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RESEARCH ARTICLE

AMELIORATION OF CURCUMIN AGAINST CADMIUM INDUCED OXIDATIVE STRESS IN LUNG OF ALBINO MICE.

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Abstract

Humans are exposed to a number of toxic elements in the environment. Cadmium, is a great environmental health problem of both humans and animals. The present study was carried out to evaluate the protective role of curcumin on lung against cadmium chloride induced oxidative stress in albino mice. Albino mice were divided into 4 groups. **Group 1** mice were kept as control. **Group 2** mice were administered an oral dose of 1mg/kg body weight of Cd on alternate days for 15 days. **Group 3** mice were given an oral dose of 1mg/kg body weight of Cd on alternate days and 100mg/kg body weight of curcumin daily for 15 days. **Group 4** mice were given an oral dose of 100 mg/kg body weight of curcumin daily for 15 days and will be kept as positive control. Autopsies were done on 15 days post treatment. A significant decrease in body weight and organ weight were observed. Biochemical analysis showed decline in antioxidant activity of superoxide dismutase (SOD), catalase (CAT), glutathione peroxidase (GPx) and increase in lipid peroxidation. However, the treatment with curcumin ameliorated Cd-induced malondialdehyde (MDA) and oxidative stress in lung tissue as it provoked the antioxidant defense system more significantly. While, co-treatment of Cd with curcumin ameliorated the antioxidant level. The results of the present research work showed the protective action of curcumin on the cadmium induced oxidative stress in the lung of mice.

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Introduction:-

Increasing industrialization all over the world has been associated with the extraction and distribution of minerals from their natural deposits which includes heavy metals (Munga et al., 2010). Cadmium (Cd) is known to be one of the most toxic environmental and industrial pollutants (El-Refaiy and Eissa, 2012). After cadmium enters human body through food chain or other approaches, it can be accumulated with biological half-life as long as 15-20 years (Son et al., 2011) and its excretion rate is very low. According to Agency for Toxic Substances and Disease Registry, it ranks 7th in top 20 hazardous substance (Attia et al., 2014) and has been classified as "category I" human carcinogen by International Agency for Research on Cancer (Sarkar et al., 2013). Human uptake of Cd is mainly through cigarette smoking, food and water intake (Barregard et al., 2014).

Cadmium has been shown to stimulate the production of intracellular reactive oxygen species (ROS) (Stohs et al., 2000). ROS may lead to cellular damage when the rate of its generation surpasses the rate of its decomposition by antioxidant defense systems, such as the enzymes superoxide dismutase (SOD), catalase (CAT), or glutathione peroxidase (GPx). The oxidative stress induced by Cd in a biological system may be due to increased lipid peroxidation, which may be attributed to alterations in the antioxidant defense system (Newairy et al., 2007).

Lung is the main target of cadmium (Kundu et al., 2009) since inhalation is one of the main exposure routes. It is reported that fumes of cadmium and air contaminated by it induce shortness of breath, lung edema, pneumonitis

(Seidal et al., 1993) and acute respiratory distress syndromes (Barbee Jr and Prince, 1999) especially for workers. Lag et al. (2002) showed that cadmium exhibited toxicity to lungs by inducing the dysfunction of individual pulmonary cells.

Various modes and methodologies are being devised to combat cadmium induced toxicity with a focus on herbal formulations. Curcumin, the major active component of curcuminoids, is a natural product found in the rhizomes of turmeric (*Curcuma longa* Linn.) of the Zingiberaceae family (Sinha et al., 2003). It is a yellow orange dye used as a spice and coloring agent in food and cosmetics. Several studies have demonstrated the beneficial pharmacological effects of curcumin, including antioxidant, anti-tumorigenic, anti-inflammatory, neuroprotective and cardioprotective properties (Lin et al., 2009). The most important feature of curcumin is that it has no side effects despite being a therapeutic agent with multiple beneficial functions (Joe et al., 2004). It acts as a scavenger of free radicals. Curcumin is considered to be an effective antioxidant against oxidative tissue damage. It can significantly inhibit the generation of reactive oxygen species (ROS) both in vitro and in vivo (Biswas et al., 2005).

Therefore in this study, protective effects of curcumin against cadmium induced biochemical changes in the lungs of Swiss albino mice have been studied.

Materials and methods:-

Animals:- Albino mice weighing 20-22 grams were procured from Central Research Institute, Kasuali. They were acclimatized for 2 weeks and were given standard mice feed and *ad libitum* access to tap water. The animals were handled with human care in accordance with the guidelines of the Institutional Animal Ethical Committee.

