Cardioprotective Effects of Lycopene against Cadmium Induced Toxicity in Albino Mice

Suman Sharma¹, P. Vijaya²

¹Professor, ²Research Scholar, Department of Zoology & Environmental Sciences, Punjabi University, Patiala.

Corresponding Author: P. Vijaya

ABSTRACT

Objective and Study Design: The present study has been undertaken to evaluate the protective efficacy of lycopene on cadmium induced toxicity in heart of albino mice.

Materials and Methods: 24 Albino mice were divided into four groups. Group I mice were kept as control. Group II animals were administered a single dose of cadmium chloride (0.32mg/kg bw) intraperitoneally. Group III animals were injected with 20mg/kg bw of olive oil (positive control). Group IV animals were injected a single dose of CdCl₂ followed by a chronic dose of lycopene (20mg/kg bw). Autopsies were done at the intervals of 1, 5, 10 and 15 days post treatment.

Results: Cadmium administration led to decrease in weight of heart in mice as compared to control. Histopathological analysis in heart showed extensive haemorrhage between the cardiac myocytes and the blood vessels showed endothelial thickening with peri-vascular infiltration of inflammatory cells. Lycopene administration to mice showed increase in weight of heart and showed significant protection by alleviating cadmium induced cardiac injury.

Conclusion: It can be concluded from the present study that that lycopene treatment is able to prevent cadmium induced cardiac injury in mice.

Keywords: Cadmium (CD), lycopene, histopathology and heart.

INTRODUCTION

Heavy metals are natural component of earth’s crust. They cannot be degraded or destroyed. [¹] Some heavy metals are essential to maintain the metabolism of the human body and other organisms. However, at higher concentration they lead to poisoning. [²] Cadmium, a known heavy metal is ubiquitous environmental pollutant and is primarily used for electroplating and galvanizing other metals (as it is relatively resistant to corrosion), in electrical contacts, in soldering alloys, in nickel cadmium batteries, in television phosphors and as stabilizers for polyvinylchloride. It is also used as a pigment in plastics, paints and plasters. [³] It is specifically significant as it has a long half life (between 4 -19 years in human liver) and can threaten human health both through environmental and occupational exposures. [⁴⁻⁵]

CD possesses a significant threat to the human population and environment. Since the biological half life of cadmium in human is found to be long, cadmium has the ability to induce severe alternation in
various organs and tissues following either acute or chronic exposure. [6] Cadmium accumulates mainly in the liver followed by heart, gut and kidney. [7] There is greater susceptibility of the heart as compared to the kidney to cadmium in the presence of high dietary selenium. Cadmium treatment results in more extensive effects on glutathione peroxidase and superoxide dismutase in the heart as compared to kidney. [8] Epidemiologically, high Cd level was found to be associated with hypertension, stroke and cardiac arrest. [9] In literature, most of the studies depicted the effects of Cd on liver [10,11,12] and kidney. [13,14,15,16,17] But, studies on the heart are relatively scanty. Moreover, the studies on heart covered the oxidative stress parameters [18,19,20,21] and very few work was found on histopathology of heart.

Lycopene is a natural pigment synthesized by plants and microorganisms. It is highly lipophilic and is most commonly located within cell membranes and other lipid components. It is therefore expected that in the lipophilic environment, lycopene will have maximum ROS scavenging effects. In epidemiological and supplementation studies on human trials, lycopene was found to reduce cardiovascular risks due to its antioxidant properties. [22] Lycopene, because of its high number of conjugated double bonds, exhibits higher singlet oxygen quenching ability compared to β-carotene or α-tocopherol. [23] Continuous administration of lycopene can protect myocardium against ischemia reperfusion injury. [24]

The present work is aimed to evaluate the protective role of lycopene on cadmium induced histopathological changes in heart of albino mice.

**MATERIALS AND METHODS**

**Animals:** Swiss albino mice weighing 20±2g were procured from GADVASU, Ludhiana. They were kept and acclimatized to the laboratory conditions for 15 days under optimal conditions of light and temperature. They had ad libitum access to tap water. The animals were handled with humane care in accordance with the guidelines of the Institutional Animal Ethical Committee.

**Chemicals:** Cadmium chloride (CdCl₂) was bought from S.D FINE CHEM LIMITED, Mumbai. It was dissolved in double glass distilled water and administered intraperitoneally (i.p.) to mice. Lycopene was obtained from PASSIM Pharmaceuticals Limited, Baddi. It was dissolved in olive oil and administered intraperitoneally to mice.

**Experimental Design:** 24 albino mice were divided into four groups of six mice each. Group I – Control animals were given distilled water. Group II – Animals were administered a single dose of 0.32 mg/kg bw (1/10th of LD₅₀) of cadmium (i.p.). Group III – Animals were kept as positive control and were injected (i.p.) 20 mg/kg bw of olive oil daily. Group IV – Animals 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. Autopsies were done on 1, 5, 10 and 15 days post treatment. Heart was removed, blotted dry and weighted.

**Histopathological Studies:** The heart tissue was fixed in Bouin’s fixative, embedded in paraffin wax (58-60°C) and 5-7µ thick sections were stained with haematoxylin and eosin stains.

