

RESEARCH ARTICLE

Microscopic Vision for a Therapeutic Effect of Carnitine and Arginine Against Cadmium Toxicity in the Histological Structure of Rat Lung

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ABSTRACT

The study is conducted to investigate the therapeutic effect of L-carnitine and L-arginine on the histological structure of the lung in rats treated with cadmium chloride. The study included 20 male rats subjected to the necessary laboratory conditions throughout the experiment. The results show the occurrence of many tissue lesions in the lung, represented by the degeneration of the lining epithelial cells and the shedding of many of these cells in the lumen of the bronchioles. In addition, there is necrosis of the interstitial tissue between the alveoli, with the presence of clumps of red blood cells in the cavities of some blood vessels in the group treated with cadmium chloride, the group treated with cadmium chloride and L-carnitine, and the group treated with cadmium chloride and L-arginine.

Keywords: Antioxidants, Cadmium chloride, L-arginine, L-carnitine.

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INTRODUCTION

Environmental exposure to tobacco smoke, indoor air pollution, fumes, and chemicals are among the most important external sources of cadmium exposure.¹ These are important risk factors for Chronic Obstructive Pulmonary Disease (COPD), the third leading cause of death worldwide. According to a WHO report, this disease caused 3.23 million deaths in 2019, more than 80% of which were in low- and middle-income countries.²

The COPD causes persistent and progressive respiratory symptoms, including difficulty in breathing, coughing, and/or sputum production. Abnormalities in the small airways of the lungs limit airflow in and out of the lungs, as well as swelling of the respiratory epithelium and airway obstruction from Mucous accumulation.³ Despite this, the disease is common and can be prevented and treated through the use of antioxidant drugs. The effects caused by cadmium toxicity are oxidative effects. Therefore, antioxidants such as carnitine and arginine may have an active role in protecting cellular components from oxidants.^{4,5}

MATERIALS AND WORKING METHODS

Chemicals

L-arginine

used in the form of 500 mg pills manufactured by the American company **Nuticost**.

L-carnitine

used in the form of 500 mg pills manufactured by the American company **Rito**.

Cadmium Chloride

obtained from the **Central Drug House Co./India**

Experimental Design

The 20 rats, aged from 12 to 51 weeks, with their weights ranging between (200–400) g, are distributed into four groups with five animals for each group, as shown below. After the preparatory period ends, these animals are treated daily for 3 weeks. It is taken into account that the weights of each group are equal to each other as much as possible before starting the treatment:

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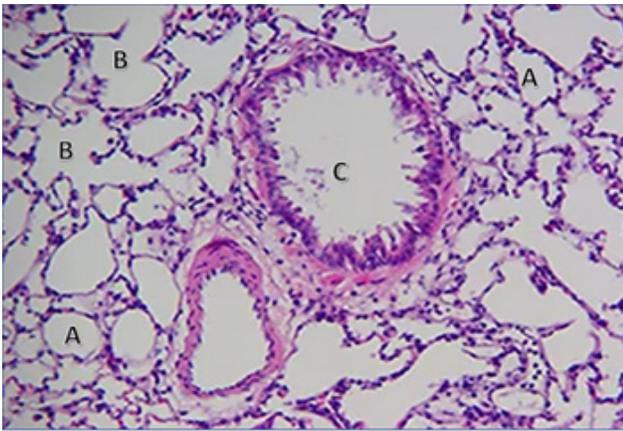


Figure 1: Lung section of a rat from the control group showing the normal histological structure of the alveoli (A), alveolar sacs (B), and respiratory bronchioles (C) (H&E, X40).

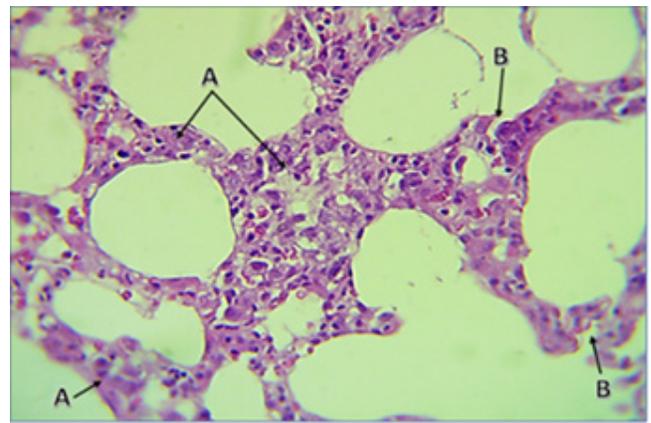


Figure 4: Lung section of a rat from the group treated with cadmium chloride showing thickening of the septa between the alveoli (A), with necrosis in some of them (B) (H&E, X40).