Chemicals:- Cadmium Chloride (CdCl_2) and Curcumin had been obtained from Himedia Laboratories Pvt. Ltd. MUMBAI. It was dissolved in distilled water and administered to mice.

Experimental Design:- Mice were divided into following 4 groups. **Group 1** mice were kept as control. **Group 2** mice were administered an oral dose of 1mg/kg body weight of Cd on alternate days for 15 days. **Group 3** mice were given an oral dose of 1mg/kg body weight of Cd on alternate days and 100mg/kg body weight of curcumin daily for 15 days. **Group 4** mice were given an oral dose of 100 mg/kg body weight of curcumin daily for 15 days and will be kept as positive control. All treated and control animals were weighed before, during and after treatment. Autopsies were done on 15 days post treatment. Mice were sacrificed and the lung was removed, freed of adipose tissue, blotted dry and were weighed separately.

Biochemical Studies: Lung homogenate was prepared with the help of tissue homogenizer in 3 ml of phosphate buffer and used for estimation of Superoxide dismutase by the method of Das et al. (2000), Catalase by the method of Aebi (1983), Glutathione peroxidase by the method of Rotruck et al. (1973) and Lipid peroxidation from tissue extract with the method of Wilbur et al. (1949).

Statistical analysis: The data was analyzed by using Student's t-test.

Results and discussion:-

A gradual increase in body weight was observed in control group (Fig. 1). But in cadmium treated group, a gradual decrease in weight was observed due to less intake of food and water which may be due to the oxidative stress by cadmium.

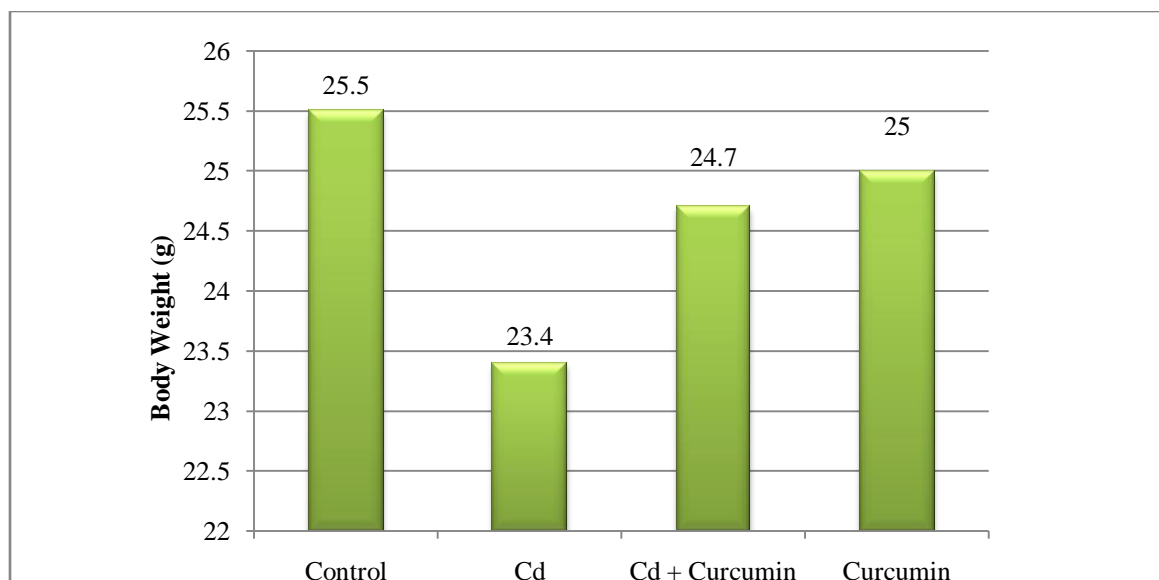


Fig. 1:- Body weight of mice in control and treated groups.

