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RESEARCH ARTICLE

EFFICACY OF *CENTELLA ASIATICA* ETHANOLIC EXTRACT ON CADMIUM INDUCED CHANGES IN BLOOD HAEMATOLOGY, HEPATIC AND NEPHRITIC FUNCTION MARKERS IN ALBINO RATS

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ABSTRACT

The present study was designed to examine the protective effect of *Centella asiatica* ethanolic leaves extract on the haematological, hepatic and nephritic function marker changes induced in the blood of cadmium chloride treated albino rats. Administration of cadmium chloride (5 mg/kg body weight) caused a considerable increase in the count of WBC, AST, ALT, ALP, LDH, total bilirubin, urea, creatinine, globulin and decrease in the levels of total haemoglobin, RBC, hematocrit, mean cell haemoglobin, mean cell haemoglobin concentrations, total serum protein and albumin. Various concentrations of *Centella asiatica* ethanolic extract (20, 40, 60, 80, 100 mg/kg body weight) or silymarin (50 mg/kg body weight) as a pre-treatment were administered for 30 days to rats treated with cadmium chloride (5 mg/kg body weight). The levels of haematological, hepatic and nephritic function markers were found to be restored to near normal levels and the effectiveness of the treatment was found to be concentration dependent. The effective concentration of *Centella asiatica* ethanolic extract was found to be 80 mg/kg body weight. At this concentration, the extract's protective effect was comparative to silymarin (50 mg/kg body weight). Altogether the results suggest that, *Centella asiatica* ethanolic extract (80 mg/kg body weight) can substantially reduce the toxic effects of cadmium and can help restore the imbalance caused in cadmium treated albino rats to near normal.

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INTRODUCTION

Cadmium (Cd) is a very toxic environmental pollutant. Occupational and environmental pollution from Cd are due to anthropogenic activities such as mining, metallurgical industries, manufacturing of Nickel–Cadmium batteries, pigments and plastic stabilizers (Friberg, *et al*., 1986; Bertin and Averbeck, 2006). It has been classified as a carcinogen by the International Agency for Research on Cancer (IARC, 1993). Cd accumulates mostly in the liver and kidney and has a long biological half-life of 17 to 30 years in humans (Hideaki *et al*., 2008).Cadmium toxicity can also induce cancer. Humans (non-smokers) get exposed to cadmium through food by phosphate fertilizer application, water and air contaminations. Cigarette smoking is another well known source of cadmium toxication in smoking population (Hassan *et al*., 2005). *Centella asiatica* L. (Apiaceae), commonly known as Asiatic pennywort or Indian pennywort, belongs to the family Apiaceae (formerly known as Umbelliferae). It is a slender, prostrate, glabrous, perennial creeping herb rooting at the nodes, with simple petiolate, palmately lobed leaves. It is widely cultivated in Southeast Asia, India, China, Sri Lanka, etc., as vegetable or spice. *Centella asiatica* L. (Apiaceae) has various pharmacological activities like memory enhancing, anti-inflammatory, antioxidant, wound healing, immune-stimulant, anti-anxiety (anti-hypertensive), anti-stress and anti-epilepsy. The diverse health benefits of *Centella asiatica* L. (Apiaceae) has lead to the increased usage of this plant in food and beverages. It has been widely used for treatment of skin diseases, rheumatism, inflammation, syphilis, mental illness, epilepsy, hysteria, dehydration, diarrhea, wounds and ulcers (Yu *et al*., 2006, Mukherjee *et al*., 2011; Meena *et al*., 2012 and Seevaratnam *et al*., 2012) This study tries to understand some of the changes in the haematological, hepatic and nephric function parameters in cadmium chloride treated albino rats and its possible reversal by *Centella asiatica* L. (Apiaceae) ethanolic leaves extract.

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MATERIALS AND METHODS

Chemicals

Cadmium chloride was obtained from SRL (Sisco Research Laboiratories Pvt. Ltd, Mumbai, India. All reagents used for

the biochemical estimations in this study were procured from Sigma Chemical Co. Ltd, USA and Himedia Laboratories Pvt Ltd, Mumbai, India.

Plant Material collection and identification

Centella asiatica L. (Apiaceae) used in this study was collected from Thanjavur district, Tamil Nadu, India. The plant was identified at the herbarium of Department of Botany, Annamalai University. A voucher specimen (Herbarium No. DDE/HER/53) was deposited in the Department Herbarium for future reference. The leaves were washed under running tap water to remove dirt and other debris. It was then spread under a clean shade for drying. The dried leaves were milled to coarse powder using a mechanical grinder and stored in an air-tight container until further use.

