Chapter 7

Studies on the hepatoprotective activity of *Swertia petiolata* and *Swertia tetragona*

7.1. Introduction

Acute hepatic failure frequently develops upon exposure of the tissue to viruses or numerous chemical agents and represents a complex process, characterized by simultaneous activation of multiple deregulated pathways that culminate in the loss of cell membrane integrity and thus, the leakage of cellular constituents (Lee, 1993). The understanding and treatment of hepatic failure has developed rapidly over the last 50 years. Many environmental toxins cause liver injury to humans, and despite new advances in hepatology, the treatment for liver diseases does not resolve the problems caused by these toxins. Furthermore, despite the increasing need for agents to protect the liver from damage, modern medicine lacks a reliable liver protective drug. Therefore, there has been considerable interest in the role of complementary and alternative medicines for the treatment of liver diseases (Galati et al., 2005).

In the present study, we used two species of *Swertia* found in Kashmir valley: *Swertia petiolata* and *Swertia tetragona* to study the hepatoprotective potential. These plant species usually contain phytochemicals found in other hepatoprotective plant extracts, and their own unique constituents. It is not clear whether one, several or all of these components are active ingredients for liver protection. It is likely that some specific ingredients of the herb play a vital role in liver protection/treatment, thereby contributing to their therapeutic potential.

7.2. Experimental design

Female Wistar rats, having weight 240-250 gm were used in this experiment. For necrogenic study, rats were divided in different groups, each consisting of six animals. Group-I animals received only saline and served as control group. Group-II animals received single dose of thioacetamide (300 mg/kg body weight), and Group-III & IV animals received aqueous and hydro-alcoholic extracts of *S. petiolata*. Group-V & VI animals received aqueous and hydro-
alcoholic extracts of *S. tetragonolobus*. Group-VII & VIII animals received the extracts of *S. petiolata* and a single dose of thioacetamide (300 mg/kg body weight). Group-IX & X animals received the extracts of *S. tetragonolobus* plus a single dose of thioacetamide (300 mg/kg body weight). The plant extract was given orally at the dose levels of 1 gm/kg body weight in case of the aqueous extract and 200 mg/kg body weight in case of the hydro-alcoholic extracts. The extracts were given for five consecutive days, and 18 hours post treatment with thioacetamide, the animals were sacrificed.

Procedure of processing of the tissue and biochemical estimations has been provided in chapter-3. Briefly, after 18 hrs of thioacetamide treatment, blood was drawn by eye vein (retro-orbital) and allowed to clot. Serum was separated by centrifuging the clotted blood at 1,500 rpm for 10 min. Liver tissue was removed immediately after sacrificing the animals and washed in ice-cold saline, blotted and kept at -80°C for subsequent operations. Hepatic tissue was homogenized and subjected to sub cellular fractionation as per methodology described in chapter 3.

To evaluate the protective effect of herbs used in this study, serum and other biochemical parameters were investigated by standard procedure described in chapter 3. The results have been presented as Mean ± S.E.M. One-way analysis of variance (ANOVA) followed by student’s t-test was applied for statistical analysis, and p<0.05 was chosen as the level of significance.

### 7.3. Results

#### 7.3.1. Morphological findings

Morphological changes were studied in the texture of vital organs as liver, spleen, kidneys, heart, and stomach with the naked eye. These organs were then weighed to assess any change in their weights. As is evident from Figure 7.1, thioacetamide caused significant reduction in the body weight of animals (average wt = 222.5 ± 2.5 p=0.007), whereas the extracts alone and in combination with thioacetamide did not cause any significant variation in the average weight of animals, which varied between 240-250 gms.
No significant change in the average weight of livers was found in any of the group (Figure 7.2). The herb treated groups also did not show any significant variation; neither did the groups treated with the herbal extract and thioacetamide. The vital organs such as heart and spleen did not show any apparent changes, while kidneys showed a significant increase in weight (Figures 7.3, 7.5 & 7.6). Also, the stomachs of herbs plus thioacetamide treated rats were bulged which could be well distinguished with other groups. There was significant increase in the average wt. of stomachs in the herb treated groups (Figure 7.4)

7.3.2. Histopathological observation

Gross morphology of the organs (Figure 7.7) and histology of the liver from control and treated rats was studied. Necrosis was found to be considerably low in the group of rats pretreated with the extracts: *Swerlia tetragona* (Figure 7.8) and *Swerlia petiolata* (Figure 7.9). Control group showed normal lobular architecture, while the necrotic liver tissue showed areas of necrosis and haemorrage. The cells were devoid of morphology.

