Protective effect of Tetrahydrocurcumin on plasma lipids and lipoproteins in cadmium intoxicated rats

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Abstract
In the present work, antihyperlipidemic activity of Tetrahydrocurcumin (THC), a polyphenolic compound from curcumin was evaluated in Cadmium (Cd) intoxicated state using male albino Wistar rats. Oral administration of Cd (5 mg/kg body weight (b.w), for 4 weeks) significantly elevated the levels of triglycerides, free fatty acids, total cholesterol, phospholipids and low density lipoprotein- (LDL-C) with a significant decrease in high density lipoprotein - cholesterol (HDL-C) in plasma. Post-oral administration of THC after three hour of Cd treatment for 4 weeks showed a significant restoration of the above changes to near normal. These results suggest that THC at the dose of 80 mg/kg b.w can effectively controls the elevated levels of lipids in the plasma of Cd intoxicated rats by regulating the lipid metabolic enzymes, protects the liver and heart against hyperlipidemic stress in Cd induced heavy metal toxicity.

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Keywords : Antihyperlipidemic, Cadmium toxicity, lipid profile, Tetrahydrocurcumin, Polyphenolic compound, Turmeric.

Introduction
Cadmium (Cd) is a soft, bluish-white metal, naturally occurring element distributed with an average concentration of 0.1 to 0.2 mg/kg in earth. It is associated in small amounts with the ores of nonferrous metals such as zinc, lead and copper and it is recovered as a byproduct in extraction, smelting and refining. Cadmium and its chemically derived products are very stable, highly insoluble, corrosion resistance, low electrical resistivity, good galvanic comparability, good plating coverage, and possess good solderability. These physiochemical properties and economical importance retains its irreplaceable position in industrial productions and humans usage. Biologically inactive cadmium exposed through occupational and environmental conditions can be able to bind with various macromolecules including DNA and proteins, disturb the orientation and functions of biomolecules. It troubles the mineral metabolism in the biological system through its most existing divalent cationic state Cd²⁺ [1]. This non-essential metal has long biological half life, gets accumulated in various organs like liver, kidney and testis [2-4], implicated in a number of clinical complications including cardiovascular diseases, anemia and diabetes mainly by affecting the of endocrine system [5-7]. The proposed molecular mechanism responsible for Cd toxicity is brought by suppressing the antioxidant system in animals and humans [8, 9]. Decrease in the levels of antioxidants and the elevated levels of lipid peroxidation end products signifies the liver damage in Cd intoxicated condition this cause to the derangement of lipid metabolism primarily regulated by liver.

Atherosclerosis is one of the major risk factors in the development of hypertension and the major death causing cardiovascular disease. Elevation in the levels of total cholesterol (TC) and changes in the level of lipoproteins in plasma are the important risk factors for the development of atherosclerosis. Studies conducted in animal models also supports the exposure of Cd causes the alterations in lipids and lipoprotein metabolism which may eventually leads to atherosclerosis [10-13]. Turmeric (Curcuma longa) is a perennial dietary spice commonly used as curry powder in Indian cuisines, coloring agent in foods and textiles and a treatment component for a wide variety of ailments. Curcumin is an active principle of turmeric, contains remarkable medicinal values and used to treat a wide variety of disorders without causing any side effects [14]. Tetrahydrocurcumin (THC) is a colorless polyphenolic compound, has almost the same physiological and pharmacological properties of curcumin and exhibits the strongest antioxidant activity among the class of curcumin derived compounds [15-17]. THC is used in the prevention of...
cancer, protects against inflammation, treatment of atherosclerotic lesions, hepatotoxicity and nephrotoxicity [18-21]. To our knowledge there are no reports available on the effect of THC on lipid profile in Cd induced toxicity in rats. Therefore, this study was designed to evaluate the antihyperlipidemic activity of the THC in cadmium intoxicated rats.

2. Materials and methods

2.1. Chemicals and kits

Tetrahydrocurcumin was a gift sample provided by Sabinsa Corporation, USA. Cadmium chloride, chloroform and methanol were obtained from Sigma chemical co., St. Louis, MO, USA. The rest of the chemicals utilized for this study were obtained from local firm (India) and were of analytical grade.

2.2. Animals

Male albino Wistar rats with the body weight of 180–200 g bred in Central Animal House, Rajah Muthiah Medical College, Annamalai University were used in this study. The animals were housed as six animals per each polypropylene cage and maintained in accordance with the guidelines of the National Institute of Nutrition, Indian Council of Medical Research, Hyderabad, India and approved by the Institutional Ethical Committee (Vide. No. : 903, 2012), Annamalai University. The animals were fed on a pellet diet (Lipton India Ltd., Mumbai, India) and allowed to drank water ad libitum. During the study period, changes in body weight, diet and water ingestion were recorded weekly.

