SUMMARY AND CONCLUSIONS
Liver diseases have serious adverse effects on health. Allopathic medicines prescribed for liver diseases have several side effects and hence modern medicine is still short of reliable and effective drugs for protection and repair of liver. There are many herbs being used to treat various liver disorders. In India, traditional medicine system and ethno-medical practices rely on several medicinal plants and their formulations to treat liver disorders.

The objective of the present study was to assess hepatoprotective activity of ayurvedic formulation and nutritional supplements that can potentially be used as hepatoprotective agent having less/no side effects. Based on the literature review, medicinal values and availability, three different forms of *Tinospora* (satwa of stem) and omega-3 fatty acids (Flax oil and fish oil) were selected to evaluate their hepatoprotective potential.

The current section summarizes organoleptic characteristics and nutritional analysis of satwa forms three *Tinospora* forms and also hepatoprotective activity of satwa from three forms of *Tinospora* as well as that of flax oil and fish oil against acetaminophen and alcohol induced hepatotoxicity.

**Methodology**

The different organoleptic characteristics and nutritional parameters like protein, carbohydrates, lipid, starch, crude fiber, and ash were analyzed from satwa, from three different forms of *Tinospora*. The hepatoprotective activity of satwa from three different forms of *Tinospora* and omega-3 fatty acids (Flax oil and fish oil) was studied by employing acetaminophen and alcohol induced hepatotoxicity in animal models. The biochemical parameters like serum SGPT, SGOT, ALP, bilirubin, total cholesterol, triglycerides, HDL cholesterol and LDL cholesterol, Hepatic antioxidant parameters like catalase, SOD, MDA, GSH, total protein and functional parameters like histopathology of liver, were studied. Further study on modulation of expression of the genes involved in lipid metabolism and inflammation was also carried out. As per the current study, maximum yield of satwa was obtained in *T. sinensis* and *Neem-giloe*. *T. sinensis* and *Neem-giloe* are rich sources of nutritional contents. The contents of lipid, ash, and carbohydrates are found to be greater in *Neem-giloe* than
*T. cordifolia* and *T. sinensis*. Protein, starch and crude fiber content is found higher in *T. sinensis* as compared with *T. cordifolia* and Neem-giloe.

Results of this study reported significant increase in serum levels of liver function tests (SGOT, SGPT, ALP, and bilirubin) and lipid profile (Total cholesterol, LDL cholesterol, VLDL, Triglycerides and decrease in HDL cholesterol levels) in the groups treated with acetaminophen and alcohol indicating induction of hepatotoxicity. It further indicated abnormal integrity of hepatocytes, resulting into liver damage. This resulted into significant elevation of lipid peroxidation with simultaneous decline in GSH, CAT, SOD and total protein levels in liver tissue.

Among the three satwa, Neem-giloe satwa and *T. sinensis* satwa exhibited higher hepatoprotective/hepatoregenerative activity in acetaminophen and alcohol induced liver toxicity. The intervention of fish oil and flax oil proved beneficial in acetaminophen and alcohol induced liver damage. The combination of Neem-giloe satwa and fish oil in acetaminophen induced liver toxicity and combination of *T. sinensis* satwa and flax oil for alcohol induced liver damage indicated improvement over their individual activities. These treatments showed significant decrease in serum levels of SGOT, SGPT, ALP, bilirubin and lipid profile (Total cholesterol, LDL cholesterol, VLDL, Triglycerides and increase in HDL cholesterol levels) and also exhibited reduction in lipid peroxidation and significant increase in levels of GSH, CAT, SOD and total protein as compared with acetaminophen and alcohol treated groups respectively. Histopathological observations showed that the above treatments also improved hepatic architecture when compared with acetaminophen and alcohol treated groups.

Expressions of FABP1 and PPARγ were down regulated while NF-κβ, TNF-α and SREBP1 were upregulated in acetaminophen and alcohol treated groups. Treatment with individual satwa and omega-3 fatty acids as well as their combinations (as indicated above) lead to downregulation of the expression of NF-κβ, TNF-α and SREBP1 and upregulation of FABP1 and PPARγ.

Herbal and nutraceutical interventions showed beneficial effects at biochemical, histological and molecular levels in chemical induced hepatotoxicity. The hepatoprotective effect of *T. sinensis* satwa, Neem-giloe satwa, fish oil and flax oil
may be due individual phytochemicals and nutritional constituents or their synergistic action.

Conclusions

The present study clearly establishes the hepatoprotective/hepato再生性 effects of *Neem-giloe* and *T. sinensis* (Herbal interventions) and flax and fish oil (Nutraceutical interventions) on hepatic disorders caused by repeated acetaminophen and alcohol dosing in rats.

- *Neem-giloe satwa* showed hepatoprotective effect against acetaminophen and *Tinospora sinensis satwa* showed hepatoprotective effect against alcohol induced hepatotoxicity.

- Fish oil and flax oil showed hepatoprotective effect against acetaminophen and alcohol induced hepatotoxicity respectively.

- Combination of *Neem-giloe* and fish oil showed hepatoprotective effect against acetaminophen and combination of *T. sinensis* and flax oil showed hepatoprotective effect against alcohol induced hepatotoxicity.

The herbal medicines and omega-3 fatty acid supplements and their combination counter the liver toxicity at the biochemical, histological and molecular levels by normalizing oxidative stress and inflammation. Their action at cellular level could be seen in the form of repair and regeneration of hepatocytes. The combination reported in the present study is worth further investigation, especially in clinical cases of liver damage due to long term alcohol abuse.
FUTURE DIRECTION

Awards

Prophylactic effect of combination of herbal and nutritional interventions against alcohol induced hepatotoxicity in rats

Hepatoprotective Effect Of Polyunsaturated Fatty Acids And Satwa From Three Tinospora Species Exhibits Differential Hepatoprotective Activity Against Repeated Alcohol Dosing In Rats

Hepatoprotective Effect Of Polyunsaturated Fatty Acids Against Repeated Subacute Alcohol Dosing In Rats

Comparative Hepatoprotective Potential Of T.cordifolia, T.sinensis and Neem-Giloe (Tinospora Cordifolia Growing On Azadirachta Indica (Neem)) Against Paracetamol Intoxication In Rats

Protein synthesis

Second prize in oral Presentation Award

Best Poster Presentation Award
Future Direction

The hepatoprotective/hepatoregenerative effects of *Neem-giloe* satwa, *T. sinensis* satwa and omega-3 fatty acids (Flax oil and fish oil) are worth further investigations in humans through well-designed clinical trials to ascertain their efficacy in clinical liver damage cases of varying severity.