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RESEARCH ARTICLE

AMELIORATING POTENTIAL OF LYCOPENE AGAINST CADMIUM TOXICITY IN KIDNEY OF ALBINO MICE

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Abstract

Cadmium is a known industrial pollutant which accumulates in the kidney and its exposure leads to the production of reactive oxygen species (ROS). The present study was carried out to evaluate the ameliorating effects of lycopene against $CdCl_2$ induced toxicity in kidney of albino mice. The biochemical alterations in kidney tissue were observed. The results showed that cadmium administration elevated serum urea and creatinine levels and showed reduction in the content of glycogen, cholesterol and total proteins in kidney. Lycopene treatment prevented degenerative changes induced by $CdCl_2$ and also aided in reduction of oxidative stress and restored the biochemical changes occurring in kidney tissue.

INTRODUCTION

Cadmium is a known hazardous environmental and occupational toxicant. It is present in drinking water, air and sometimes in food also (Klos, 2001). It is absorbed from the alimentary tract and in combination with thionein protein forms metallothioneins which play significant role in further distribution of cadmium in the different organs. Kidney is known to be the most sensitive organ to cadmium exposure and is quite prone to oxidative stress (Ryan et al., 2000). It has been evaluated that, for the treatment of cadmium toxicity chelating compounds have been used such as calcium disodium versenate, dimercaprol and mesomercaptosuccinic acid (Piotrowski et al., 1974). In recent years in scientific investigations, attention has been drawn to the "health-promoting" activity of natural products derived from plants.

Lycopene acts as a therapeutic agent, found in plenty in tomatoes and may alleviate chronic diseases such as coronary heart diseases, eye disease, male infertility, inflammation and osteoporosis. No adverse effects have been reported in association with the consumption of lycopene-containing foods (Selvan et al., 2011). Tomato lycopene content varies considerably, reflecting the influence of variety, maturity and both agronomic and environmental conditions during growing (Kaur et al., 2006). Tomato waste product also contains lycopene and beta carotene and has exhibited the cognitive enhancing effect in normal and impaired conditions (Thukhammee et al., 2012).

The aim of this study was to evaluate the protective efficacy of lycopene against $CdCl_2$ induced renal toxicity .The protective efficacy of lycopene against nephrotoxicity was determined by considering renal function markers in albino mice.

MATERIALS AND METHODS

Animals: Albino mice weighing 20±2 gm were procured from GADVASU, Ludhiana. They were kept and acclimatized to the laboratory conditions for 15 days .The animals were given standard mice feed and water *ad libitum.* The animals were handled in accordance with the guidelines of the Committee for Purpose of Control and

Supervision of Experiments on Animals (CPCSEA), India. Institutional animal ethical committee has approved the present study.

Chemicals: Cadmium chloride ($CdCl_2$) was dissolved in double distilled water and administered intraperitoneally (i.p.) to mice. Lycopene was dissolved in olive oil and administered intraperitoneally to mice. Thus olive oil is used as a vehicle to inject lycopene.

Experimental Design: Animals were randomly divided into four groups as follows: **Group 1 –**Animals were given distilled water and kept as control. **Group 2** – Albino mice were treated with a single dose of 0.32 mg/kg b.w of cadmium (i.p.). **Group 3** – (taken as positive control) albino mice were injected (i.p.) 20 mg/kg bw of olive oil daily. **Group 4 –** Mice were injected an acute dose of 0.32 mg/kg bw of cadmium i.p. followed by a daily dose of 20 mg/kg bw of lycopene for 15 days.

Biochemical Studies: Kidney homogenates were prepared with the help of tissue homogenizer in 3 ml of phosphate buffer and used for estimation of glycogen, cholesterol and protein content by the methods of Montgomery et al. (1957), Zlatkis et al. (1953) and Lowery et al. (1951). On the day of autopsy, 1ml of blood was collected from each mouse under ether anesthesia. Blood was pooled in separate eppendrof tubes, centrifuged (3000 rpm at 2^oC for 15 minutes) and serum was collected in separate clean tubes. It was then used for various biochemical analyses. Serum urea and creatinine were determined by using appropriate kits provided by Reckon Diagnostics P.Ltd., Vadodara, India.

