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HYPOLIPIDEMIC EFFECT OF *COLEUS AROMATICUS* LINN., ON CCL4 INDUCED HEPATOTOXICITY IN SWISS ALBINO RATS

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ABSTRACT

The present study has been carried out to evaluate the effect of *coleus aromaticus* leaves on CCl4 induced hepatotoxicity in swiss albino rats. Elevation of bilirubin, total cholesterol, triglyceride, and decrease in A/G ratio, total protein and phospholipid was noted in CCl_4 administred rats. Total reversal of all the above said parameters was noted in both ethanolic extract of coleus aromaticus treated and Silymarin treated rats. The efficacy of the plant drug has been found to be more than the standard drug Silymarin.

KEYWORDS: Biochemical analysis, *Coleus aromaticus* and CCl_4.

INTRODUCTION

The liver is the largest organ in the body and weighs about 105kg making up about 2-3% of the total body weight, the basic functional unit of the liver is the liver lobule. The lobules are made up of columns of hepatic cells whose outlines are distinc forming a syncytium. The sinusoid lining is made up of the typical endothelial cells as well as a large number of phagocytic cells called kupffer cells, which engulf pathogens, cellular debris and damaged blood cells. Most other chemicals are not biologically active but can be converted to reactive toxic metabolites, which then act on target cells. This modification is usually accomplished by the cytochrome p-450 mixed function oxidase in the liver and other organs. These metabolites cause membrane damage and cell injury by involves the formation of reactive free radicals and subsequent lipid per oxidation. [1]

Cabon tetrachloride (CCl_4) is of considerable industrial and environmental importance and is a natural product. The toxic effect of CCl_4 on the liver has been studies extensively by a large number of investigators.[2]

Karpuravalli (*Coleus aromaticus* L.) with its distinctive smelling leaves is a common home remedy for infantile cough, cold and fever. They are useful in cephalagia, anorexia, dyspepsia, colic, diarrhea and cholera especially in children, halitosis, convulsions, epilepsy, chronic asthma, bronchitis, renal vesical calculi stroangury, hepatopathy and malarial fever. Juice is mixed with sugar is give to children in colic. Its also useful for gonorrhea, piles. Crushed leaves are used as a local application of the head in headache and relieve the pain and irritation caused by sting centipedes.[3]

MATERIALS AND METHODS

Plant material

The leaves of *Coleus aromaticus* were collected from S.T.E.T Medical plant garden, Mannargudi, Thiruvarur District and authenticated by Botany Department of A.V.V.M. Sri Pushpam College, Poondi. After anthentification the plant material were washed under running tap water.

Preparation of Plant Extract

Coleus aromaticus leaves were dried (without direct sunlight) and converted to powder form. The powder obtained was successively extracted in methanol and distilled water by using soxhlet apparatus. It was stored at 4°C until used when needed the residual extract was suspended in distilled water and used in the study.

Animals

A healthy swiss albino rats were housed in well ventilated hygienic atomosphere. Animals with 100 – 150g were used our study. Animals were fed with commericial rat feed (Saidurga feeds & foods, Bangalore) and tap water adlibitum. After randamization into various groups, the rats were acclimatized for a period of 2-3 days in the new environment before initiation of experiment.

Chemicals

All of the chemicals were of analytical grades and were obtained from Central Drug House Pvt. Ltd (New Delhi, India).

Experiment design

In the experiment, a total of 24 rats were used. The rats were divided in to following 4 groups of 6 each.

Group I : Control

Group II : CCl_4 treated (Intraperitoneal administration of CCl_4 at a dosage of 1.5ml/kg/body weight for 14 days).

Group III : CCl_4 and silymarin (Intraperitoneal administration of CCl_4 as the above mentioned dose along with oral administration of 25mg of silymarin/ml of paraffin/kg/body weight for 14 days).

GroupIV : CCl_4 and *coleus aromaticus* treated (Intraperitoneal administration of CCl_4 as the above of 300mg of *coleus aromaticus* 1 ml of paraffin/kg/bodyweight for 14 days).

Sample Collection

After 14 days of herbal treatment, the blood sample were collected from the anaesthetized rats by puncturing the orbital sinus. After the collection of blood, it was allowed to stand for 10 mts.

Biochemical measurements

Tissue and plasma Bilirubin[4], A/G ratio[5], Total protein[6], Total cholesterol[7], Phospholipid[8],[9] and Triglyceride[10] were determined.

Statistical analysis

Results are expressed as mean ± SE from six observations.

RESULT AND DISCUSSION

Table 1 shows that the levels of bilirubin, A/G radio and total protein in serum of normal and that of experimental rats. Compared with Group I animals. Group II animals showed alterations in the above parameters after CCl_4 treatment. The increased bilirubin level (0.73±0.03mg) indicates that toxicity induced by CCl_4 in Group II, Group III, Group Iv animals.

