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Pathogenic Effect of Different Doses of Arsenic Trioxide on White Rat

A Research

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BY

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بِيْ مِ اللَّهِ ٱلرَّحْمَزِ ٱلرَّحِيمِ

فَتَعَالَى اللّهُ الْمَلِكُ الْحَقُّ وَعُنِهُ وَقُلْ رَبِّ وَلَا تَعْجَلْ بِالْقُرْآنِ مِنْ قَبْلِ أَنْ يُقْضَىٰ إِلَيْكَ وَحْيَهُ وَقُلْ رَبِّ وَلَا تَعْجَلْ بِالْقُرْآنِ مِنْ قَبْلِ أَنْ يُقْضَىٰ إِلَيْكَ وَحْيَهُ وَقُلْ رَبِّ وَلَا تَعْجَلْ بِالْقُرْآنِ مِنْ قَبْلِ أَنْ يُقْضَىٰ إِلَيْكَ وَحْيَهُ وَقُلْ رَبِ

صدق الله العلي العظيم

طه ۱۱۶

SUPERVISOR CERTIFICATION

I certify that this research entitled (Pathogenic Effect of Different Doses of Arsenic Trioxide on White Rat), was prepared by Yousif Ibrahim Yousif And Rand Najm Abd Mizhur under my supervision at the College of Veterinary Medicine/University of Al-Qadisiyah in partial fulfillment of the requirements for the degree of Bachelor of Science in Veterinary Medicine Sciences / Veterinary Surgery.

Assist. Prof Dr. Khalil G. Chelab

April 2017

CERTIFICATE OF INSTRUCTOR

We certify that Yousif Ibrahim Yousif And Rand Najm Abd Mizhur completed the fulfillment of their graduation research entitled Pathogenic Effect of Different Doses of Arsenic Trioxide on White Rat) For the year 2016/2017 under our construction.

Instructor Dr. Muthanna Hadi Hussain

Head of Department of Internal and Preventive
Medicine
Dr. Muthanna Hadi Hussain
April 2017

DEDICATION

To our country Peace and safety
The light of our eyes our parents

Acknowledgments

By the name of god first who deserve all thanks & pleasure for granting me with well strength & help with which this dissertation has been accomplished peace & prayer on my Bachelor. Guide Prophet Mohammed & his household.

We would like to gratefully thank my supervisor Assist. Prof Dr. Khalil G. Chelab for his invaluable guidance. Also we thank very much our teachers & our friends.

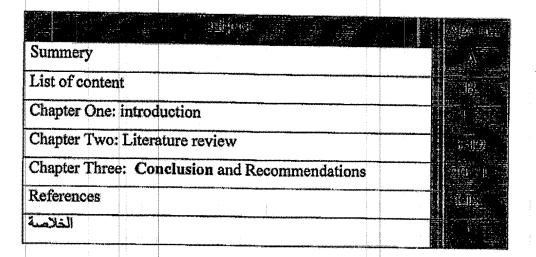


Abstract

This study was performed to investigat on the toxicity of arsenic trioxide on the different body systems like nervous system, skin, respiratory system and liver through collection of previous studies which related with arsenic trioxide. also the broaching to the studies which performed on the arsenic trioxide through histroy of arsenic, chemical and physical properties and source of arsenic.

We concluded that arsenic trioxide is very common element in the nature, it present in the soil and ground water so that the human and animal exposed directly to it . also arsenic trioxide is almost highly toxic to all body system specially nervous system, respiratory system and skin, and it cause acute and chronic toxicity.

List of Content



Introduction

Arsenic (AS) is ubiquitous element in the environment. Weathering of rocks converts sulfides to arsenic trioxide, which enters the arsenic cycle as dust or by dissolution in rain, rivers, or ground water (Mandal and Suzuki, 2002). Arsenic is a very toxic metal, and also an environmental and industrial pollutant which is present in soil, water, air and food (Cullen, 1989).

