INTRODUCTION

Hepatotoxicity is a chronic health disease raised due to the altered diet practice and alcoholism. Diabetes mellitus is characterized by changes in protein metabolism by a negative nitrogen (N) balance and loss of nitrogen from most organ systems (Almdal and Viltstrup, 1987). Increased urea nitrogen production in diabetes may be accounted for by enhanced catabolism of both liver and plasma proteins (Jorda et al., 1982). Liver has an important role in metabolism (Lavoie et al., 2005) and also maintains the glucose level in the blood by storing the glucose as glycogen. Liver has involved in metabolic functions (carbohydrate, lipid, protein, mineral and vitamin metabolisms), excretory function (bile pigments, cholesterol), storage function (glycogen, vitamin A, D and B12 and trace element iron) and detoxification function (conversion of ammonia to urea).

The liver helps to maintain normal blood glucose concentration in the fasting and postprandial states. Loss of insulin effect on liver leads to glycogenolysis and an increase in hepatic glucose production. Abnormalities of triglyceride storage and lipolysis in insulin-sensitive tissues such as the liver are early manifestation of conditions characterized by insulin resistance and are detectable earlier than fasting hyperglycemia. The exact genetic, environmental and metabolic factors lead to the underlying insulin resistance is not fully understood (Lewis et al., 2002). Chronic hyperinsulinemia in animals cause insulin resistance in liver where there is a failure of insulin to signal an increase in insulin receptor substrate-2. Upregulation of sterol regulatory element-binding
protein 1c (SREBP-1c) also occurs, leads to increased lipogenesis (Shimomura et al., 2000). Despite down-regulation of the insulin receptor substrate-2-mediated insulin signaling pathway in insulin-resistant states, the up-regulation of SREBP-1c and subsequent simulation of de novo lipogenesis in the liver leads to increased intracellular availability of triglycerides promoting fatty liver. This also increases VLDL assembly and secretion (Lewis et al., 2002). Thus, hyper insulinenia might directly lead to hepatic insulin resistance with associated fatty changes.

The excess of free fatty acids found in the insulin-resistant state is known to be directly toxic to hepatocytes. Putative mechanisms include cell membrane disruption at high concentration, mitochondrial dysfunction, toxin formation and activation and inhibition of key steps in the regulation of metabolism (Neuschwander-Tetri and Caldwell, 2003). The elevation in ALT, a gluconeogenic enzyme whose gene transcription is suppressed by insulin, could indicate impairment in insulin signaling rather than purely hepatocyte injury (O’Brien and Granner, 1991). Individuals with type 2 diabetes have a higher incidence of liver function abnormalities than individuals who do not have diabetes (Elizabeth, 2005).

Oxygen free radical initiates glycation of proteins and inactivates enzymes in diabetic condition (Baynes, 1991). More oxidative stress affects the liver cells. Hence, the activity of liver is impaired and therefore it is very important that the drugs should have the protective effect on liver to maintain the normal metabolic activities.

The liver function test is the biochemical investigation which will help to detect the abnormalities and the extent of liver damage (Satyanarayana and Chakrapani, 2007). Liver function tests (LFTs) are commonly used in clinical practice to screen for
liver disease, to monitor the progression of known disease and to monitor the effects of potentially hepatotoxic drugs. The most common LFTs include the serum aminotransferases, alkaline phosphatase and bilirubin. Aminotransferases, such as alanine aminotransferase (ALT) and aspartate aminotransferase (AST) measure the concentration of intracellular hepatic enzymes that have leaked into the circulation and serve as a marker of hepatocyte injury. Alkaline phosphatase (ALP) and bilirubin act as markers of biliary function and cholestasis.

Tremendous advances made in allopathic medicine but there are no effective hepatoprotective drugs. Plant drugs are known to play a vital role in the management of liver diseases (Subramaniam and Pushpangadan, 1999). Hence, the present study was undertaken to assess the hepatoprotective effects of *N.crenulata* extracts on streptozotocin induced diabetic rats.

