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Normalisation of Lipoprotein Phenotypes by *Chromolaena odorata-Linn.* in Carbon Tetrachloride Hepatotoxicity-Induced Dyslipidaemia

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ABSTRACT

The major functions of the liver can be detrimentally altered by liver injury resulting from acute or chronic exposure to toxicants. Dyslipidemia is often found in such toxicity resulting from chemical damage. Normalisation of atherogenic indices by *Chromolaena odorata* (*C. odorata*) in carbon tetrachloride-induced liver toxicity was evaluated in 30 male rabbits divided into 5 groups of 6 animals each. Normal Control (NC) received food and water only. Carbon tetrachloride intoxicated control (CCl_4) received a single dose of CCl_4 (0.2 mL kgbw^{-1} in liquid paraffin 1:1). *C. odorata* test animals (ETECO TEST) received a single dose of CCl_4 + ethanol extract of *C. odorata* at 400 mg/kg/day in two divided doses of 200 mg kg^{-1} morning and night, for 6 days. *C. odorata* control animals (ETECO CTRL) received ethanol extract of *C. odorata* at 400 mg/kg/day in two divided doses of 200 mg kg^{-1}. Group five (Sylimarin) received sylimarin 50 mg/kgbw prior to CCl_4 intoxication. Carbon tetrachloride-induced toxicity resulted in liver injury which was seen from the significant ($p<0.05$) elevation of the activities of serum Aspartate Aminotransferase (AST), Alanine aminotransferase (ALT), Lactate Dehydrogenase (LDH) and gamma-Glutamyl Transferase (γ-GT), significantly decreased protein and albumin and significantly increased total bilirubin concentrations; altered lipid and lipoprotein phenotypes in favour of increased atherogenic indices. Pre-treatment with *C. odorata* extract prevented these biochemical alterations and normalized the lipoprotein phenotypes. *C. odorata* may be useful not only as a hepatoprotective agent, but also in the reduction and/or prevention of adverse cardiovascular events.

Key words: *Chromolaena odorata*, hypolipidemia, anti-hepatotoxicity, cardioprotective

INTRODUCTION

The liver is a versatile organ in the body having a specialized function, reflected in its anatomy and metabolic activity. It regulates internal chemical environment (Gole *et al.*, 1997) and plays a central processing and distributive role in metabolism. The liver plays a significant role in the body as the organ saddled with the responsibility of metabolising toxic substances that enter the body. The major functions of the liver can be detrimentally altered by liver injury (Singh *et al.*, 2011) resulting from acute or chronic exposure to toxicants (Khadr *et al.*, 2007) or by situations affecting both β-oxidation and the respiratory chain enzymes. Altered free fatty acid metabolism and impaired aerobic respiration as found in animals on high fat diet, have frequently been associated with accumulation of lactate and Reactive Oxygen Species (ROS). The presence of ROS further

disrupts mitochondrial DNA and brings about the damage to hepatic cells. Still other pathways to injury may develop when drugs damage mitochondria, disrupting fatty-acid oxidation and energy production. When drugs bind to and disable respiratory-chain enzymes, increased formation of ROS in mitochondria results. This increases oxidative stress and a secondary attack on mitochondrial DNA, with ensuing anaerobic metabolism, lactic acidosis and triglyceride accumulation (microvesicular fat within cells) (Pessayre *et al.*, 2001).

Carbon tetrachloride (CCl_4) has been one of the most intensively studied hepatotoxicants to date and provides a relevant model for other halogenated hydrocarbons that are used widely (Dahm and Jones, 1996; Weber *et al.*, 2003; Adinarayana *et al.*, 2011). It consistently produces liver injury in many species, including non-human primates and man (Achudume and Ogunyemi, 2007; Moundipa *et al.*, 2007; Noori *et al.*, 2009). Carbon tetrachloride is well known to be converted by cytochrome P-$_{450}$-mixed function oxygenases in smooth endoplasmic reticulum of liver into toxic metabolite, mainly trichloromethyl radical ($CCl_3{}^\bullet$). This free radical in the presence of oxygen may cause peroxidation of lipids on target cell resulting in extensive damage. Liver damage (hepatotoxicity) remains one of the most serious health problems (Lee, 2003). Antioxidation agents of natural origin have attracted special interest because they can protect human body from free radical damage (Raja *et al.*, 2007; Babu *et al.*, 2001; Gupta *et al.*, 2006) and can also protect the liver from damage initiated by hyperlipidaemia (Alisi *et al.*, 2008).

