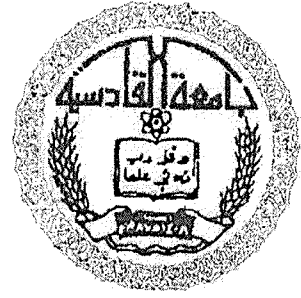


Republic of Iraq  
Ministry of Higher Education  
and Scientific Research  
University of Al-Qadissiya  
College of Veterinary Medicine



# **Histopathological effect of cadmium on organs of rats**

A Research Submitted to  
Veterinary Medicine collage / University of AL-Qadissiyah in  
Partial Fulfillment of the Requirements For The Degree of  
Bachelors of Science in Veterinary Medicine .

By

**Mohammad Jafar Mohammad**

Supervised by

**Lecture . Hala Abbas Naji**

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بسم الله الرحمن الرحيم

فَتَعَالَى اللَّهُ الْمَلِكُ الْحَقُّ ۖ وَلَا تَعْجَلْ بِالْقُرْآنِ مِنْ قَبْلِ أَنْ  
يُقْضَىٰ إِلَيْكَ وَحْيُهُ ۚ وَقُلْ رَبِّ زِدْنِي عِلْمًا ﴿١١٤﴾

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سورة طه.. الآية 114

# Certificate of Supervisor

I certify that the research entitled (Histopathological effect of cadmium on organs of rats) was prepared under my supervision at the college of veterinary medicine / University of Al-Qadissiya .




SUPERVISOR

lecture. Hala Abbas Naji

Dept. of pathology and poultry disease  
College of vet.medicine /University of Al-Qadissiya

# Certificate of Department

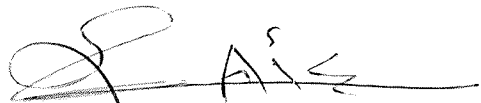
We, head of dept. of Int. and prev. med. , certify that ( Mohammad Jafar Mohammad) is adequate for the debate of graduation project of Bachelor degree in science in veterinary medicine



Instructor

**Dr.Muthanna Hadi Hussain**

21.4.2016



**Head of Dept. of Int. and prev. med.**

**Dr. Asaad Jasim abd**

# الاهداء

إلى أصحاب الفضل بعد الله في تربيته ونشأته

والدي ووالدتي

إلى كل من أعانني وقدم لي جهداً لانجاز دراستي

أساتذتي الكرام

إلى من بذل جهداً في إكمال البحث

الدكتورة

م. هالة عباس ناجي

## شكر وتقدير

الحمد لله الذي له ما في السماوات وما في الأرض وله الحمد في الأولى وفي الآخرة والصلاة والسلام على سيد الخلق أجمعين محمد الهادي الأمين وعلى اله الطيبين الطاهرين وصدق رسول الله صلى الله عليه واله وسلم القائل : (من لم يشكر المخلوق لم يشكر الخالق ) وإيماننا من ذلك أوجه شكري وتقديري إلى أساتذتي الكرام جميعا لما قدموا لي من توجيهات قيمة وأراء سديدة وبذلوا جهدا سخيا إثناء سنوات الدراسة ادعوا البارى عز وجل إن يكرمهم جميعا بدوام الصحة والموفقية كما أتقدم بالشكر الجزيل إلى عمادة كلية الطب البيطري لدورها في توفير مستلزمات الدراسة خلال سنوات الدراسة كما يسعدني إن أقدم شكري وامتناني إلى الدكتور هاله عباس ناجي لما قدمت لي من جهود طبية ومساعدة في إكمال بحثي ويسعدني إن أقدم شكري وامتناني إلى زملائي الذين لهم أعمق الأثر في نفسي لتجاوز كل الصعوبات خلال دراستي وأقدم لهم كل الحب والاعتزاز واطمأن منهم بالذكر الإخوان كرار محمد علي واحمد هيثم ومحمد حسن وحسين كامل واحمد رشيد وحسن صباح واحمد محمد مطر وليث مهند وآخر دعوانا الحمد لله رب العالمين والصلاة والسلام على خاتم الأنبياء والمرسلين سيدنا أبي القاسم محمد صل الله عليه واله الطاهرين وصحبه المنتجبين والتابعين لهم بإحسان إلى يوم الدين .



