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Research Article

PROTECTIVE EFFECT OF *CURCUMA LONGA* ADMINISTRATION ON LUNG OF MICE EXPOSED TO CADMIUM

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ABSTRACT

Objective: Cadmium (Cd) is a toxic heavy metal which is introduced into the environment by various anthropogenic and natural activities. It can cause various health problems even at low concentration by inducing oxidative damage in tissues of organisms. Nowadays, the focus has been raised toward the use of herbal treatment against the heavy metal toxicity. Hence, the present study was aimed to investigate the protective effect of curcumin (Cur) against Cd-induced toxicity in the lung of albino mice.

Materials and Methods: Albino mice were divided into 4 groups and 5 mice were kept in each group. The experiment was carried out for 15 and 45 days. Group 1 mice were kept as control. Group 2 mice were given an oral dose of 1mg/kg body weight of Cd on alternate days. Group 3 mice were administered an oral dose of 1mg/kg body weight of Cd on alternate days and 100 mg/kg body weight of Cur daily. Group 4 mice were received an oral dose of 100 mg/kg body weight of Cur daily. Autopsies were done on 15 and 45 days post-treatment.

Result: Biochemical observations showed an increased level of lipid peroxidation and decreased activity of antioxidant enzymes, i.e., superoxide dismutase, catalase, and glutathione peroxidase. However, Cur administration improved the level of malondialdehyde and oxidative stress in lung tissue by its antioxidant activity. Furthermore, cotreatment of Cd and Cur ameliorated the antioxidant level.

Conclusion: The results of the present experiment showed the protective action of Cur on the Cd-induced oxidative damage in the lung of mice.

Keywords: Oxidative damage, Antioxidant enzymes, Ameliorate and toxicity.

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INTRODUCTION

Heavy metals are natural components of the Earth's crust, and the concentration of several heavy metals has increased in the environment as a result of anthropogenic activities. Environmental contamination due to heavy metals is becoming a global issue because of the toxicological damage posed by such metals to human health [1]. Cadmium (Cd) is one such heavy metal which is causing various health hazards. The agency for toxic substances and disease registry ranks Cd as 7th in the list of top 20 hazardous substances [2] and also it has been classified as "Category I" human carcinogen by International Agency for Research on Cancer [3].

Cd causes the tissue injury by generating oxidative stress and physiological defects [4-7]. Cd leads to the formation of reactive oxygen species (ROS) by affecting mitochondrial electron transport chain. Reactive oxygen species cause the cellular damage when there is an imbalance between ROS and antioxidant defense system, i.e., superoxide dismutase, catalase (CAT), Glutathione peroxidase (GPx), or reduced GSH [8,9].

Human exposure to Cd mainly occurs by inhalation or ingestion. Ingesting contaminated food or water is the main source of Cd toxicity [10-12]. Cd enters the body through the respiratory tract in people who are occupationally exposed to Cd and in cigarette smokers [13]. By inhaling Cd, respiratory tract gets injured. However, lung epithelium is an effective barrier for harmful molecules, but Cd can pass through the alveolar cells and can reach the blood [14]. In workers, inhaling fumes of Cd and contaminated air could cause lung edema, shortness of breath, pneumonitis [15], and acute respiratory distress syndrome [16].

Nowadays, herbal formulations are gaining lots of interest against heavy metal poisoning. Curcumin (Cur), a yellow color compound is obtained from the rhizome of *Curcuma longa* Linn. (Family Zingiberaceae) [17]. It is a used as a spice and coloring agent in food and cosmetics. Cur has been shown to possess many biological properties, for example, anti-inflammatory, anticarcinogenic, antioxidant, anticoagulant, antimutagenic, antidiabetic, antifungal, antibacterial, antiviral, anticoagulant, antiulcer, hypercholesterolemia, hypotensive, and cardioprotective [18-23]. Antioxidants play a critical role in preventing oxidative stress in the human body [24]. Cur, an antioxidant can remarkably inhibit the generation of ROS both *in vitro* and *in vivo* [25]. Hence, the present research work was carried out to investigate the ameliorating efficacy of Cur against Cd-induced toxicity in the lungs of albino mice.