Numerous medicinal plants and their formulations are used for liver disorders in ethno-medical practices (Chavda *et al.*, 2010) as well as in traditional systems of medicine in Africa, India and indeed Asia (Yen *et al.*, 2001; Rao *et al.*, 2006; Koneru *et al.*, 2011). *Chromolaena odorata* (L.) R. KING and H. ROBINSON (formerly *Eupatorium odoratum* L.), a perennial belonging to the plant family Asteraceae (Compositae), is a diffuse, scrambling shrub that is mainly a weed of plantation crops and pastures of Southern Asia and Western Africa. This common plant is called Siam weed. The plant is known among the Igbos of the South-Eastern Nigeria as Elizabeth Independence leaf, 'Enugu plantation weed and 'Awolowo leaf (Alisi and Onyeze, 2009). Results of a number of studies showed that the extract of the leaves of *C. odorata* inhibited the growth of some bacteria (Irobi, 1997). Enhancement of haemostasis and blood coagulation with use of *C. odorata* extract has also been reported. *C. odorata* has demonstrated anti-inflammatory, astringent and diuretic activities (Owoyele *et al.*, 2006; Rao *et al.*, 2010). We already demonstrated a nitric oxide scavenging ability of ethyl acetate fraction of methanol leaf extracts of *Chromolaena odorata* (Alisi and Onyeze, 2008). Biochemical mechanisms of wound healing using ethanol extract of *Chromolaena odorata* have also been previously reported. The ethyl acetate fraction of methanol extract of *C. odorata* has been demonstrated *in vitro* to scavenge hydroxyl radicals (Alisi and Onyeze, 2009).

Patients with hyperlipidaemia have elevations in aminotransferases levels due to non-alcoholic fatty liver disease (Mayes and Botham, 2003). It is well known that hyperlipemia induces liver damage (Mukai *et al.*, 2002; Milionis *et al.*, 2004). Dyslipidaemia accompanies Carbon tetrachloride-induced liver toxicity. Dyslipidemia, as low HDL-cholesterol, high Triglyceride (TG) and elevated LDL-cholesterol, increase cardiovascular disease risk (Wilson *et al.*, 1991; Austin *et al.*, 1998). Low density lipoprotein cholesterol (LDL), HDL and TG are all independent and significant predictors of cardiovascular risk. High blood cholesterol is one of the greatest risk factors contributing to the prevalence and severity of coronary heart disease (Wilson *et al.*, 1998). The Total Non HDL Cholesterol (TNH-CHOL) is the single greatest predictor of cardiovascular risk and can be used as a surrogate measure of lowering the cardiovascular risk. In addition, there is a well known

association between hypertension and dyslipidemia, particularly high levels of serum LDL cholesterol. Furthermore, the magnitude of the reduction in cardiovascular events is a function of the extent of LDL cholesterol lowering. A decrease of 40 mg per deciliter (1.0 mmol L^{-1}) in LDL cholesterol will correspond to a 24% reduction in major cardiovascular events (Baigent *et al.*, 2005). The adoption of crude extracts of plants, such as infusions, for self-medication by the general public (Houghton, 1995), has arisen in the possibility that the impact of several diseases may be either ameliorated or prevented by improving the dietary intake of natural nutrients (Raja *et al.*, 2007). We are not aware of any studies on the normalisation of atherogenic indices by *Chromolaena odorata* in carbon tetrachloride-induced liver toxicity. The purpose of this study was to evaluate hypolipidaemic vis-α-vis antihepatic effects of *Chromolaena odorata* extracts in carbon tetrachloride-induced liver damage.