Statistical analysis: The biochemical data was analyzed statistically by using Student's *t*-test, and ANOVA.

RESULTS AND DISCUSSION

Cadmium (Cd) is a potent toxic metal and is extremely harmful to the environment as well as to humans because it can accumulate in tissues causing metabolic, histological and pathological changes (Dzobo and Naik, 2013).

Glycogen content in Cd treated kidneys was found to be reduced significantly ($p<0.0001$) in the present study (Fig.1). Ivanova-Chemishanska (1982) suggested the changes in the levels of glycogen to be either due to increased catabolism of the biomolecules to meet the enhanced energy demand of animals under stress or their reduced synthesis due to impaired tissue function.

Cadmium exposure in the present study caused significant decrease ($p<0.05$) in kidney cholesterol (Fig.1). These observations are in accordance with the findings of Khan (1980); Purohit et al. (1993).

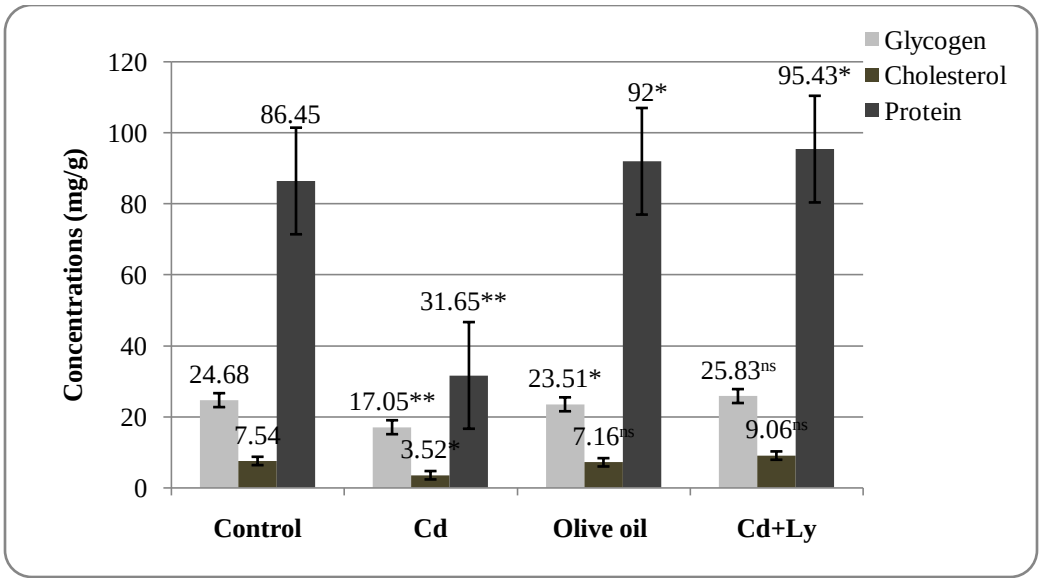
A significant decrease ($p<0.0001$) in protein content of kidneys was observed (Fig.1) which indicated that the amount of total proteins is adversely affected by cadmium. Omata et al. (1978) suggested that the decrease in protein synthesis can be correlated to direct toxic effects of heavy metals. They also believed that ribosomes can be intoxicated by heavy metals which led to their deterioration and reduction in protein synthesis. Swamy et al. (1992) suggested that decrease in total proteins and soluble proteins indicate their metabolic utilization. They also correlated the increase in proteases with decrease of soluble and total proteins.

In lycopene treated mice, total glycogen, total cholesterol and total proteins were found to attain almost normal values and showed marked make over in the presence of the protective agents as shown in Fig.1.

