Iran. J. Ichthyol. (Special Issue 1, 2022): 348-354

P-ISSN: 2383-1561; E-ISSN: 2383-0964
http://www.ijichthyol.org

## Research Article

# Histological comparison of rat heart after treatment with L-carnitine and L-arginine against cadmium toxicity

Khulood N. RASHEED*[1], Abdul Monem K. ABDULLAH[2]
[1]*Department of Anatomy and Histology, College of Medicine, University of Tikrit, Iraq.*
[2]*Department of Biology, College of Science, University of Tikrit, Iraq.*
[*]*Email: khuloodnaji@tu.edu.iq*

**Abstract**
The study aimed to investigate the therapeutic effect of L-carnitine and L-arginine on the histological structure of the heart in rats exposed to cadmium chloride. The study includes 20 male rats divided inthetreatmentsof (1) control group, given drinking water and food daily for 21 days, (2) group treated with cadmium chloride as 5mg/kg as 2.5g added into distilled water daily for 21 days, (3) group treated with cadmium chloride as 5mg/kg per day for 21 days and L-carnitine from day eighth as 7.2mg/kg for 14 days, and (4) group treated with cadmium chloride as 5mg/kg for 21 days and L-arginine from day eighth as 7.2mg/kg for 14 days. The results showed the occurrence of many tissue lesions in the heart, represented by the occurrence of necrosis in some cardiac muscle fibers and rupture of the cytoplasm, with disintegration between muscle fibers. Moreover, there is infiltration of macrophages in the connective tissue of the fascia, extensive damage and a lack of connection for many muscle fibers. In addition, there is the occurrence of congestion and hemolysis in the group treated with cadmium chloride, and the group treated with cadmium chloride and L- arginine. A significant improvement is also observed in the group treated with cadmium chloride and L-Carnitine, which is represented by a normal appearance of muscle fiber bundles and Purkinje fibers.

**Keywords:** L-arginine and L-carnitine, cadmium chloride, Heart, Antioxidants.

**Citation:** Rasheed, K.N. & Abdullah, A.M.K. 2022. Histological comparison of rat heart after treatment with L-carnitine and L-arginine against cadmium toxicity. Iranian Journal of Ichthyology 9(Special Issue 1, 2022): 348-354.

## Introduction

Cardiovascular disease (CVD) causes 17.3 million deaths annually (Sacks et al. 2017). Current records estimate an annual global average of 30 million cases of cardiac dysfunction, with a projected 2-3-fold increase over the next 20-30 years (Wang et al. 2018). Although drugs such as β-blockers and angiotensin-converting-enzymes are commonly prescribed to control CVD risk, they can cause side effects such as hepatotoxicity, renal toxicity, and hematological changes (Margalef et al. 2018). Therefore, it is necessary to find alternatives such as L-carnitine and L-arginine to control the internal factors that contribute to the progression of the disease. L-Carnitine acts as an antioxidant and its intake through dietary and intravenous modalities serve as an appropriate preventive strategy against ventricular dysfunction, ischemia, and arrhythmia (Vacante et al. 2018). L-arginine acts as a basic substrate for nitric oxide production to regulate blood pressure and immunity (Kan et al. 2015). Aside from being a structural component of many proteins, L-arginine is important in several roles in most cardiovascular diseases (Rodrigues-Krause et al. 2018). In addition, both L-carnitine and L-arginine reduce hypertension, hyperlipidemia, hyperglycemia, insulin resistance, and obesity, which promote cardiovascular disease (Hong et al. 2018; Fathi et al. 2020). The study aimed to investigate the therapeutic effect of L-carnitine and L-arginine on