MATERIALS AND METHODS

Collection and preparation of plant samples: Fresh aerial parts of *Chromolaena odorata* were collected from Egbu and Ihiagwa in Owerri, Imo State (2008) and authenticated by a plant taxonomist, at the Department of Plant Science and Biotechnology, Imo State University, Owerri, Nigeria. Voucher specimen has been retained at the authors' laboratory.

The leaves were shed, dried at 30°C and then reduced to a coarse powder in a mill (Kenwood BL357). A 500 g portion was extracted with 2 L ethanol by shaking for 48 h. Soluble extract was recovered by distillation under reduced pressure at 49°C in a Buchi rotavapour (Switzerland). The extract was then dried to solid form in vacuum desiccator (CNS Simax) and stored in a freezer (4.0°C) until used.

Animals: Thirty white New Zealand male rabbits acquired from an animal breeder in Owerri, Imo State, Nigeria were maintained under standard environmental condition (28-30°C, 60-70% relative humidity, 12 h dark/light cycle) in stainless steel cages with free access to standard laboratory animal diet (Vital finisher) and drinking water.

Induction of hepatic injury: Seven days after acclimatization, animals were distributed into five groups of six animals each. Group I served as Normal Control (NC) which received food and water only throughout the treatment period. Group II served as intoxicated controls (CCl_4 group) which received food and water *ad libitum* and carbon tetrachloride (0.2 mL kg b.wt.$^{-1}$ in liquid paraffin 1:1) on day 7. Groups III served as intoxicated tests (ETECO test) that received food and water *ad libitum*, received ethanol extracts of *C. odorata* (400 mg kg^{-1} body weight of animal) in two divided equal daily doses and carbon tetrachloride (0.2 mL kg b.wt.$^{-1}$ in liquid paraffin 1:1) on day 7. Group IV received food and water *ad libitum* and received ethanol extracts of *C. odorata* (400 mg kg^{-1} body weight of animal) in two divided equal daily doses but did not receive carbon tetrachloride. Group V received food and water *ad libitum* and received Sylimarin (50 mg kg^{-1} body weight of animal) daily and CCl_4 on day 7. At the end of the seven-day pre-treatment and subsequent intoxication with carbon tetrachloride, animals were allowed for 48 h. Animals were anaesthetized and sacrificed by cervical dislocation as permitted by University Ethical Committee.

Biological assays: Blood collected from the ear blood vessels under mild chloroform anesthesia was kept for 45 min at 4°C to clot. Serum was separated by centrifugation at 600 g for 15 min and

analyzed for various biochemical parameters. Serum enzyme activities (aspartate aminotransferase (AST), Alanine aminotransferase (ALT), gamma-Glutamyl Transferase (γ-GT), Lactate Dehydrogenase (LDH), were assayed using a chemistry analyzer (Ciba-Corning 550 Express Plus. USA). Total bilirubin estimation exploits the use of deoxidized sulphanilic acid as described by Pearlman and Lee (1974). The Biuret method as described by Gornall *et al.* (1949) was employed for the determination of protein concentration in serum. Serum albumin concentration was estimated by the method employing bromocresol green as described by Doumas *et al.* (1971).

Total cholesterol, triglyceride, HDL-cholesterol and LDL-cholesterol concentrations were measured spectrophotometrically (Pharmacia LKB Ultospec III) using assay kits (Biosystems S.A. costa Brava Barcelona Spain) while LDL/HDL-ratio and the total non-HDL cholesterol concentration (TNHCHOL) were simply calculated.

Statistical analysis: Results of groups are calculated as Means±SD. and subjected to one-way Analysis of Variance (ANOVA). Significant difference between means were determined at alpha = 0.05. Analysis was done using Analyst v.2.2 (Leeds UK) on Microsoft Excel platform.