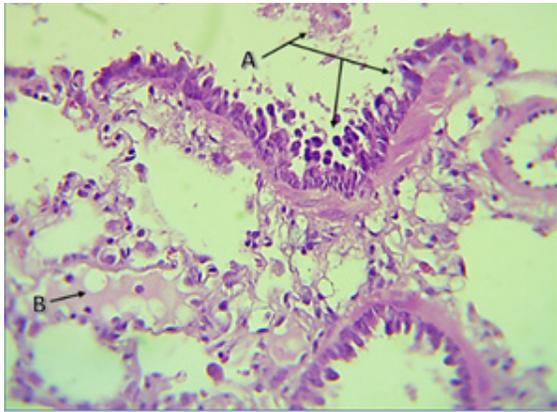


Figure 2: Lung section of a rat from the cadmium chloride-treated group showing degeneration, necrosis and desquamation of the epithelium lining the bronchiole (A), and inflammatory edema of another bronchiole (B) (H&E, X40).

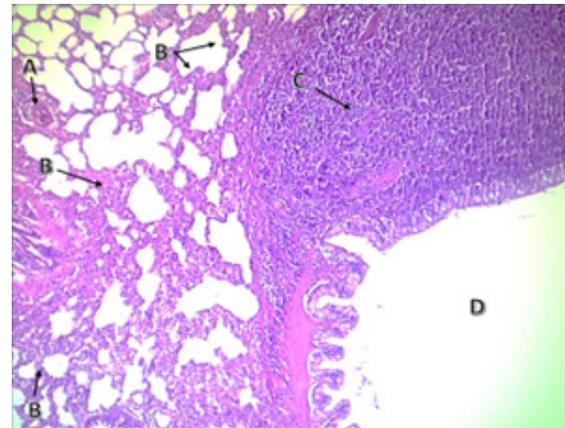


Figure 5: Lung section of a rat from the group treated with cadmium chloride and L-carnitine showing cellular infiltration around a blood vessel (A), partial thickening of the inter-alveolar septa (B), lymph node (C) around a bronchus. (H&E, X40).

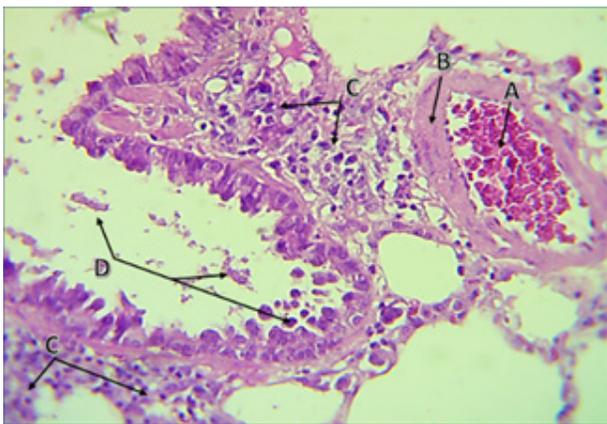


Figure 3: Lung section of a rat from the cadmium chloride-treated group showing acute congestion in a blood vessel (A) thickening of its walls (B), inflammatory cell infiltration (C), necrosis and desquamation of the epithelium lining the trachea (D) (H&E, x40).