2.3. Experiment Protocol

Animals were randomized and divided into four groups of which each group containing six rats. The toxic dose of the Cd was selected based on the studies from Renugadevi and Prabu [22].

Group I: Control rats were orally administered with isotonic saline and corn oil (2mL/ kg b.w /day) for 4 weeks.

Group II: Rats were orally administered with THC (80 mg/kg b.w/day) suspended in corn oil for 4 weeks.

Group III: Rats were orally administered with Cd as Cadmium chloride (5 mg/kg b.w /day) in isotonic saline for 4 weeks.

Group IV: Rats were orally administered with Cd (5 mg/kg b.w /day) and THC (80 mg/kg b.w /day, post orally after 3 hrs of Cd administration) in corn oil for 4 weeks.

2.4. Sample Preparation

At the end of the experimental duration, rats were fasted overnight and anaesthetised by intramuscular injection of Ketamine hydrochloride (30 mg/kg b.w) [23] then euthanized by cervical decapitation. Blood samples were collected in the tubes containing heparin as anticoagulant for plasma analysis. Plasma separated by centrifuging the blood samples at 3000 x g for 5 min, was used for various biochemical estimations. Tissues were dissected out, cleared off blood and immediately kept in ice-cold saline. Tissue samples were homogenized in appropriate buffer using OMNI international tissue homogenizer (TH 4212) and the tissue homogenate was utilized for the enzyme activity.

2.5. Biochemical studies

2.5.1. Extraction of Lipids

Lipids in plasma were extracted by the method of Folch et al. [24] using chloroform - methanol mixture (CHCl₃:CH₃OH) (2:1 v/v) for separation and the non-lipid components were washed using 0.1 M potassium chloride. The organic layer was used for the used for the analysis of total cholesterol, triglycerides, free fatty acids and phospholipids.

2.5.2. Estimation of Total Cholesterol

Level of total cholesterol in plasma was estimated by the method of zlatkis et al. [25] by using a reagent kit from Sigma Diagnostics (I) Pvt. Ltd. (Baroda, India). To 0.1 ml of the plasma 9.9 ml of ferric chloride-acetic acid reagent was added, allowed to stand for 15 min and then centrifuged. 5 ml of the supernatant was mixed with 3 ml of con. H₂SO₄ and the color developed were read at 560 nm after 20 min using reagent blank and a set of standards. Values were expressed as mg/dL in plasma.

2.5.3. Cholesterol in the lipoprotein fractions

HDL-cholesterol fraction was separated from plasma sample by the precipitation techniques following Burnstein et al. [26]. 1 ml of plasma was mixed with 0.18 ml of heparin-manganese chloride reagent. The solution was allowed to stand at 4°C for 30 min and then centrifuged in a refrigerated centrifuge at 1800 x g for 30 min. An aliquot of supernatant containing the HDL-C fraction was used for cholesterol estimation. The values were expressed as mg/dL in plasma.

The very low density lipoprotein- Cholesterol (VLDL-C) and LDL cholesterol concentrations were calculated from the Friedewald’s equation. LDL Cholesterol = Total cholesterol - (HDL cholesterol + VLDL cholesterol) and VLDL cholesterol = Triglycerides/5. The values were expressed as mg/dL in plasma.

2.5.4. Estimation of Triglycerides (TG)

The levels of triglycerides in plasma was estimated by the method of Fossati and Lorenzo [27] by using a reagent kit from Sigma Diagnostics (I) Pvt. Ltd, Baroda, India. An aliquot (0.5 mL) of lipid extract was evaporated to dryness. To this, 0.1 ml of methanol was added followed by 4 mL of isopropanol and 0.4 g of alumina and the tubes were shaken well for 15 min then centrifuged. 2.0 mL of the supernatant was treated with 0.6 mL of the saponifying agent and 0.5 mL of acetyl acetone, mixed and then saponified by kept in a water bath at 65°C for 15 min. A series of standards in the concentration 8-40 µg of triolein were treated similarly along with a blank containing the reagents alone. All the tubes were cooled and read at 405 nm. The triglyceride content was expressed as mg/dL in plasma.