This metal enters surface water from the industrial and found in soil by leaching of sewage sludge through soil (Antman, 2001). So, the population can be affected by arsenic through food consumption, drinking water and incidental ingestion of soil contaminated by arsenic (Celik et al., 2008). It is used in foods preservatives, herbicides, insecticides and rodenticides (Akter et al., 2005). Arsenic (As) is a widespread environmental toxin, it enters the organisms by dermal contact, inhalation, or ingestion of contaminated drinking water and affects nearly entire organ systems of the body (Ratnaike, 2003). Arsenic compounds are quite effectively incorporated from the gastrointestinal tract (Zielhuis and Wibowo, 1984). After absorption, It transports in the plasma is bound to albumin and accumulated mainly in kidney and liver. Arsenic occurs both organic and inorganic forms in nature but inorganic species of arsenic (ASIII and ASV) represent a potential threat to the environment, human and animal health due to their carcinogenic and other effects (Singh et al., 2004). Arsenic trioxide is a trivalent inorganic compound (Saxena et al., 2008).

Arsenic can result in acute and chronic toxicity. The characteristics of chronic effects of arsenic toxicity are degenerative inflammatory and neoplastic changes of the skin, respiratory, haemopoitic, cardio vascular, nervous, hepatic, endocrine and renal system (Hughes, 2002). Also causes

an oxidative stress through lipid peroxidation and consumption of some antioxidant systems (Yamauchi et al., 2004; Kitchen, 2001).

Previous studies showed that arsenic contamination may cause wide variety of diseases such as cancers (National research council, 2001), diabetes mellitus (Tseng et al., 2000), cardiovascular disorders (Das et al., 2004; Wang et al., 2002), reproductive toxicity (Ahmed et al., 2008) as well immunotoxicity (Patterson et al., 2004; Soto-Pena et al., 2006). Chronic exposure to arsenic, in addition to its general toxicity may affect lymphocyte, monocyte and macrophage activity in many mammals, resulting in immunosupperssion (Yang and Frenkel, 2002; Wu et al., 2003; Duker et al., 2005; Sakurai et al., 2006).

CHAPTER TWO

Literatures of Review

Literatures Review

2-1-Arsenic trioxide review:

2-1-1- History of Arsenic:

It is unclear when and who discovered arsenic, historical records show that it was used by the ancient Greeks, Persians, and Chinese. It is best known as a poison, as a one of its earliest uses (Boffetta, 2004). It was almost the perfect poison difficult to detect because it lacks color, odor and taste (Hazardous substance fact sheet, 2010).

An early historical reference to arsenic as a poison is by a Greek physician named Discordia's who was in the court of Emperor Nero (54-68 AD) (Smith, 2005). Arsenic has been used in medicine for more than 2400 years for a variety of ailments including ulcers, the plague and malaria (Waxman and Anderson, 2001).

Arsenic is known to mankind since the dawn of human civilization as an ideal homicidal poison and was used umpteen times with criminal intent (Arsenic poisoning, 2008). The poison was molded into a medicine in the 1700s, when Thomas Fowler developed a solution of arsenic trioxide in potassium bicarbonate (1%W/V) for the treatment of asthma, cholera, eczema, pemphigus, and psoriasis (Fowler's solution, 2008). It was also used empirically for the treatment of a variety of diseases, including leprosy, syphilis and yaws (Anonymous Arsenic, 2008). The art of arsenic therapy suffered a blow when this metalloid was identified as the culprit for major public health problem after exposure via drinking water in the early 1900s in Argentina, Chile, Mexico and Thaiwan (Zaldivar, 1974). In India the problem of arsenicosis due to ground water contamination was first identified in the state of west Bengal in 1984, (Garai et al., 1984; Saha, 1984) and a survey report in 2001 suggest that around 150 million people are at risk from arsenic—contaminated ground water in the combined areas

*Group B (Low Dose Group):

Examination of liver sections of rats which injected with low dose of arsenic trioxide showed that the severity of lesions was reduced significantly which revealed a preserved cytoarchitecture of hepatic lobules consisting of central veins and radially arranged hepatocytes (as in Fig. (4-9); (4-10)). However, few infiltrations of inflammatory cells, the central veins were showed slightly congested and mild dilation of the hepatic sinusoids as in Fig. (4-10).

*Control group:

Control group which received only PBS showed no histopathological changes in the liver sections of this group animals and these microscopic appearance showed that the central veins and radially arranged cords of hepatocytes with blood sinusoids lined by flat endothelial and Kupffer cells located between them. The hepatocytes were large polyhedral with acidophilic cytoplasm and rounded nuclei with prominent nuclei, some cells were binucleated as in Fig. (4-11).