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

**RESULTS AND DISCUSSION**

CD administration does not produce any discernible signs and symptoms of sickness in mice. Also, no mortality was observed during the entire period of experiment. A reduction in weight of heart...
was also observed in mice treated with cadmium in comparison to control group. This reduction may be attributed to the damaging effects of cadmium on heart tissue. Anderson H et al. [25] suggested that organ toxicity can be evaluated by considering the weight of the organs after exposure to toxicant in animal toxicity studies. In Cd + lycopene treated group, increase in weight of heart was observed. Thus improvement in organ weight indicates the protection afforded by lycopene (Figure1).

![Figure 1](image1.png)

**Figure 1:** Weight of heart (gm/100gm body weight) in control, cadmium and antioxidant treated groups.

Histopathological examination of the heart of control group showed normal arrangement of cardiac muscles and nuclei. Endocardium, myocardium and epicardium were normal (Figure 2). Histology of heart of olive oil treated group showed normal structure at all the intervals of the experiment (Figure 3).

![Figure 2](image2.png)

**Figure 2:** Showing normal heart structure. A semi-thin section in the cardiac myocytes showing a longitudinal section. The cells show branching with each other. Cross striations (arrows) and central nuclei (N) are seen. X400.

![Figure 3](image3.png)

**Figure 3:** Heart of olive oil treated group. Showing normal cardiac myocytes. X400.

However, animals treated with Cd showed loss of normal heart architecture including extensive haemorrhage between the cardiac myocytes and the blood vessels showed endothelial thickening with peri-vascular infiltration of inflammatory cells (Figure 4, 5). Also, a focal area of degenerated cells was seen. This is in agreement with Lei W et al. [26] who observed myocardial oedema, vascular degeneration and infiltration of inflammatory cells in crab heart after cadmium exposure. Ferramola ML et al. [27] observed foci of myocardial fibre necrosis in rats exposed to cadmium-induced oxidative stress. On the other hand, Zaslavina SV et al. [28] studied the structural changes of rat myocardium in the mother-foetus system exposed to cadmium and observed the reduction in volume of cardiomyocytes and blood vessels
in both mother and foetus with signs of diffuse oedema of myofibrils and dilatation of intercellular spaces.

**Figure 4:** Heart of cadmium treated group showing an oblique section. Extensive haemorrhage (H) is seen between the cells. The blood vessels (BV) show endothelial thickening with peri-vascular infiltration of inflammatory cells. X400.

**Figure 5:** Heart of cadmium treated group showing hyperaemia, vacuolation between the cardiac myocytes. X400.

Ferramola ML et al. [27] observed profound ultrastructural damages of the heart tissue in rats exposed to cadmium. Also, Patai K and Balogh I [29] found that CdCl₂ causes apparent changes in rat foetal myocardium with simultaneous mitochondrial impairments. Many authors studied the mechanism of cadmium toxicity, Ferramola ML et al. [21] suggested that, cadmium acts as a catalyst in the oxidative reactions of biological macromolecules and therefore, the toxicity associated with the metal might be due to the oxidative damage. Manca D et al., [30] Pathak N and Khandelwal S, [31] and Ercal N et al. [32] stated that, cadmium causes an increase in the production of reactive oxygen species (ROS) such as superoxide anion free radical, hydroxyl free radical as well as hydrogen peroxide. An enhanced production of ROS results in oxidative stress. Cells under oxidative stress display various dysfunctions due to lesions caused by ROS to lipid, proteins and DNA.

Messaoudi I et al. [33] added that, the degree of cell damage under the heavy metal stress depends on the rate of ROS formation and on the efficiency and capacity of detoxification and repair mechanisms. The cellular defence system against toxicity from ROS includes superoxide dismutase, catalase and glutathione peroxidases. Mitra E et al. [34] demonstrated that, the cadmium-induced cardiac damage is due to generation of oxidative stress as evident from elevated levels of tissue lipid peroxidation and protein carbonyl content and a decreased tissue level of reduced glutathione, the well known bio-markers of oxidative stress. Membrane lipids are highly susceptible to free radical damage. In the presence of free radicals, lipids can undergo highly damaging chain reaction of lipid peroxidation. Moreover, the heavy metal binds to other relevant biomolecules found in subcellular membrane, endoplasmic reticulum, mitochondria or within the nucleus causing their damage. [34] The cadmium also showed adverse effects on the structure of cardiac myocytes.

Lycopene treated group showed mild edema with significant reduction in infarction, showing normal myocardial architecture (Figure 6, 7).
Figure 6: Heart of cadmium + lycopene treated group showing less hyperaemia with occasional loss of muscle fibre. X400.

Figure 7: Heart of cadmium + lycopene treated group showing almost normal histoarchitecture of heart tissue. X400.

The present study showed that lycopene supplementation (20 mg/kg/bw) reduced the cardiac cellular changes induced by cadmium, indicating that lycopene contributes to the protection against, cardiac-morphological injury.

CONCLUSION

It is concluded that foods containing lycopene could protect cardiac tissue against heavy metal induced especially, cadmium-induced oxidative cardiac impairment. At this stage the precise mechanism of protection played by lycopene is not fully clear. Further researches are necessary to investigate the detailed molecular protective mechanism played by lycopene against cadmium-induced cardiac injury.

ACKNOWLEDGEMENT

The authors gratefully acknowledge the Department of Zoology & Environmental Sciences, Punjabi University, Patiala, for providing the necessary facilities to pursue the research work.

REFERENCES


How to cite this article: Sharma S, Vijaya P. Cardioprotective effects of lycopene against cadmium induced toxicity in albino mice. Int J Health Sci Res. 2015; 5(8)507-513.