A reduction in lung weight was also observed in mice treated with cadmium in comparison to control group (Fig. 2). This reduction may be attributed to the damaging effects of cadmium on various tissues, which is in agreement with earlier reports (Bhatia et al., 2001; Nwachukwu et al., 2014)

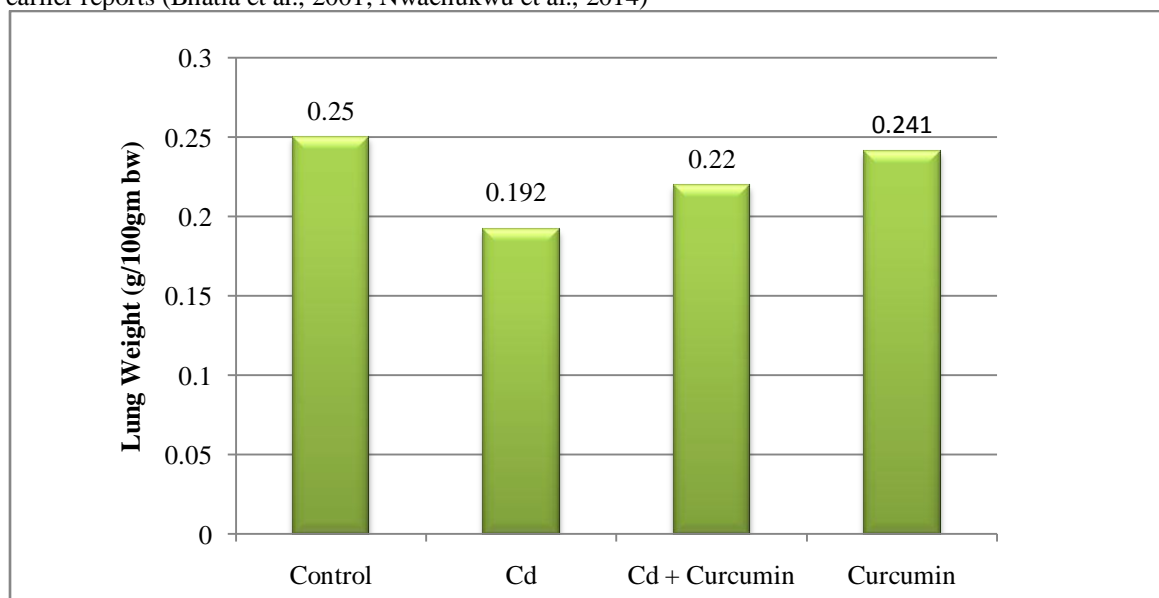


Fig. 2:- Weight of Lung in control and treated groups.

The endogenous antioxidant enzymes such as SOD, CAT, GPx present the first line of cellular antioxidative defense against free-radical damage (Hassani et al., 2015). The results of the present study showed that there was a decrease in activities of antioxidant enzymes SOD, CAT (Fig. 3 and Fig. 4) in lung tissue of cadmium chloride treated mice. In this study, depletion of SOD and CAT activities could be attributed to the increased production of reactive oxygen species as is evident from the increased lipid peroxidation levels due to cadmium chloride treatment (Kaur et al., 2015). However, some studies have reported that superoxide radicals could also inhibit CAT activity and the elevated hydrogen peroxide level resulting from CAT inhibition could eventually inhibit SOD activity (Zama et al., 2007).

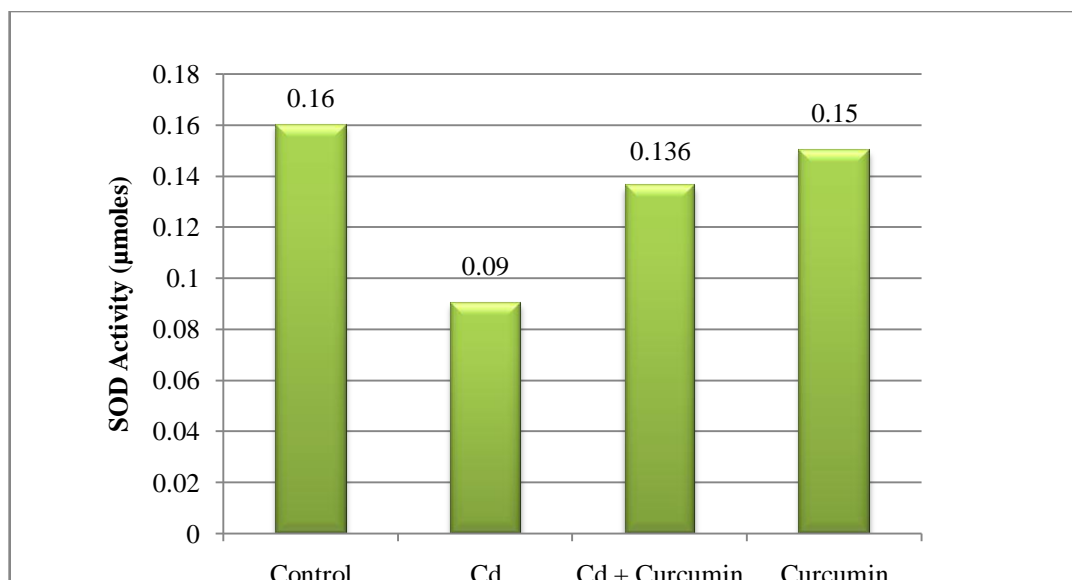


Fig. 3:- SOD activity in lung of control and treated groups.

