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Effect of curcumin on brain and liver lipids in experimental hepatotoxicity

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Abstract

Excitotoxins, the dietary toxins, are specially added to food to enhance the taste. The present study has been designed to observe the effect of these excitatory amino acids in rats and also to assess whether curcumin an aromatic kitchen master ingredient, could counteract the effect of excitotoxin induced lipid alterations in rat brain and liver. The lipid changes resulting from curcumin also correlated well with its ability to protect due to the exposure of toxins. The brain and liver lipids and histopathologiocal examination was carried out to evaluate the damage induced by excitotoxin. These results imply that curcumin could be used therapeutically to reduce these toxins, thus potentially reducing the toxicity and tissue damage. It would be appropriate to consider the effect of this wonder drug in the case of organ injury due to dietary toxins.

Keywords: Excitotoxin, Curcumin, liver damage, lipids.

Introduction

Liver injury induced by chemicals has been recognized as a toxicological problem for over 100 years. Lipids perform various functions that in each cell which are essential for proper functioning of our body. The fatty acids protect cells against invasion by microorganism or damage by chemicals.[1] Certain man made dietary components, if consumed in large amounts repeatedly, could be challenging to the functional and structural integrity of such lipid components and thus perturbing the vital organs then the whole system.In certain cases, damage to other vital organs such as brain will also lead to liver injury secondarily affecting its function.[2]

The study has been designed to observe the alteration in protective lipids during exposure to liver and brain toxicants, namely phenyl alanine and aspartate based on John W.onley report and to

assess the efficacy of Curcumin, antioxidant in the efficacy of treating tissue damage caused by these excitotoxins.

Materials and Methods

Experimental design

Pure bred, Wistar strain, albino rats weighing 150-200 gm, obtained from veppery, TANUVAS Chennai. The animals are maintained at an ambient temperature of 25 ± 2 ^{0} C under at 12'hr light, 12 hr dark cycle Bihrnger[3] with food pellets (supplied by Lipton India Ltd. Bangalore), and clean drinking water. Curcumin was dissolved in olive oil and 80g/kg, was i.p injected daily for 15days followed by the induction of Excitotoxin 1g / kg bodyweight for 10 days. (Oral administration) and the rats were sacrificed for histopathological and lipid analysis.

Extraction of lipids

Total lipid was extracted from the liver tissues according to the method of Folch et al.,[4]

Estimation of Total cholesterol.

Tissue cholesterol content was estimated by the method of Parekn and jung.,[5]

Estimation of Triglycerides

Triglycerides in brain and liver was estimated by the method of Foster and Dunn.[6]

Estimation of Free Fatty acids:

Free Fatty acids was estimated by the method of Horn.*et a*l,[7]

Estimation of Lipoproteins.

Lipoproteins were estimated by the method Burnstein *et a*l.,[8]

Statistical analysis

The results were calculated by one way analysis of variance (ANOVA) using SPSS software package. Results were expressed as mean ± SD. The mean difference is significant at the 0.5 level.

Results and Discussion

Histological results evaluating the extent of damage induced by ET, in rat liver after 2-10 days of ET treatment were presented in plate I and plate II respectively. There wont be any significant change observed after 2 days and 4 days of treatment (b and c of plate I and II) and showing similar pattern as control histology (plate I-a and plate II- a). After 6th day and 8th day of treatment, tissue damage could be encountered (d and e of plate I and II) based on John W.onley[9] report. However, significant changes were observed after 10 days of treatment has evident from plate I f and II- f). Hence, the latter period of 10 days of amino acid administration was selected, and used throughout for inducing damage and to assess the efficacy of curcumin.

Plate I and II exhibit histological pattern of control, ET treated and CT rats, in liver. Plate I and II a shows normal architecture of control liver. Both Plate I-b and Plate II-b (ET treated liver), present derangement of cells and damaged regions liver, when compared to control. Plate I c – f and Plate II c-f exhibit tissue architecture on exposure to curcumin (c-80, d-160, e-240, f-320 mg/kg bw) showing near normal picture. The result suggests the hepato protective nature of the drug against the injury.[10]

HISTOPATHOLOGICAL CHANGES ENCOUNTERED IN RAT LIVER ADMINISTERED ASPARTATE AND PHENYL ALANINE (ET) AT 1 g/kg OF BODY WEIGHT FOR DIFFERENT NO. OF DAYS

