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PROTECTIVE ROLE OF LYCOPENE ON CADMIUM INDUCED LUNG INJURY

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ABSTRACT The present study has been undertaken to evaluate the protective efficacy of lycopene on cadmium induced toxicity in lungs of albino mice. 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 20 mg/kg bw of olive oil (positive control). **Group IV** animals were injected a single dose of $CdCl_2$ 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. Cadmium treatment leads to decrease in weight of lungs. Histopathological analysis of treated lungs revealed atrophy, hyperaemia, lymphocytic infiltration and thickening of bronchiolar wall. Lycopene administration to mice increased the weight of lungs and showed significant protection in the alleviation of cadmium induced pulmonary injury.

KEYWORDS : Cadmium (Cd), lycopene, histopathology and lungs.

INTRODUCTION

Heavy metals are natural components 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 high concentrations they lead to poisoning (2). Cadmium, a known heavy metal is ubiquitous environmental pollutant, is primarily used for electroplating and galvanizing works, in soldering alloys, in nickel cadmium batteries and is also used as a pigment in plastics and paints (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).

The cadmium can affect liver, central nervous system, lungs, kidneys and other vital organs (5). Cadmium in tobacco smoke may contribute to the development of pulmonary emphysema (6). The absorption through inhalation in the lungs is thought to be much higher than that from food, via the intestine and as a result cadmium concentration in blood can be up to four to five times higher in smokers (7-9). But very little is known about the deposition of cadmium in the lungs.

For the last couples of decades, natural products derived from plants, fruits, herbs etc have been the main focus of research to ameliorate the threat posed by chemicals, toxins etc from endogenous and exogenous sources (10). Lycopene belongs to a class of compounds known as carotenoids (11) and can be ingested by people as a component of certain foods, most notably in tomatoes (12). It has also been suggested that lycopene can prevent carcinogenesis by protecting vital biomolecules including DNA, proteins, enzymes and lipids (13).

The main aim of the present study was to evaluate the protective role of lycopene on cadmium induced histopathological changes in lungs of albino mice.

MATERIALS AND METHODS

Animals: Swiss albino mice weighing 20-25g were procured from Animal house, GADVASU, Ludhiana, Punjab, India (Reg no. 107/1999/CPCSEA/2014-33). They mice 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 and were provided with standard pellet diet. The animals were handled with humane care as per the guidelines and principles of the Institutional Animal Ethical Committee.

Chemicals: Cadmium chloride ($CdCl_2$) 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 (Himachal Pradesh-India). It was dissolved in olive oil and administered intraperitoneally to mice. Thus olive oil is used as a vehicle to inject lycopene.

Experimental Design: The 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 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.

Lungs were excised, freed of adipose tissue, blotted dry and weighted.

Histopathological studies: The lungs were fixed in Bouin's fixative for 24 hrs. After 24 hrs, tissue was washed in 70% alcohol, dehydrated, cleared in xylene and embedded in paraffin wax (58-60°C) followed by their microtome sectioning at 5-7mμ thick sections. These sections stained with routine Haematoxylin and eosin staining technique (14). The final slides were studied for light microscopy.

Statistical analysis: The data was analyzed by using Student's *t*-test and two way ANOVA to examine the significance of difference between the various groups.

RESULTS AND DISSCUSSION

Cd administration does not produce any discernible signs and symptoms of sickness in mice. Also, there was observed no mortality during the entire period of experiment. A significant reduction ($p \leq 0.001$) in weight of lung was also observed in mice treated with cadmium in comparison to control group at all the intervals of the experiment. This reduction may be attributed to the damaging effects of cadmium on lung tissue. Anderson *et al*. [15] 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 lung was observed. Thus improvement in organ weight indicates the protection afforded by lycopene (Fig.1).

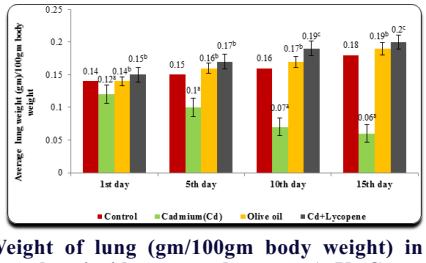

Fig.1: Weight of lung (gm/100gm body weight) in control, cadmium and antioxidant treated groups. (a Vs Control; b,c Vs Cd)

The rate of cadmium absorption depends on the duration of cadmium administration [16]. Lehman and Klaassen [17] reported that the retention of cadmium by a single oral administration is also dosage dependent and increased at higher cadmium dosages. They further suggested that cadmium at low dosages may be more extensively bound to metallothionein (Mt) and is less freely available for absorption in comparison to that to higher dosages. The distribution of cadmium also showed variations in organ cadmium accumulation rate which is in accordance with the results of the other workers [18].