RESULTS

Effect of ethanol extract of *C. odorata* on plasma alanine amino transferase (ALT) Activity in carbon tetrachloride induced hepatotoxicity: Result showed that ALT activity in Carbon tetrachloride-intoxicated animals were elevated significantly ($p<0.05$) (115.93 ± 11.8 U L^{-1}) when compared to normal control (40.86 ± 4.0 U L^{-1}), ethanol extract of *C. odorata* control (62.72 ± 7.2 U L^{-1}) and ethanol extract of *C. odorata* treated group (77.88 ± 6.8 U L^{-1}). Sylimarin (52.6 ± 4.4 U L^{-1}) was however, more effective in protecting the hepatocytes against Carbon tetrachloride-induced damage (Fig. 1a).

Effect of ethanol extract of *C. odorata* on plasma aspartate amino transferase (AST) activity in carbon tetrachloride-induced hepatotoxicity: Result showed that AST activity in Carbon tetrachloride-intoxicated animals was elevated significantly ($p<0.05$) (194.0 ± 17.8 U L^{-1}) when compared to normal control (31.0 ± 3.2 U L^{-1}), ethanol extract of *C. odorata* control (47.0 ± 3.9 U L^{-1}) and ethanol extract of *C. odorata* treated group ($143.\pm15.4$ U L^{-1}). Sylimarin (80.82 ± 10.5 U I^{-1}) was however, more effective in protecting the hepatocytes against Carbon tetrachloride-induced damage (Fig. 1b).

Effect of ethanol extract of *C. odorata* on lactate dehydrogenase (LDH) activity in carbon tetrachloride-induced hepatotoxicity: Result showed that LDH activity in carbon tetrachloride intoxicated animals was elevated significantly ($p<0.05$) (4833 ± 540 IU L^{-1}) when compared to normal control (2740 ± 294 IU L^{-1}), ethanol extract of *C. odorata* control (2992 ± 246 IU L^{-1}) and ethanol extract of *C. odorata* treated group (3543 ± 600 IU L^-).[1] Ethanol extract of *C. odorata* was comparable to sylimarin (3200 ± 85 IU L^{-1}) in restoring the LDH activity to normalcy (Fig. 1c).

Effect of ethanol extract of *C. odorata* on gamma glutamyl transferase (γ-GT) activity in carbon tetrachloride-induced hepatotoxicity: Result showed that γ-GT activity in carbon tetrachloride intoxicated animals was elevated significantly ($p<0.05$) (26.0 ± 4.5 IU L^{-1}) when compared to normal control (8.33 ± 1.12 IU L^{-1}), ethanol extract of *C. odorata* control
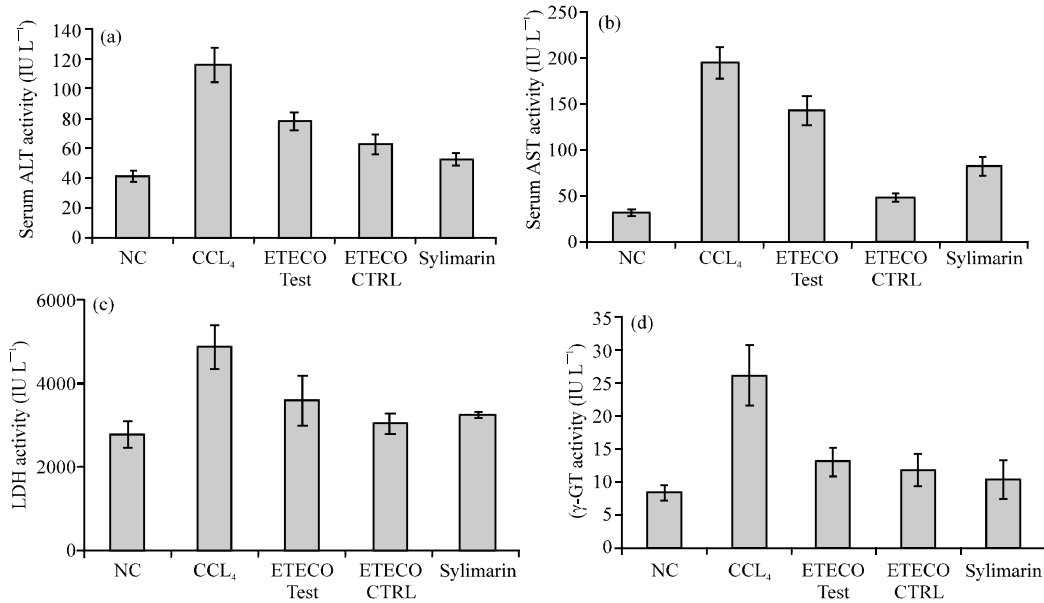
Fig. 1 (a-d): Effect of Ethanol extract of *C. odorata* (400 mg kg^{-1}) on some serum indicators (enzymes) of liver injury (a) ALT, (b) AST, (c) LDH and (d) γ-GT