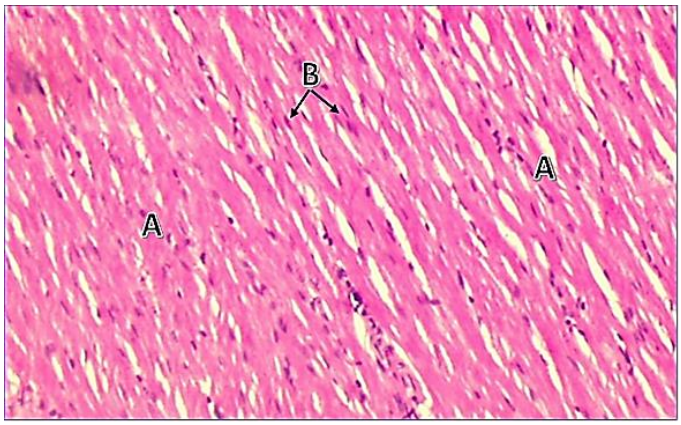


**Fig. 1.** Heart section of a rat from the control group showing the normal structure of muscle fibers (A), and their oval central nuclei (B) (H&E, X40).

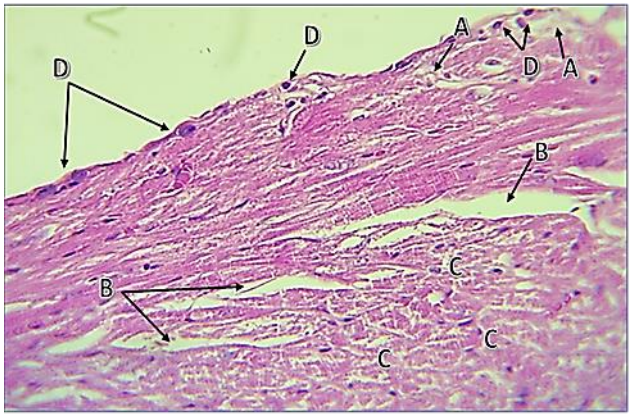


**Fig. 2.** Heart section of a rat from the group treated with cadmium chloride showing necrosis (A), disintegration (B) of cardiac muscle fibers, as well as eruption of the cytoplasm in a number of them (C), and infiltration of inflammatory cells (D). (H&E, X40).

the histological structure of the heart in rats treated with cadmium chloride.

## Materials and Methods

The used chemicals were L-arginine and L-carnitine in 500mg pills (USA) and Cadmium Chloride from the Central Drug House Company (India). A total of 20male rats, aged from 12 to 51 weeks, and their weights ranging 200-400g, are distributed into four groups with five animals per group. And experiment lasts for three weeks.

The weights of each group were equal before starting the experiment with treatments of (1) control group: given drinking water and food daily for 21 days, (2) group treated with cadmium chloride as 5mg/kg prepared by adding 2.5g of cadmium chloride to 1000ml of distilled water (Rodrigues-Krause et al. 2018) daily for 21 days, (3) group treated with cadmium chloride as 5mg/kg per day for 21 days and L-carnitine from day eighth as 7.2mg/kg for 14 days, and (4) group treated with cadmium chloride as 5mg/kg for 21 days and L-arginine from day eighth as 7.2mg/kg via a single dose daily for 14 days. Preparation of histological slides according to the standard method (Fixation, washing, dehydration, clearing, infiltration, embedding, trimming and sectioning, staining, and mounting) based on Luna (1968).

## Results

**Control Group:** Histological examination showed a normal structure of the heart tissue, where the cardiac muscle fibers are aligned with each other with an oval central nucleus (Fig. 1).

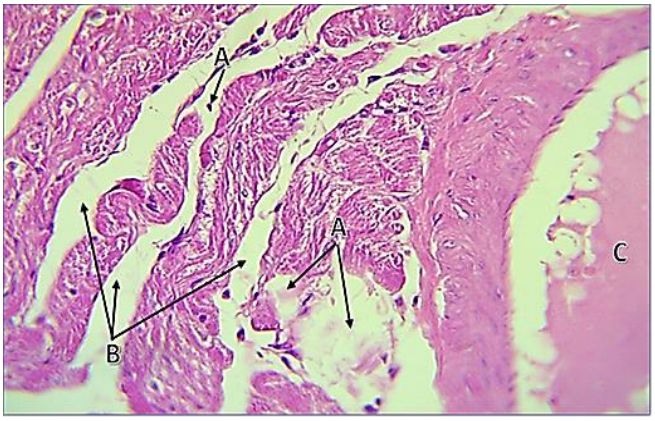


**Fig. 3.** Heart section of a rat treated with cadmium chloride showing acute necrosis (A) and extensive disintegration (B) of cardiac muscle fibers, and hemolysis (C). (H&E, X40).

