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BIOCHEMICAL CHANGES OF SERUM GLUTATHIONE AND MALONDIALDEHYDE BY TIN DICHLORIDE ON ADULT MALE REPRODUCTIVE SYSTEM OF RABBITS

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Abstract

This experiment aimed to investigate the Toxicopathological effect of tin dichloride on the adult male rabbit's reproductive system testes, epididymis) liver, lung, kidney, stomach, intestine, and brain. Eighteen adult male rabbits were randomly divided into 4 groups which administrated orally and daily for four weeks as follows: distilled water(C), 3mg $SnCl_2$ Kg B.wt (T_1), 3mg /Kg B.wtSncl$_2$ (T_2) (T_3) respectively. Blood samples were collected after 2and 4weeks for the estimation of the biochemical parameters (serum glutathione and MDA).The trends of glutathione were significantly different ($P < 0.05$) across the periods in all groups. In the T_1, T_2 groups showed a significant decrease at 4 weeks. On the other hand, the T_3 showed a significant increase ($P < 0.05$) within 4 weeks.The results showed the means of Glutathione were significantly lowered in T1 and T_2 as compared with control. While the MDA shows a significant increase ($P < 0.05$) in the T_1 and T_2 during the experiment periods ascompared with the control group, while group (T_3) shows a significant decrease ($P <0.05$) in MDA concentration compared with a control group. In conclusion, MDA increased in rabbits treated with tin dichloride, while the glutathione is decreased in the same groups.

Key words : Tin dichloride, Serum Glutathione, MDA, Rabbits.

Introduction

Tin is a natural element within the crust of the earth. Tin metal is used to cover the food, drink, and aerosol bottles. It may combine to form inorganic tin compounds (*i.e.*, stannous chloride, stannous sulfide, stannic oxide) with chemicals such as chlorine, sulfur, or oxygen, such is used in toothpaste, perfumes, soaps, and Meat coloring, and colorants. Tin can also be mixed with carbon to form organotin compounds (*i.e.*, dibutyltin, tributyltin, triphenyltin) (Goullé, 2005).

Both natural and anthropogenic sources, inorganic tin are released into the environment. Conversely, organotin compounds are produced primarily from anthropogenic sources. Food consumption, notably canned foods, and beverages are considered a major source of human exposure to inorganic forms of tin (Ostrakhovitch, 2014).

Stannous chloride (Tin) is a chemical reducing agent found in a variety of man-made products, sncl$_2$ can produce reactive oxygen species (ROS). The present research was therefore conducted to investigate the antioxidant role of l-ascorbic acid (AA) in reducing the toxicity of SnCl2 to lipid peroxidation, an antioxidant enzyme and biochemical parameters in male white New Zealand Honeys (Yousef *et al.,* 2007).

Stannous chloride's biological effects include relaxation accompanied by central nervous system agitation in laboratory animals (JECFA, 2001). Stannous chloride ($SnCl_2$) is believed to suppress the rodent's immune response and cause the thyroid gland to produce tumors. There was general regarding its genotoxicity, and it has been discussed that the effects of this salt depend on the physicochemical conditions and route of its administration (Silva *et al.,* 2002).

Tin dichloride has been shown to facilitate neuromuscular transmission; $SnCl_2$ is also capable of

promoting reactive oxygen species (ROS) production that is responsible for oxidative stress that can damage DNA (Silva *et al.,* 2002).

Compounds of inorganic tin are poorly absorbed following oral, inhalation, or dermal exposures, the gastro-intestinal tract absorbs only 3 percent of the stannic compounds and less than 1 percent of the stannic compounds (Rudel, 2003). The bulk of an oral dose of inorganic tin is excreted in the feces, while urine removes only a small portion of the ingested tin (Rudel, 2003). The organotin compounds are better absorbed than inorganic tins, especially trimethyltin and triethyltin compounds (Okoro *et al.,* 2011), Tissue distribution of tin from these organometallic compounds shows the highest concentration in muscle, spleen, heart, brain, bone, liver, kidney, and lung (Fang *et al.,* 2017).

Exposure to organotin compounds such as tributyltin and triethyltin in pregnant animals can induce developmental and endocrine detrimental effects (ATSDR, 2005). Some organic tin compounds are highly neurotoxic, particularly triethyltin and trimethyltin, and cause encephalopathy and cerebral edema (Rohl *et al.,* 2009). Inorganic tin compounds are used in the ceramic and textile industries as pigments (Ecker-Ehrhardt and Wessels, 2011).

Therefore, inorganic tin, organotin compounds are known to be more toxic, and laboratory studies had identified several organotin compounds, especially tributyltin, as environmental obesogens (Zuo *et al.,* 2011; Heindel *et al.,* 2017).

Glutathione is designed to combat the harm caused by responsive oxygen species, such as free radicals, peroxides, lipid peroxides, and significant metals to essential cell parts (Pompella *et al.,* 2003), Glutathione (GSH), tripeptide containing cysteine, Plays a role as a cellular defense factor against tissue-generated reactive oxygen species (Meister, 1991) Glutathione has been found to bind and activate ionotropic receptors that are not the same as some other exciting amino-corrosive receptors and may constitute glutathione receptors, probably making it a neurotransmitter (Oja *et al.,* 2000).

The organic compound containing the nominal formula $CH_2(CHO)_2$ is malondialdehyde (MDA). Malondialdehyde, a colorless liquid, is a highly reactive compound that exists as the enol (Nair *et al.,* 2008). In the clinical setting, the direct measurement of ROS formation in cells is extremely difficult. Instead, several indirect methods for measuring free radicals and their metabolites were developed, such as malondialdehyde (MDA; the final product of lipid peroxidation) (Lykkesfeldt, 2007).