Table 1: Effect of ethanol extract of *C. odorata* (400 mg kg bw^{-1}) on some liver function parameters

Extract	Normal control	Carbon tetrachloride (CCl$_4$)	ETECO test	ETECO control	Silymarin
Bilirubin-Total (mg dL^{-1})	15.34±.33	40.34±3.60*	19.31±1.57†	14.77±1.32†	16.43±1.70†
Protein (g dL^{-1})	76.55±3.83	50.20±2.50*	57.56±3.40†*	68.81±3.50†	70.12±3.46†
Albumin (g dL^{-1})	49.76±1.47	32.63±1.87*	43.92±2.86†*	44.73±3.32†	48.40±5.50†

Values are Mean±S.D. (n = 6). *p<0.05 vs. normal control. † p<0.05 vs. CCl$_4$ control

(11.67±2.5 IU L^{-1}) and ethanol extract of *C. odorata* treated group (13.0±2.16 IU L^{-1}). Sylimarin (10.3±2.9 IU L^{-1}) was comparable to ethanol extract of *C. odorata* in restoring the γ-GT activity to normalcy (Fig. 1d).

Effect of ethanol extract of *C. odorata* on total bilirubin concentration in carbon tetrachloride-induced hepatotoxicity: Result showed that total bilirubin concentration in carbon tetrachloride intoxicated animals was elevated significantly (p<0.05) (40.34 μmol L^{-1}) when compared to normal control (15.34 μmol L^{-1}), ethanol extract of *C. odorata* control (14.77 μmol L^{-1}) and ethanol extract of *C. odorata* treated group (19.31 μmol L^{-1}). Ethanol extract of *C. odorata* was comparable to sylimarin (16.43±1.70 μmol L^{-1}) in restoring the total bilirubin concentration to normalcy (Table 1).

Effect of ethanol extract of *C. odorata* on serum protein concentration in carbon tetrachloride induced hepatotoxicity: Table 1 showed that total protein concentration in carbon tetrachloride intoxicated animals was significantly (p<0.05) decreased (50.20±2.5 gl L^{-1}) when compared to normal control (76.6±3.83 g L^{-1}), ethanol extract of *C. odorata* control (68.81±3.5 g L^{-1}) and ethanol extract of *C. odorata* treated group (57.56±3.4 g L^{-1}).

Effect of ethanol extract of *C. odorata* on serum albumin concentration in carbon tetrachloride induced hepatotoxicity: Table 1 showed that total albumin concentration in carbon tetrachloride intoxicated animals was significantly ($p < 0.05$) decreased (32.63 ± 1.87 gl L^{-1}) when compared to normal control (49.76 ± 1.47 g L^{-1}), ethanol extract of *C. odorata* control (44.73 ± 3.32 g L^{-1}) and ethanol extract of *C. odorata* treated group (43.92 ± 2.86 g L^{-1}).