Plate I

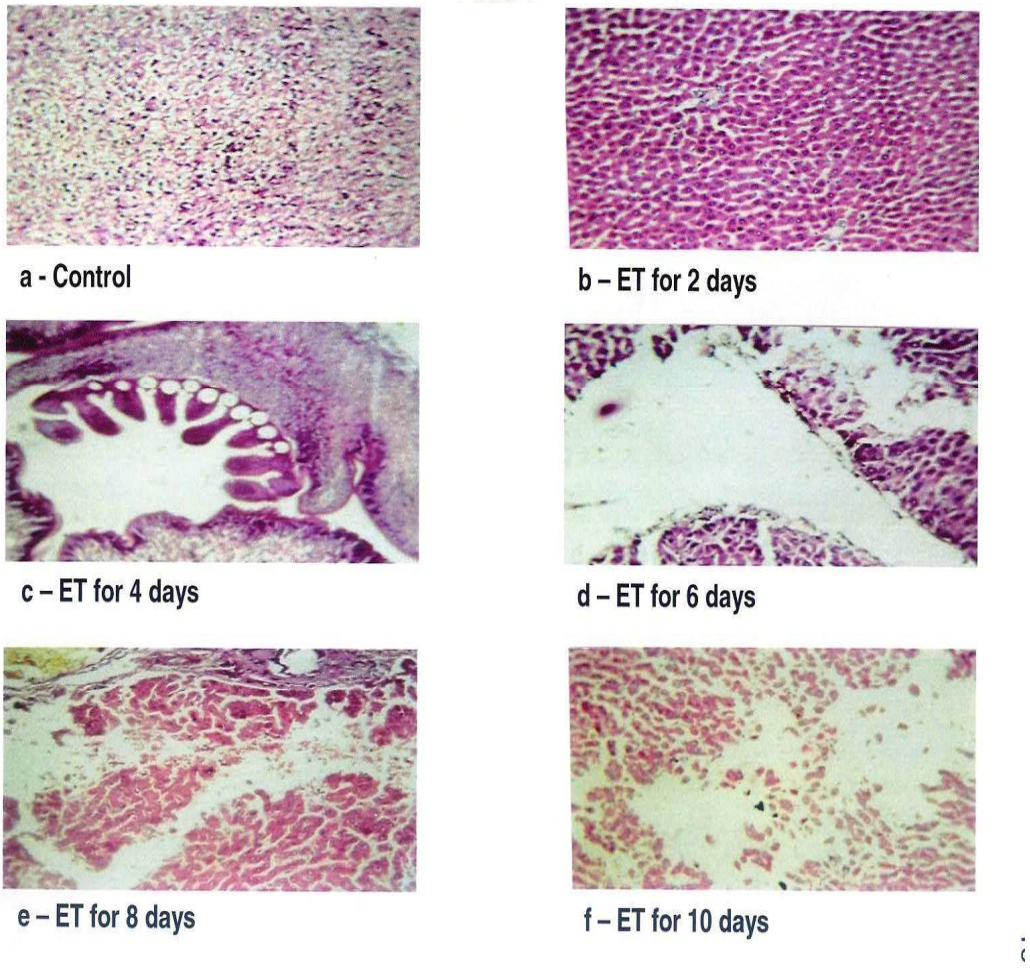


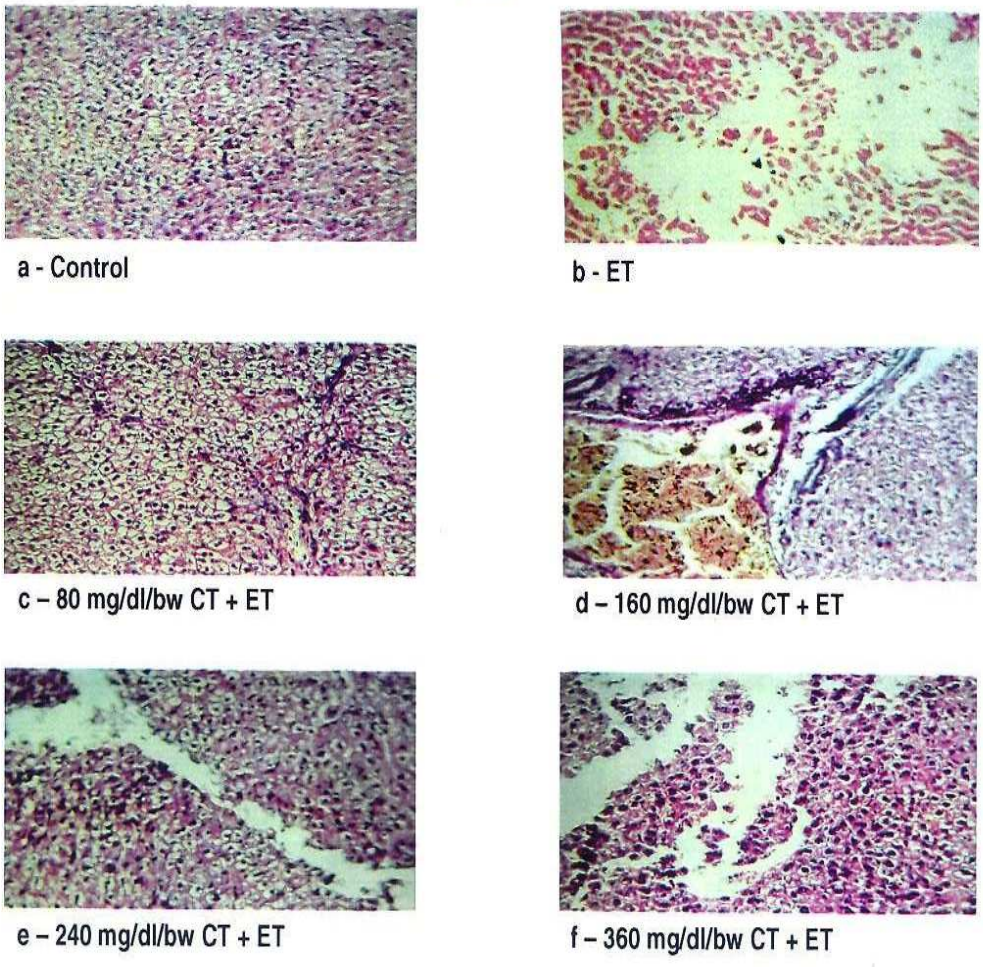
Table 1. Levels of cholesterol, triglycerides and free fatty acids in brain of control, ET and curcumin treated rats. Values are expressed mean ± SD

Groups	Tissue cholesterol mg/g tissue	Triglyceride mg/g tissue	Free fatty acid, mg/g tissue
Group I (Control)	93.6 ± 1.70	55.5 ± 1.16	2.15 ± 0.58
Group II (ET)	66.8 ± 0.13	39.6 ± 1.14	1.45 ± 0.83
Group III a (80 mg)	93.8 ± 0.40 *	55.83 ± 0.40*	2.05 ± 0.50*
Group III b (160)	66.0 ± 0.10*	42.8 ± 0.70*	2.0 ± 0.49*
Group III c (240)	44.0 ± 0.50	31.0 ±01.50	1.75 ± 0.38
Group III d (320)	50.0 ± 0.40*^{NS}	38.8 ± 0.70*^{NS}	1.72 ± 0.35*^{NS}

*n=6, The mean difference is significant at the 0.5 level.; * p<0.5- Group I Vs Group II, Group II Vs Group III; NS Group III a-b vs Group I*

HISTOPATHOLOGICAL CHANGES ENCOUNTERED IN RAT LIVER PRETREATED CURCUMIN (15 DAYS) FOLLOWED BY ET ADMINISTERATION

Plate II



The functional behavior of any biological membrane critically depends upon its chemical composition. Any change in the membrane components is bound to affect its function. Cholesterol a type of lipid is a substance found in cell membrane that helps in maintains the physical integrity of cells. The liver synthesizes cholesterol, which is then packaged and distributed to the body to be used of excreted in to bile for removal from the body. Under pathological conditions, high levels of lipid metabolites generated by are involved in neuroinflammation, oxidative stress, and neural cell injury.[11]

Table 2. Levels of cholesterol, triglycerides and free fatty acids in liver of control, ET and curcumin treated rats. Values are expressed mean ± SD