7.3.3. Biochemical investigations

To study the effect of extracts on the liver, serum aminotransferases (ALT, AST), alkaline phosphatase (ALP), and gamma glutamyl transpeptidase (GGT) activities were measured in different groups in order to assess the damage induced by thioacetamide. As evident from Figures (7.10, 7.11, 7.12, and 7.13), administration of thioacetamide caused significant increase in these enzyme levels, which were decreased by *swertia* extracts.

Hepatic lipid peroxidation was measured in terms of the hepatic malondialdehyde (MDA) levels in the tissue. MDA is an index of oxidative stress and increased significantly after the induction of liver necrosis and decreased in extract treated rats (Figure 7.14). Marked reduction in the levels of reduced glutathione were observed in necrotic group and increased in extract treated experimental animals (Figure 7.15). The Mo–Fe–S flavin enzyme xanthine oxidase plays an important role in the metabolism of drugs and toxins. Figure 7.16 shows that XO activity increased significantly in TAA, and decreased in extract pretreated groups.
Glutathione reductase (Figure 7.17), glutathione peroxidase (Figure 7.18), and catalase (Figure 7.19) were decreased by thioacetamide, and normalized by the extracts. Results of the analysis of G6PD and SOD also decreased in TAA groups and normalized by extracts are shown in (Figure 7.20-7.21).
Figure 7.1: Effect of the Swertia extracts on the average body weight of rats. Data represents mean ± S.E.M \((n=6)\). *\( p < 0.05 \) which are statistically significant compared to the necrotic group (TAA). NS: group receiving normal saline and serving as normal control group; S.P (H/A) & (Aq): *Swertia petiolata* hydro-alcoholic and aqueous extracts; S.T (H/A) & (Aq): *Swertia tetragona* hydro-alcoholic and aqueous extracts; TAA: necrotic group received thioacetamide; S.P & S.T + TAA: respective herbal extracts plus thioacetamide.
Figure 7.2: Effect of the Swertia extracts on the average Liver weight of rats. Data represents mean ± S.E.M (n=6). *p <0.05 which are statistically significant compared to the necrotic group (TAA). NS: group receiving normal saline and serving as normal control group; S.P (H/A) & (Aq): Swertia petiolata, hydro-alcoholic and aqueous extracts; S.T (H/A) & (Aq): Swertia tetragona hydro-alcoholic and aqueous extracts; TAA: necrotic group received thioacetamide; S.P & S.T + TAA: respective herbal extracts plus thioacetamide.
Figure 7.3: Effect of the Swertia extracts on the average kidney weight of rats. Data represents mean ± S.E.M (n=6). Significant p < 0.05 values were found in pretreated necrotic animals when compared with necrotic group (TAA). NS: group receiving normal saline and serving as normal control group; S.P (H/A) & (Aq): Swertia petiolata, hydro-alcoholic and aqueous extracts; S.T (H/A) & (Aq): Swertia tetragona hydro-alcoholic and aqueous extracts; TAA: necrotic group received thioacetamide; S.P & S.T + TAA: respective herbal extracts plus thioacetamide.
Figure 7.4: Effect of the Swertia extracts on the average stomach weight of rats. Data represents mean ± S.E.M (n=6). *p <0.05 which are statistically significant compared to the necrotic group (TAA). NS: group receiving normal saline and serving as normal control group; S.P (H/A) & (Aq): Swertia petiolata, hydro-alcoholic and aqueous extracts; S.T (H/A) & (Aq): Swertia tetragona hydro-alcoholic and aqueous extracts; TAA: necrotic group received thioacetamide; S.P & S.T + TAA: respective herbal extracts plus thioacetamide.
Figure 7.5: Effect of the Swertia extracts on the average Spleen weight of rats. Data represents mean ± S.E.M (n=6). *p <0.05 which are statistically significant compared to the necrotic group (TAA). NS: group receiving normal saline and serving as normal control group; S.P (H/A) & (Aq): *Swertia petiolata*, hydro-alcoholic and aqueous extracts; S.T (H/A) & (Aq): *Swertia tetragona* hydro-alcoholic and aqueous extracts; TAA: necrotic group received thioacetamide; S.P & S.T + TAA: respective herbal extracts plus thioacetamide.
Figure 7.6: Effect of the Swertia extracts on the average heart weight of rats. Data represents mean ± S.E.M (n=6). *p <0.05 which are statistically significant compared to the necrotic group (TAA). NS: group receiving normal saline and serving as normal control group; S.P (H/A) & (Aq): Swertia petiolata, hydro-alcoholic and aqueous extracts; S.T (H/A) & (Aq): Swertia tetragona hydro-alcoholic and aqueous extracts; TAA: necrotic group received thioacetamide; S.P & S.T + TAA: respective herbal extracts plus thioacetamide.
Figure 7.7: Excised vital organs of experimental rats a), livers of normal control animals b), necrotic group c), necrotic group pretreated with extracts d). While figure e), and f) show the experimental animals during study.