2.5.5. Estimation of Phospholipids

Phospholipids in plasma were estimated by the method of Zilversmit and Davis [28]. To 0.1 mL of plasma 1 mL of 5N H₂SO₄ and con HNO₃ were added and digested to a colorless solution. The inorganic phosphorous content in the extract was determined according to the method of Fiske and Subbarow [29] by using a diagnostic kit from Sigma Diagnostics (I) Pvt. Ltd (Baroda, India). The color developed was read spectrophotometrically at 640 nm using reagents blank. The values were expressed as mg/dL in plasma.

2.5.6. Estimation of Free Fatty Acids

Free fatty acids in plasma were estimated by the method of Falholt et al. [30]. 0.1 mL of plasma was evaporated to dryness. To the residue 6 mL of lipid extraction solvent, 1 mL of phosphate buffer and 2.5 mL of copper reagent were added, tubes were shaken vigorously, treated with 200 mg of activated silicic acid and kept aside for 30 min. To 3 mL of
aqueous layer 0.5 mL of diphenyl carbazide was added, mixed and the absorbance was read at 550 nm. The values were expressed as mg/dL in plasma.

2.5.7. Assessment of activity of the lipid metabolic key enzymes

The activity of HMG-CoA reductase was assayed indirectly by assessing the ratio of HMG-CoA to mevalonate in hepatic tissue described by Philipp and Shapiro [31]. Equal volumes of liver homogenate (10%) and perchloric acid were mixed, kept for 5 min in room temperature and then centrifuged at 2000 rpm for 10 min. To 1 mL filtrate, 0.5 mL of freshly prepared hydroxylamine reagent (Mevalonate - Equal volumes of hydroxylamine hydrochloride (2 M/L) and water, for HMG CoA – Equal volumes of hydroxylamine hydrochloride (2 M/L) and sodium hydroxide (4.5 M) solution were mixed freshly before use) was added, followed by 1.5 mL of ferric chloride, mixed and the readings were taken after 10 min at 540 nm using saline-arsenate blank. The ratio of HMG-CoA to mevalonate was calculated. The lower ratio indicates higher enzyme activity and vice-versa.

Activity of lecithin cholesterol acyl transferase (LCAT) in Plasma was assayed by the method of Hitz et al. [32]. 0.6 mL of the substrate (HDL-C) was mixed with equal volume of enzyme source (plasma) and 0.2 mL of this mixture was mixed with 1 mL of isopropanol while the remaining mixture was incubated at 27°C for 90 min. Amount of cholesterol present in the protein free filtrate was estimated by Zlatkis method [25] and the value express the cholesterol present in the test sample at zero time. Activity of the LCAT was assayed by incubating the reaction mixture to different time period (60, 120 and 180 min), the reaction was arrested and the cholesterol content was estimated as above with the control containing substrate alone. LCAT activity was expressed as a function of the disappearance of free cholesterol during the incubation period with the unit of µmoles of cholesterol esterified / hr / mL of plasma.

Plasma lipoprotein lipase (LPL) activity was assayed by the method of Korn [33]. 0.1 mL of plasma was mixed with 20 mL of acetone, filtered and the precipitate was scrapped off, washed and suspended in 1 mL of ammonia for 30 min at 0°C for complete extraction of enzymes. This extract was used for enzyme study. The incubation mixture containing 0.3 mL of ammonia buffer, 0.1 mL of calcium chloride, 0.4 mL of substrate and 0.2 mL of plasma was incubated at 37°C for 60 min. At the end of the incubation period, reaction was arrested by the addition of 1 mL of 0.2 N H₂SO₄. Glycerol liberated in the reaction was estimated by taking the aliquot with 0.1 mL of periodate, mixed and allowed to stand in room temperature for 5 min then 9 mL of chromotropic acid was added, mixed and kept in boiling water for 10 min. Intensity of the colour developed was read at 570 nm using reagent blank and standard glycerol. Values were expressed as µmoles of glycerol liberated / hr / mL of plasma.

2.6. Statistical analysis of the Data

Values are given as mean ± S.D. for six rats in each group. The data for various biochemical parameters were analyzed using analysis of variance (ANOVA) and the group means was compared by Duncan’s Multiple Range Test (DMRT) [34]. Values were considered statistically significant when p < 0.05 and the values sharing a common superscript did not differ significantly.

3. Results

Table 1 depicts the effect of Cd and THC on food and water intake, body weight gain and hepatic index (%) in control and experimental rats. In Cd treated condition, water and pellet diet consumption were significantly decreased (p < 0.05) with decrease in body weight gain and an increase (p < 0.05) in hepatic index. Post-oral administration of THC (80 mg/kg b.w.) in Cd intoxicated rats significantly reversed the changes near normal without making any change in THC alone.