# *Abstract*

# ABSTRACT

Cadmium is a heavy metal that occurs as a natural constituent in earth's crust. Cadmium is vastly used in batteries, coating, plating, alloys etc. in various industries. Humans & animal are commonly exposed to cadmium by inhalation and ingestion. Cadmium enters in air and bind to small particles where it can combine with water or soil causing contamination of fish, plants and animals in nanoform. Cadmium waste streams from the industries end up in soil which can pollute both soil and surface water. The organic matter in the soil absorbs cadmium increasing the risk of survival of various plants and also increases the uptake of this toxic metal in food. The bioaccumulation of cadmium in human & animal bodies in food chain leads to acute and chronic intoxications due to biomagnification. Health effects includes diarrhea, stomach pains, Bone fracture, Reproductive failure and possibly even infertility, damage to the central nervous system and immune system, psychological disorders, etc. Cadmium can also cause the transformation of normal epithelial cells into carcinogenic cells by inhibiting the biosynthesis of protein. This review is about the study of histopathological effect of cadmium toxicity in animals.



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*CHAPTER  
ONE*

*Introduction*

# Introduction

That contaminated food is the major source of population exposure to cadmium (10-11). In persons occupationally exposed to cadmium, the main route of entry into the body is cadmium inhalation, but also the intake of cadmium via digestive tract and skin contributes to the total exposure. Once cadmium enters the circulation, it is transported to certain depots, and the most important are kidneys, liver and muscles. Cadmium is eliminated from the body through the digestive tract and urine, but due to the low level of excretion from the body and its excessive accumulation in the blood and depots, it has a biological half-life of up to 30 years (19).

Chronic exposure to cadmium is associated with increased incidence of various neoplastic and non-neoplastic diseases of kidney, liver, lungs, bone, brain, thyroid gland and other organs (12-13). It was also found that cadmium has a neurotoxic effect because it affects the integrity of the blood-brain barrier (14), but the report on structural changes in the myocardium under the influence of cadmium are rarely found in literature (15). Cadmium (Cd) can disturb mechanisms of vascular tone regulation and induce hypertension in experimental models, and its effect is dose-dependent. Given in small doses, it induces hypertension due to vascular dysfunction. Used in large doses, it is responsible for renal tubules destruction and intraparenchymal fibrosis leading to nephrogenic hypertension. Mechanisms of Cd vascular effect vary and involve nervous, hormone and intracellular signaling pathways. Cadmium influences renin-angiotensin-aldosterone systems and atrial natriuretic peptide concentration (16-18).



*CHAPTER  
TWO*

*Literatures of  
Review*

# Literature Review

## History

Cadmium was independently discovered by German chemist Karl Hermann in 1818. Hermann had noticed an unexpected yellow color in zinc sulfide. The yellow was assumed to be from arsenic impurities, but Hermann realized that it was actually due to a previously unknown element. <sup>(1,2,3)</sup>

The cadmium used within the United States was used for the second application, which was for red, orange and yellow pigments based on sulfides and selenides of cadmium.<sup>(9)</sup> The stabilizing effect of cadmium-containing chemicals like the carboxylates cadmium laureate and cadmium stearate on PVC led to an increased use of those compounds in the 1970s and 1980s. The use of cadmium in applications such as pigments, coatings, stabilizers and alloys declined due to environmental and health regulations in the 1980s and 1990s; in 2006, only 7% of total cadmium consumption was used for plating and coating and only 10% was used for pigments.<sup>[3]</sup> The decrease in consumption in other applications was made up by a growing demand of cadmium in nickel-cadmium batteries, which accounted for 81% of the cadmium consumption in the United States in 2006.<sup>(10)</sup>

## 2-1 Uses of Cadmium

Cadmium's major use is in batteries (especially rechargeable nickel-cadmium, NiCad, batteries). As a result of its low coefficient of friction and its high fatigue resistance, cadmium is used in alloys for bearings (1). It is also used in electroplating. Compounds containing cadmium are used in black and white television phosphors, and in the blue and green phosphors for color television picture tubes. Cadmium sulfide is used as a yellow pigment, and cadmium selenide is used as a red pigment, often called cadmium red(3).

Cadmium and tellurium can be compounded into CdTe thin-film photovoltaic modules whose physical characteristics are ideal for solar cell production(2).