Histopathological examination of the lungs of control group showed normal histological structure of the lung. The interalveolar septa were seen to be thin and the alveoli and alveolar sacs appeared clear and patent (Fig.2). Histology of lung of olive oil treated group also shows normal structure (Fig.3). However, animals treated with Cd showed loss of normal lung architecture including loss of continuity of alveolar epithelium, extensive thickening and distortion of the interalveolar septa with dilatation and congestion of the pulmonary blood vessels and perivascular and peribronchial cellular infiltration. Lymphocytic infiltration and hyperaemia were observed along with numerous macrophages in the surrounding area of the lesions. The increased number of lymphocytes is one of the indicators for inflammation (Fig.4). Increased macrophages a1re possible because of increased production of surfactant by the hyperplastic cells [19].

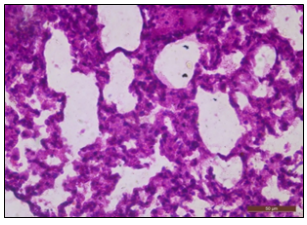

Fig. 2 Showing normal lung structure. Alveoli with interalveolar septa, alveolar sacs and pulmonary blood vessels. X400.

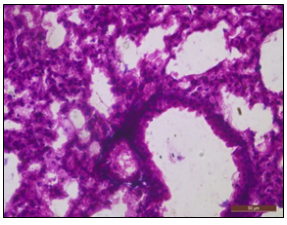

Fig. 3 Lung of olive oil treated group. Showing normal alveoli with alveolar sacs.X400.

The lung tissue of rats treated with Cd in the present study revealed severe inflammation and cell proliferation. The chronic exposure of cadmium compound induces lung cell proliferation which may be independent of lung inflammation [20]. They hypothesised that cadmium exposure induces the inflammatory cytokines along with the cell proliferating factors in the lung. El-Sokkary and Awadalla [21] revealed different changes induced by cadmium (5 mg/kg body weight) in the lung of rat. Lung lesions consist of vascular severe inflammation in both alveoli and bronchioles with oedema and congestion. Also, these histopathological changes are in agreement with the findings of Shin *et al*. [22] who reported that the lung is a primary target organ of systemic exposure to cadmium. Because cadmium is mainly absorbed through the inhalation of industrial pollution and tobacco smoke, the result is the accumulation of this metal in the lung. Also, Yamada *et al*. [23] noticed a dramatic increase in the number of alveolar neutrophilic leukocytes 6–48 h after intra-bronchial instillation of 1 mg cadmium chloride into the lungs of dogs.

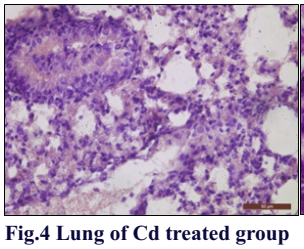

Fig.4 Lung of Cd treated group showing oedema, hyperaemia, air space enlargement, thick interalveolar septa and lymphocyte infiltration in connective tissue surrounding lung bronchiole. X400.

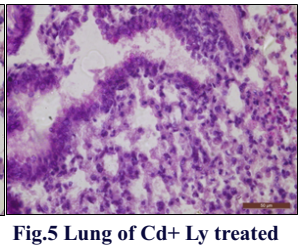

Fig.5 Lung of Cd+ Ly treated group showing less oedema, hyperaemia and almost normal structure similar to that of control. X400.

However, Driscoll *et al*. [24] reported that inhalation of Cd has been implicated in the development of emphysema and pulmonary fibrosis. Mckenna *et al*. [25] found that Cd-exposed lungs showed acute and more chronic pulmonary inflammation in both rats and mice with bronchiolar and alveolar lesions. Cd exposure was deleterious to the lung tissue causing mild to severe inflammation[26].