Plasma total cholesterol, triglycerides, free fatty acids and phospholipids of control and experimental rats were shown in Fig 1. Significant elevation in the levels of total cholesterol, triglycerides, free fatty acids and phospholipids in plasma of Cd treated rats. Administration of THC in Cd intoxicated rats significantly decreased these elevated plasma lipids towards near normal.

![Fig.1 Changes in the levels of lipids in plasma of control and experimental rats](image1)

Cd-Cadmium; THC- Tetrahydrocurcumin; Values are mean ± SD for 6 rats in each group. In each row, means with different superscript letter differ significantly at p<0.05 (DMRT)

![Fig.2 Changes in the levels of lipoprotein cholesterol in the plasma control and experimental rats](image2)

Cd-Cadmium; THC- Tetrahydrocurcumin. Values are mean ± SD for 6 rats in each group. a-c In each row, means with different superscript letter differ significantly at p<0.05 (DMRT).

Fig. 2 shows the changes in the levels of lipoprotein cholesterol (HDL-C, LDL-C and VLDL-C) in plasma of control and experimental rats. Significant (p < 0.05) increase in the levels of LDL-C and VLDL-C with decreased level of HDL-C in plasma was observed in Cd treated rats. In the case of THC treatment in Cd intoxicated rats, variations observed...
once in

g with the

y weight and alterations in

body, regulating and maintaining lipid homeostasis [38]. It has

the membrane integrity of the cells [36, 37].

activity of the anabolic enzymes in Cd toxicity and dismantles

the decreased protein synthesis. Strong interaction of Cd with

to the increased degeneration of lipids and proteins and also

hepatic

subnormal development of bod

of Cd toxicity includes the decreased food and water intake,

lipoproteins and free cholesterol with the common symptoms

study, significant increase in the levels of plasma lipids,

lipoproteins m

Every year [35]. Elevation in the levels of lipids and

disorder roughly accounts for 20% of mortality in the world in

diseases that affects the heart and blood vessels, this major

Cardio vascular diseases (CVD) are a heterogeneous group of

4.

crease in the activities of LPL and LCAT in plasma of control and

experimental rats. It might be due

hepatic index were observed in Cd treated rats. It might be due

impairment of liver function caused by the imbala

plasma in experimental rats [43

which was pre

increase in the level of HDL were noticed in Cd administered

elevated levels of LDL

agreement with the study conducted by Skoczyńska [46],

antioxidant defense system in Cd intoxicated rats. In

Environmental toxicant cadmium primarily gets accumulated

characterized by distinct cha

changes from a normal plasma lipid

and lipoprotein profile [39].

Cd toxicity leads to a variety of
derangements in metabolic and regulatory processes in lipids,

which in turn leads to dyslipidemia, the most common

metabolic complication observed in heavy metal toxicity

characterized by distinct changes from a normal plasma lipid

and lipoprotein profile [39].

Environmental toxicant cadmium primarily gets accumulated

in the liver and responsible for the dysfunction of liver by

disturbing the activity of lipid metabolic enzymes antioxidant

homeostasis [40]. Impairment of antioxidant function in Cd

toxicity may facilitate the lipid peroxidation and the release of

free fatty acids (FFA) in plasma. The increased concentration

of FFA in Cd toxicity was attributed by the inhibition of β

oxidation process in

mitochondria [41], which eventually leads

were significantly changed to near normal.

Activities of the enzymes HMG-CoA reductase in liver, LPL and LCAT in plasma of control and experimental rats were shown in Table 2. Activity of the rate limiting enzyme HMG-CoA reductase was significantly elevated in the liver of Cd administered rats along with the decreased activities of LPL and LCAT in plasma when compared to the control rats. On administration of THC to Cd intoxicated rats, results indicating the significant (p < 0.05) decrease in the activity of HMG-CoA reductase in liver with the increase in the activities of LPL and LCAT in plasma when compared to Cd alone treated rats.

4. Discussion

Cardio vascular diseases (CVD) are a heterogeneous group of disorders that affects the heart and blood vessels, this major disorder roughly accounts for 20% of mortality in the world in every year [35]. Elevation in the levels of lipids and lipoproteins may prone to CVD in Cd administered rats. In our study, significant increase in the levels of plasma lipids, lipoproteins and free cholesterol with the common symptoms of Cd toxicity includes the decreased food and water intake, subnormal development of body weight and alterations in hepatic-index were observed in Cd treated rats. It might be due to the increased degeneration of lipids and proteins and also the decreased protein synthesis. Strong interaction of Cd with membrane lipids and membrane bound proteins impairs the activity of the anabolic enzymes in Cd toxicity and dismantles the membrane integrity of the cells [36, 37].