The renal indices: serum urea and creatinine reflect kidney function and renal structural integrity. There was observed a statistically significant increase ($p<0.05$) in serum urea and creatinine in cadmium treated group (Figs.2). These results are in confirmation with the results of many workers (Rana et al., 1996; Yiin et al., 1999). Further, heavy metals have been found to cause alterations in the blood biochemical attributes (El-Demerdash et al., 2004; Sidhu et al., 2004, 2005). According to Gaurav et al. (2010) urea and creatinine levels are used to monitor renal function and their levels will not rise until at least half of the kidney nephrons are destroyed.

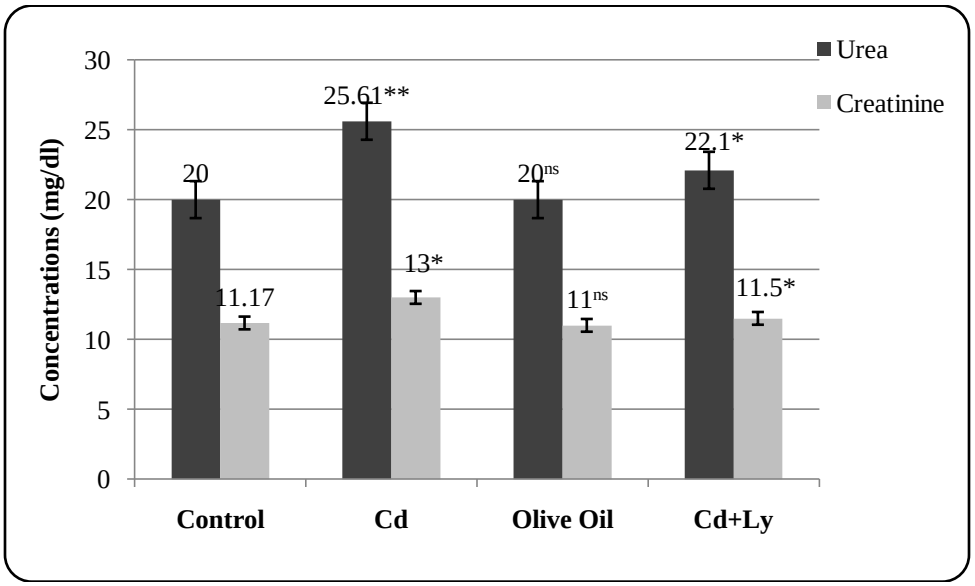
Harper et al. (1979) correlated the elevated urea with increased protein catabolism in mammals and for the conversion of ammonia to urea as a result of increased synthesis of arginase enzyme involved in urea production. According to Lee et al. (2006) the nephrotoxic metal cadmium at micro molar concentrations induces apoptosis of proximal tubule cells within 3-6 hours of exposure which involves a complex and sensitive interplay of signaling cascades involving mitochondrial pro apoptotic factors, calpins and caspases, whose activation is determined by cadmium concentration and the duration of cadmium exposure. Also, non-protein nitrogenous (NPS) substances such as urea and creatinine are increased only when renal function is below 30% of its original capacity. Plasma urea appears to be most useful variable for detections of pre-renal causes of renal failure (Kaneko et al., 1997).

Treatment with lycopene brought back the enzyme level to near normal indicating clearly the therapeutic value of lycopene. In lycopene treated mice concentrations of urea and creatinine reached almost near to their normal concentrations.



ns Non-Significant difference at p>0.05
** Highly Significant variations at p<0.0001 (Control vs Cd)
* Significant variations at p<0.05 (Cd vs antioxidant groups)

Fig.2 Kidney markers in various treated groups.



ns Non-Significant difference at p>0.05
** Highly Significant variations at p<0.0001 (Control vs Cd)
* Significant variations at p<0.05 (Cd vs antioxidant groups)

Fig.1 Variations in biochemical parameters of kidney in various treated groups.

Conclusion:

It could be concluded that lycopene acts as a potential antioxidant that prevents renal toxicity induced by cadmium in albino mice. Though supplementation with lycopene resulted in beneficial effects against renal toxicity, but it was dose dependent. As lycopene showed quite encouraging amelioration, it can help us fight against hazardous environmental pollution.

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