Lycopene treated group showed mild neutrophil infiltration, perivascular and alveolar edema, and aided in preventing the progression of lung damage (Fig.5). Thus, lycopene rich diet can play an important role in preventing injury to lungs which are prone to oxidative stress. Many epidemiological studies had also shown an inverse association between the occurrence of lung cancer and more consumption of fruits and vegetables [27]. This further confirms that people having high serum levels of lycopene and β-carotene were less prone to lung diseases [28]. So, carotenoids (i) function as antioxidants [29] (ii) are precursors of retinoic acid [30, 31] (iii) enhance communication in gap junctions [32] (iv) function as immune enhancers [33] (v) inhibit cell proliferation [34] (vi) induce cell apoptosis [35] (vii) induce carcinogen-metabolizing enzymes [36].

The histopathological studies of the present study showed the promising protective role of lycopene. Animals fed lycopene with cadmium showed normalization of most of the alveolar tissue and bronchioles but still few bronchioles showed congestion of blood vessels.

CONCLUSION:

The present study concluded that cadmium is quite toxic to lungs but lycopene ameliorated most of the histopathological lesions produced by cadmium. Though we can,t avoid environmental pollution but intake of antioxidant rich food can help us to bear with such environment and keep us healthy.

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REFERENCES

1. Pinot F, Kreps SF, Bachelet M, Hainaut P, Bakonyi M. and Polla BS. Cadmium in the environment: sources, mechanisms of biotoxicity and biomarkers. Res. Environ. Health. 2000; 15: 299-323.
2. Ferner DJ. 2001. Toxicity heavy metals. eMed. J. 2: 1.
3. Waisberg GM, Joseph P, Hale H. and Beyersonann D. Molecular and cellular mechanism of cadmium carcinogenesis. Toxicol. 2003; 192: 95-117.
4. Duruibe JO, Ogwuegbu MOC. and Egwurugwu JN. Heavy metal pollution and human biotoxic effects. Int. J.Physiol. Sci. 2007; 2 (5): 112-118.
5. Casolino E, Calzaratti G, Sblano C. and Landriscina C. Molecular inhibitory mechanisms of antioxidant enzymes in rat liver and kidney by cadmium. Toxicol. 2000; 179: 37-45.
6. Ganguly K, Levänen B, Palmberg L, et al. Cadmium in tobacco smokers: a neglected link to lung disease? Eur Respir Rev. 2018; 27: 170122 [https://doi.org/10.1183/16000617.0122-2017].
7. Agency for Toxic Substances & Disease Registry (ATSDR). Toxicological Profile for Cadmium. Atlanta, GA, U.S. Department of Health and Human Services, Public Health Service, 2012.
8. Nair AR, Degheselle O, Smeets K, et al. Cadmium-induced pathologies: where is the oxidative balance lost (or not)? Int J Mol Sci. 2013; 14: 6116-6143.
9. Barregard L, Fabricius-Lagging E, Lundh T, et al. Cadmium, mercury, and lead in kidney cortex of living kidney donors: impact of different exposure sources. Environ Res. 2010; 110: 47-54.
10. Steven G, Thomas D, Haffner J, Kroetsch T, Davidson SR, James WE. and Hugson RL. Effect of short-term lycopene supplementation and postprandial dyslipidemia on plasma antioxidants and biomarkers of endothelial health in young, healthy individuals. J. Vas. Health Risk Manage. 2008; 4 (1): 213-222.
11. Rao AV. and Agarwal S. Role of antioxidant lycopene I cancer and heart disease. J. American Coll. Nutr. 2000; 19: 563-569.
12. Selvan VK, Vijayakumar A, Kumar KS. and Singh G N. Lycopene's effect on health and diseases. Natural Med J. 2011; 3: 3.
13. Scolastici C, Alvas De Lima RO, Barbisan LF, Ferreira AL, Ribeiro A. and Salvadori DMF. Lycopene activity against chemically induced DNA damage in Chinese hamster ovary cells. Toxicol. In vitro. 2007; 21: 840-845.
14. Drury RA. and Wallington EA. Carleton's Histological Techniques, 5th ed, Oxford University Press. London, New York Toronto, 1980; 1: 653-661.
15. Anderson H, Larsen S, Splid H. and Christenson ND. Multivariate statistical analysis of organ weights in toxicity studies. Toxicol. 1999; 136: 67.
16. Grosicki A. and Kowalski B. Whole-body and organ retention of cadmium after repeated administration to rats. Bull. Vet. Inst. Pulawy, 2002; 46: 143-147.
17. Lehman LD. and Klaassen CD. Dosage-dependent disposition of cadmium administered orally to rats. Toxicol. Appl. Pharmacol. 1986; 84: 159-167.
18. McKinney J. Cadmium. In: Metal bioavailability and disposition kinetics research needs workshop. Toxicolol. Envir. Chem. 1991; 38: 44-49.
19. Dixon D, Herbert RA, Sills RC. and Boorman GA. Lungs, pleura, and mediastinum. In: R. R. Maronpot (ed.), Pathology of the Mouse, Vienna, IL: Cache River Press, 1999; 293-323.
20. Kundu S, Sengupta S, Chatterjee S, Mitra S. and Bhattacharya A. Cadmium induces lung inflammation independent of lung cell proliferation: a molecular approach. J. Inflamm. 2009; 12: 6-19.
21. El-Sokkary GH. and Awadalla EA. The protective role of vitamin C against cerebral and pulmonary damage induced by cadmium chloride in male adult albino rat. Open Neuroendocrinol. J. 2011; 4:1-8.
22. Shin HJ, Lee BH, Yeo MG, Oh SH, Park JD, Park KK, Chung JH, Moon CK. and Lee MO. Induction of orphan nuclear receptor Nur77 gene expression and its role in cadmium induced apoptosis in lung. Carcinogen. 2004; 25 (8): 1467-1475.
23. Yamada H, Damiano VV, Meranze DR, Glasgow J, Abrams WR. and Weinbaum G. Neutrophil degranulation in cadmium chloride induced acute lung inflammation. American J. Pathol. 1982; 109 (2): 145-156.