Liver is regarded as one of the central metabolic organs in the body, regulating and maintaining lipid homeostasis [38]. It has been demonstrated that Cd toxicity leads to a variety of
derangements in metabolic and regulatory processes in lipids,

which in turn leads to dyslipidemia, the most common

metabolic complication observed in heavy metal toxicity

characterized by distinct changes from a normal plasma lipid

and lipoprotein profile [39].

Cd toxicity may facilitate the lipid peroxidation and the release of free fatty acids (FFA) in plasma. The increased concentration of FFA in Cd toxicity was attributed by the inhibition of β

oxidation process in mitochondria [41], which eventually leads to the increased accumulation of FFA in circulation.

Alterations in lipid profile and total cholesterol were observed in Cd administered animals [42]. Exposure to Cd has been associated with a wide variety of cardiovascular diseases such as atherosclerosis, hypertension, stroke and cardiac arrest which was pre-cautioned by the lipoprotein abnormalities in plasma in experimental rats [43-45]. This might be due to the impairment of liver function caused by the imbalance in antioxidant defense system in Cd intoxicated rats. In agreement with the study conducted by Skoczyńska [46], elevated levels of LDL-C and VLDL-C followed by the decrease in the level of HDL were noticed in Cd administered rats.in our study, administration of THC at the dose of 80 mg/kg b.w. effectively controls the derangement of lipoprotein levels in Cd intoxicated rats. This might be because of the chelating property of the THC with the Cd and renders the

<table>
<thead>
<tr>
<th>Groups</th>
<th>Control</th>
<th>Normal+THC(80mg/kg)</th>
<th>Normal+Cd (5mg/kg)</th>
<th>Cd (5mg/kg)+THC(80mg/kg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Body weight</td>
<td>183.33 ± 13.22</td>
<td>185.00 ± 14.86</td>
<td>190.00 ± 14.60</td>
<td>186.67 ± 14.74</td>
</tr>
<tr>
<td>Initial (g)</td>
<td>215.00 ± 15.85</td>
<td>218.33 ± 17.18</td>
<td>205.00 ± 14.64</td>
<td>210.00 ± 15.26</td>
</tr>
<tr>
<td>Body weight gain (%)</td>
<td>17.27</td>
<td>18.01</td>
<td>7.89</td>
<td>12.49</td>
</tr>
<tr>
<td>Food intake (g/100 g body weight/day)</td>
<td>10.92 ± 0.78^a</td>
<td>11.31 ± 0.82^a</td>
<td>7.62 ± 0.62^b</td>
<td>9.18 ± 0.71^c</td>
</tr>
<tr>
<td>Water intake (mL/100 g body weight /day)</td>
<td>7.82 ± 0.66^a</td>
<td>8.14 ± 0.56^a</td>
<td>4.60 ± 0.37^b</td>
<td>6.94 ± 0.48^c</td>
</tr>
<tr>
<td>Hepatic index (%) #</td>
<td>2.68 ± 0.17^a</td>
<td>2.72 ± 0.22^a</td>
<td>3.64 ± 0.24^b</td>
<td>2.93 ± 0.18^c</td>
</tr>
</tbody>
</table>

Cd-Cadmium; THC- Tetrahydrocannabinol. # Liver weight - body weight ratio. Values are mean ± SD for 6 rats in each group. ^a-c In each rows, means with different superscript letter differ significantly at p<0.05 (DMRT).

<table>
<thead>
<tr>
<th>Groups</th>
<th>Control</th>
<th>Normal+THC(80mg/kg)</th>
<th>Normal+Cd (5mg/kg)</th>
<th>Cd (5mg/kg)+THC(80mg/kg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>HMG-CoA reductase</td>
<td>1.86 ± 0.14^a</td>
<td>1.92 ± 0.14^a</td>
<td>1.23 ± 0.09^b</td>
<td>1.61 ± 0.14^c</td>
</tr>
<tr>
<td>(HMG-CoA/ Mevalonate ratio in liver)</td>
<td></td>
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<tr>
<td>LCAT</td>
<td>36.01 ± 2.37^a</td>
<td>38.42 ± 3.14^a</td>
<td>19.68 ± 1.56^b</td>
<td>29.69 ± 2.07^c</td>
</tr>
<tr>
<td>(µmoles of cholesterol esterified/hr/mL of plasma)</td>
<td></td>
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</tr>
<tr>
<td>LPL</td>
<td>68.01 ± 5.37^a</td>
<td>71.42 ± 6.54^a</td>
<td>44.68 ± 2.56^b</td>
<td>60.69 ± 4.07^c</td>
</tr>
<tr>
<td>(µmoles of glycerol liberated/hr/mL of plasma)</td>
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</table>

