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MODULATORY EFFECT OF CURCUMIN ON ENDOSULFAN INDUCED ANOMALIES IN THE KIDNEY FUNCTION OF *MUS MUSCULUS*

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ABSTRACT
The present study investigated the effect of curcumin on endosulfan induced anomalies in the kidney function of *Mus musculus*. Administration of endosulfan (3.0 mg/kg) resulted in marked increase in the values of blood urea (17.63%, 39.20% and 63.68%) and serum creatinine (20.37%, 44.64% and 105.55%) and reduction in the total protein concentration (5.14%, 16.20% and 29.13%) after 7, 14 and 28 d respectively. Analysis of variance showed that the level of blood urea and creatinine increased significantly ($p \geq 0.05$) from control however, the total protein concentration decreased significantly ($p \geq 0.05$) from control after 7, 14 and 28 d of endosulfan administration. The result also indicated that endosulfan induced anomalies in the kidney function was remarkably prevented by treatment with Curcumin. Curcumin restored renal function in *Mus musculus* as judged by the increase in total protein while decrease in blood urea and creatinine. These data suggest that administration of curcumin is a promising approach in the treatment of disturbed kidney function caused by endosulfan.

INTRODUCTION

Large scale manufacture and tremendous utilization of a variety of pesticides and their formulation for the control of crop pests and vectors of communicable diseases has caused global concern (Vengateshwarlu *et al.,* 2000). Pest control chemicals are poisons and they may present immediate danger to user if used improperly. Some of them highly toxic and may cause serious metabolic disorders and even death if inhaled or ingested through oral route (Frank and Brawn, 1984). Endosulfan is one of the synthetic organochlorine insecticide of the cyclodine group with a mixture of two stereo isomer: α- and β- endosulfan in the ratio of 70:30. It has widespread use in agriculture and forestry to control a wide varicty of insect pests and on non food crops such as cotton and tobacco (Khan and Kumari, 2012). Endosulfan is known to be one of the highly toxic agricultural pesticides commonly used in our societies (Uboh *et al.,* 2011). In India about 1000 metric tons of endosulfan and its formulations have been in use (Romeo and Quijano, 2000). Once the insecticides enter the body; it is transported to different parts of it through the blood. The kidney is the main excretory organ, it removes the wastes which are toxic to the animal body. The effect of pesticide poisoning can be easily seen on this organ. The administration of pesticides, therefore, affects the biochemical environment of kidney. Considering this fact the nephrosis caused by endosulfan in the form of biochemical changes was observed through kidney function test.

There is an increasing interest towards medicinal plants and their active ingredient since 1980. Medicinal plants serve as therapeutic alternatives, safer choice, or in some cases, as the only effective treatment. People in different cultures and places have used particular plants to treat certain medical problems. A larger number of these plants and their extract have shown beneficial therapeutic effects, including anti-oxidant, anti-inflammatory, anti-cancer, anti-microbial, and immunomodulatory effects (Qin *et al*., 2008; Brown *et al*., 2009; Al-Attar and Al-Taisan, 2010). Medicinal plants show also rejuvenating and restorative properties. Many of physiological disorders including productive abnormalities can be effectively prevented by use of active principles of medicinal plants in adequate dose and duration. Among the promising medicinal plants, the turmeric (*Curcuma longa*) plant, a perennial herb belonging to the ginger family, cultivated extensively in south and southeast tropical Asia is an amazing herb with a rich historical and religious background. The rhizome of this plant, also referred to as the "root" is the most useful part of the plant for culinary and medicinal purposes. The most active component of turmeric is curcumin, which makes up 2–5% of the spice.

Several lines of evidence suggest reactive oxygen species (ROS) as the principal mediator in the development of nephrosis caused by endosulfan. The hypothesis was proposed, that if endosulfan nephrotoxicity is related to free radical formation and lipid peroxidation then antioxidant therapy may protect endosulfan toxicity in kidney (Uzun and Kalender, 2011). Curcumin, the yellow pigment isolated from turmeric, represents a class of anti-inflammatory (Srivastava and Srimal, 1985), antioxidant (Joe *et al.,* 2004) reported to be a potent

inhibitor of ROS formation. It has been found to be at least 10 times more active as an antioxidant than even vitamin E (Khopde *et al.,* 1999). Therefore, the present study was undertaken to evaluate the protective effect of curcumin against endosulfan caused adverse biochemical changes in the kidney function of *Mus musculus*.

MATERIALS AND METHODS

In the present investigation, experiment was performed on 3-4 months old Swiss albino mice. The mice were divided into 4 groups as first group (n = 10) was control group, second group (n = 10) was Endosulfan treated group for 7 days, third group (n = 10) was Endosulfan treated group for 14 days, fourth group (n = 20) was Endosulfan treated group for 28 days. Half of the animals from fourth group treated with Endosulfan for 4 week were further treated with turmeric extract for 28 days. The oral LD_{50} value of Endosulfan for mice was estimated by standard interpolation method, which was 7.0 mg/kg b.w. The standard data reference for LD_{50} value of Endosulfan for mice is 7.36 mg/kg b.w. (EXTOXNET, 1996). Endosulfan manufactured by Excel Industries, Mumbai (EC 35%) was dissolved in distilled water to prepare sublethal dose of 3.0 mg/kg b.w. was administered by gavage method. The control group of mice was served with equal volume of distilled water by gavage method. The maximum permissible dose for curcumin was 200 mg/kg. b.w. Blood samples were collected from all groups on 7th, 14th and 28th day of experiment.

Data are expressed as means ± SEM. Statistical comparison between different groups were done using one way analysis of variance (ANOVA) followed by Bonferroni multiple comparison test using SPSS version 16.0 for windows. Values of $p \leq 0.05$ were considered statistically significant.