**MATERIALS AND METHODS**

As a biomarker potential of normal hepatic function some hepatic enzyme parameters like Alkaline phosphatase (ALP), Total liver and serum protein, Alanine transaminase (ALT), Aspartate transaminase (AST) and serum bilirubin were assessed in the following experiment to validate the hepatotoxicity

**Estimation of total protein (Lowry et al., 1951)**

Proteins react with Folin-Ciocalteau reagent to give a coloured complex. The colour so formed was due to the reaction of alkaline copper with protein and the reduction of phosphomolybdate by tyrosine and tryptophan present in the protein. The intensity of the colour depends on the amount of these aromatic aminoacids present.
Reagents

a. Alkaline copper reagent

Solution A - 2% sodium carbonate in 0.1 N sodium hydroxide.

Solution B - 0.5% copper sulphate in water.

Solution C - 1% sodium potassium tartarate in water.

50 ml of solution A was mixed with 0.5 ml of solution B and 1 ml of solution C just before use.

b. Folin’s phenol reagent: 100g of sodium tungstate, 24g sodium molybdate, 700 ml water, 50 ml 85% O-phosphoric acid and 100 ml concentrated HCl were taken in a 1500 ml round bottomed flask. The mixture was refluxed gently for 10 hours. To this 150g lithium sulphate, 50 ml water and a few drops of bromine were added and the mixture was boiled for 15 minutes to remove excess bromine. This was diluted to 1:2 with double distilled water before use.

c. Standard bovine serum albumin (BSA): A stock solution was prepared by dissolving 100mg of BSA in 100 ml water in a standard flask. Small quantities of sodium hydroxide were added to complete the dissolution of BSA. 10 ml of the stock was diluted to 100 ml to obtain a working standard of concentration 100 µg/ml.

Procedure

0.1ml of liver and serum tissue homogenate was diluted to 10 ml with saline. 1 ml of diluted tissue homogenate was taken and added 1 ml of 10% TCA. The mixture was centrifuged at 300 rpm for 15 minutes. The supernatant was discarded and residue was suspended in 1.0 ml of 0.5 N sodium hydroxide. From this 0.1 ml was taken and made upto 1 ml. to this 4.5 ml of alkaline copper reagent was added. The contents were allowed
to stand at 37°C for 10 minutes. Then 0.5 ml of Folin’s phenol reagent was added and mixed well. The tubes were shaken well and kept at the laboratory temperature for 30 minutes. A series of standards of concentration range from 20 to 100µg and a blank were processed similarly. The blue colour developed was read at 620 nm against a reagent blank in UV Spectrophotometer. Bovine serum albumin (Sigma Chemicals Co.,) was used to construct the standard graph. The protein content is expressed in mg/g wet weight of tissue and mg/dl in serum.

**Estimation of serum alkaline phosphatase (ALP) (King and Armstrong, 1988)**

Phosphatases are enzymes which catalyse the splitting up of phosphoric acid from monophosphoric esters. Alkaline phosphatase acts on sodium β-glycero phosphate at pH 10 to liberate inorganic phosphorous. This phosphorous was allowed to react with molybdic acid to give phosphomolybdate which in turn was reduced by 1-amino, 2-napthol, 4-sulphonic acid (ANSA) to molybdenum blue.

**Reagents**

Substrate-0.1 ml sodium β-glycero phosphate was dissolved in 100 ml sodium carbonate-bicarbonate buffer (0.1 m, pH 10)

- **a.** Sodium carbonate-bicarbonate buffer (0.1 m, pH 10)
- **b.** 10%TCA
- **c.** Ammonium molybdate-2.5% in 3 N sulphuric acid
- **d.** ANSA-500 mg ANSA was dissolved in a mixture of 195 ml of 15% sodium bisulphate and 5 ml of 20% sodium sulphite solution.
e. Standard phosphorous: 35.1 mg potassium dihydrogen phosphate was dissolved in 100 ml glass distilled water 10 ml of this solution was diluted to 100 ml to prepare a working standard containing 8 µg/ml phosphorous.