Figure 7.8: Summary of histopathological analysis of experimental rats. Normal control group received saline solution showing normal hepatocytes a), necrotic group showing area of necrosis and sinusoidal dilatation b). There are no changes in animals receiving aqueous extract c) and hydro-alcoholic extract e), while necrotic animals that received aqueous extract d) and hydro-alcoholic extract f) of *Swertia tetragona* showed congested vessels.
Figure 7.9: Summary of histopathological analysis of experimental rats. Normal control group received saline solution showing normal hepatocytes a), necrotic group showing area of necrosis and sinusoidal dilatation b). There are no changes in animals receiving aqueous extract c) and hydro-alcoholic extract e), while necrotic animals that received aqueous extract d) and hydro-alcoholic extract f) of *Swertia petiolata* showed sinusoidal dilatation.
Figure 7.10: Effect of two *Swertia* species on AST activity in rat model of liver necrosis. Data represents mean ± S.E.M (n=6). *p <0.05* which are statistically significant compared to the necrotic group (TAA). Group I: group receiving normal saline and serving as normal control group; II & III: *Swertia petiolata*, hydro-alcoholic and aqueous extracts; IV & V: *Swertia tetragona* hydro-alcoholic and aqueous extracts; VI: necrotic group received thioacetamide; VII & VIII: Necrotic groups pretreated with *Swertia petiolata*, hydro-alcoholic and aqueous extracts; IX & X: Necrotic groups pretreated with *Swertia tetragona*, hydro-alcoholic and aqueous extracts. Results are expressed in units/ml.
Figure 7.11: Effect of two *Swertia* species on ALT activity in rat model of liver necrosis. Data represents mean ± S.E.M (n=6). *p <0.05 which are statistically significant compared to the necrotic group (TAA). Group I: group receiving normal saline and serving as normal control group; II & III: *Swertia petiolata*, hydro-alcoholic and aqueous extracts; IV & V: *Swertia tetragona* hydro-alcoholic and aqueous extracts; VI: necrotic group received thioacetamide; VII & VIII: Necrotic groups pretreated with *Swertia petiolata*, hydro-alcoholic and aqueous extracts; IX & X: Necrotic groups pretreated with *Swertia tetragona*, hydro-alcoholic and aqueous extracts. Results are expressed in units/ml.
Figure 7.12: Effect of two *Swertia* species on serum alkaline phosphatase activity in rat model of liver necrosis. Data represents mean ± S.E.M (n=6). *p < 0.05 which are statistically significant compared to the necrotic group (TAA). Group I: group receiving normal saline and serving as normal control group; II & III: *Swertia petiolata*, hydro-alcoholic and aqueous extracts; IV & V: *Swertia tetragona* hydro-alcoholic and aqueous extracts; VI: necrotic group received thioacetamide; VII & VIII: Necrotic groups pretreated with *Swertia petiolata*, hydro-alcoholic and aqueous extracts; IX & X: Necrotic groups pretreated with *Swertia tetragona*, hydro-alcoholic and aqueous extracts. Results are expressed in Eq. units/ml.
Figure 7.13: Effect of two *Swertia* species on gamma glutamyl transpeptidase activity in rat model of liver necrosis. Data represents mean ± S.E.M (n=6). *p <0.05 which are statistically significant compared to the necrotic group (TAA). Group I: group receiving normal saline and serving as normal control group; II & III: *Swertia petiolata*, hydro-alcoholic and aqueous extracts; IV & V: *Swertia tetragona* hydro-alcoholic and aqueous extracts; VI: necrotic group received thioacetamide; VII & VIII: Necrotic groups pretreated with *Swertia petiolata*, hydro-alcoholic and aqueous extracts; IX & X: Necrotic groups pretreated with *Swertia tetragona*, hydro-alcoholic and aqueous extracts. Results are expressed in nmole p-nitroanilide/mg protein.
Figure 7.14: Effect of two *Swertia* species on lipid peroxidation activity in rat model of liver necrosis. Data represents mean ± S.E.M (n=6). *p < 0.05 which are statistically significant compared to the necrotic group (TAA). Group I: group receiving normal saline and serving as normal control group; II & III: *Swertia petiolata*, hydro-alcoholic and aqueous extracts; IV & V: *Swertia tetragona* hydro-alcoholic and aqueous extracts; VI: necrotic group received thioacetamide; VII & VIII: Necrotic groups pretreated with *Swertia petiolata*, hydro-alcoholic and aqueous extracts; IX & X: Necrotic groups pretreated with *Swertia tetragona*, hydro-alcoholic and aqueous extracts. Results are expressed in nmole of MDA/mg protein.
Figure 7.15: Effect of two Swertia species on reduced glutathione activity in rat model of liver necrosis. Data represents mean ± S.E.M (n=6). *p <0.05 which are statistically significant compared to the necrotic group (TAA). Group I: group receiving normal saline and serving as normal control group; II & III: Swertia petiolata, hydro-alcoholic and aqueous extracts; IV & V: Swertia tetragona hydro-alcoholic and aqueous extracts; VI: necrotic group received thioacetamide; VII & VIII: Necrotic groups pretreated with Swertia petiolata, hydro-alcoholic and aqueous extracts; IX & X: Necrotic groups pretreated with Swertia tetragona, hydro-alcoholic and aqueous extracts. Results are expressed in μmole of GSH/g tissue.