Ethanolic extraction of plant material

Approximately 1 kg of powered *Centella asiatica* L. (Apiaceae) was used for ethanolic extraction using Soxhlet apparatus. The dark green extract obtained was subjected to ultracentrifugation followed by micro-filtration. The final clear dark extract was then concentrated in a rotary evaporator under reduced pressure. The final dried extract was lyophilized and was stored in a glass vials at -20°C for further use.

Percentage yield of plant extract

The percentage yield of the extract was determined gravimetrically using the dry weight of the crude extract obtained (X) and dry weight of plant powder used for the extraction (Y) by using the following formula:
Percentage yield = X/Y * 100

Animals

Male Wistar albino rats of body weight 160–180 g were used for this study. The animals were bred and maintained at Central Animal House, Rajah Muthiah Medical College, Annamalai University, Annamalainagar, Chidambaram, India. Rats were fed on standard pellet diet ((Lipton India Ltd., Mumbai, India) and water *ad libitum*. The animals were housed in polycarbonate cages in a room with a 12 h day–night cycle. The protocol (Proposal No. 1022, 2013) of this study was approved by the Institutional Ethical Committee of Annamalai University.

Experimental Design

The rats were divided into nine groups each comprising of six rats. For oral administration, cadmium chloride and the extract were dissolved in saline and 0.5% DMSO respectively.

Group 1: Normal control rats (saline and 0.5% DMSO) (n =6)
Group 2: Cadmium chloride treated rats (5 mg/kg body weight, intragastrically) (n =6)
Group 3: *Centella asiatica* ethanolic leaves extract (20 mg/kg body weight; pre-treatment before 1 hour) + Cadmium chloride (5 mg/kg body weight) (n =6)
Group 4: *Centella asiatica* ethanolic leaves extract (40 mg/kg body weight; pre-treatment before 1 hour) + Cadmium chloride (5 mg/kg body weight) (n =6)
Group 5: *Centella asiatica* ethanolic leaves extract (60 mg/kg body weight; pre-treatment before 1 hour) + Cadmium chloride (5 mg/kg body weight) (n =6)
Group 6: *Centella asiatica* ethanolic leaves extract (80 mg/kg body weight; pre-treatment before 1 hour) + Cadmium chloride (5 mg/kg body weight) (n =6)
Group 7: *Centella asiatica* ethanolic leaves extract (100 mg/kg body weight; pre-treatment before 1 hour) + Cadmium chloride (5 mg/kg body weight) (n =6)
Group 8: *Centella asiatica* ethanolic leaves extract treated rats (100 mg/kg body weight) (n =6)
Group 9: Silymarin (50 mg/kg body weight; pre-treatment before 1 hour) + Cadmium chloride (5 mg/kg body weight) (n =6)

All the treatments were administered orally using an intragastric tube daily for a period of 30 days (El-Demerdash *et al*., 2004). The experiment was terminated at the end of 30 days and the animals were fasted overnight, weighed and sacrificed by cervical decapitation. Blood was collected in EDTA tubes for the estimation of haematological parameters. Fresh blood samples were centrifuged to collect serum for biochemical parameters.

Evaluation of haematological parameters

The total red blood cells (RBC) and white blood cells (WBC), haemoglobin (Hb), haematocrit (Ht), mean cell haemoglobin (MCH/MEH) and mean cell haemoglobin concentration (MCHC), were determined and calculated by adopting the method of Dacie and Lewis, 1984.

Assessment of hepatic and nephritic functions

The total serum protein (TSP) concentration was determined using the Lowry *et al.* (1951), method and the albumin concentration by the method of Doumas *et al*. (1971). The globulin concentration was calculated as the difference between albumin concentration and the total protein concentration. Activities of serum aspartate aminotransferase (EC. 2.6.1.1), alanine aminotransferase (EC. 2.6.1.2), alkaline phosphatase (EC.3.1.3.1) and lactate dehydrogenase (EC. 3.1.3.1) were determined using commercially available diagnostic kits from Sigma diagnostics (I) Pvt. Ltd., Baroda, India. The level of total bilirubin was measured using the method of Malloy and Evelyn, (1937). The levels of kidney function markers urea and creatinine were also determined using commercially available diagnostic kits from Sigma diagnostics (I) Pvt. Ltd., Baroda, India.