**Procedure**

To 1 ml buffered substrate added, 0.2 ml liver homogenate and incubated at 37 °C for one hour. The tubes were removed and 1 ml 10% TCA was added mixed and centrifuged for 10 minutes. To 1 ml supernatant, 1 ml ammonium molybdate and0.4 ml ANSA was added. The colour developed was read in a UV-spectrophotometer at 680 nm. A system devoid of enzyme served as control. A series of standard in the concentration 0.156 to 0.781 µmoles were also processed similarly and the enzyme activity was expressed as IU/L

**Activities of Aspartate Transaminase (AST) and Alanine Tranaminase (ALT)**

Activities of AST and ALT were assayed by the method of Reitmann and Frankel (1957). AST catalyses the transfer of an amino group from dL-aspartate (dL-ASP) to α-ketoglutарате (α-KG) to yield oxaloacetate and L-glutamate. ALT catalyses the transfer of an amino group from dL-alanine (dL-Ala) to α-ketoglutarate to yield pyruvate and L-glutamate. The liberated oxaloacetate and pyruvate reacts with 2, 4-dinitrophenyl hydrazine to form 2, 4-dinitrophenyl hydrazone, which was read at 540 nm.

\[
\text{L - ASP} + \alpha - \text{KG} \rightarrow \text{Oxaloacetic} + \text{L – Glutamate}
\]

**Reagents**

1. Phosphate buffer-0.1M, pH 7.5
2. Substrate
a) Aspartate transaminase: 0.30 g of dL-aspartic acid and 50 mg of α-keto glutaric acid were dissolved in 20 ml of phosphate buffer. The pH was adjusted to 7.5 with 1 N sodium hydroxide and made up to 100 ml with phosphate buffer.

b) Alanine transaminase: 5.0 g of dL-alanine and 20 mg of α-ketoglutaric acid were dissolved in 20 ml of phosphate buffer. The pH was adjusted to 7.5 with 1 N sodium hydroxide and made up to 100 ml with phosphate buffer.

3. DNPH: 200 mg of 2, 4-dinitrophenylhydrazine (DNPH) was dissolved in hot 1 N hydrochloric acid and made up to 100 ml with the same.

4. Aniline-citrate reagent: 50 g of citric acid were dissolved in 50 ml of distilled water and to this added an equal volume of redistilled aniline.

5. Sodium hydroxide-0.4 N.

6. Standard pyruvate solution: 12.5 mg of sodium pyruvate was dissolved in 100 ml of phosphate buffer.

**Procedure**

One ml of substrate was incubated for few minutes at 37 °C. Then 0.2 ml of liver homogenate was added and incubated for one hour in case of aspartate transaminase and 30 minutes for alanine transaminase, then added 2 drops of aniline-citrate reagent to both test and control. To the control, liver homogenate was added after incubation. The reaction was arrested using 1.0 ml of DNPH solution and the tubes were kept at room temperature for 20 minutes. 1.0 ml of 0.4 N sodium hydroxide was added to all the tubes. Sets of standards were also treated in the similar manner. The colour developed was read at 540 nm. Activities of aspartate and alanine transaminase were expressed as 1I/L.
**Estimation of serum Bilirubin**

Serum bilirubin was estimated by the method of Melloy and Evelyn (1937). Serum bilirubin was estimated by Vanden Bergh reaction. It was based on the formation of purple colored azobilirubin when bilirubin reacts with diazotized sulphanilic acid.

**Reagents**

1. Absolute methanol
2. Hydrochloric acid-1.5%
3. Diazo reagent

Solution A: 1.0g of sulphanilic acid was dissolved in 15 ml of conc. hydrochloric acid and made up to 1 litre with water.

Solution B: 0.5g of sodium nitrate was dissolved in water and made up to 100 ml. Freshly prepared before use by adding 0.3 ml of solution B to 10 ml of solution A.

standard bilirubin solution: 10mg/100 ml chloroform.

**Procedure**

0.2 ml of serum was diluted to 2.0 ml with distilled water in two tubes marked as test and blank. To the test, 0.5 ml of the diazo reagent and to the blank, 0.5 ml of 1.5% hydrochloric acid was added. Finally to both tubes, 2.5 ml of methanol was added and the tubes were kept at room temperature for 30 minutes. The color developed was read at 540 nm. For a standard curve, one in five dilutions of stock standard in methanol was made to obtain a solution containing 2 mg/ml. Serum bilirubin was expressed as mg/dl.
RESULTS

Hepatoprotective effect of *N. crenulata* in the present experiment comes up with promising results.

TOTAL PROTEIN LEVEL

Table.6 shows the status of total protein levels estimated in serum of control and diabetic induces rats.

