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EVALUATION OF NEPHROPROTECTIVE ACTIVITY OF HERBAL ADAPTOGEN *CURCUMA LONGA* ON CADMIUM INDUCED NEPHROTOXICITY IN CHICKEN

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Abstract: The present investigation carried out to evaluate the nephroprotective activity of herbal adaptogen *Curcuma longa* on cadmium induced nephrotoxicity in chicken. Twenty seven number of chicken were equally divided in to three groups. In group II and III cadmium chloride given in drinking water at the dose rate of 100ppm/L for 29 days, additionally group III was treated with *Curcuma longa* (2g/kg in feed), while group I was control. Group III birds showed significantly reduced blood urea nitrogen and plasma creatinine level compared to group II. Lipid per oxidation and superoxide dismutase significantly decrease in group III compared to group I. Histopathology of kidney revealed mononuclear cells infiltration in interstitial space and coagulative necrosis in the lining of tubular cells. *Curcuma longa* is useful in preventing and treating the toxicity induced by cadmium chloride.

Keywords: Cadmium, nephroprotective, *Curcuma longa,* Lipid per oxidation, superoxide dismutase

INTRODUCTION

Cadmium is a soft bluish-white metal with atomic no 48 and atomic weight 112.4. It is a toxic metal that is widely used in electroplating and galvanizing, as a colour pigment in paints and batteries. The increased release of cadmium from industrial process, waste disposal and cigarette smoke in the environment lead to a general concern for the potential toxic effect of cadmium. Many of poultry industries those are located near highway and in the proximity of industries that liberate cadmium as a pollutant. The poultry kept as a layer or broiler may accumulate cadmium from polluted environment or feed contaminated cadmium. Shellfish such as mussels ,scallops and oysters and other fish accumulate cadmium and may become a major source of cadmium exposure for poultry and other livestock fed with fish meal and oyster shell grid as calcium source (Sashikumar *et al.* 2006). Low dietary levels of cadmium intake by broiler chicken results in its progressive accumulation in various tissues such as liver, kidney, muscle and bone (El-Dein,*et al*.2000) causing oxidative stress and may affect

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the performance and serum biochemical parametars, beside damaging kidney, liver and bursa of fabrics (Uyanik, *et al.*2001) Cadmium inhibits Ca^{2+} -ATPase in cell membrane /endoplasmic reticulum and prevents Ca^{2+} export from the cytoplasm. Ca^{2+}activates the enzyme that generates oxygen free radical (O_2^-) (Goyeret al., 2001) Cadmium also participates in Fenton reaction leading to generation of hydroxyl radical (HO-) (Liochevet al., 1999). Cadmium is known to cause stress by increasing lipid peroxidation or by changing intracellular glutathione (GSH) level and to affects the ubiquinin/ATP dependent proteolytic pathway (Figueiredoet al., 1998). Cadmium forms a covalent attachment with sulfhydryl groups of proteins and reduced glutathione (Quiget al., 1998). Cadmium competes with Zn and Cu and may affects the dependent enzymes such as Cu-Zn superoxide dismutase (Valiniece et *al*,. 1999). *Curcuma longa* is a mandatory spice present in every Indian kitchen. It is a member of zingiberaceae, a perennial herb with short and thick rhizomes. Turmeric is comprised of a group of three curcuminoids: curcumin (diferuloylmethane), demethoxycurcumin and bisdemethoxycurcuminas as well as volatile oils (tumerone, atlantone and zingiberone) sugars, proteins, and resins. It has been shown to have a wide spectrum of biological actions that includes anti-inflammatory, anti-carcinogenic, anti-mutagenic and antibacterial activities (Aggarwal*et al*., 2003; Egan *et al.,* 2004; Singh *et al.,* 2007: Deevika*et al*., 2012).

MATERIAL AND METHODS

Chemical and Reagent

The chemical used in the present study was cadmium chloride monohydrate (Merck Limited), MTT, Thibarbituric acid, Thioacetic acid, Sulfuric acid, Nitric acid, Dimethyl sulfoxide, Pyragallol, potassium dihydrogenphosphate. ERBA Diagnostics kits (Mannheim, Germany) were procured for estimation of the serum bio-marker levels.