Source: Cadmium most often occurs in small quantities associated with zinc ores, such as sphalerite (ZnS). Greenockite (CdS) is the only cadmium mineral of any consequence. Almost all cadmium is obtained as a by-product of zinc, copper, and lead ore refining operations(5).

### **2-1-1 Physical properties**

Cadmium is a soft, malleable, ductile, bluish-white divalent metal which is easily cut with a knife. It is similar in many respects to zinc but forms complex compounds.<sup>(4)</sup> Unlike most other metals, cadmium is resistant to corrosion and as a result it is used as a protective layer when deposited on other metals. As a bulk metal, cadmium is insoluble in water and is not flammable; however, in its powdered form it may burn and release toxic fumes.<sup>(5)</sup> Cadmium tarnishes in air and is soluble in acids but not in alkalis(8) .

### **2-1-2 Chemical properties**

Cadmium burns in air to form brown amorphous cadmium oxide (CdO); the crystalline form of this compound is a dark red which changes color when heated, similar to zinc oxide. Hydrochloric acid, sulfuric acid and nitric acid dissolve cadmium by forming cadmium chloride (CdCl<sub>2</sub>), cadmium sulfate (CdSO<sub>4</sub>), or cadmium nitrate (Cd(NO<sub>3</sub>)<sub>2</sub>). The oxidation state +1 can be reached by dissolving cadmium in a mixture of cadmium chloride and aluminium chloride, forming the Cd<sub>2</sub><sup>2+</sup> cation, which is similar to the Hg<sub>2</sub><sup>2+</sup> cation in mercury(I) chloride.<sup>(6,4)</sup>

### **2-1-3 Biological role**

Cadmium has no known useful role in higher organisms, but a cadmium-dependent carbonic anhydrase has been found in some marine diatoms, The diatoms live in environments with very low zinc concentrations and cadmium performs the function normally carried out by zinc in other anhydrases(11,12) .

The discovery was made using X-ray absorption fluorescence spectroscopy (XAFS)<sup>(13)</sup>.

The highest concentration of cadmium has been found to be absorbed in the kidneys of humans, and up to about 30 mg of cadmium is commonly inhaled throughout childhood and adolescence.<sup>(14)</sup> Cadmium can be used to block calcium channels in chicken neurons.<sup>(15)</sup> Analytical methods for the determination of cadmium in biological samples have been reviewed.<sup>(16)</sup>

#### **2-1-4 Cadmium poisoning**

The bioinorganic aspects of cadmium toxicity have been reviewed.<sup>(17)</sup> The most dangerous form of occupational exposure to cadmium is inhalation of fine dust and fumes, or ingestion of highly soluble cadmium compounds<sup>(13)</sup>. Inhalation of cadmium-containing fumes can result initially in metal fume fever but may progress to chemical pneumonitis, pulmonary edema, and death<sup>(18)</sup>. Cadmium is also an environmental hazard. Human & animal exposures to environmental cadmium are primarily the result of fossil fuel combustion, phosphate fertilizers, natural sources, iron and steel production, cement production and related activities, nonferrous metals production, and municipal solid waste incineration<sup>(3)</sup>.

Bread, root crops, and vegetables also contribute to the cadmium in modern populations.<sup>(19)</sup> In the decades leading up to World War II, mining operations contaminated the Jinzū River in Japan with cadmium and traces of other toxic metals. As a consequence, cadmium accumulated in the rice crops growing along the riverbanks downstream of the mines. Some members of the local agricultural communities consuming the contaminated rice developed itai-itai disease and renal abnormalities, including proteinuria and glucosuria<sup>(20)</sup>.

The victims of this poisoning were almost exclusively post-menopausal women with low iron and other mineral body stores. Similar general population

cadmium exposures in other parts of the world have not resulted in the same health problems because the populations maintained sufficient iron and other mineral levels. Thus, although cadmium is a major factor in the itai-itai disease in Japan, most researchers have concluded that it was one of several factors (3). Cadmium is one of six substances banned by the European Union's Restriction on Hazardous Substances (RoHS) directive, which bans certain hazardous substances in electrical and electronic equipment but allows for certain exemptions and exclusions from the scope of the law(21). The International Agency for Research on Cancer has classified cadmium and cadmium compounds as carcinogenic to humans & animals(22).