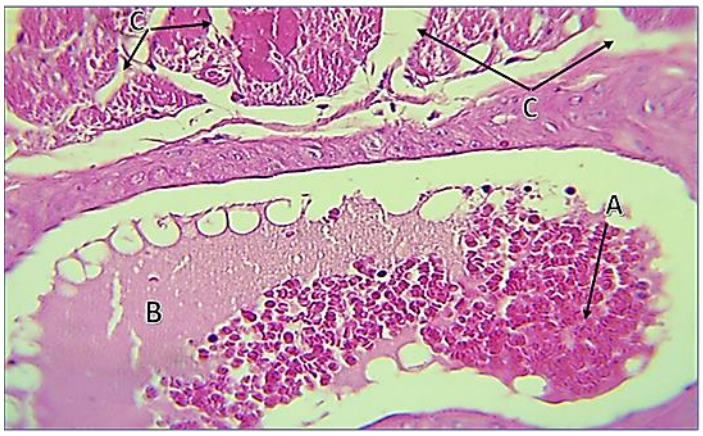


**Fig.4.** Heart section of a rat from the group treated with cadmium chloride showing congestion (A), hemolysis (B), and degeneration and dissociation of cardiac muscle fibers (C). (H&E, X40).

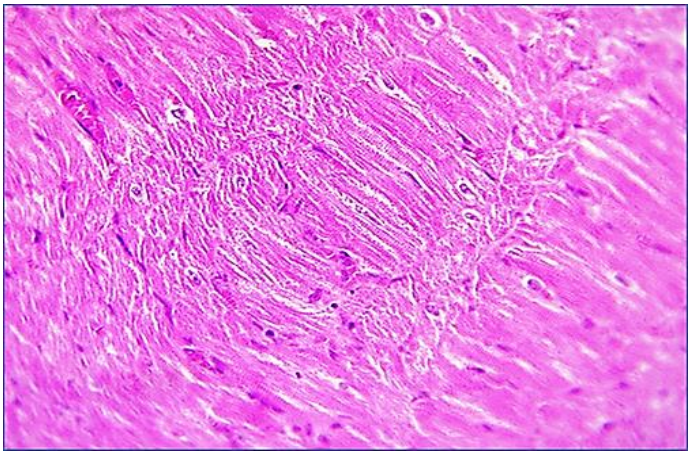

**Fig.5.** Heart section of a rat from the group treated with cadmium chloride and L-carnitine, showing the quasi-normal structure in the entire histological section. (H&E, X40).

**Group treated with cadmium chloride:** The histological examination of the heart in the rats of this group showed necrosis in some cardiac muscle fibers and cytoplasmic eruption, with dissociation between muscle fibers, infiltration of macrophages in the connective tissue of the fascia. It also showed extensive damage and a lack of association between many muscle fibers and the occurrence of congestion

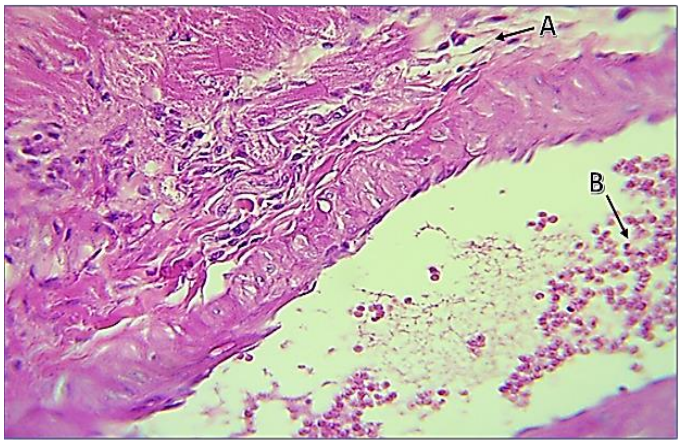


**Fig. 6.** Heart section of a rat from the group treated with cadmium chloride and L-carnitine, showing necrosis of some cardiac muscle fibers (A), and partial blood congestion (B). (H&E, X40).