In the present study diabetic induced hepatic damage caused severe decline in tissue protein level. STZ induced diabetic rats reflected a phenomenal decline in protein level of 5.53±0.58 mg/dl (Fig.10). At the same time *N. crenulata* extract treated diabetic groups exhibited a drastic increase in enzymatic and tissue protein level. *N. crenulata* methanolic extract treated animals showed 5.52±0.58mg/dl and 6.66±0.55 mg/dl of protein level. Acetone extract treated group exhibited 6.52±0.58 mg/dl which is relatively lesser than that of standard anti diabetic drug glibenclamide (Fig.20).

ALKALINE PHOSPHATASE AND ASPARTATE TRANSAMINASE

The levels of ALP and AST were found highly increase in diabetic rats 130.33±7.58 IU/L and 78.23±3.6 IU/L, while there was a significant lowering in ALP and AST in methanolic *N. crenulata* extract treated rats 81.33±4.83 IU/L and 55.09±3.28 IU/L respectively. Hence there was a lowering effect of ALT and ASP on *N. crenulata* treated groups (Table.6 and Fig. 21-22).

ALANINE TRANSAMINASE

Likewise ALT was observed more 31.75±2.82IU/L in streptozotocin treated diabetic rats as compared to that of normal control 21.10±2.02 IU/L. It was found to be declined level in *N. crenulata* extract treated rats 24.06±1.92 IU/L (Fig. 23).
BILIRUBIN LEVEL

Bilirubin contents increased in diabetic group up to a level of 1.15±0.08mg/dl and its level were well regulated in the diabetic group treated with N.crenulata extract treated which was found 0.78±0.19 mg/dl near to that of standard glibenclemide treated 0.74±0.10 mg/dl as shown in (Fig. 24).

Table. 6. Effect of N.crenulata extract on Serum total proteins, ALP, ALT, AST and billirubin of normal and diabetic rats.

<table>
<thead>
<tr>
<th>Groups</th>
<th>Total serum protein (mg/dl)</th>
<th>ALP (IU/L)</th>
<th>AST (IU/L)</th>
<th>ALT (IU/L)</th>
<th>Bilirubin (mg/dl)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>7.01±0.72a</td>
<td>75.45±4.85a</td>
<td>49.09±3.13a</td>
<td>21.10±2.02a</td>
<td>0.65±0.14a</td>
</tr>
<tr>
<td>Diabetic</td>
<td>5.53±0.58b</td>
<td>130.33±7.58d</td>
<td>78.23±3.6d</td>
<td>31.75±2.82c</td>
<td>1.15±0.08c</td>
</tr>
<tr>
<td>N.crenulata (M)/300</td>
<td>6.58±0.84a</td>
<td>90.86±3.56a</td>
<td>60.09±3.13a</td>
<td>25.14±2.12a</td>
<td>0.89±0.21a</td>
</tr>
<tr>
<td>N.crenulata (M)/600</td>
<td>6.66±0.55a</td>
<td>81.33±4.83a</td>
<td>55.09±3.28a</td>
<td>24.06±1.92a</td>
<td>0.78±0.19a</td>
</tr>
<tr>
<td>N.crenulata (A)/300</td>
<td>6.73±0.68a</td>
<td>110.13±7.58d</td>
<td>68.14±3.22a</td>
<td>28.44±3.92a</td>
<td>0.92±1.62a</td>
</tr>
<tr>
<td>N.crenulata (A)/600</td>
<td>5.82±0.58b</td>
<td>91.42±2.36a</td>
<td>61.55±2.13a</td>
<td>26.32±1.92a</td>
<td>0.83±2.61a</td>
</tr>
<tr>
<td>Glibenclamide</td>
<td>6.71±0.61a</td>
<td>80.08±5.08b</td>
<td>52.09±5.55b</td>
<td>22.89±2.12b</td>
<td>0.74±0.10a</td>
</tr>
</tbody>
</table>

Values are given as mean ± SD (n=6 rats)
Values that are not sharing a common superscript letter in the same column differ significantly at p<0.05
Fig. 20. Effect of *N. crenulata* extract on the Total Protein level of diabetic induced rats

Fig. 21. Effect of *N. crenulata* extract on Total ALP level of diabetic induced rats
Fig. 22. Effect of *N. crenulata* extract on Total AST level of diabetic induced rats

Fig. 23. Effect of *N. crenulata* extract on Total ALT level of diabetic induced rats
Fig. 24. Effect of *N. crenulata* extract on Total Bilirubin level of diabetic induced rats
TOTAL HEPATIC PROTEIN LEVEL

Table 7 shows the status of total hepatic protein, levels estimated in liver of control and diabetic induces rats.