Although occupational exposure to cadmium is linked to lung and prostate cancer, there is still a substantial controversy about the carcinogenicity of cadmium in low, environmental exposure. Recent data from epidemiological studies suggest that intake of cadmium through diet associates to higher risk of endometrial, breast and prostate cancer as well as to osteoporosis in humans (23,24,25,26). A recent study has demonstrated that endometrial tissue is characterized by higher levels of cadmium in current and former smoking females(27).

Although some epidemiological studies show a significant correlation between cadmium exposure and occurrence of disease conditions in human populations, a causative role for cadmium as the factor behind these effects remains yet to be shown. In order to prove a causative role, it will be important to define the molecular mechanisms through which cadmium in low exposure can cause adverse health effects (25). One hypothesis is that cadmium works as an endocrine disruptor because some experimental studies have shown that it can interact with different hormonal signaling pathways. For example, cadmium can bind to the estrogen receptor alpha, and affect signal transduction along the estrogen and MAPK signaling pathways at low doses.(23,25)



Tobacco smoking is the most important single source of cadmium exposure in the general population. It has been estimated that about 10% of the cadmium content of a cigarette is inhaled through smoking. The absorption of cadmium from the lungs is much more effective than that from the gut, and as much as 50% of the cadmium inhaled via cigarette smoke may be absorbed(28). On average, smokers have 4–5 times higher blood cadmium concentrations and 2–3 times higher kidney cadmium concentrations than non-smokers. Despite the high cadmium content in cigarette smoke, there seems to be little exposure to cadmium from passive smoking. No significant effect on blood cadmium concentrations has been detected in children exposed to environmental tobacco smoke(29).

There have been a few instances of general population toxicity as the result of long-term exposure to cadmium in contaminated food and water, and research is ongoing regarding the estrogen mimicry that may induce breast cancer(17,19). Cadmium exposure is a risk factor associated with early atherosclerosis and hypertension, which can both lead to cardiovascular disease(28,29).

## **2-2 CADMIUM INDUCED TOXICITY**

Cadmium is considered as a toxic metal and is hazardous to both human and wild life. It acts as a mitogen and promotes cancer in a number of tissues. It also stimulates cell proliferation, inhibit DNA repair and inhibit apoptosis. On the one hand it induces the cell death which leads to tissue damage in kidney,liver ,bone ,brain ,thyroid gland &other organs In cell culture systems, cadmium at low concentration cause apoptosis and with increase in concentration necrosis become evident . Cadmium also affects the renal function when exposed to the environment. (30,31) .

The role of cadmium in induction of atherosclerosis in rabbits. Effect of the cadmium has determined in various tissues of the rabbits for a period of 6 months on histopathological changes and biochemical alterations of profiles. Before and at the end of cadmium treatment. Histopathological studies of the

coronary artery revealed that the atherosclerotic changes occur due to the toxic effect of the cadmium. It leads to total increase of lipids, cholesterol, free fatty acids and phospholipids , Triglyceride in heart and kidney and decrease in serum and liver(32).

Cadmium -induced hepatic and renal injury in chronically exposed rats: likely role of hepatic cadmium in nephrotoxicity . When cadmium is injected in rat, cadmium level in liver and kidney(31).

Cadmium exposure has been reported to be a risk factor for infertility ,studies have shown that exposure to cadmium causes lipid peroxidation , which is associated with cadmium toxicity in testes (33).

(34) it was also found that cadmium has a neurotoxic effect because it affects the integrity of the blood –brain barrier.



# Chapter Three

## *Conclusions and Recommendations*

## CONCLUSION

Cadmium is heavy metal hazardous to all living organisms here its effect on various organisms were studied. Cadmium involves different machineries to induce its harmful effect on many biological activities in humans, animals and various other organisms . In humans cadmium adverse effect is not only restricted to kidney and bone but it includes almost every organ and tissue where it accumulates which argues needs for public health measures aimed at reducing exposure. There are many methods by which this heavy metal can be suppressed in its activities forming the future prospective for reduced metal toxicity involving

cadmium. The preventive measures in high -risk patients must be practiced and it is important to make population-based preventive strategies, such as promoting public and private smoke-free environments, reviewing food safety policies maintaining cadmium safety standards, and limiting cadmium industrial releases into the environment helping to avoid cadmium toxicity.