Experimental animals

A total twenty seven chickens weighing 477-490 grams maintained in poultry farm, Ranchi Veterinary College. The protocol of the experiment was approved by the Institutional Animal Ethical Committee. The experimental chickens were given standard feed and water *ad-libitum*.

Experimental design

A totaltwenty seven number of layer chickens were equally divided in to three groups. In group II cadmium chloride was given in drinking water @100ppm/L for 29 days. Group III was treated with *curcuma longa* @ 2 gram /kg in feed for 29 days and same dose of cadmium

chloride as in group II. The control group was kept untreated with either cadmium chloride or *curcuma longa*.

Sample collection and Biochemical analysis

Blood samples were collected from the wing vein on 14th and 29th day from all the chicken with anticoagulant (EDTA). Serum blood urea nitrogen (BUN) and creatinine were estimated using the Erba-semi auto analyzer. The pieces of kidney thus collected after sacrifice of the experimental birds were washed in ice cold saline and 200mg of kidney tissue sample was weighted and kept in 2 ml of ice-cold saline. The homogenate was prepared in the Remi-Homogeniser and was centrifuged at 3000 rpm for 10 min. The supernatant was used for estimation of oxidative stress indices. Superoxide dismutase (SOD) was estimated as per the method of Madesh, and Balasubramanian (1998). The extent of Lipid peroxidation was evaluated in term of MDA production and determined by the thiobarbituric acid method. The reduced glutathione (GSH) level was assessed by DTNB method.

Cadmium analysis

The cadmium concentration in kidney was quantitivelyanalyses with the help of Atomic absorption spectrophotometry (AAS) by the method of Troloson (1969). 1gm of tissue was taken in digestion tube and 5ml concentrated nitric acid and 1ml of concentrated sulfuric acid were added and mixed well. The samples were kept overnight at room temperature followed by digestion on low heat using heat block, until the volume of sample reduced to about 1ml. To this 3ml of double acid mixture was added and low heat digestion continued until the digested sample becameclear and emitted white fumes. Digested clear white sample were filtered through Whatman filter paper no-42. Repeated washing of digestion tube and filter paper were done taking 0.5 ml Millipore water. The working standards were as follows 5,10,20 and 40 ml/L and prepared it by same procedure test sample.

Histopathology

Formal saline fixed kidney were routinely processed, cut at 5µm and stained with H&E stain.

Statistical analysis

Statistical way was analyzed using ANOVA. A value $p \leq 0.05$ and $p \leq 0.01$ were considered significantly at 5 percent and 1 percent level respectively.

RESULT

Table 1: Effect of cadmium chloride along and with Curcuma longa on various parameters in chicken (mean±S.E)

Group	Creatinine(mg/ dl)		BUN(mg/dl)		Cadmium (ppm)	
	14^{th} day	29^{th} days	14^{th} day	29^{th} days	14^{th} day	29^{th} days
I	0.51±0.04	0.65±0.17	20.70±1.17	24.81±0.71	0.32±0.06	0.31±0.03
II	1.18±0.30	2.31±0.27	46.97±7.61	73.64±4..90	*14.05*±0.78	24.72±3.69
III	1.02±18	1.08±0.06**	32.88±5.29	52.88±5.5**	12.07±3.37	23.07±3.44

Table 2: Effect of cadmium chloride along and with curcuma longa on various parameters in chicken (mean±S.E)

Group	SOD(U/mg of protein)		LPO (nM/MDA/g)		GSH(µmol/gm of protein)	
	14^{th} day	29^{th} days	14^{th} day	29^{th} days	14^{th} day	29^{th} days
I	3.94±0.21	3.99±0.31	0.51±0.1	0.47±0.15	7.54±025	7.02±0.65
II	5.60±0.47	7.14±0.74	2.58±0.35	7.62±1	3.58±0.67	2.98±092
III	4.91±0.22*	5.44±0.26**	1.48±0.63*	4.02±0.99**	4.82±0.57*	5.71±0.82*

**P ≤ 0.01; *P ≤ 0.05;

Serum biochemical parameters

There was significant increase in Creatinine and BUN values of group I and also in group II with that of control on 14^{th} day. Similarly, on 29^{th} day significant increase in Creatinine and BUN levels of group I and group II were found (Table 1).