RESULTS

Data of the serum biochemical analyses after 7, 14 and 28 d of endosulfan administration followed by curcumin treatment were represented in Table 1. Administration of endosulfan (3.0 mg/kg) resulted in marked increase in the values of blood urea (17.63%, 39.20% and 63.68%) and serum creatinine (20.37%, 44.64% and 105.55%) and reduction in the total protein concentration (5.14%, 16.20% and 29.13%) after 7, 14 and 28 d respectively. The result also indicates that the duration of endosulfan exposure also affected significantly the biochemical parameters. Analysis of variance showed that the level of blood urea and creatinine increased significantly ($p \leq 0.05$) from control however, the total protein concentration decreased significantly ($p \leq 0.05$) from control after 7, 14 and 28 d of endosulfan administration. Curcumin treatment (200 mg/kg) for 28 d significantly attenuated the level of blood urea, creatinine as well as total protein in endosulfan treated mice for 28 d (Table 1).

DISCUSSION

The present investigation indicates that exposure to endosulfan caused significant alterations in serum renal function biochemical parameters. Serum levels of urea, total protein and creatinine are useful tools in diagnosis as any disturbances to the system early enough to allow for projection and possible remedies. This study evaluated kidney function by measuring serum urea, total protein and creatinine values. Endosulfan treatment is found to elevate urea and cratinine levels in serum. These observations are generally in agreement with other investigators on pesticides inducerelative effects (Eraslan *et al*., 2007; Omurtag *et al*., 2008). Al-Attar and Al-Taisan (2010) reported a significant increase in the values of serum urea (20.42% and 65.33%) and creatinine (63.01% and 101.25%) after 3 and 6 weeks of diazinon administration respectively. Urea and creatinine are waste products of protein metabolism that need to be excreted by the kidney, therefore a marked increase of these parameters, as observed in this study, confirms an indication of functional damage to the kidney (Panda, 1999). Urea level can be increased by many other factors such as dehydration, antidiuretic drugs and diet, while creatinine is more specific to the kidney, since kidney damage is the only significant factor that increases the serum creatinine level (Cheesbrough, 1998). Increased blood urea and creatinine is correlated with an increased protein catabolism resulting in the marked decrease in the total protein concentration.

The results of this study indicated that curcumin given orally for 7, 14 and 28 d attenuated the extensive changes in the biochemical parameters in endosulfan- treated mice. The exact mechanisms by which curcumin exert their protective effects against endosulfan- induced toxicity is not yet known. It has been shown that the curcumin have appreciable free radical scavenging properties. Generation of free radicals may be, at least partially, the basis of many human diseases and conditions. Therefore, the antioxidant action of curcumin may explain its claimed usefulness in folk medicine. This antioxidant

Table 1: Effect of curcumin on endosulfan induced changes in kidney function profile of *Mus musculus*

Parameters		7 d	14 d	28 d
Blood Urea(mg/dL)	CNT	16.5 ± 0.05	16.3 ± 0.07	16.3 ± 0.06
	END	$19.41 \pm 0.07^{*\spadesuit¥}$	$22.69 \pm 0.04^{*\spadesuit¥}$	$26.68 \pm 0.04^{*\spadesuit¥}$
	CUR	$23.86 \pm 0.30^{\alpha\beta\mu}$	$21.27 \pm 0.07^{\alpha\beta\mu}$	$19.33 \pm 0.08^{\beta\mu}$
Total Protein(mg%)	CNT	6.03 ± 0.02	6.11 ± 0.02	6.11 ± 0.03
	END	$5.72 \pm 0.01^{*\spadesuit¥}$	$5.12 \pm 0.03^{*\spadesuit¥}$	$4.33 \pm 0.3^{*\spadesuit¥}$
	CUR	$4.63 \pm 0.01^{\alpha\beta\mu}$	$5.17 \pm 0.03^{\alpha\mu}$	$5.8 \pm 0.01^{\beta\mu}$
Creatinine(mg/dL)	CNT	0.54 ± 0.02	0.56 ± 0.02	0.54 ± 0.02
	END	$0.65 \pm 0.00^{*\spadesuit¥}$	$0.81 \pm 0.00^{*\spadesuit¥}$	$1.11 \pm 0.00^{*\spadesuit¥}$
	CUR	$0.98 \pm 0.00^{\alpha\beta\mu}$	$0.79 \pm 0.00^{\alpha\mu}$	$0.62 \pm 0.00^{\beta\mu}$

CNT: Control; END: Endosulfan; CUR: Curcumin; * $p \leq 0.05$: compared to control 7 d; ♠ $p \leq 0.05$: compared to control 14 d; ¥ $p \leq 0.05$: compared to control 28 d; α $p \leq 0.05$: compared to endosulfan 7 d; β $p \leq 0.05$: compared to endosulfan 14 d; μ $p \leq 0.05$: compared to endosulfan 28 d; Values represent mean ± SEM (n = 10).

property would explain its action against several chemically induced liver, kidney, heart, gastric and colon injuries and diseases (Kanter *et al*., 2006; Uz *et al*., 2008; Al-Attar and Al-Taisan, 2010). However, results obtained from the present study showed that the curcumin could prevent the kidney from severe alterations induced by exposure to endosulfan. We suggest that these protective effects of curcumin could be due to their anti-peroxidative and antioxidant influences. The turmeric extract can be considered as a promising therapeutic agent against nephrotxicity induced by endosulfan and may be against other chemical pollutants, environmental contaminants and pathogenic factors. Finally, in view of the present findings, the repeated use of turmeric as a therapeutic agent in pharmacological and pathological researches should be encouraged.

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