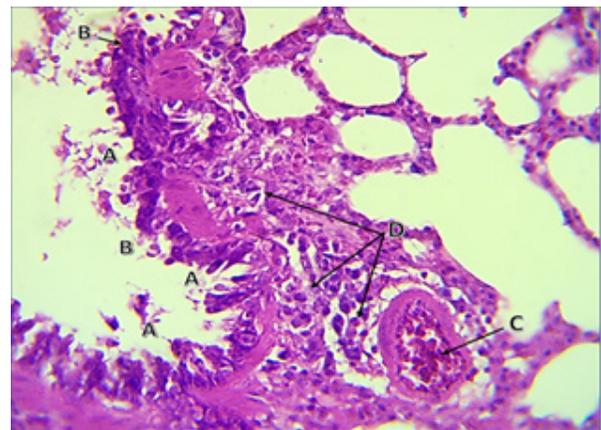


Figure 6: Lung section of a rat from the group treated with cadmium chloride and L-Carnitine, showing necrosis and desquamation of the bronchial endothelium (A), necrosis of smooth muscle fibers in its wall (B), congestion of a blood vessel (C), inflammatory cell infiltration (D) . (H&E, X40).

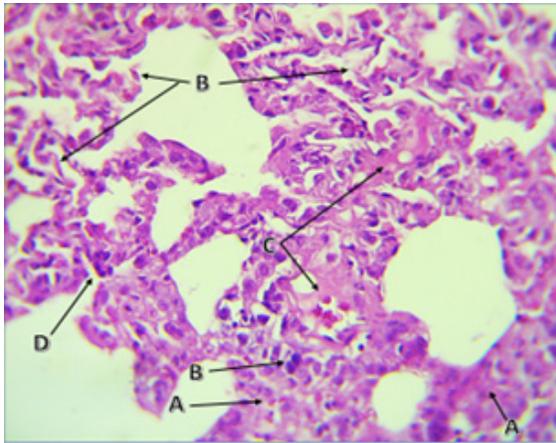


Figure 7: Lung section of a rat from the group treated with cadmium chloride and L- arginine showing hyperplasia of a part of the interstitial tissue between the alveoli (A), necrosis of another part (B), with the appearance of an inflammatory exudate (C), as well as an inflammatory cell infiltration (D) (H&E, X40).

- Control group: given drinking water and food daily for 21 days.
- Group treated with cadmium chloride: dosed with cadmium chloride (5) mg/kg, prepared by adding 2.5 g of cadmium chloride to 1000 ml of distilled water⁶ daily for a period of 21 days.
- Group treated with cadmium chloride followed by L-carnitine: treated with cadmium chloride (5) mg/kg in one dose per day for 7 days. On the eighth day, it is treated with L-carnitine (7.2) mg/kg *via* a single dose per day for 14 days while continuing the treatment with chloride Cadmium until the end of the experiment.
- Group treated with cadmium chloride followed by L-arginine: treated with cadmium chloride 5 mg/kg *via* one dose daily for a period of 7 days. On the eighth day, it is treated with L-arginine 7.2 mg/kg with a single dose daily for 14 days while continuing the treatment with chloride Cadmium until the end of the experiment.

Preparation of Tissue Sections

Using the working methods and employing the standard system, the Luna method⁷ is adopted to prepare the tissue sections according to the following steps: (Fixation, Washing, Dehydration, Clearing, Infiltration, Embedding, Trimming and sectioning, Staining, and Mounting).

RESULTS

Control Group

Microscopic examination reveals the normal structure of the lung tissue, showing the alveoli with cavities of different sizes, the alveolar walls containing the alveolar squamous cells, as well as the normal appearance of bronchioles lined with cuboidal cells (Figure 1).

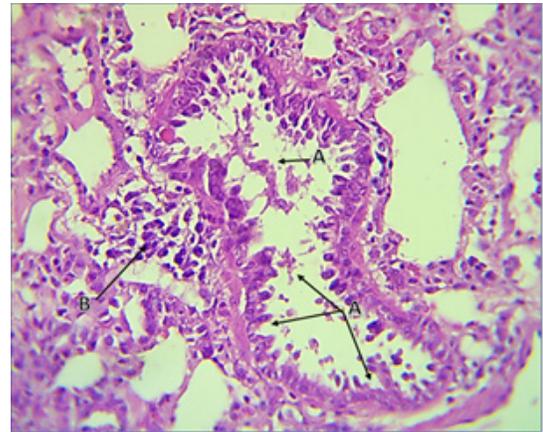


Figure 8: Lung section of a rat from the group treated with cadmium chloride and L-arginine showing necrosis and desquamation of the bronchial endothelium (A), and inflammatory cell infiltration (B). (H&E, X40).