Oxidative stress indices

There was significantly decrease in SOD and LPO value of group II as compared to Group I on both 14^{th} and 29^{th} day, but value were increase as compared to 0 days.

GSH level in kidney were significantly decreased in group I compared to control, but improved in group II (Table 2).

Cadmium concentration

There was significant amount of cadmium deposited in the kidney of chicken, but accumulation was not varied significantly after treatment of *curcuma longa.*

Histopathology

The microscopic section of kidney of chicken treated with cadmium @100ppm collected after 14th days and 29th days of experiment exhibited degenerative change in renal tubules and glomeruli varying from reversible to irreversible stage of cell injury (Fig 1). The microscopic changes of kidney of chicken treated with cadmium along with curcuma longa showed consistent decrease in severity of granular, vacuolar and necrotic changes of the tubular epithelia cell along with congestive haemorrhagic and infiltrative changes.(Fig 2)

DISCUSSION

An increase in BUN reflects an accelerated rate of protein catabolism (Swapna *et al.,* 2011). In the present study, the serum creatinine and BUN levels were significantly increased in toxic controls at the end of 29 days as compared to the remaining groups. This could be attributed to the free radical induced oxidative damage on kidney by cadmium. Cadmium may exert toxic effects on several organ systems, but those in the kidney are the most insidious. Treatment in group- III with, curcuma longa and cadmium resulted in significant decrease in serum creatinine and BUN as compared to Cd toxic control group- II, which further confirms the protective/preventive role of the *Curcuma longa* in present study Ghoniem *et al*.,(2012). This finding suggests the prophylactic potential of *Curcuma longa* to prevent cadmium induced toxic manifestations, though there was no complete prevention of the changes. The beneficial renal protective actions of drugs in present study may be attributed to their antioxidant / free radical scavenging actions and protection of protein thiols from deleterious actions of cadmium in kidney (Attia *et al*.2014). The antioxidant defense profile was studied in order to assess the extent of Cd -induced free radical damage in the biological system. In the present study, kidney LPO and SOD activities were significantly increased and GSH production decrease in the toxic group suggesting the ongoing peroxidative stress (Karimi *et al*.2012). It has been reported earlier that Cadmium impairs the antioxidant defenses of cells and render them more susceptible to oxidative attacks (Bharvi *et al*., 2011). *Curcuma longa* has been reported to reduce lipid peroxidation, SOD and improve GSH concentration in kidney (Tarasub *et al.,* 2011).

CONCLUSION

Curcuma longa (2 g/kg in feed) along with cadmium chloride showed mild protection against the toxic effects caused by cadmium in layer birds. It has shown potent antioxidant activity, nephroprotective activity against cadmium induced toxicity. Supplementation of this plant may protect tissues from the toxic effects of cadmium.

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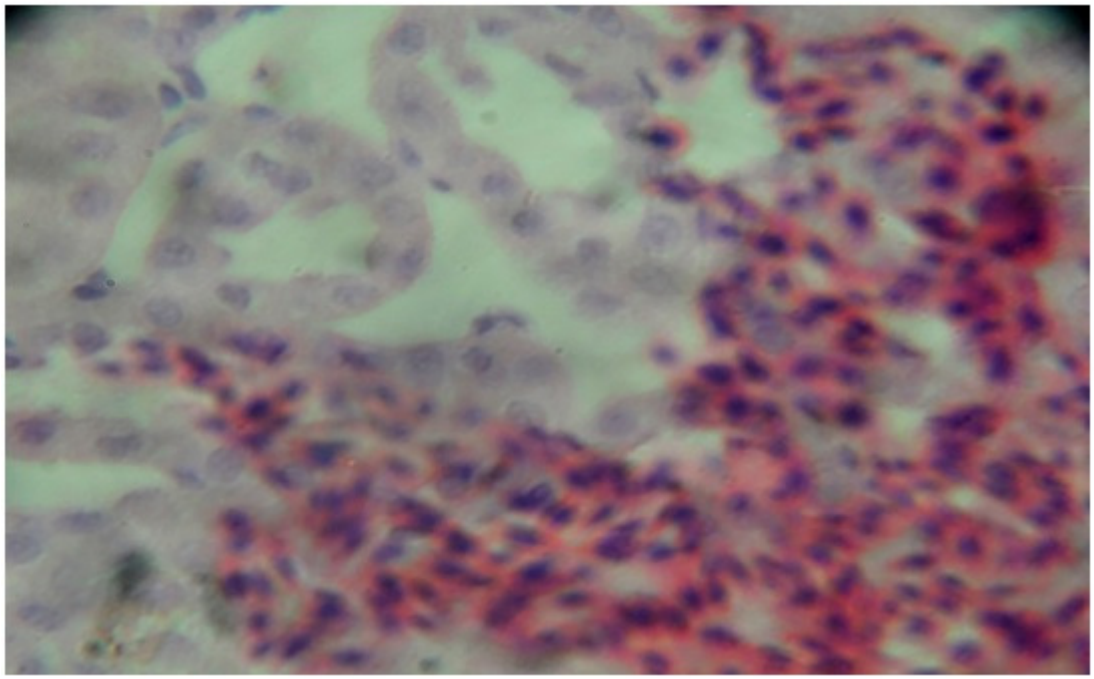