STZ induced diabetic rats reflected a phenomenal decline in protein level of 4.41±0.71 mg/g (Fig. 25). *N. crenulata* methanolic extract treated animals showed 7.89±0.1 mg/g and 6.24±1.3 mg/g of protein level. Acetone extract treated group exhibited 6.22±0.4 mg/dl which is greater significant than drug treated group.

HEPATIC ALKALINE PHOSPHATASE AND ASPARTATE TRANSAMINASE

The levels of ALP and AST were found highly increase in diabetic rats 0.27±1.58 IU/L and 754.21±1.6 IU/g (Fig. 26&27). Methanolic *N. crenulata* extract treated rats exhibited significant enzyme restoration level of 0.24±0.1 IU/g and 639.4±0.1 IU/g respectively. Hence there was a lowering effect of ALT and ASP on *N. crenulata* treated groups.

HEPATIC ALANINE TRANSAMINASE

Likewise ALT was observed more 1014.21±1.2 IU/g in streptozotocin treated diabetic rats as compared to that of normal control 941.14±18.6 IU/g. It was found to be declined level in *N. crenulata* methanolic extract treated rats 914.5±0.4 IU/g (Fig. 28).
Table 7. Effect of *Naringi crenulata* on Liver protein, ALP/AST/ALT level.

<table>
<thead>
<tr>
<th>Groups</th>
<th>Total protein (mg/g)</th>
<th>ALP (IU/g)</th>
<th>AST (IU/g)</th>
<th>ALT (IU/g)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>8.30±0.4&lt;sup&gt;a&lt;/sup&gt;</td>
<td>0.23±1.1&lt;sup&gt;a&lt;/sup&gt;</td>
<td>625.14±1.4&lt;sup&gt;a&lt;/sup&gt;</td>
<td>941.14±18.6&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Diabetic</td>
<td>4.41±0.71&lt;sup&gt;b&lt;/sup&gt;</td>
<td>0.27±1.58&lt;sup&gt;cd&lt;/sup&gt;</td>
<td>754.21±1.6&lt;sup&gt;d&lt;/sup&gt;</td>
<td>1014.21±1.2&lt;sup&gt;e&lt;/sup&gt;</td>
</tr>
<tr>
<td><em>N.crenulata</em> (M)/300</td>
<td>6.24±1.3&lt;sup&gt;a&lt;/sup&gt;</td>
<td>0.25±1.0&lt;sup&gt;a&lt;/sup&gt;</td>
<td>689.1±0.1&lt;sup&gt;b&lt;/sup&gt;</td>
<td>989.4±0.1&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
<tr>
<td><em>N.crenulata</em> (M)/600</td>
<td>7.89±0.1&lt;sup&gt;a&lt;/sup&gt;</td>
<td>0.24±0.1&lt;sup&gt;a&lt;/sup&gt;</td>
<td>639.4±0.1&lt;sup&gt;b&lt;/sup&gt;</td>
<td>914.5±0.4&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td><em>N.crenulata</em> (A)/300</td>
<td>5.47±3.0&lt;sup&gt;a&lt;/sup&gt;</td>
<td>0.26±1.4&lt;sup&gt;b&lt;/sup&gt;</td>
<td>710.4±0.6&lt;sup&gt;a&lt;/sup&gt;</td>
<td>999.1±0.4&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td><em>N.crenulata</em> (A)/600</td>
<td>6.22±0.4&lt;sup&gt;a&lt;/sup&gt;</td>
<td>0.25±0&lt;sup&gt;b&lt;/sup&gt;</td>
<td>682.4±1.5&lt;sup&gt;a&lt;/sup&gt;</td>
<td>962.4±0.4&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Glibenclamide</td>
<td>8.1±0.4&lt;sup&gt;a&lt;/sup&gt;</td>
<td>0.22±1.7&lt;sup&gt;a&lt;/sup&gt;</td>
<td>624.77±1.1&lt;sup&gt;a&lt;/sup&gt;</td>
<td>940.4±1.2&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

Values are given as mean ± SD (n=6 rats)  
Values that are not sharing a common superscript letter in the same column differ significantly at p<0.05

![Effect of *N.crenulata* on Liver protein level](image)

Fig.25. Effect of *N.crenulata* extract on liver protein level of diabetic induced rats
Fig. 26. Effect of *N. crenulata* extract on liver ALP level of diabetic induced rats.