MATERIALS AND METHODS

Animals

Albino mice weighing 20–22 g were procured from Central Research Institute, Kasauli. They were acclimatized for 10–15 days and given standard mice feed and *ad libitum* access to tap water. The animals were handled with proper human care in accordance with the guidelines of the Institutional Animal Ethical Committee.

Chemicals

Cd chloride ($CdCl_2$) and Cur were purchased from HiMedia Laboratories Pvt., Ltd., Mumbai. $CdCl_2$ was dissolved in distilled water and was administered to mice orally. An aqueous suspension of Cur was made [26] and administered orally to mice.

Experimental design

Mice were divided into the 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 and 45 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 Cur daily for 15 and 45 days. Group 4 mice were given an oral dose of 100 mg/kg body weight of Cur daily for 15 and 45 days.

Autopsies were done on 15 and 45 days post-treatment. All control and treated animals were sacrificed, and the lung was removed, freed of adipose tissue, and blotted dry and were processed for biochemical analysis.

Biochemical studies

Lung homogenate was prepared with the help of tissue homogenizer in 3 ml of phosphate buffer and used for estimation of lipid peroxidation from tissue extract with the method of Wilbur *et al*. [27], SOD was assessed by the method of Das *et al*. [28], CAT by themethod of Aebi [29], and GPx by the method of Rotruck *et al*. [30].

Statistical analysis

The data were analyzed using the Student's t-test.

RESULTS AND DISCUSSION

In the present study, toxic effects of $CdCl_2$ and protective effects of Cur on lungs of albino mice were studied and the results obtained from the study are discussed.

Malondialdehyde (MDA) is the main byproduct of lipid peroxidation, and it can be effectively linked to oxidative injuries in tissues [31]. A significant ($p<0.0001$) increase in MDA content in the Cd-treated mice was observed in comparison to control at both 15 and 45 days post-treatment. However, the increase in MDA content was more significant at 45 days. Whereas, the Cur treatment significantly decreased the MDA level in Cd+Cur-treated mice in comparison to control group and but no significant ($p>0.05$) changes were observed in only Cur-treated groups at both the intervals (Fig. 1). This is in accordance with the previous studies in which heavy metals elevated the MDA level in the lung tissue [32]. Lipid peroxidation basically denotes free-radical generation. Oxidative damage of the cell membrane can induce damage to other cellular components through the reaction between metal ions and cell organelles. According to Manca *et al.* [33], lipid peroxidation is an advanced and sensitive reaction to Cd toxicity. Rana and Verma [34] also reported that increased intake of Cd results in its retention and peroxidative damage in soft tissues.

Superoxide dismutase (SOD) activity was significantly decreased ($p<0.0001$) in the Cd-treated group in comparison to the control group of mice at both the intervals. Cur administration ameliorated the decreased SOD activity in Cd+Cur-treated group. Whereas, Cur-treated group showed no significant ($p>0.05$) changes as compared to control at both intervals (Fig. 2). These results are in agreement with the work of other authors [35,36] who reported that as SOD is a metalloenzyme; reduction and depletion in its activity may be because of dysfunctional conformational change which can be due to the replacement of Zn^{2+} present in SOD by Cd. Furthermore, Cd replaces other metals mostly manganese is resulting in inhibition of SOD activity [37]. The tissue toxicity at increased ROS production is associated with decreased level of an antioxidant enzyme such as SOD [38,39].

A highly significant ($p<0.0001$) decrease in CAT was observed in Cd-treated mice as compared to control at days 15 and 45. Cd+Cur-treated group showed decreased CAT activity as compared to the Cd-treated group, and Cur alone treated group showed normal CAT activity at both intervals (Fig. 3). Cd causes enzyme inhibition by separating the iron in the catalytic subunit of CAT [40]. Decreased CAT activity may also be due to the high generation of reactive oxygen species that are above the detoxification capacity of antioxidant enzymes resulting in the development of tissue damage [41]. It is in agreement with the results of other authors [42,43]. According to Abu-Taweel [24], Cur enhanced the activity of antioxidant enzymes (SOD, CAT, and GSH) in rats against heavy metal toxicity. Jamakala and Rani [44] explained that CAT activity gets declined because of high accumulation of H_2O_2 in the tissues and as a resulting in Cd-induced peroxidation of lipids in Cd-treated mice.