Fig 1: Kidney showing degenerative change in renal tubules and glomeruli

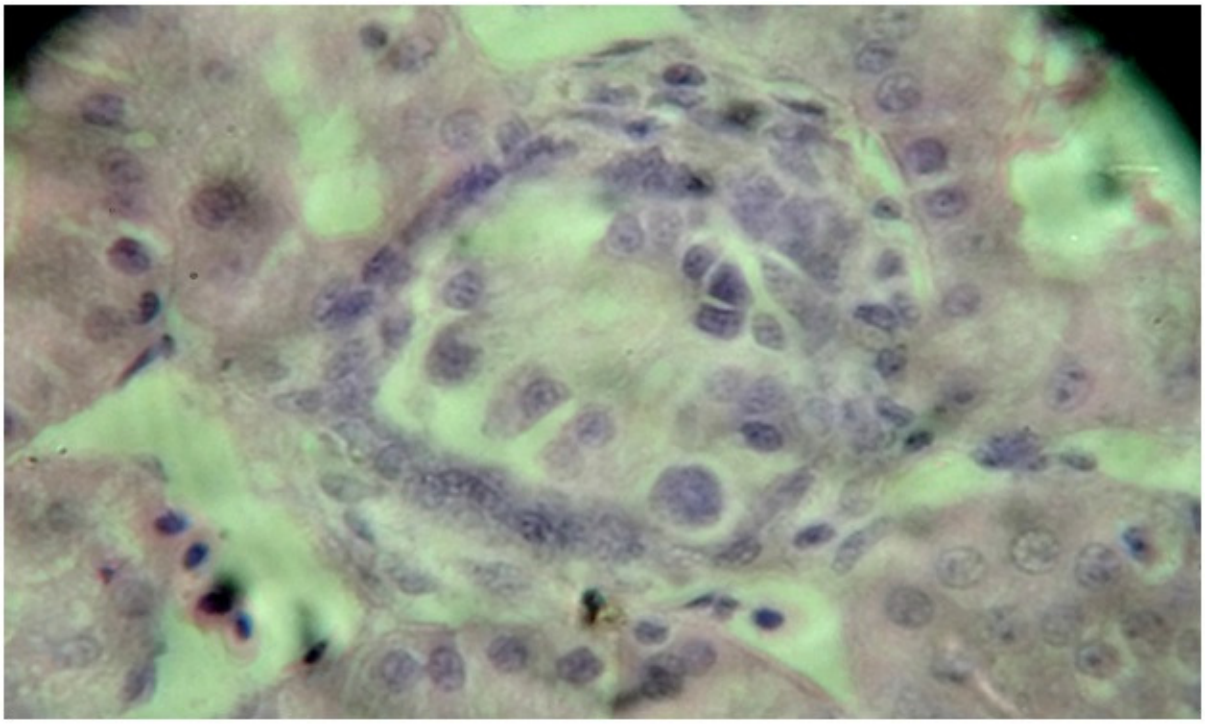

Fig 2: Kidney of chicken treated with cadmium along with *Curcuma longa*