Effect of ethanol extract of *C. odorata* on serum total cholesterol concentration of carbon tetrachloride-induced hepatotoxicity: Figure 2a showed that total cholesterol concentration in carbon tetrachloride intoxicated animals was significantly ($p < 0.05$) increased (6.89 ± 1.31 mmol L^{-1}) when compared to normal control (3.22 ± 0.19 mmol L^{-1}) and ethanol extract of *C. odorata* control (3.07 ± 0.26 mmol L^{-1}). Ethanol extract of *C. odorata* treated group (4.95 ± 0.37 mmol L^{-1}) had significantly lower cholesterol concentration than the intoxicated group, but were significantly ($p < 0.05$) higher than normal controls.

Effect of Ethanol extract of *C. odorata* on serum triacylglycerol concentration of carbon tetrachloride-induced hepatotoxicity: Figure 2b showed that serum triacylglycerol concentration in carbon tetrachloride intoxicated animals was significantly ($p < 0.05$) increased (1.56 ± 0.22 mmol L^{-1}) when compared to normal control (1.015 ± 0.056 mmol L^{-1}) and ethanol extract of *C. odorata* control (0.766 ± 0.07 mmol L^{-1}). Ethanol extract of *C. odorata* treated group (1.094 ± 0.1 mmol L^{-1}) had significantly lower triacylglycerol concentration than the intoxicated group, but were significantly ($p < 0.05$) higher than ethanol extract of *C. odorata* controls.

Effect of ethanol extract of *C. odorata* on serum LDL-cholesterol concentration of carbon tetrachloride-induced hepatotoxicity: Figure 2c showed that serum LDL-cholesterol concentration in carbon tetrachloride intoxicated animals was significantly ($p < 0.05$) increased (2.17 ± 0.13 mmol L^{-1}) when compared to normal control (1.37 ± 0.11 mmol L^{-1}) and ethanol extract of *C. odorata* control (1.726 ± 0.17 mmol L^{-1}). ethanol extract of *C. odorata* treated group (1.698 ± 0.212 mmol L^{-1}) had significantly lower LDL-cholesterol concentration than the carbon tetrachloride intoxicated group but were significantly ($p < 0.05$) higher than normal controls.

Effect of ethanol extract of *C. odorata* on serum HDL- cholesterol concentration of carbon tetrachloride-induced hepatotoxicity: Figure 2d showed that serum HDL-cholesterol concentration in carbon tetrachloride-intoxicated animals was significantly ($p < 0.05$) decreased (1.003 ± 0.008 mmol L^{-1}) when compared to normal control (2.47 ± 0.002 mmol L^{-1}) and ethanol extract of *C. odorata* control (2.16 ± 0.005 mmol L^{-1}). Ethanol extract of *C. odorata* treated group (1.697 ± 0.003 mmol L^{-1}) had significantly ($p < 0.05$) higher HDL-cholesterol concentration than the intoxicated group but were significantly lower than normal controls.