**Effect of *N. crenulata* on ALP level**

![Bar diagram showing ALP levels in different groups.](image)

- Control
- Diabetic
- *N. crenulata M/300*
- *N. crenulata M/600*
- *N. crenulata A/300*
- *N. crenulata A/600*
- Glibenclamide

ALP level IU/g

Fig. 27. Effect of *N. crenulata* extract on liver AST level of diabetic induced rats.

**Effect of *N. crenulata* on Liver AST level**

![Bar diagram showing AST levels in different groups.](image)

- Control
- Diabetic
- *N. crenulata M/300*
- *N. crenulata M/600*
- *N. crenulata A/300*
- *N. crenulata A/600*
- Glibenclamide

AST level IU/g
Fig. 28. Effect of *N. crenulata* extract on liver ALT level of diabetic induced rats

**DISCUSSION**

Oxidative stress is currently suggested as one of the mechanism underlying diabetes mellitus, which affects carbohydrate, lipid and protein metabolism. Several alterations in diabetic individuals are oxidative in nature or may depend on increased oxidative stress (Baynes *et al.*, 1991). Glycation (Vlassara *et al.*, 1994) and hyperglycaemic pseudohypoxia (Williamson and Lilo, 1993) can generate a redox imbalance inside the cells, especially in the liver (Gallou *et al.*, 1993). Assessment of liver function can be made by estimating the activities of serum AST and ALT (which are some of the enzymes originally present in higher concentrations in the cytoplasm), as well as levels of total and conjugated bilirubin. When there is hepatopathy, these enzymes leak into the blood stream conformity with the extent of liver damage (Plaa and Charbonneau, 1994; Venukumar and Latha, 2004). The elevated level of these marker enzymes observed in the diabetic rats in this present study correlated with the extensive liver damage induced by alloxan and the subsequent generation
of oxidative radicals and stress. However, the reduced concentrations of ALT and AST, as well as total and conjugated bilirubin following A-Polyherbal extract administration might be due, at least, in part to the presence of some antioxidant polyphenolic components in the extract (Raphael et al., 2002; Vauzour et al., 2010; Nijveldt et al., 2001). Thus, the tendency of these marker enzymes and biochemicals to return to a near-normal level when administered the methanolic extract of A-Polyherbal, comparable to the group administered glibenclamide (Table.2) strongly suggests a clear manifestation of the antihepatotoxic effect of *N.crenulata* formulation. Hence, these results demonstrate that *N.crenulata* extract possess strong anti-hepatotoxicity capacity for the alleviation and management of diabetes and related complications, including, oxidative stress, hyperglycemia, development of micro and macro vascular diabetic complications arising from elevated plasma lipids and decreased levels of antioxidant defense systems, as well as reduced erythrocyte survival.

The significantly boosted enzymatic antioxidant defense system including superoxide dismutases (SODs) and catalases (CATs) by administration of the *N.crenulata* extract can decompose superoxide and hydrogen peroxide in the cells, and hence *N.crenulata* extract boosts the main defense against oxidative injuries. Besides, the role of SOD in blocking pathways of hyperglycemic damage is well established (Nishikawa et al., 2000).

**SUMMARY AND CONCLUSION**

The present study investigated the possible protective effect of *N.crenulata* extracts on certain biochemical markers in streptozotocin (STZ)-induced diabetes in rats. STZ treatment caused a hyperglycemic state that led to various physiological and biochemical alterations. Activities of diagnostic marker enzymes including aspartate aminotransferase (AST), alanine amino transferase (ALT), alkaline phosphatase (ALP) and γ-glutamyl
transpeptidase (γ-GT), dismutase (SODs) and catalases (CATs) in plasma, liver and kidney were markedly altered in STZ diabetic rats. Oral administration of *N. crenulata* extract of methanolic and acetone extract (300 mg/kg and 600mg/kg bw) for 45 days restored all these hepatic biochemical parameters to near normal levels. Thus, the present results have shown that *N. crenulata* extract has the potent hepatoprotective effect and consequently may alleviate liver damage associated with STZ-induced diabetes in rats.