Figure 7.16: Effect of extract treatment on xanthine oxidase. Pretreatment with the extracts could significantly decrease the elevated levels of xanthine oxidase in the necrotic rats. Data represents mean ± S.E.M (n=6). p <0.05, which are statistically significant compared to the necrotic group (TAA). Group I: group receiving normal saline and serving as normal control group; II & III: *Swertia petiolata*, hydro-alcoholic and aqueous extracts; IV & V: *Swertia tetragona* hydro-alcoholic and aqueous extracts; VI: necrotic group received thioacetamide; VII & VIII: Necrotic groups pretreated with *Swertia petiolata*, hydro-alcoholic and aqueous extracts; IX & X: Necrotic groups pretreated with *Swertia tetragona*, hydro-alcoholic and aqueous extracts. Results are expressed in μmole of uric acid/mg protein.
Figure 7.17: Effect of two Swertia species on glutathione peroxidase activity in rat model of liver necrosis. Data represents mean ± S.E.M (n=6). *p <0.05 which are statistically significant compared to the necrotic group (TAA). Group I: group receiving normal saline and serving as normal control group; II & III: Swertia petiolata, hydro-alcoholic and aqueous extracts; IV & V: Swertia tetragona hydro-alcoholic and aqueous extracts; VI: necrotic group received thioacetamide; VII & VIII: Necrotic groups pretreated with Swertia petiolata, hydro-alcoholic and aqueous extracts; IX & X: Necrotic groups pretreated with Swertia tetragona, hydro-alcoholic and aqueous extracts. Results are expressed in nmole of NADPH oxidized/min/mg protein.
**Figure 7.18:** Effect of two *Swertia* species on glutathione reductase activity in rat model of liver necrosis. Data represents mean ± S.E.M (n=6). *p <0.05* which are statistically significant compared to the necrotic group (TAA). Group I: group receiving normal saline and serving as normal control group; II & III: *Swertia petiolata*, hydro-alcoholic and aqueous extracts; IV & V: *Swertia tetragona* hydro-alcoholic and aqueous extracts; VI: necrotic group received thioacetamide; VII & VIII: Necrotic groups pretreated with *Swertia petiolata*, hydro-alcoholic and aqueous extracts; IX & X: Necrotic groups pretreated with *Swertia tetragona*, hydro-alcoholic and aqueous extracts. Results are expressed in nmole of NADPH oxidized/min/mg protein.
Figure 7.19: Effect of two Swertia species on catalase activity in rat model of liver necrosis. Data represents mean ± S.E.M (n=6). *p <0.05 which are statistically significant compared to the necrotic group (TAA). Group I: group receiving normal saline and serving as normal control group; II & III: Swertia petiolata, hydro-alcoholic and aqueous extracts; IV & V: Swertia tetragona hydro-alcoholic and aqueous extracts; VI: necrotic group received thioacetamide; VII & VIII: Necrotic groups pretreated with Swertia petiolata, hydro-alcoholic and aqueous extracts; IX & X: Necrotic groups pretreated with Swertia tetragona, hydro-alcoholic and aqueous extracts. Results are expressed in n mole of H₂O₂ consumed/min/mg protein.
Figure 7.20: Effect of two *Swertia* species on glucose-6-phosphate dehydrogenase activity in rat model of liver necrosis. Data represents mean ± S.E.M (n=6). *p <0.05 which are statistically significant compared to the necrotic group (TAA). Group I: group receiving normal saline and serving as normal control group; II & III: *Swertia petiolata*, hydro-alcoholic and aqueous extracts; IV & V: *Swertia tetragona* hydro-alcoholic and aqueous extracts; VI: necrotic group received thioacetamide; VII & VIII: Necrotic groups pretreated with *Swertia petiolata*, hydro-alcoholic and aqueous extracts; IX & X: Necrotic groups pretreated with *Swertia tetragona*, hydro-alcoholic and aqueous extracts. Results are expressed in n mole of NADP reduced/min/mg protein.
Figure 7.21: Effect of two *Swertia* species on superoxide dismutase activity in rat model of liver necrosis. Data represents mean ± S.E.M (n=6). *p <0.05 which are statistically significant compared to the necrotic group (TAA). Group I: group receiving normal saline and serving as normal control group; II & III: *Swertia petiolata*, hydro-alcoholic and aqueous extracts; IV & V: *Swertia tetragona* hydro-alcoholic and aqueous extracts; VI: necrotic group received thioacetamide; VII & VIII: Necrotic groups pretreated with *Swertia petiolata*, hydro-alcoholic and aqueous extracts; IX & X: Necrotic groups pretreated with *Swertia tetragona*, hydro-alcoholic and aqueous extracts. Results are expressed in units/mg protein.
7.4. Discussion