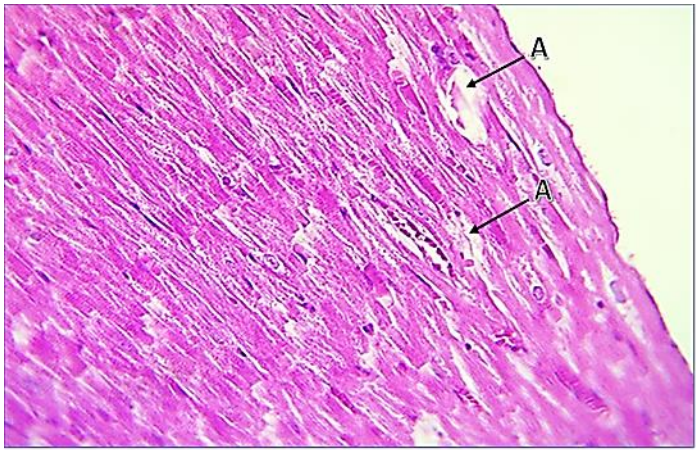


**Fig.7.** Heart section of a rat from the group treated with cadmium chloride and L-carnitine, showing the quasi-normal structure, except for a slight dent in the cardiac muscle fibers (A). (H&E, X40).

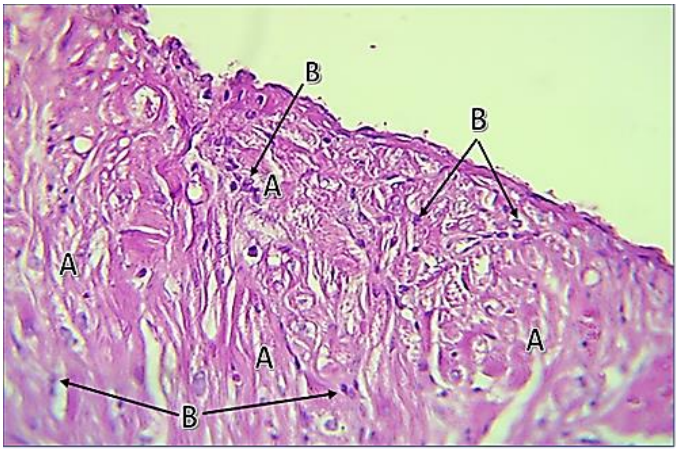


**Fig.8.** Heart section of rats from the group treated with cadmium chloride and L-arginine showing extensive degeneration, necrosis and rupture in cardiac muscle fibers (A), and with inflammatory cells infiltration (B). (H&E, X40).

and hemolysis (Figs. 2, 3, 4).

**Group treated with cadmium chloride and L-carnitine:** The histological examination of the heart shows the appearance of muscle fibers in the form of bundles parallel to each other and the nuclei of muscle fibers in a normal manner, with a very limited

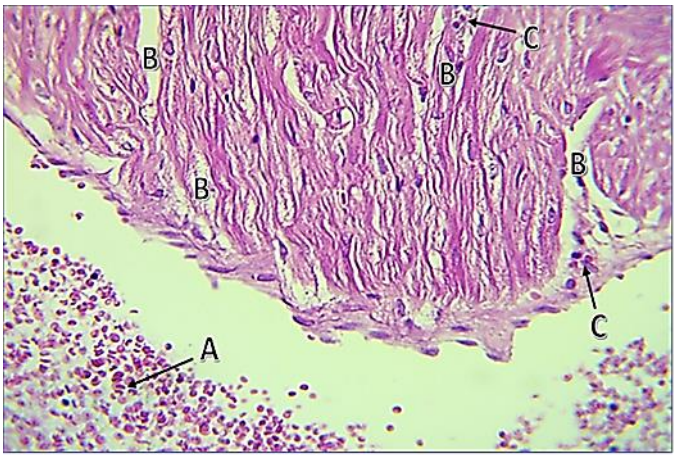


**Fig.9.** Heart section of a rat from the group treated with cadmium chloride and L- arginine showing blood congestion (A), degeneration and disintegration of cardiac muscle fibers (B), and inflammatory cell infiltration (C). (H&E, X40).