Cd-Cadmium; THC- Tetrahydrocannabinol; HMG-CoA- Hydroxy methyl glutaryl Coenzyme A, LCAT- Lecithin Cholesterol Acyl Transferase, LPL - Lipoprotein lipase. Values are mean ± SD for 6 rats in each group. ^a-c In each rows, means with different superscript letter differ significantly at p<0.05 (DMRT).
oxidant character of Cd by its active para hydroxy and keto functional groups.

Hypercholesterolemia is a major risk factor for cardiovascular disease and the common cause of morbidity and mortality. The degree of hypercholesterolemia is directly proportional to the severity of liver damage in toxic condition which attributes derangement in lipid homeostasis [47]. HDL fraction carries the free and esterified cholesterol from the peripheral tissues to the liver, where the cholesterol is metabolized into bile acids and excreted [48]. This good cholesterol plays an important role in reducing cholesterol levels in circulation and peripheral tissues thereby inhibiting atherogenesis. Decrease in the level of HDL has been observed in Cd toxic condition may be due to the decreased production of HDL in liver. Administration of THC exerts potential antihyperlipidemic activity inferred by the decrease in levels of LDL-C, VLDL-C and increase in the level of HDL-C in Cd intoxicated rats.

HMG-CoA reductase converts HMG-CoA to mevalonate in cholesterol biosynthesis [49]. Increase in the activity of HMG-CoA reductase leads to the excessive production and accumulation of cholesterol and initiate the development of atherosclerosis [50]. Decrease in the ratio of HMG-CoA/mevalonate indicates increased activity of the enzyme HMG-CoA reductase. Heavy metal like Cd alters the cholesterol as well as the overall lipid metabolism by inducing the changes in the activity of HMG-CoA reductase. Studies conducted in inflammatory cytokines such as TNF-α and IL-1β have been reported that the increased gene expression of HMG-CoA reductase (HMGR) and suppression of cholesterol 7α-hydroxylase, a catalytic enzyme of cholesterol in the liver of Cd administered rats [51, 52]. By substantiating this, marked elevation in the activity of HMG-CoA was resulted in Cd intoxicated rats. This might cause the hypercholesterolemia and hypertriglyceridemia and favors the mobilization of lipids from the adipose tissue to the plasma by forming LDL-C, which is the major coronary risk factor in Cd intoxicated rats. In THC treated rats, marked decrease in total cholesterol infers the reduction in the activity HMG-CoA by down regulating the gene expression in rats.

Lecithin cholesterol acyl transferase (LCAT) is the key enzyme responsible for the esterification and transesterification of cholesterol moiety in between the lipoprotein fractions like HDL, VLDL and LDL present in circulation [53, 54]. In correlation with the previous study [40], decreased activity of LCAT noted in Cd intoxicated rats, promotes the accumulation of free cholesterol and of remnant lipoprotein in plasma which may accelerate the atherogenesis [55]. Treatment of THC in Cd toxic rats prevents the accumulation of cholesterol by activating the expression of LCAT and catabolic enzymes of cholesterol degradation pathway.

Lipoprotein lipase (LPL) plays vital role in catabolism of TGs and releases the FFA from chylomicrons and VLDL, thereby regulating the level of TGs in circulation. Previous studies evident that Cd decreases the activity of LPL which results in hypertriglyceridemia and increased LDL-C [56, 40]. In our study, reduction in the activity of LPL may contribute the hypertriglyceridemia in plasma and inducts the organization of LDL, aggregation and the oxidation of LDL potentiates the atherogenesis in similar way reported by Taskinen et al. [57]. Administration of THC may activate LPL there by increasing the HDL and decreasing the LDL through the reduction of TGs.

In conclusion, the present investigation reveals that the administration of THC in Cd intoxicated rats altered the plasma lipids by regulating the lipid metabolizing enzymes to near normal levels. It can be stated that, the tetrahydrocurcumin has beneficial effects and protects the liver and heart from the dyslipidemia associated complications in cadmium toxicity.

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