Hepatic injury was induced by using intra-peritoneal injection of thioacetamide, which is known to cause hepatotoxicity in experimental rats and can produce hepatic necrosis (Ali et al., 2008). Thioacetamide induced hepatic injury is an experimental model widely used in hepatoprotective drug screening. This study shows, pre treatment of medicinal plants can prevent the acute hepatic damage induced by TAA. TAA is a thiono-sulfur-containing compound, which has liver-damaging and carcinogenic effects. Shortly after administration, it undergoes extensive metabolism by the mixed function oxidase system to acetamide, which has no liver necrotising properties, and thioacetamide-S-oxide. Thioacetamide-S-oxide is metabolized by cytochrome P-450 mono-oxygenases to further compounds, including the very reactive compound, thioacetamide-S-dioxide. The binding of this metabolite to tissue macromolecules may be responsible for hepatic necrosis, induction of apoptosis, perturbation of mitochondrial activity, and elevation of serum enzyme levels. Numerous studies in rats indicated the involvement of oxidative stress in the etiology of TAA-induced liver damage (Bruck et al., 2002).

In the present study, a model of liver necrosis was produced by thioacetamide to evaluate the efficacy of our selected medicinal plants of *Swertia*. *Swertia tetragona* and *Swertia petiolata* which show hepatoprotective activity. In this regard, morphological and biochemical analyses were studied. In the morphological characteristics, there were no apparent pharmacological changes in the liver of rats treated with *Swertia* extracts; neither any other organ (heart, kidneys, and spleen) showed any apparent change. However, the stomachs of the *Swertia* treated animals showed bulginess, which could be due to the laxative action of the extracts.

Experimental animals treated with thioacetamide alone developed significant hepatocellular damage as was evident from a significant increase in the serum levels of AST, ALT, ALP, and GGT when compared with control (Fontana et al., 1996). In the figures (7.10, 7.11, 7.12, and 7.13), the rise in serum levels of AST, ALT, ALP and GGT has been attributed to the damaged structural integrity of liver (Chenoweth & Hake, 1962), because these are cytoplasmic in location and are released into the circulation after cellular damage (Kew, 2000). The results indicate towards the protective role of extracts in liver necrosis. The extracts when
given prophylactically could effectively prevent the liver injury induced by thioacetamide, as evidenced by decrease in the serum levels of ALT, AST, GGT, and ALP. Among the various phosphatases, ALP has attained much attention because of its location in the plasma membrane and possible role in active transport (Mehendale et al., 1994).