Materials and Methods

Preparation of Tin (II) chloride ($SnCl_2$)

14.700 mg $Sncl_2$ was dissolved in 100ml distilled water to prepare a stock solution and prepare other doses The doses were administered daily to male rabbits using gastric intubation (Chen *et al.,* 2017).

Blood collection

Blood samples were collected at different intervals of the experiment using disposable medical syringes (5ml) via cardiac puncture. Blood samples from each rabbit were stored in disposable tubes that were retained for at least four hours until serum isolation. Samples were centrifuged for 15 minutes at a speed of 2500 rpm and then serum samples were placed in a freezer at -18°C before Testosterone and Malonyldialdehyde (MDA) and Glutathione were used for the hormonal assay.

Experimental animals

In this experiment a total of eighteen (18) adult weighted male rabbits (1200-1800 g) were used. Their ages domain between weeks (10-14). Experimental animals were housed in a metal cage (120 x 60 x 60 cm) at (22-25 ° C) in the Department of Pathology / College of Veterinary Medicine at the University of Baghdad., Through using ventilation vacuum, the air in the room and the controlled lightening were adjusted continuously. We were left to acclimatize themselves with the laboratory conditions for two weeks. During the experimental period, animals had free access to water and a normal pellet diet (Hafez, 1970). For this experiment, we used eighteen adult male rabbits. After two weeks of acclimatization they were divided into three classes equally as follows:

Group one control (C): This group received distilled water daily for 4 weeks

Group two (T_1): This group received (147 mg & 2ml/ Kg B.wt) $Sncl_2$ daily for 4 weeks.

Group three (T_2): This group received (73.5 ml/Kg B.wt) $Sncl_2$ daily for 4 weeks.

The experiment lasted for 4 weeks. Blood samples were tested for concentrations of Testosterone, MDA, and Glutathione after 2, 4 weeks of the experiment. Body weight was assessed at experimental weeks 0,1,2,4. During the experiment, three animals from each group were an esthetized and killed for the histological study of testes, epididymis.

Statistical analysis

Statistical analysis of data was performed using SAS

(Statistical Analysis System - version 9.1). One-way, two ways ANOVA and Least significant differences (LSD) post hoc test were performed to assess significant differences among means. $P < 0.05$ was considered statistically significant (SAS, 2010).

Results

Serum Glutathione concentration

Glutathione concentration in response to oral administration of Tin dichloride, Tin dichloride T_1 147 mg/Kg B.wt. and T_2 73.5 mg/Kg B. wt.in adult male rabbits for four weeks is shown in (Table 1).

Table 1: Glutathione concentration in response to oral administration of Tin dichloride doses.

Group	GSH
C	419.98±2.30a
T_1	118.80±5.02c
T_2	259.60±16.51b
LSD	30.983

Means with a different letter in the same column are significantly different (P<0.05).

The results revealed that the trends of glutathione significantly different ($P < 0.05$) across the periods in all groups. In the T_1 it was shown a significant decrease at 4 weeks. In the T_1 it was shown a significant decrease at 4 weeks, while the T_2 showed a significant decrease in the 3 and 4 weeks.

The results showed that the means of Glutathione in T_1 and T_2 were significantly (P<0.05) lowered than control.

Table 2: Serum MDA level (pg/ml) in response to oral administration of Tin dichloride, Tin dichloride T_1 147 mg/Kg B.wt. and T_2 73.5 mg/Kg B.wt. in adult male rabbits for four weeks is shown in (Table 2).

Group	MDA
C	0.23±0.01b
T_1	8.44±0.85a
T_2	1.44±0.09b
LSD	1.5324

Means with a different letter in the same column are significantly different (P<0.05).

Malondialdehyde (MDA) concentration: The effect of different doses of Tin dichloride on mean values of MDA concentration is shown in (Table 2). This Table shows a significant increase ($P < 0.05$) in MDA concentration in treated groups (T_1) and (T_2) along the experimental periods comparing with the control group. In the meantime, the highest concentration of MDA is shown in (T_2) as compared to other groups. Within the time, the concentration of MDA reveals no significant difference ($P < 0.05$) between the second and fourth weeks in control and T1 groups. However, this difference is significant in T_2 *i.e.* the table showed a significant increase ($P > 0.05$) in the MDA level after the 4th week in comparison to the 2nd and 4th week in T_2.

Discussion

Glutathione (GSH) is also called the master antioxidant of the body. GSH is a vitally essential defensive cell. They specifically quench reactive hydroxyl-free radicals, other oxygen-centered free radicals, and DNA and other biomolecules with radical centers. GSH is a primary protective against radiation damage to the retina, cornea, lens, and skin and other biochemical foundations of P450 detoxification in the liver, kidneys, lungs, intestines, epithelia, and other organs (WHO, 2005; Halprinand Ohkawara, 1967). The findings showed that, compared with control one, GSH decreased in both treated groups and this is in agreement (Guoyao, *et al.,* 2004). Although the MDA has resulted in an increase in one treated relative to the control one.

MDA naturally occurring and is a marker for oxidative stress. (Nair *et al.,* 2008) and that pointed to tin dichloride treated groups which reported an increase in MDA. Oxidative stress tends to chronically inflammatory tissues (Gheita and Kenawy, 2014). Malondialdehyde (MDA), it is one of the final components of lipid peroxidation in the membrane. (Al-Okialy, 2018).

Conclusion

Malondialdehyde (MDA) and glutathione are markers of oxidative damage. Tin side effects on the concentration of Glutathione serum and MDA identified from this analysis by low glutathione peroxidase levels and high (MDA) levels. The animals are exposed to stressful conditions 1\10LD50, 1\20LD50 of Tin dichloride) These have been linked to the increase of reactive oxygen species that attack unsaturated lipids and other biomolecules of the cell membrane and thus induce oxidation.

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