Effect of ethanol extracts of *C. odorata* on serum total non-HDL cholesterol of carbon tetrachloride-induced liver damage: Intoxication of rabbits with carbon tetrachloride produced an elevated total non-HDL-cholesterol (5.88 mMol L^{-1}) which was significantly ($p < 0.05$) higher than the normal controls (0.742 mMol L^{-1}) and the ethanol extract of *C. odorata* treated controls (0.910 mMol L^{-1}) (Fig. 2e). Treatment with ethanol extract of *C. odorata* significantly ($p < 0.05$) lowered TNHC (3.25 mMol L^{-1}) in the intoxicated animals.
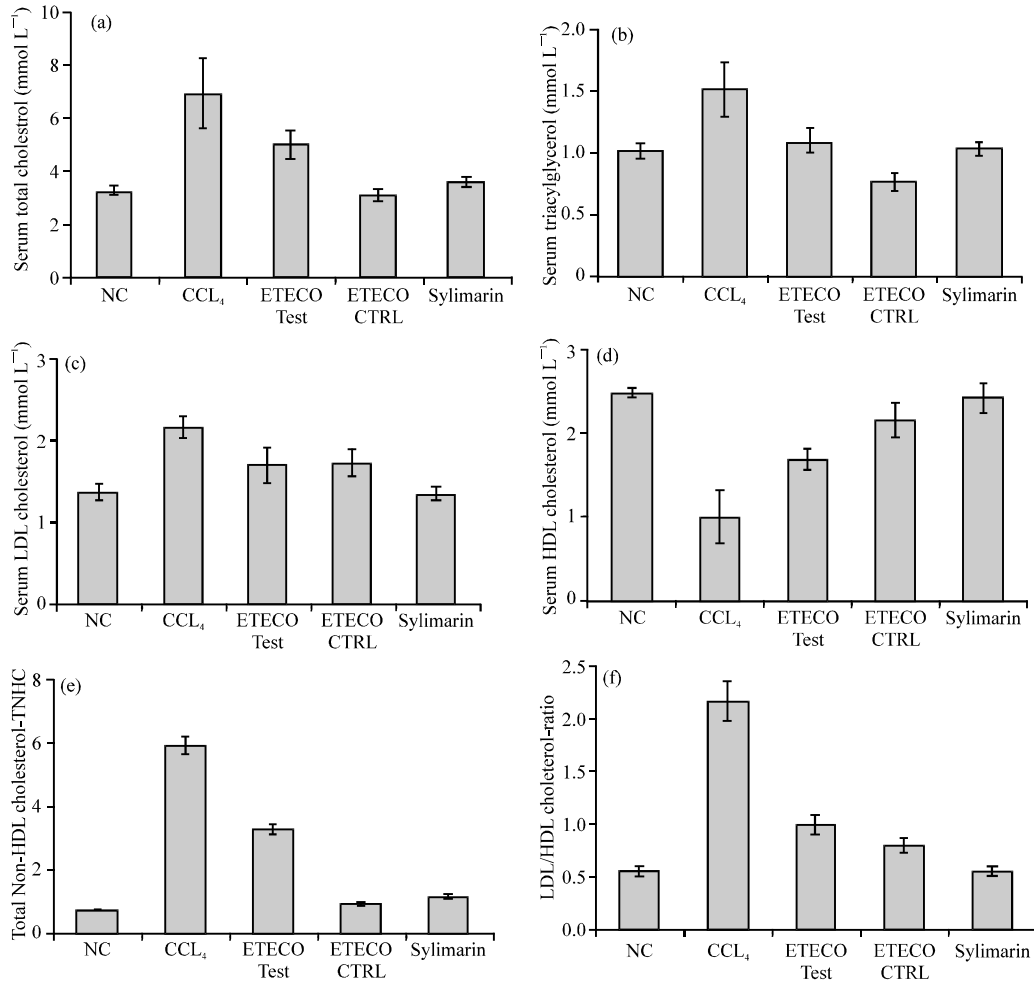
Fig. 2 (a-f): Effect of ethanol extract of *C. odorata* on serum lipid/lipoprotein phenotype of carbon tetrachloride intoxicated rabbit liver (a) Serum total cholesterol, (b) Serum triacylglycerol, (c) Serum LDL cholesterol, (d) Serum HDL cholesterol, (e) Total Non-HDL cholesterol and (f) LDL/HDL cholesterol ratio

Effect of ethanol extracts of *C. odorata* on LDL/HDL cholesterol ratio in carbon tetrachloride induced liver damage: Result obtained (Fig. 2f) showed that intoxication of rabbits with carbon tetrachloride produced an elevated LDL/HDL (2.159 ± 0.194) which was significantly ($p<0.05$) higher than the normal controls (0.553 ± 0.050) and the ethanol extract of *C. odorata* treated control (0.798 ± 0.072). Treatment with ethanol extract of *C. odorata* significantly ($p<0.05$) lowered LDL/HDL ratio (1.001 ± 0.090) in the intoxicated animals.