Groups	Tissue cholesterol mg/g tissue	Triglyceride mg/g tissue	Free fatty acid, mg/g tissue
Group I (Control)	46.0 ±01.5	173.3 ± 1.90	2.96 ± 0.56
Group II (ET)	76.6 ± 0.81	141.1 ± 0.40	1.45 ± 0.83
Group III a (80 mg)	46.5 ± 0.04*	169.3 ± 0.50*	2.80 ± 0.50*
Group III b (160)	36.5 ± 0.30*	119.0 ± 0.01*	2.10 ± 0.47*
Group III c (240)	34.3 ± 0.60*	84.0 ± 0.70*	2.0 ± 0.38*^{NS}
Group III d (320)	80.0 ± 0.40*^{NS}	164 ± 0.50*^{NS}	2.12± 0.40

*n=6, The mean difference is significant at the 0.5 level, * p<0.5- Group I Vs Group II, Group II Vs Group III, NS Group III a-b vs. Group I*

Table 3. Levels of plasma lipoproteins, HDL cholesterol, LDL cholesterol and VLDL cholesterol of control, ET and curcumin treated rats. Values are expressed mean ± SD.

Groups	HDL cholesterol mg/ dl	LDL mg/ dl	VLDL mg/ dl
Group I (Control)	9.50 ± 1.0	9.00 ± 0.12	35.16 ± 1.2
Group II (ET)	5.0 ± 0.6	29.0 ± 0.17	41.16 ± 0..26
Group III a (80 mg)	10.30 ± 0.3*	9.5 ± 1.0*	25.3 ± 0..6*
Group III b (160)	11.00 ± 1.0*^{NS}	28.16 ± 0.24*	35.6 ± 1.3*^{NS}
Group III c (240)	11.80 ± 0..9	30.16 ± 0.1.9	20.0 ± 0.09
Group III d (320)	11.60 ± 0.8*^{NS}	46.0 ± 0.89	36.3± 1.07*^{NS}

*n=6, The mean difference is significant at the 0.5 level, * p<0.5- Group I Vs Group II , Group II Vs Group III, NS Group III a-b vs Group I*

In the present study ET treated rats registered a decreased levels of TG and FFA both in liver and brain and decreased levels of cholesterol in the case of brain only (Table 1&2)when compared to control (p<0.5 group II vs control). Free fatty acids are markers of secondary cellular injury following traumatic brain injury. [12] When the drug treated group (CT) was compared to ET animals, the level of FFA and TG were found to be increased and maintained at near normal levels. (p<0.5, group III a in brain and liver vs group II, NS group III a brain and liver vs control) suggesting the protective action of drug.[13]

When the levels of liver cholesterol were analyzed in the experimental animals, a contrast observation to those of brain was obtained. The level of cholesterol was found to be elevated in the liver of ET rats when compared to control (p<0.5). On treatment with the drugs, the levels were reduced and were maintained near to the normal one (NS group III a liver vs control). This reduction on drug administration in the study well coincides with the report of Bapu S *et al [14]*, which suggest that could enhance the catabolism of accumulated cholesterol.

Lipoproteins, the ‘fat protein’ combination molecules circulating in the blood and tissues can move the body, if they are surrounded by protein because fats are not soluble in water. When the

level of HDL of ET rats were compared to the control rats the levels of HDL was found to be decreased ($p<0.5$). In CT rats the levels were maintained to near normal level (NS, group III vs control). In the amino acid induced (ET) rats the, other lipoprotein levels were found to be elevated when compared to control ($p<0.5$). When the CT group was compared to ET rats, the level of LDL, and VLDL were found to be decreased ($p<0.5$. groupIII vs group II) when compared to ET animals, showing near normal levels (NS, group III vs control). This observation very much correlates with the report showing that curcumin, in a dose dependent manner, could decrease the susceptibility of LDL to lipid peroxidation.[15] The low levels of LDL and VLDL - cholesterol in the circulation observed in present study in CT rats were supported by the observation of hypolipidemic effect of curcumin in vivo due to alteration in fat metabolism.[16]

Conclusion

In the present study, curcumin, a naturally occurring medicinal compound, was investigated for its protective effect against excitotoxin-induced damage in a dose dependent manner. At the end of the experiment, tissue (liver and brain) lipid levels (i.e. cholesterol, free fatty acids, triglycerides and phospholipids) were analyzed, which were significantly increased in the excitotoxin-treated group, whereas curcumin at a dose of 80 mg/kg b.w. was found to be more effective when compared with the other doses. The results suggest that curcumin exerts its hepato protective action against excitotoxin-induced tissue damage through its antioxidant and antihyperlipidemic properties.

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