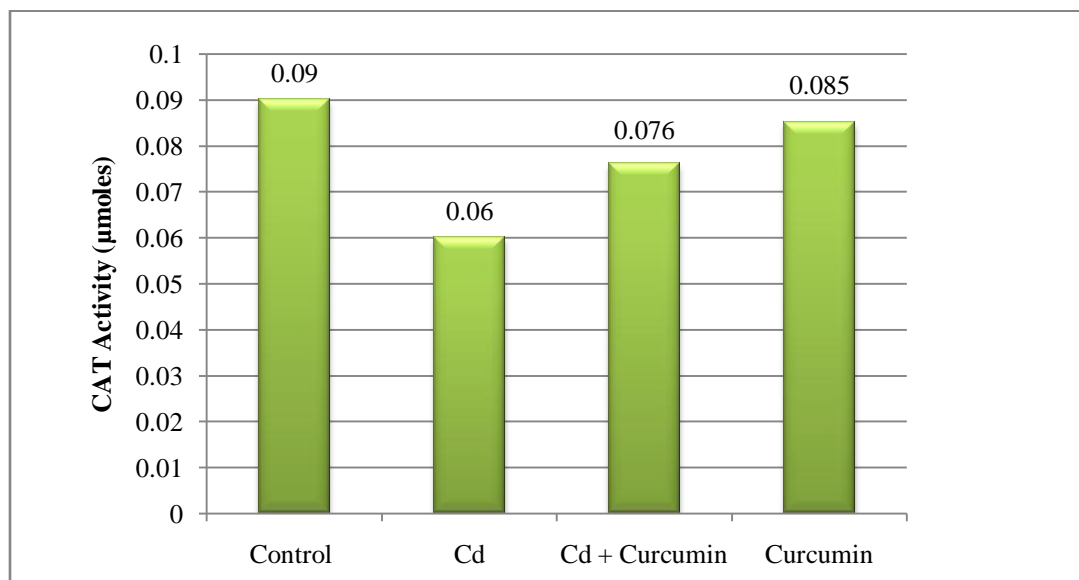


Fig. 4:- CAT activity in lung of control and treated groups.

In the present study, cadmium chloride treatment resulted in decrease of Glutathione peroxidase activity in the mice (Fig. 5). The major function of this enzyme is the removal and detoxification of hydrogen peroxide and lipid hydroperoxides in the presence of oxidized GSH (Kanbur et al. 2009). The decrease in GPx activity could be due to the increased free radicals on Cd toxicity.