A significant ($p<0.0001$) decrease in GPx activity was observed in mice treated with Cd as compared to control mice at 15 and 45 days post-treatment. Cur significantly increased the gpx activity in Cd+Cur-treated mice as compared to Cd-treated group (Fig. 4). GPx is also one of the antioxidant enzymes directly affected by Cd as it replaces the selenium present in the enzyme [45,46]. The main function of gpx is the removal

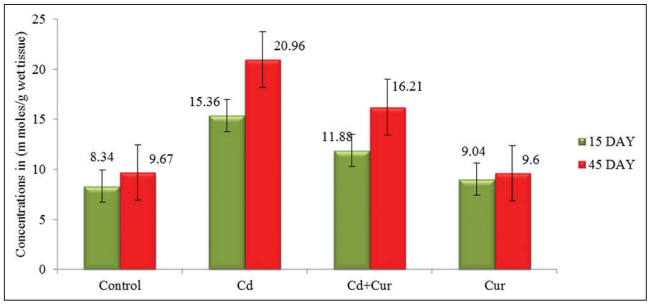

Fig. 1: Malondialdehyde level in control and treated groups at 15 and 45 days treatment

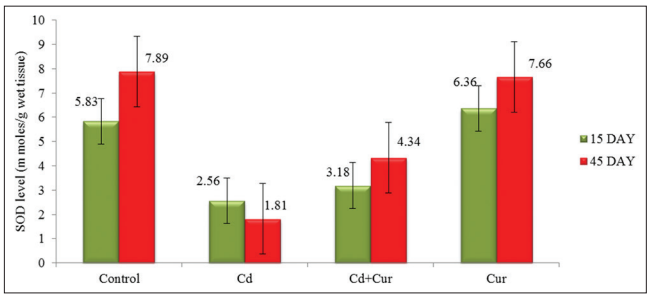

Fig. 2: Superoxide dismutase activity in control and treated groups at 15 and 45 days treatment

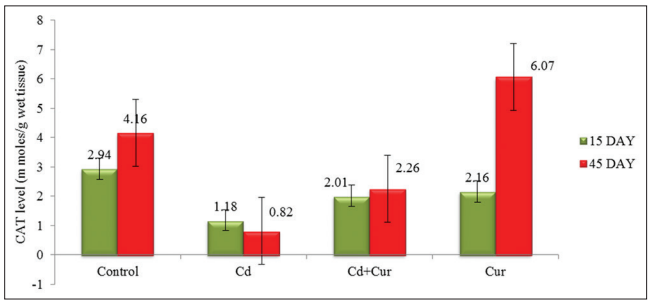

Fig. 3: Catalase activity in control and treated groups at 15 and 45 days

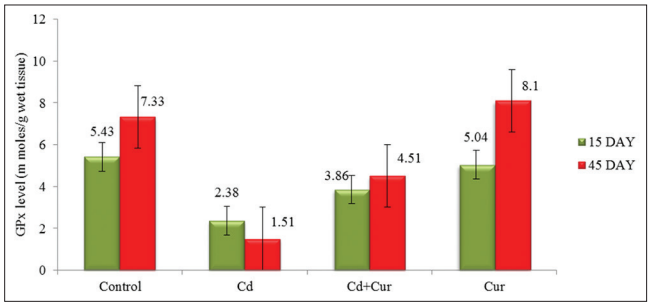

Fig. 4: Glutathione peroxidase activity in control and treated groups at 15 and 45 days

and detoxification of hydrogen peroxide and lipid hydroperoxides in the presence of oxidized GSH [47]. The decrease in gpx activity could be due to the increased free radicals induced by Cd toxicity.

CONCLUSION

$CdCl_2$ is one of the hazardous heavy metals. In the present study, Cd-induced the oxidative stress in lungs which resulted in elevated lipid peroxidation and declined activity of antioxidant enzymes (SOD, CAT, and GPx). Whereas, Cur administration ameliorated the Cd-induced changes in MDA, SOD, CAT, and GPx activities. Therefore, it is recommended that daily intake of Cur can overcome the Cd toxicity in organisms.

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AUTHORS' CONTRIBUTIONS

Both the authors have contributed equally.

CONFLICTS OF INTEREST

The author declares that there are no conflicts of interest regarding the publication of this paper.

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