Statistical analysis

The data were expressed as mean ± SD (n = 3). Statistical analysis of the data was carried out by one-way analysis of variance (Anova) followed by Duncan's Multiple Range Test (DMRT) using a statistical package program (SPSS v11.5 for Windows) $p<0.05$ were considered as statistically significant.

RESULTS

Percentage yield of plant extract

Table 1 shows the percentage yield of *Centella asiatica* (Ca) ethanolic extract and was found to be 2.418%.

Table 1. Percentage yield of plant extract

Plant	Solvent	Method	Weight of crude extract (g)	% yield
Centella asiatica	Ethanol	Soxhlet extraction	12.09	2.418

Body weight

Table 2 shows the body weight of control and experimental animals in each group. The mean body weight was significantly decreased (p<0.05) in cadmium chloride ($CdCl_2$) treated rats as compared to control animals. The body weight was found to be increased in $CdCl_2$ treated rats for both 1 hour pre-treatment with the reference drug silymarin (50 mg/kg body weight) group and in Ca ethanolic leaves extract treated groups in a concentration dependent manner. Extract at a concentration of 80 mg/kg body weight was found to be most effective.

Evaluation of haematological parameters

The total RBC, Hb, Ht, MCH/MEH and MCHC, were found to be significantly decreased (p<0.05) in cadmium chloride treated group, when compared with control group. Whereas, a significant increase (p<0.05) in the white blood cells (WBC) level was found in the $CdCl_2$ treated group.

These levels were found to be restored in the reference drug silymarin (50 mg/kg body weight) and Ca extract pre-treated groups in a concentration dependent manner, with 80 mg/kg body weight to be the most effective concentration (Table 3).

Assessment of hepatic and nephritic functions

The changes in the level of TSP, albumin, globulin, activities of serum AST, ALT, ALP, LDH, and total bilirubin (liver function tests) (Table 4a & b); urea and creatinine (kidney function tests) (Table 5), in $CdCl_2$ and Ca extract treated groups are summarized in Table 4 and 5. A significant decrease (p<0.05) in the levels of TSP and albumin were observed in $CdCl_2$ treated group.

Table 2. Body weight of control and experimental animals in each group. Values are expressed as mean ±SD (n=6). Values not sharing a common superscript letter differ significantly at p<0.05 (DMRT)

Groups	Body weight (g)	
	Initial	Final
Group 1	178.00±10.24^{a}	218.00±4.73^{de}
Group 2	175.00±11.30^{a}	182.00±3.59^{a}
Group 3	181.00±8.64^{a}	190.10±9.56^{ab}
Group 4	180.00±10.16^{a}	196.00±11.20^{b}
Group 5	179.00±9.32^{a}	200.00±10.12^{bc}
Group 6	178.00±6.28^{a}	207.50±12.34^{cd}
Group 7	177.00±11.19^{a}	208.00±8.96^{cd}
Group 8	180.00±9.47^{a}	220.00±4.46^{e}
Group 9	177.00±5.67^{a}	209.00±11.22^{cd}

Table 3. Effect of Centella asiatica leaf ethanolic extract on Cd induced haematological parameter changes in control and experimental animals. Values are expressed as mean ±SD (n=6). Values not sharing a common superscript letter differ significantly at p<0.05 (DMRT)

Groups	RBC x10^{6}/mm^{3}	WBC x10^{3}/mm^{3}	Haemoglobin mg/dl	Ht%	MCH pg	MCHC%
Group 1	6.98± 0.31^{c}	5.32±1.77^{a}	16.50±0.10^{g}	43.15±3.60^{d}	23.67±0.90^{d}	38.45±2.98^{d}
Group 2	4.25±0.23^{a}	7.59±1.38^{b}	6.62±0.02^{a}	27.35±2.35^{a}	15.61±0.79^{a}	24.35±2.01^{a}
Group 3	4.50±0.30^{a}	7.42±1.68^{ab}	7.85±0.09^{b}	27.18±2.34^{a}	17.50±1.00^{b}	29.04±2.19^{b}
Group 4	5.12±0.25^{b}	6.95±1.57^{ab}	9.95±0.04^{c}	29.18±1.40^{ab}	19.47±0.87^{c}	34.17±1.48^{c}
Group 5	5.15±0.16^{b}	6.15±1.84^{ab}	12.97±0.03^{d}	31.01±1.16^{b}	25.20±0.75^{e}	35.87±1.46^{e}
Group 6	6.90±0.16^{c}	5.49±1.30^{ab}	15.79±0.01^{e}	40.08±1.15^{c}	22.90±0.52^{d}	37.42±1.10^{d}
Group 7	6.97±0.29^{c}	5.40±1.32^{ab}	15.85±0.08^{e}	40.15±1.37^{c}	22.96±0.86^{d}	37.49±1.13^{d}
Group 8	6.99±0.27^{c}	5.35±1.74^{a}	16.59±0.10^{h}	43.02±2.33^{d}	23.75±0.79^{d}	38.65±1.85^{d}
Group 9	6.94±0.27^{c}	5.38±1.70^{a}	16.01±0.01^{f}	41.27±2.24^{cd}	23.09±0.90^{d}	38.89±2.08^{d}