Oxidative stress and its consequent lipid peroxidation have been considered involved in hepatic injury. Studies on thioacetamide-induced liver injury have demonstrated the generation of reactive oxygen species (ROS) and initiation of peroxidation reactions (Ali et al., 2001). The ROS either extract a hydrogen atom from unsaturated membrane lipids to initiate lipid peroxidation or reacts with the sulfhydryl compounds, triggering a chain of peroxidation reactions. These changes lead to cell injury. This study on *Swertia* extract demonstrates that the extract could inhibit the injury induced by thioacetamide in rat. Measurement of lipid peroxidation (Figure 7.14) and glutathione (reduced form, GSH, Figure 7.15) provided a clear indication towards the antioxidant role of the extract. Lipid peroxidation represents a degradative process in the tissue arising from the production and propagation of free radical reactions primarily involving membrane polyunsaturated fatty acids and the production of end products such as malondialdehyde and 4-hydroxynonenal (Poli, 2000). Data have been reported showing a progressive reduction in the activity level of lipid peroxidation and elevated level of reduced glutathione in necrotic animals (Bruck et al., 2001). In this study, we reported similar changes in the model, pretreatment of herbal extracts reversed this effect.

To evaluate the involvement of oxygen radicals in hepatic damage and potential defence of herbal extracts, we have measured activity of xanthine oxidase (Figure 7.16). In this study, TAA induced necrosis provokes xanthine oxidase activity which produces oxidative stress by generating ROS, indicating its role in this type of liver injury. Significant decrease of xanthine oxidase activity was observed in pretreated rats with herbal extracts followed by thioacetamide, which is in accordance with results of Pawa and Ali (2004).

In addition to hepatic glutathione level, activity of enzymes involved in the glutathione redox cycle such as glutathione reductase was also determined (Figure 7.17). While in necrotic rats it decreased markedly, in the test extracts treated animals the activity increased and reached

*Ph.D Thesis* 157 *University of Kashmir*
almost up to normal value. The peroxide metabolizing enzyme, glutathione peroxidase, showed a similar pattern suggesting the generation of peroxides in hepatic injury (Figure 7.18). Catalase is known to catalyze the removal of hydrogen peroxide and therefore its upregulation may provide a compensatory or adaptive response against elevation in hydrogen peroxide (Pillai and Gupta, 2005) (Figure 7.19). Over-production of ROS normally induces oxidative stress unless it was scavenged with endogenous antioxidants. Thus, overproduction of ROS could be attributed to the depletion of antioxidants.

Glucose-6-phosphate dehydrogenase being a cytoplasmic enzyme, its main metabolic role is the production of NADPH in the monophosphate pathway and the defense against oxidizing agents. The results indicate a significant increase in glucose-6-phosphate dehydrogenase activity in necrotic groups, which are pretreated with the extracts (Figure 7.20).

The antioxidant defense system is composed mainly of three enzymes such as superoxide dismutase, catalase, and glutathione peroxidase. The superoxide dismutases convert superoxide anion into H$_2$O$_2$ and O$_2$. Catalase catalyzes the dismutation of H$_2$O$_2$, forming neutral products as O$_2$ and H$_2$O. Glutathione peroxidase catalyzes the reductive destruction of hydrogen and lipid hydroperoxides, using glutathione as an electron donor (Harris, 1992). A significant decline in the level of liver superoxide dismutase (Figure 7.21) in necrotic rats was observed in this study.

The findings suggest that the extracts can protect the liver injury (necrosis), which is produced by the excessive production of ROS. However, the mechanism by which this effect is produced is not very clear. The effect appears to be due to the ability of extracts to somehow strengthen the antioxidant status of tissue, which is evident from results.
7.5. **Conclusion**

It can thus be concluded that the two *Swertia* species under investigation show good hepatoprotective activity against thioacetamide induced liver injury. Biochemical evidences as normalization of serum parameters, oxidative stress parameters, free radical scavengers, phase II drug metabolizing enzymes, glutathione metabolizing enzymes, and histopathological evidences provide support to these findings.