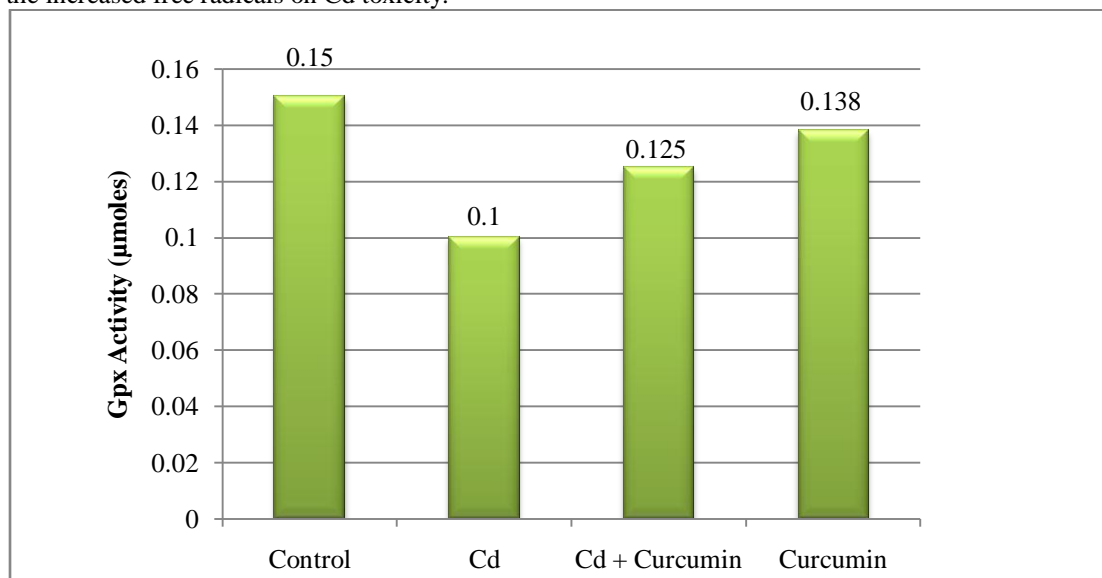


Fig. 5:- GPx activity in lung of control and treated groups.

In present study cadmium chloride treatment resulted in a significant increase in the MDA level in the lung tissue (Fig. 6). Malondialdehyde is a stable metabolite of lipid peroxidation induced by the oxidative stress in the cells (Boroushaki et al., 2014). Previous studies have shown that heavy metals induced elevated MDA level in the lung tissue (Karaca and Eraslan, 2013). However, the enhanced MDA level might be conclusion of increased formation of free radicals. Similar oxidative stress due to increased MDA level in mammals is also reported by other researchers with other metals and pesticides (Sharma et al., 2015; Dhalla et al., 2016).

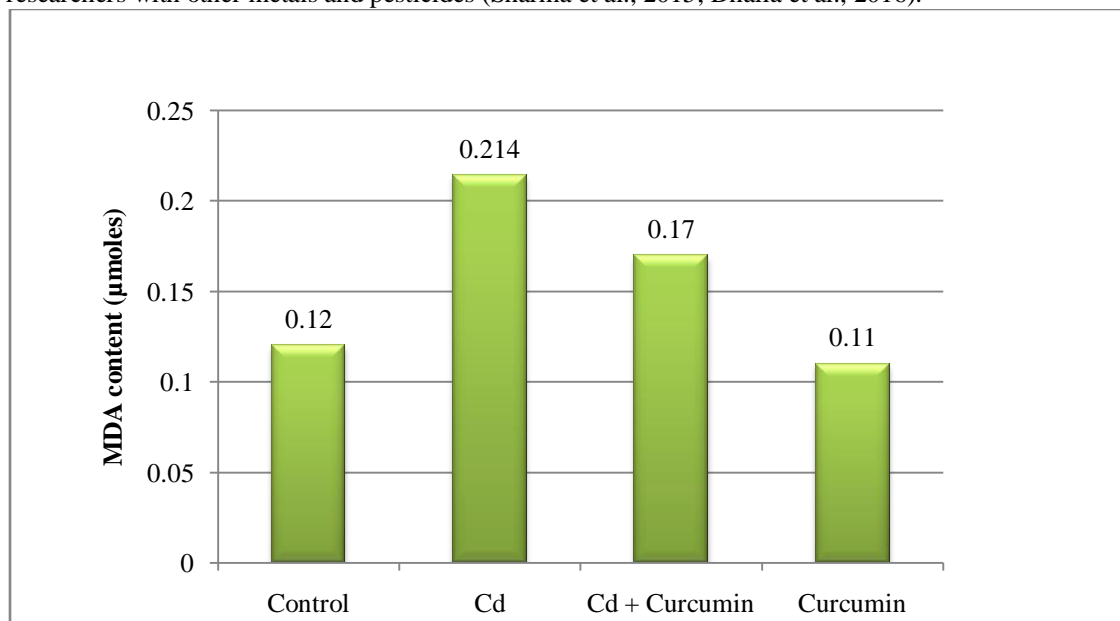


Fig. 6:- MDA activity in lung of control and treated groups.

A decrease in oxidative damage was observed when mice were co-treated with cadmium and curcumin. Treatment with curcumin was effective in decreasing changes induced by Cd which resulted in increased MDA concentration and decreased activity of antioxidant enzymes. Curcumin was capable of inhibiting formation of ROS through its high antioxidant activity (Venkatesan et al., 2000). According to Masuda et al. (2001) the preventive action of curcumin may be attributed to its specific conjugated structure of two methoxylated phenols and an enol form of β -diketone. This structure might be responsible for free radical trapping ability as a chain breaking antioxidant.

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