Table 4a. Effect of Centella asiatica leaf ethanolic extract on Cd induced changes in total serum protein, albumin and globulin in control and experimental animals. Values are expressed as mean ±SD (n=6). Values not sharing a common superscript letter differ significantly at p< 0.05 (DMRT)

Groups	Protein g/dl	Albumin g/dl	Globulin g/dl
Group 1	6.21±0.22^{c}	5.50±0.45^{e}	0.71±0.18^{b}
Group 2	4.32±0.33^{a}	2.01±0.09^{a}	2.31±0.24^{de}
Group 3	4.49±0.21^{a}	2.04±0.50^{a}	2.45±0.37^{e}
Group 4	5.01±0.44^{b}	2.92±0.19^{b}	2.09±0.25^{d}
Group 5	5.19±0.23^{b}	3.12±0.14^{b}	2.07±0.09^{d}
Group 6	5.25±0.22^{b}	4.20±0.20^{c}	1.05±0.02^{c}
Group 7	5.48±0.26^{b}	4.40±0.39^{c}	1.00±0.12^{c}
Group 8	6.20±0.20^{c}	5.49±0.02^{e}	0.71±0.18^{b}
Group 9	5.27±0.33^{b}	4.85±0.18^{d}	0.41±0.16^{a}

Table 4b. Effect of Centella asiatica leaf ethanolic extract on Cd induced changes in AST, ALT, ALP, LDH and bilirubin in control and experimental animals. Values are expressed as mean ±SD (n=6). Values not sharing a common superscript letter differ significantly at p< 0.05 (DMRT)

Groups	AST IU/L	ALT IU/L	ALP IU/L	LDH IU/L	Bilirubin mg/dl
Group 1	67.51±4.66^{a}	46.03±4.23^{a}	110.20±4.54^{b}	105.09±11.19^{a}	0.33±0.04^{a}
Group 2	132.45±8.29^{e}	120.62±4.67^{e}	231.61±3.96^{g}	185.05±11.29^{d}	1.42±0.10^{e}
Group 3	130.72±2.36^{e}	110.25±2.22^{d}	228.72±3.60^{g}	171.07±12.48^{d}	1.39±0.02^{e}
Group 4	100.21±5.19^{d}	81.34±7.08^{c}	191.41±2.33^{f}	156.35±11.94^{c}	1.20±0.05^{d}
Group 5	85.08±5.80^{c}	65.11±3.92^{b}	142.32±6.06^{e}	131.20±13.90^{b}	0.95±0.10^{c}
Group 6	74.05±4.43^{b}	50.23±3.76^{a}	129.90±4.22^{d}	118.23±13.76^{ab}	0.49±0.01^{b}
Group 7	72.05±3.58^{b}	48.24±3.78^{a}	128.06±5.05^{d}	116.20±13.05^{ab}	0.40±0.03^{ab}
Group 8	68.62±3.79^{ab}	45.21±3.35^{a}	105.28±4.66^{a}	108.51±10.17^{a}	0.30±0.11^{a}
Group 9	69.59±3.51^{ab}	49.45±3.22^{a}	118.73±1.65^{c}	115.71±11.21^{a}	0.44±0.14^{b}

Table 5. Effect of Centella asiatica leaf ethanolic extract on Cd induced changes in kidney function tests in control and experimental animals. Values are expressed as mean ±SD (n=6). Values not sharing a common superscript letter differ significantly at p<0.05 (DMRT)

Groups	Creatinine mg/dl	Urea mg/dl
Group 1	0.51±0.03^{a}	26.80±1.42^{a}
Group 2	1.71±0.07^{f}	49.90±2.13^{f}
Group 3	1.42±0.16^{e}	47.31±1.99^{e}
Group 4	1.01±0.09^{d}	40.12±1.46^{d}
Group 5	0.82±0.01^{c}	37.03±1.98^{c}
Group 6	0.65±0.04^{b}	32.40±1.32^{b}
Group 7	0.63±0.02^{b}	31.20±1.24^{b}
Group 8	0.50±0.04^{a}	26.10±1.31^{a}
Group 9	0.61±0.06^{b}	30.70±2.10^{b}

A significant increase (p<0.05) were observed in the activities of AST, ALT, ALP, LDH, globulin, total bilirubin, urea and creatinine in $CdCl_2$ treated group, when compared with control group. These levels were found to be restored in the reference drug silymarin (50 mg/kg body weight) and the Ca extract pre-treated groups, in a concentration dependent manner, with 80 mg/kg body weight being the most effective concentration.

