells. (Garber et al., 2011 & Perfetti et al., 2000)

To understand the pathological damage to pancreas, histological photomicrographs of pancreas were taken in normal, diabetic and treated rats. Histological slides of pancreas in diabetic (HFD-STZ) control group showed significant damage to islets of pancreas as compared to normal control group (Figure 5.53 & 5.54). Histological slides of pancreas in treated groups like ENEE showed recovery in pancreatic beta cells and established normal architecture of islet of pancreas as compared to diabetic (HFD-STZ) control rats (Figure 5.55, 5.56 & 5.57). This action might be due to increase in activity of GLP-1 and GLP-1 receptor sensitivity which causes regeneration, proliferation and decrease in apoptosis rate of beta cells of pancreas.

In the present study Glibenclamide to compare potency of ENEE in the treatment of diabetes. Over all data showed that ENEE 200 mg/kg and 400 mg/kg dose dependent effect on FBG, lipid profile, insulin, liver glycogen and Glycated heamoglobin.