After herbal drug administered, the increased bilirubin get decreased (0.070±0.02mg) to that of Group I animals. The decreased level of total protein and A/G ratio in Group II animals showed alternations after herbal drug administration. The levels were found to be

0.9900±0.06 and 5.02±1.43 on compared with Group II. It was observed that, administration of herbal extract produced significant effect on the above parameters with that of the effect produced by the standard drug silymarin (group III).

The administration of CCl_4 caused significant hepatotoxicity, recognized by a dramatic increase in serum bilirubin (0.73mg) level.

Bilirubin formed in the peripheral tissue is transport to the liver by plasma albumin and the further metabolism of bilirubin occurs primarily in the liver. When bilirubin in the blood exceeds 1mg hyperbilirubinemia exists due to the production of more bilirubin than the normal liver can excrete, or it may result from the failure of a damaged liver to excrete bilirubin produced in normal amount. In abnormal condition, bilirubin reaches a concentrated approximately 22.5 mg/dl [11]. Bilirubin level is very high in the hepatocellular bilirubin[12]. Levels of bilirubin altered in group II rats after CCl_4 administration as compared to normal controls *Coleus aromaticus* (300mg/kg/bw) extract treatment caused significant recovery in group IV rats.

Serum albumin level is an index of seventy and prognosis in patients with chronic hepatic disease. In patients with chronic hepatic disease, serum albumin level was midly depresse, where as globulin level was midly elevated in acute hepatic disease[13]. In the present study the serum albumin/globulin ratio in CCl_4 treated rats was less than the normal control rats. In contrary, levels of albumin and globulin were maintained at near normal values in *Coleus aromaticus* treated animals.

Numerous pathophysiological changes observed in CCl_4 intoxicated rats can be ascribed to the insult by free radicals (CCl_3) produced during the metabolism of CCl_4. These radical binds to lipids in endoplasmic reticulam. These radical also bind hepatocyte membrane and lead to limination of protein impairment of mitochondrial glutathione redox status,[14] and elucit LPO, disturb Ca^{2+} homeostasis and finally results in cell death.[15]

The attainment of near normal protein content in serum of CCl_4 and *Coleus aromaticus* treated rats contributory hepatoprotective mechanism, which accelerates the regeneration process of the liver cells.[16]

Table 2 indicates the mean values of total cholesterol, triglyceride and decreased the level of phospholipid than that of normal control in liver homogenate the levels are 13.37, 27.50 and

32.28. A remarkable recovery was seen in the Group IV rats which received the herbal extract.

The treatment of *Coleus aromaticus* produced significant changes in the above parameters when compared with Group II rats. The levels were found to be 10.01±3.46, 28.90±3.54 and 20.27±3.09. The moderate changes produced by herbal drug was seen 14th day of our experiment. In Group III animals which received the standard drug silymarin, the level of total cholesterol, phospholipid and TG were found to be 9.58±3.48, 29.30±3.38 and 18.02±3.32 compared between Group III and Group IV animals, Group IV animals produced effect was similar to that of the effect produced by Group III.

Marked alteration in lipid metabolism have been reported in chronic CCl_4 administration. Our result showed increased level of cholesterol in plasma and liver homogenate. The measurement of total plasma cholesterol has long been used as a liver function test. The total cholesterol level tends to wise in condition with either extrahepatic (or) intro hepatic biliary obstruction and sometimes rises to high in patients with primary biliary cirrhosis[17]. The liver plays are important role in the synthesis and removal of cholesterol from the circulation. Disease status impair bile duct obstruction, may lead to increased serum cholesterol level. In many cause with hepatocellular injury have been decreased in the percentage of cholesteryl esters, a result of LCAT deficiency. These cause also have marked elevation in unesterified cholesterol [18]. The deficiency of lecithin cholesterol acyl transfarase (LCAT – the enzyme that esterifies cholesterol) lipolytic defects that result in hyper triglyceridemia and due to low levels of lipoprotein lipase, and elevations of biliary lipids into plasma.[19]

Phospholipids are vital components of biomembrane. They are primary target of peroxidation and can be altered by CCl_4. The decrease in the level of phospholipids in liver may be due to increased activity of phospholipids in these tissue.

120 – day survival of the circulating red cell is dependent on preservation of the permeability of its membrane. The red cell membrane in composed of 50 prercent protein, 40 percent lipid and 10 percent carbohydrate. It is bilayer consisting of molecules of phospholipid and cholesterol in a 1.2:1 molar rats assembled in a stacked arrays that the hydrophobic portions of the molecules are oriented toward the interior while the polar side groups are either on the external surface of the cell (or) on the inner cytoplasmic surface.

Administration of CCl_4 induces the increase concentration of triglyceride in liver and plasma as compared to that of the normal rats. CCl_4 decrease the level of LCAT as a result triglyceride concentration is increased[20]. Triglycerides are mainly stored in adipose tissue stated that triglyceride level is found to be higher during liver injury. The plasma lipoprotein are major sources of fattyacids to synthesize triglycerol. The disorder of lipid metabolism, which is cholesterol by increase level of triglyceride. CCl_4 increase the synthesis of fatty acids and triglycerides, from acetate and also increase the rate of lipid esterification[21].