DISCUSSION

Cadmium is widely used in various industries and imposes a threat on environment as well as on human health (Hideaki *et al*., 2008). The present study was undertaken to understand the efficacy of *Centella asiatica ethanolic* (Ca) ethanolic leaves extract on cadmium chloride ($CdCl_2$) induced toxicity in albino rats. Previous finding by Antony *et al*. (2006), showed that Ca alcoholic extract had hepatoprotective effect in chemically (CCl_4) induced liver injury. Based on the acute toxicity works of Abdulla *et al.,* 2010, the ethanolic extract of Ca at a dose of 2g and 5g per kg body weight for 14 days did not manifest any significant visible signs of toxicity. The $CdCl_2$ treated animals showed a significant decrease (p<0.05) in body weight (Table 2), was in agreement with previous study by Milton Prabu *et al*. (2012) who found a decrease in body weight in cadmium chloride treated rats.

Another study by Rahman *et al*. (1988), suggested that prolonged cadmium exposure was associated with diabetes mellitus. Study by Kaltreid *et al*. (2001), linked low levels of heavy metals with impairment of glucocorticoid system. Glucocorticoid hormones are very important in glucose, carbohydrate and protein metabolism, which in turn affects increase/decrease in body weight. This impairment of glucocorticoid system may be the cause of body weight loss in cadmium treated groups. The body weights of rats were significantly restored (p<0.05) to near normal levels (Table 2) in the group administered with reference drug silymarin (50 mg/kg body weight) or Ca ethanolic leaves extract (in a concentration dependent manner). This may be attributed to the antioxidant properties of compounds present in *Centella asiatica* (Meena *et al*., 2012; Seevaratnam *et al*., 2012 and Ghosh & Indra, 2014).

Cadmium is known to cause anaemia by inducing hemolysis, renal anaemia as well as iron deficiency accompanied by abnormalities in iron metabolism (Horiguchi *et al*., 2011). The decrease in RBC and Haemoglobin (Hb) (Table 3) in $CdCl_2$ treated rats are in agreement with the results of Karmakar *et al*. (2000), El-Demerdash *et al*. (2004) and Singh *et al*. (2013). The lower levels of Hb content can be attributed to the increased rate of erythrocyte destruction or reduction in production of erythrocytes in bone marrow (El-Demerdash *et al*., 2004).

In the present study, we found a decrease in RBC, Hb, Ht, MCH/MEH and MCHC in $CdCl_2$ treated albino rats (Table 3). These parameters were restored to near normal in the groups treated with Ca extract (in a concentration dependent manner), with 80 mg/kg body weight being the most effective concentration or reference drug silymarin (50 mg/kg body weight).

WBCs are primarily involved in protecting the body at the event of any infection or injury. T and B lymphocyte cells play a very important role in the immune-defence system of the body (Bagley, 2014). Previous study by El-Demerdash *et al*. (2004), found an increase in leukocytes in $CdCl_2$ treated rats, indicating an increase in immune activity of the animal (Table 3). The present study found an increase in WBC levels in $CdCl_2$ treated rats indicating increase in immune activity and reversal by Ca extract treatment (in a concentration dependent manner), with 80 mg/kg body weight being the most effective concentration or reference drug silymarin (50 mg/kg body weight) (Table 3).

Liver is the main organ involved in detoxification of hormones, xenobiotics and drugs. During xenobiotic detoxification, the metabolised produced can damage the liver cells (Hutchison, *et al*., 2011). Previous study by El-Demerdash *et al*. (2004), have indicated a decrease in albumin levels and increase in serum total protein and serum globulin in cadmium treated rats. The estimation of TSP helps in differentiating amidst normal and damaged liver function. This is because, most of the serum proteins like albumins and globulins are bio-synthesised in the liver (Thapa and Walia, 2007). During hepatocellular injury, total protein may be reduced a little, but there is always a sharp decrease in albumin level and increase in globulin level (Singh *et al*., 2011). A decrease in the levels of albumin indicates liver dysfunction (Santosh *et al*., 2007). In the current study, a decrease in the TSP and serum albumin, and an increase in serum globulin were observed in cadmium chloride treated rats (Table 4a). This may be due to damage and dysfunction of liver by $CdCl_2$ administration. The hepatoprotective effect of Ca extract (in a concentration dependent manner), with 80 mg/kg body weight being the most effective concentration Or reference drug silymarin (50 mg/kg body weight) treated $CdCl_2$ groups may be the reason of restored levels of TSP, serum albumin and globulin to near normal (Table 4a).