24. Driscoll KE, Maurer JK, Poynter J, Higgins J, Asquith T. and Miller NS. Stimulation of rat alveolar macrophage fibronectin release in a cadmium chloride model of lung injury and fibrosis. Toxicol. Appl. Pharmacol. 1992; 116 (1): 30-37.
25. Mckenna IM, Waalkes MP, Chen LC. and Grdn T. Comparison of inflammatory lung responses in Wister rats and C57 and DBA mice following acute exposure to cadmium oxide fumes. Toxicol. Appl. Pharmacol. 1997; 146 (2): 196-206.
26. Bell RR, Nonavinakere VK. and Soliman MR. Intratracheal exposure of the guinea pig lung to cadmium and/or selenium: a histological evaluation. Toxicol Lett. 2000; 114 (1): 101-109.
27. Kim J. and Kim Y. Animal models in carotenoids research and lung cancer prevention. Treansl.Oncol. 2011; 4(5): 271-281.
28. Comstock GW, Alberg AJ, Huang HY, Wu K, Burke AE, Hoffman SC, Norkus EP, Gross M, Cutler RG, Morris JS, et al. The risk of developing lung cancer associated with antioxidants in the blood: ascorbic acids, carotenoids, α-tocopherol, selenium, and total peroxyl radical absorbing capacity. Am J Epidemiol. 2008; 168: 831-840.
29. Krinsky NI. Actions of carotenoids in biological systems. Annu Rev Nutr. 1993; 13: 561-587.
30. Napoli JL. and Race KR. Biogenesis of retinoic acid from β-carotene. Differences between the metabolism of β-carotene and retinal. J Biol. Chem.1988; 263: 17372-17377.
31. Wang XD. and Krinsky NI. The bioconversion of β-carotene into retinoids. Subcell Biochem.1998; 30: 159-180.
32. Sies H. and Stahl W. Carotenoids and intercellular communication via gap junctions. Int J Vitam Nutr Res. 1997; 67: 364-367.
33. Hughes DA. Effects of carotenoids on human immune function. Proc Nutr Soc. 1999; 58: 713-718.
34. Ben-Dor A, Steiner M, Gheber L, Danilenko M, Dubi N, Linnewiel K, Zick A, Sharoni Y, and Levy. Carotenoids activate the antioxidant response element transcription system. Mol Cancer Ther. 2005; 4: 177-186.
35. Stahl W, von Laar J, Martin D, Emmerich T, and Sies H. Stimulation of gap junctional communication: comparison of acyclo-retinoic acid and lycopene. Arch Biochem Biophys. 2000; 373: 271-274.
36. Edes TE, Thornton W Jr, and Shah J. β-Carotene and aryl hydrocarbon hydroxylase in the rat: an effect of β-carotene independent of vitamin A activity. J Nutr. 1989; 119: 796-799.