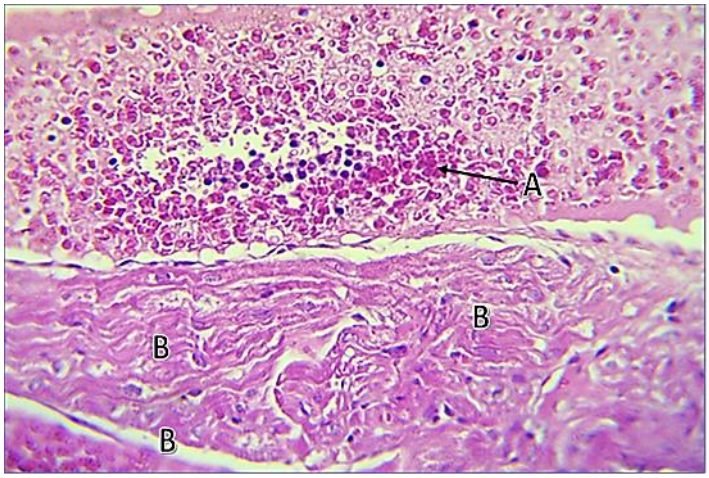


**Fig.10.** Heart section of a rat from the group treated with cadmium chloride and L- arginine, showing severe blood congestion (A), disintegration of cardiac muscle fibers (B). (H&E, X40).

degeneration of some of those muscle fibers, in addition to the appearance of Purkinje fibers in a normal manner (Figs. 5, 6, 7).

**Group treated with cadmium chloride and L-arginine:** The results showed the occurrence of disintegration and atrophy in many muscle fibers, and the eruption of the cytoplasm in some muscle fibers with infiltration of some inflammatory white blood cells in the fascia of cardiac muscle fibers (Figs. 8, 9, 10).

## Discussion

Cadmium chloride transports to the heart through the blood as bound to metallothionine, and it enhances the generation of free radicals and the production of ROS, which leads to oxidation in the tissue of the heart muscle and the occurrence of necrosis and programmed cell death in the exposed tissue cells (Zhang et al. 2018). Cadmium can displace some essential minerals such as zinc, iron, and calcium, and its direct effects in inducing toxicity may explain the degenerative changes of cardiomyocytes in rats. Low-dose exposure affects tissue structure and myocardial integrity by increasing ROS production and affects the cardiac conduction system by interfering with calcium-mediated physiological and biochemical processes. It also affects calcium channels and potassium current, leaving the ventricular muscle cells (Shen et al. 2000; Vassallo et al. 2018; Borné et al. 2018).

The group treated with cadmium chloride and L-carnitine showed a significant improvement in the

bundles of muscle fibres, nuclei and Purkinje fibres. These results are consistent with the findings of Song et.al. (2017) who report that L-carnitine supplementation can reduce the clinical effects of heart disease, by improving factors associated with metabolic syndrome and cardiovascular disease such as arterial hypertension, cholesterol levels, impaired glucose tolerance and insulin resistance.

There is a strong relationship between heart disease and a deficiency of nitric oxides NO. In addition, L-arginine works to increase nitric oxides, which leads to the expansion of blood vessels to control blood pressure, as a neurotransmitter, as well as regulating the contraction of the heart (Costa et al. 2016). Studies also indicate that coronary artery disease (CAD) is associated with defects in the generation or functioning of nitrogen oxide (Godo & Shimokawa 2017), but our results in the group treated with cadmium chloride and L-arginine show many tissue lesions that may be attributed to the short period of treatment with L-arginine, and the high toxicity of cadmium chloride.

## Conclusions

L-Carnitine has a high therapeutic effect in the treatment of cadmium chloride-induced toxicity in the histological structure of the heart, in contrast to L-arginine, which shows no therapeutic effect on the histological structure of the heart.

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