Dysfunction or damage in liver is accompanied by increased levels of hepatic enzymes in serum, indicating hepatic cellular damage and loss of cell membrane functional integrity (Zimmerma and Seef, 1970). ALT and AST are primarily better parameters for detecting liver damages (Thapa and Walia, 2007). Elevated levels of ALP and bilirubin are correlated with liver function. Increased biliary function leads to an increased synthesis of ALP and elevated levels of serum bilirubin (Hutchison *et al*., 2011). Hepatotoxicity causes cirrhotic liver condition, leading to defective biliary functioning and increased bilirubin release in blood circulation (Lei *et al*., 2007). Increased bilirubin may also be a result of increased hemolysis (El-Demerdash *et al*., 2004). LDH, which is an intracellular enzyme, is an indicator of hepatic cell damage (Kim *et al*., 2001). Several studies have reported elevated serum levels of hepatic marker enzymes and bilirubin in cadmium exposed rats (Amin *et al*., 2006, Selvarajan *et al*., 2007, Milton Prabu *et al*., 2012 and Ibiam *et al*., 2013). In the present study, an increase in hepatic enzymes and bilirubin was observed in serum of cadmium treated rats. This may be due to cellular damage caused by cadmium in the liver of rats. The levels of AST, ALT, ALP, LDH and bilirubin were significantly ($p<0.05$) restored to near normal in the group treated with reference drug silymarin (50 mg/kg body weight) and Ca ethanolic leaves extract (in a concentration dependent manner) (Table 4b). The increased level of bilirubin is in agreement with the decrease in RBC count (Table 3). The hepatoprotective activity may be due to the antioxidant properties of compounds present in *Centella asiatica*, which help in healing as well as protecting the liver cells from cadmium toxicity and decrease the levels of hepatic cellular enzymes and bilirubin in serum of cadmium treated rats. Based on previous study, Ca ethanolic leaves extract has very good *in vitro* antioxidant and free radical scavenging activity. This may be attributed due to the presence of various antioxidant compounds present in *Centella asiatica* (Meena *et al*., 2012; Seevaratnam *et al*., 2012 and Ghosh & Indra, 2014).

After liver, the toxic secondary metabolites produced by phase I and II metabolising enzymes in the liver gets excreted out of the body through the kidneys. The second organ which gets affected by cadmium chloride toxicity are the kidneys. Decrease in haematological parameters partly contributes to $CdCl_2$ induced renal toxicity. Patients chronically exposed to cadmium experiences renal failure. Thus nephrotoxicity can lead to an incomplete filtration of the toxicants like urea and creatinine, leading to increased levels of these toxicants in the blood circulation (Ibiam *et al*., 2012). The present study found an increase in blood urea and creatinine (Table 5) in $CdCl_2$ treated rats indicating kidney dysfunction. These findings are in agreement with the results obtained by El-Demerdash *et al*. (2004) and Ibiam *et al*. (2012), in albino rats. These adverse effects on kidneys were restored to near normal in the groups administered with reference drug silymarin (50 mg/kg body weight) or Ca leaves extract (in a concentration dependent manner) with 80 mg/kg body weight being the most effective concentration (Table 5). Antioxidant and chelating activity of *Centella asiatica* may be the reason for its nephroprotective activity against $CdCl_2$ toxicity (Meena *et al*., 2012; Seevaratnam *et al*., 2012 and Ghosh & Indra, 2014).

The present study collectively demonstrates that the pre-treatment of $CdCl_2$ treated rats with *Centella asiatica* ethanolic leaves extract (80 mg/kg body weight) can reduce the possible side effects of the cadmium treatment in blood haematology, liver as well as kidney marker enzymes. The present work also provides future avenues to study the molecular mechanism involved in the protective effect of Centella asiatica ethanolic leaves extract in Cd intoxicated albino rats, and also isolation and characterization of potent molecules responsible for this protective effect.

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