The accumulate of triglyceride the liver might be due to the suppression of lysosomal acid triglyceride lipase activity in addition to the inhibition of VLDL triglyceride secretion [22] . The level of triglyceride is reduced to normal after the treatment of formation of *Coleus aromaticus* administration.

Table 1

Table 1: showing level of bilirubin, A/G ratio and total protein in serum of normal and experimental group.

S.No	Groups	Bilirubin (mg/dl)	A/G ratio (mg/dl)	Total protein (gm/dl)
1.	GP-I	0.050 ± 0.015	1.53 ± 0.34	6.63 ± 1.81
2.	GP-II	0.73± 0.03	0.5 ± 0.03	4.04 ±1.24
3.	GP-III	0.070 ± 0.02	1.040 ± 0.206	5.98 ± 1.59
4.	GP-IV	0.10 ± 0.03	0.9900 ± 0.06	5.02 ± 1.43

(Values are mean ± S.E from 6 rats in each group)

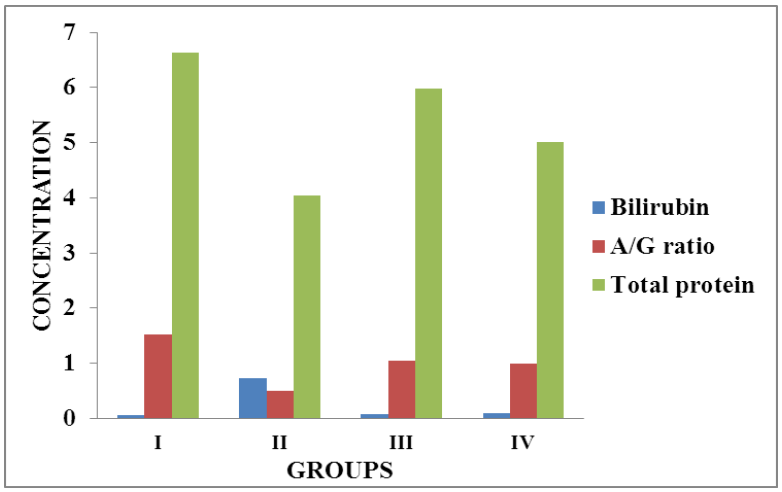

Figure 1

Table 2: showing level of total cholesterol, phospholipid and triglyceride in serum of normal and experimental groups.

S.No	Groups	Total cholesterol (mg/dl)	Phospholipid (mg/dl)	Triglyceride (mg/dl)
1.	GP-I	56.47± 3.10	124.33 ± 2.71	54.45 ± 3.47
2.	GP-II	82.60± 2.51	91.70 ± 2.96	150.30 ± 1.62
3.	GP-III	58.62 ± 2.28	120.40 ± 2.50	60.05 ± 2.50
4.	GP-IV	62.42 ± 3.24	110.20 ± 3.68	67.00 ± 2.78

(Values are mean ± S.E from 6 rats in each group)

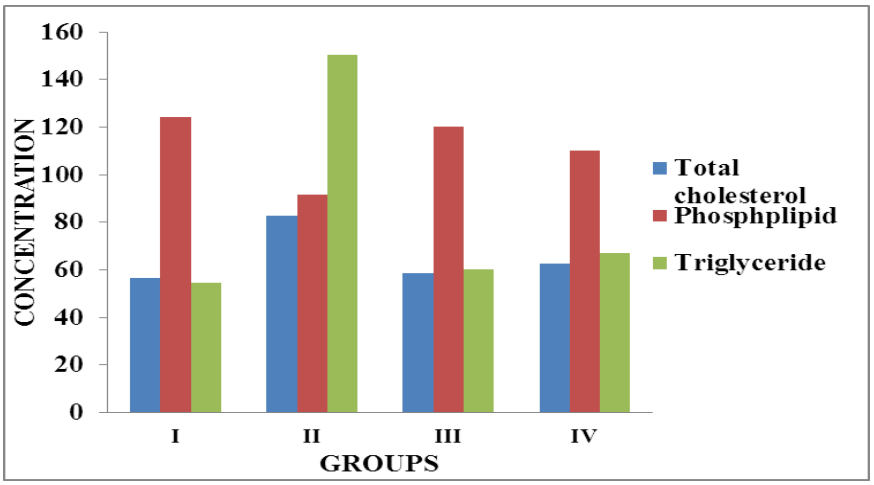

Figure 2

CONCLUSION

Thus, our study shows that *coleus aromaticus* at a dose of 300mg/kg body weight effectively protects the tissues against CCl_4-induced hyperlipidemia. They offer a safer alternative to synthetic chemicals and can be obtained at a very low cost. *coleus aromaticus* can be used for effective protection of hepatic disorders, their potential under field conditions needs to be evaluated. Further investigation regarding the hepatoprotective principles of *coleus aromaticus* should be carried out in future.

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