Group Treated with Cadmium Chloride

The results of the histological examination of the lung in the rats of this group show the occurrence of degeneration of the lining epithelial cells and shedding of many of them in the lumen of the bronchioles, as well as necrosis of the interstitial tissue between the alveoli, with the presence of masses of red blood cells in the cavities of some blood vessels, as in Figures 2, 3 and 4.

Group Treated with Cadmium Chloride Followed by L-carnitine.

The results of the histological examination of the lung in the rats of this group show severe degeneration of the epithelium lining the bronchioles with the loss and shedding of many of them in the lumen of these bronchioles, as well as being surrounded by a thickening of smooth muscle fibers, and infiltration of inflammatory cells around the walls of the alveoli and around the blood vessels containing a blood clot as in Figures (5 and 6).

Group Treated with Cadmium Chloride Followed by L-arginine.

The results of the histological examination of the lung in the rats of this group show a thickening between the walls of the alveoli, cellular degeneration of the epithelium lining the cavities of a number of them, hyperplasia of the epithelium of other alveoli, as well as infiltration of inflammatory white blood cells with edema in the tissue (Figures 7 and 8).

DISCUSSION

The widespread presence of cadmium chloride in the environment has led to a global increase in respiratory diseases. Its effects on the structure and function of the liver and kidneys have been extensively studied, but the respiratory system is often overlooked as a target. The Agency for Toxic Substances and Disease Registry (ATSDR) (2012) has indicated that cadmium can lead to damage the tissue structure of the

lungs, and long-term exposure to low levels of cadmium in the air, food or water leads to the accumulation of cadmium in the lungs and thus exacerbate the damage.⁸ Therefore, this research is designed to study the possible structural changes in lung tissue of male rats after oral exposure to cadmium and the therapeutic role of L-carnitine and L-arginine for 21 days. The results of the histological examination of the lung in the group treated with cadmium chloride show degeneration of the lining epithelial cells and sloughing off many of these cells in the bronchioles' lumen necrosis of the interstitial tissue between the alveoli. These results are consistent with what Naidoo *et al.* has reported.⁹ Some studies have indicated that cadmium chloride binds to metallothionein and antioxidants inside the lung tissue. Prolonged exposure to cadmium chloride leads to depletion of antioxidants that are the first lines of defense in the rat lung, thus increasing oxidative stress, persistent inflammation, lipid peroxidation, loss of lung function and increased alveolar volume. These are established phenomena in the pathogenesis of cadmium-related lung diseases, including COPD, chronic bronchitis and emphysema.¹⁰

Concerning the results of the group treated with cadmium chloride and L-carnitine, it shows degeneration of the lining epithelial cells and shedding of many of these cells in the lumen of the bronchioles, inflammatory cell infiltration, and the occurrence of a blood clot. These lesions are due to the acute toxicity caused by cadmium chloride and the short treatment period by L-Carnitine. These results are consistent with a study conducted by Unsal *et al.*,¹¹ where they reported that giving oral doses of cadmium chloride to male rats for 10 days causes a decrease in lung weight, with the appearance of non-specific lung lesions. A study performed by Salama *et al.*⁴ mentions that giving oral doses of L-carnitine at a concentration of 25 mg/kg to white male rats treated with chromium at a concentration of 2 mg/kg has a therapeutic effect in acute lung injury caused by chromium in acting as an antioxidant and anti-inflammatory mediated by the nuclear factor-erythroid 2-related factor 2 (Nrf2) pathways.

The group treated with cadmium chloride followed by L-arginine shows degeneration of the epithelial cells lining the bronchioles, hyperplasia of the interstitial tissue between the alveoli, infiltration of inflammatory cells in addition to inflammatory edema. These results do not agree with what Scott *et al.* mention 5 in that L-arginine can protect lung tissue by acting as an antioxidant, as well as its role in the production

of nitric oxides, which have therapeutic benefits against oxidants and improve the inner lining of blood vessels. The reason for the persistence of these tissue lesions in our current results may be due to the short treatment period.

CONCLUSIONS

L-Carnitine and L-Arginine have no therapeutic effect on the histological structure of the lung against cadmium chloride-induced toxicity.

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