DISCUSSION

In this study, rabbits treated with single dose of CCl_4 developed a significant hepatic damage which manifested as a substantial increase in the activities of serum marker enzymes, ALT, AST (Alqasoumi *et al.*, 2009), LDH and γ-GT. This was indicative of cellular leakage and loss of functional integrity of cell membrane in liver (Mukherjee, 2003, 2002). Hepatotoxicity induced by

Carbon tetrachloride, impaired function of the hepatic cells in this study. Impairment of hepatic function is evidenced by decreased serum protein and albumin concentration and increased bilirubin concentration (Table 1). This is in agreement with previous reports in which liver damage impaired function and decreased protein and albumin concentrations in serum (Alisi *et al.*, 2008). In this study, increases in ALT, AST, LDH and γ-GT activities showed damage to the tissues while elevations in total bilirubin, decreases in total protein and albumin concentrations showed impairment of hepatic functions. Most circulating proteins are synthesized in the liver and concentrations indicate synthetic ability of the liver (Deepak *et al.*, 2000).

Liver injury resulting from carbon tetrachloride toxicity was followed by a concomitant induction of abnormal lipoprotein phenotype. Increase in cholesterol, triacylglycerol, low density lipoprotein cholesterol, total non-high density lipoprotein cholesterol, LDL/HDL-ratio and decrease in HDL-cholesterol concentrations were indicative of abnormal lipoprotein phenotype. The results obtained from this study indicated that ethanol extracts of *C.odorata* was hypolipidemic. The extract was able to normalize lipoprotein phenotype (HDL, LDL, LDL/HDL-ratio and total non-HDL-cholesterol) which was altered by the induction of hepatotoxicity with carbon tetrachloride in the rabbits. In the presence of Carbon tetrachloride-intoxication, hypertriglyceridaemia resulted. In this condition, there is increased VLDL concentration because of the action of hepatic lipase. The HDL becomes overloaded with triglyceride; they reduce in size, losing apoA$_1$ and the concentration of HDL-cholesterol falls. This fall in HDL-cholesterol concentration represents an alteration of the lipoprotein phenotype. Effectiveness of *C. odorata* extracts in the normalization of lipoprotein phenotype in serum (Fig. 2a-f) was seen in the restoration of lipid profile values to their respective normal values. Normalization of lipid profile values could be a mechanism of/or a consequence of hepatoprotection. More generally, normalization of lipoprotein phenotype by the extracts could point to their potential to reduce cardiovascular disease risk. Hypercholesterolaemic serum increases the permeability of endothelial cells through zonula occludens-1 with phosphatidylinositol 3-kinase signaling pathway (Chang *et al.*, 2009). Increased endothelial cell permeability will result in loss of endothelial relaxing factor and increased vascular complication. Inhibition of the processes resulting to hypercholesterolemia and by implication increased endothelial cell permeability by *C. odorata* extracts may be a mechanism of reduction of vascular complication. It is well known that total cholesterol, triglyceride, LDL-cholesterol, HDL-cholesterol, LDL/HDL-ratio and total non-HDL cholesterol are all independent and significant predictors of cardiovascular disease risk (Wilson *et al.*, 1998). The reduction in the total-non-HDL-cholesterol is most interesting since it is the single greatest predictor of cardiovascular risk. Measurement of total-non-HDL-cholesterol has been shown to be as good as or better than apo-lipoprotein fractions in the prediction of cardiovascular risk. There has been an association between hypolipemic potential and hepatoprotective effect (Alisi *et al.*, 2008). *C. odorata* ethanol extract, may be furthering its hepatoprotective effect by hypolipidemic mechanism. *Chromolaena odorata* normalises lipoprotein phenotypes in carbon tetrachloride toxicity-induced dyslipidemia.

CONCLUSION

In conclusion, present investigation revealed that *C. odorata* leaf extract has got the ability to prevent dyslipidemia that would normally result from Carbon tetrachloride-induced oxidative damage. The mechanism of this action is not fully understood. However, the protection conferred

on the liver by the extract would have preserved the liver cell to function in the maintenance of lipoprotein phenotype. Intake of *C. odorata* extract as drug or as supplement in diet may offer useful benefit in the preservation of lipoprotein phenotype. This will also be beneficial in the reduction of cardiovascular risk associated with dyslipidemia.

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