4-1-2-Kidney:

* Group A (High Dose Group):

Examination of kidneys of arsenic trioxide-exposed rats with high dose (group A) showed the histopathological abnormalities like loss of integrity with severe necrosis of epithelial cells which lining of the proximal convoluted tubules, inflammatory cellular infiltrations, atrophied and disorganized glomeruli with distorted Bowman's capsule as in Fig. (4-12). The higher magnification of the kidney showed that the cells which lining

the proximal and distal convoluted tubules appeared with severe necrosis and their nuclei showed either pyknotic or karyolysis with atrophied glomeruli as in Fig. (4-13). Also there is congestion within the kidney tissue. The proximal convoluted tubules appeared dilated as in Fig. (4-14).

* Group B (Medium Dose Group):

In this group (B) as in the liver sections, the kidneys of arsenic trioxide-exposed rats with low dose also showed significant reduction in the severity of lesions which revealed normal organized glomeruli with mild dilation of proximal convoluted tubules and regenerative cortical tubular basophilia were seen as in Fig. (4-15). There is tubular basophilia of proximal convoluted tubules (regeneration of epithelial cells of proximal convoluted tubules) seen as in Fig. (4-16). Also there is no hemorrhage or congestion of blood vessels in the kidney tissue.

*Control Group:

The kidneys in control group showed normal histological structures which having normal arrangement of cortical and medullary elements (normal glomeruli with high cellularity and normal renal convoluted tubules) as in Fig. (4-17).

4-1-3-Testes and Epididymus:

* Group A (High Dose Group):

Examination of testicular sections of rats which injected with high dose of arsenic trioxide showed the testis had lost its characteristic architecture. There is vacuolation of seminiferous tubules and suppression of spermatogenesis and pronounced reduction in sperm numbers in the lumen of seminiferous tubules and many tubules are totally devoid of sperms. Also

increased diameter of seminiferous tubule's lumen as in Fig. (4-18). Desquamation of germ cells resulting in several small spaces showed inside the seminiferous tubule. There is vacuolation of spermatogonia and its detached from basal lamina of seminiferous tubules, with presence of spermatid multinucleate giant cells which indicate severe degeneration within the seminiferous tubules as in Fig. (4-19); (4-20).

The epididymal tubules showed severe changes which characterized by dilated lumen and empty of sperms as in Fig. (4-21); (4-22).

* Group B (Medium Dose Group):

The histopathological changes of testicular sections of arsenic trioxide-exposed rats with low dose showed a significant amelioration and reduction in the lesion severity. The histological changes characterized by complete spermatogenesis without vacuolation or spaces within the seminiferous tubules. Presence of mild to moderate numbers of sperms in the lumen of these tubules as in Fig. (4-23); (4-24). Also there is presence of characteristic architecture of seminiferous tubules which appeared circled, and compact with decreased diameter of seminiferous tubule's lumen as in Fig. (4-24).

The epididymal tubules showed less affected some these tubules filled with sperms but others were empty as in Fig. (4-25).

*Control Group:

The testicular sections of control group did not demonstrate any changes which characterized by normally arranged seminiferous tubules which showed circled and compact. Complete spermatogenesis in which

spermatogonia, spermatocytes and spermatids were regularly arranged with spermatozoa in the lumen of seminiferous tubules as in fig. (26).

The epididymal tubules showed normally dilated and fully filled with sperms as in fig. (27).

Chapter Three

Conclusions and Recommendations

Conclusion

Via the previous study, we conclude the following;

- 1- Arsenic trioxide is highly common in the nature, it presents in the soil and ground water.
- 2- Arsenic trioxide have special chemical and physical properties which it make very toxic.
- 3- Arsenic trioxide is highly toxic to human, animals and plants.
- 4- Arsenic trioxide is very toxic to different body system specially nervous system, respiratory system, skin and livers.

Recommendation;-

- 1- Procedure study to investigate on the effect of arsenic trioxide on other system like male and female reproductive system, endocrine, digestive system....ect.
- 2- Procedure molecular study to know the effect of arsenic trioxide on the oncogenes and know the role of arsenic trioxide in the induction of cancer.
- 3- Procedure immunohisto chemical study to know the role of arsenic trioxide in the immunity of the body.
- 4- Protection of the environment in Iraq through make the continuous measurements of arsenic trioxide and other heavy metals specially in the ground water.