Chapter VI

SUMMARY

AND

CONCLUSIONS
The present study was undertaken to evaluate the biochemical efficacy of *Tribulus terrestris* in lowering hyperoxaluria. The salient findings of this study are summarized as follows:

1. Hyperoxaluria was induced in the male adult rats by feeding sodium glycolate (100 mg/100 BW/day) for 30-days as described by Murthy *et al.*, (1981).

2. Three indigenous drugs, available in this region, i.e. Achyranthus aspera, Crataeva nurvala and *Tribulus terrestris* were evaluated for their beneficial effect in lowering hyperoxaluria.

3. Among these three drugs, *T. terrestris* showed the maximum efficacy (50%) in terms of lowering hyperoxaluria, whereas C. nurvala and A. aspera lowered the hyperoxaluria by 30% and 10% respectively.

4. Efficacy of *T. terrestris* was monitored in hyperoxaluric conditions by feeding the drug extract from 0-day and from 15th day of sodium glycolate feeding.

5. Urinary excretion of calcium, phosphorus and uric acid was unaltered in all the groups.

6. The normal rat urine exhibited a significant inhibitory activity (I.A.) towards calcium oxalate monohydrate crystal growth in a metastable solution of calcium chloride and $^{14}$C-sodium oxalate. The urinary I.A was unaltered in *T. terrestris* fed group. The urinary I.A of sodium glycolate fed animals was significantly low as compared to control group. Administration of *T. terrestris* alongwith sodium glycolate from 0-day resulted in an increased I.A. as compared to the sodium glycolate fed group, whereas *T. terrestris* feeding from 15th day could not increase the mean I.A.

7. Sodium glycolate feeding resulted in significant increase in the activities of oxalate biosynthesizing enzymes viz. GAO, GAD and LDH in the liver as compared to control animals. *T. terrestris* feeding (0-day) alongwith
sodium glycolate caused a significant decrease in both GAO and GAD, but LDH remained unaltered as compared to sodium glycolate fed animals. *T. terrestris* (15-day) also caused a decrease in GAO and GAD levels but to a lesser extent while LDH remained unaltered.

8. Kidney LDH was significantly decreased by feeding sodium glycolate but *T. terrestris* administration alongwith sodium glycolate (either from 0-day or 15- day) resulted in an elevation of kidney LDH.

9. Isoenzyme distribution pattern of kidney LDH showed a significant reduction in LDH5 isoenzyme by sodium glycolate, while *T. terrestris* alone and with sodium glycolate showed an opposite effect to sodium glycolate i.e. LDH5 isoenzyme was increased. The isoenzyme LDH1 remained unaltered in all the groups.

10. Renal uptake of oxalate by kidney cortical brush border membrane vesicles revealed a biphasic transport mechanism (a saturable carrier mediated mechanism at extravesicular oxalate concentrations from 0.1 to 0.8 mM and a nonsaturated passive diffusion at 0.1-1.0 mM) in all groups.

11. The rate of oxalate uptake was significantly enhanced in sodium glycolate fed group as compared to normal. *T. terrestris* feeding from 0-day simultaneously with sodium glycolate resulted in decreased reabsorption of oxalate by renal BBM. The oxalate uptake was also found to be low in sodium glycolate +*T. terrestris* (15-day) fed group but not at all the concentrations tested.

12. Lipid composition of renal BBM in sodium glycolate fed group showed a decrease in cholesterol content and an increase in phospholipid content, thus decreasing the cholesterol/phospholipid ratio, as compared to control group. *T. terrestris* feeding from 0-day revealed an increased cholesterol/phospholipid ratio as compared to sodium glycolate fed group.
Total lipid, glycolipid and triglyceride contents remained unaltered in these groups.

Among the individual phospholipids lysophospholipids and phosphatidyl ethanolamine contents were unchanged in sodium glycolate as well as *T. terrestris* fed groups. A significant decrease in phosphatidyle serine + phosphatidyl inositol (PS + PI) and an increase in phosphatidyl choline (PC) contents were observed in sodium glycolate fed group whereas a reverse effect i.e. increase in PS + PI and decrease in PC content, has been seen in *T. terrestris* fed group.

From the above observations, it can be concluded that sodium glycolate feeding in rats for 30 days leads to increased oxalate biosynthesis, which is mediated by increased hepatic GAO, GAD and LDH activities and by increased reabsorption of oxalate by kidneys resulting in hyperoxaluria. *T. terrestris* shows a beneficial effect in lowering hyperoxaluria through its action on endogenous oxalate biosynthesizing enzymes as well as through renal membrane lipid composition, resulting in decreased reabsorption and excretion of oxalate by the kidneys. However, oxalate lowering effect is more when it is fed from 0-day simultaneously with sodium glycolate, rather than fed after 15 day pretreatment of sodium glycolate, thereby indicating a prophylactic efficacy of the drug in stone disease. Further, studies are required to characterize the active component of *T. terrestris* which is responsible for observed changes and enables it to lower hyperoxaluria.