Chapter VII

SUMMARY AND CONCLUSION
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Indigenous drugs are used widely for the treatment of many diseases. Many of the herbal drugs are said to be rich sources of antioxidants. It has been proved that without continuous supply of antioxidants that can scavenge oxygen radicals, survival of aerobic living beings would be impossible. Clinical and epidemiological studies have conclusively indicated that nutrients with antioxidant activity are effective in the prevention of diseases. Molecular and cellular approaches have demonstrated that ROS and antioxidants can directly affect the cellular signaling apparatus and consequently the control of gene expression. This provides a link between ROS and antioxidants in the mechanism of disease processes and prevention.

A wide range of antioxidants, both natural and synthetic has been proposed for use in the prevention and treatment of human diseases where the role of oxygen free radicals have been implicated. Number of useful antioxidants is rather limited and discovery of new antioxidants will be highly valued in this context. The present study thus was an attempt to identify the antioxidant activity of the plant Acalypha indica with a view of understanding its hepatoprotective / curative activity in albino rats along with isolation of the chemical constituents of the active extract.
Ethanol extract of A. indica was found to be a potent inhibitor of lipid peroxidation in liver homogenate induced by Fe^{2+}-ascorbate system. It produced 50% inhibition of lipid peroxidation at a concentration of 800μg/ml. It was also found to inhibit hydroxyl radical generated by the Fe^{3+}-ascorbate – EDTA – H$_2$O$_2$ system (Fenton reaction). Concentration required for 50% inhibition of hydroxyl radical scavenging activity by deoxyribose degradation method was 190μg/ml. It produced 50% inhibition on superoxide radical generation also.

Phytochemical studies could lead to the isolation of two tannin compounds namely gallic acid and ellagic acid, one flavone - quercetin – and two kauranes. So far no report has come regarding the isolation of gallic acid, quercetin and kauranes from this plant. As tannins and flavones are known antioxidants and kauranes being known anti-inflammatory agents, the activity of the ethanol extract can normally be assumed to be due to the presence of these antioxidants.

Administration of CCl$_4$/ paracetamol produced an increase in the serum biochemical parameters like AST, ALT, ALKP and total bilirubin. But oral administration of A. indica extract was found to reduce the hepatotoxicity induced by CCl$_4$ and paracetamol in rats significantly. This was evident from the decreased levels of serum enzymes like AST, ALT, ALKP and total bilirubin. As elevated levels of these enzymes in blood indicate liver damage,
the present result is an evidence of recovery. There was an increase in the levels of total protein and albumin also. Effective control of bilirubin level points towards secretory mechanism of the hepatocytes. Histopathological studies showed that *A. indica* at a dose of 100 mg/kg could prevent necrosis in CCl₄ - treated rat liver and also reduced the inflammation so as to bring back the liver to the normal stage as exhibited by normal architecture of the tissue. In the paracetamol - treated animals also the swelling and ballooning of the hepatocytes was reversed by the administration of the drug.

In the choleretic study also, the drug exhibited a very significant increase in bile flow indicating its efficacy in the cure of hepatitis.

Liver regeneration study, after the administration of the drug, could bring out a very promising result. The RNA, DNA, protein and cholesterol estimation in hepatectomised rats (treated) brought out significant elevation in the levels of these parameters between 36 and 120 hrs though there was chance of hyperplasia after hepatectomy. The untreated and sham operated group of animals could not exhibit this result proving that the elevation of the above parameters are not due to normal hyperplasia alone which is possible after hepatectomy.

The antioxidant studies of the liver of drug treated rats could reveal that the possible mechanism of hepatoprotective effect is due to the presence
of active constituents like polyphenols, flavonols, and kauranes present / isolated in the active fraction of the extract.

The observed effects of *A. indica* lead to the conclusion that ethanol extract of the drug is a potent antioxidant due to its free radical scavenging activity. The active fraction contained chemical constituents like polyphenols, flavonols, kauranes etc. which are known antioxidants and hepatoprotectives. Also it produced choleretic property. Moreover the ethanol extract exhibited significant effect on liver regeneration as evidenced by increase in the content of RNA, DNA, protein and cholesterol after partial hepatectomy.

Since *Acalypha indica* produced marked antioxidant and free radical scavenging effect along with hepatoprotective activity, comparable to silymarin, it can be used for the treatment of liver ailments especially chemical-induced hepatitis. Also it may be used as an anti inflammatory and anti neoplastic agent. As chronic toxicity study did not produce any adverse results in the hematological and biochemical parameters, except mild inflammation in the hepatocytes in the highest dose, this can be subjected to further clinical studies. Also further studies against viral hepatitis using the same is worth investigating.