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Study of the effect of coenzyme Q10 on some hematological and biochemical parameters in male albino rats treated with melamine

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Abstract

This study aimed to determine the toxic effects of melamine in some blood and biochemical parameters, in addition to evaluating the role that each of the enzymatic cofactors can play in reducing the toxic effects of melamine in male rats for a period of 30 days. A random sample of male white rats (40) was used in this study, divided randomly into four groups, the control group (C): was dosed with physiological saline NaCl at a concentration of 0.9% for 30 days and counted as the control group. The first treatment group ((T1):was dosed with melamine at a concentration of 50 mg/kg of body weight per day for 30 days. The second treatment group (T2):was dosed with coenzyme Q10 at a concentration of 10 mg/kg of body weight per day for 30 days. The third treatment group (T3): Melamine was dosed at a concentration of 50 mg/kg of body weight and coenzyme Q10 at a concentration of 10 mg/kg of body weight simultaneously daily for 30 days.After the end of the experiment, the following criteria were studied: Lipids (cholesterol, triglycerides, and high-density lipids) as well as Antioxidants and blood parameters, including (red blood cell count, hemoglobin concentration, and packed cell volume) in male rats.The results showed that dosing rats with melamine led to a significant decrease ($P<0.05$) in the number of RBC, Hb and PCV in (T1) compared with the control group.In contrast, the results showed a significant increase ($P < 0.05$) in the average ofRBC,Hb andPCV in animals of group (T3) compared with group (T1). The current results indicated that the treatment with melamine led to a significant increase ($P<0.05$) in the levels of total cholesterol, triglycerides, LDL and VLDL in the blood with a significant decrease in the level of HDL compared with the control group, on the other hand, the current results showed a significant decrease In the level of lipids andincrease in HDL in the blood of animals dosed Q10 with melamine compared with animals dosed only melamine. The results of the current study showed a significant decrease in the level of (GSH) and (CAT), accompanied by a significant increase in the level of (MDA) in the group (T1) when compared with the control group. In addition, the present results showed that decreased the level of MDA and increased the level of GSH and CAT compared to the animals given only melamine.

Keywords: coenzyme Q10, melamine, SOD, MDA, blood, GSH.

Introduction

Milk is an important food source for humans in the various stages of their life, especially in childhood, because of its content of essential nutrients, which make milk or its products one of the most integrated foods rich in nutritional value (Hassan, 2008). It also contributes to the high economic growth rates of the producing countries. And exported to him, as it is an important material in the export (Al-Rubaie, 1983). The high nitrogen content of melamine and its cheap price make it used in many countries where the performance of quality control and oversight is low in adulteration of food products and animal feed (Wei et al., 2010). The aim behind this addition is to raise the value of nitrogen, which leads to an increase in the value of Apparent protein in food products (Feng et al., 2012). Many methods of protein determination depend on the nitrogen present in it, and they usually do not differentiate between protein nitrogen and non-protein nitrogen, as is the case in the Keldahl method (Hon et al., 2011). Milk is adulterated with it to compensate for the lack of protein in it (Hon et al., (2011). Because milk is the main food source for feeding children during their early stages of growth, as well as their physiological differences from adults (Chan et al., 2008), their consumption of contaminated milk causes many One of the health problems for children, especially renal failure, as it was proven that it formed kidney stones that exported melamine crystals (Gossner et al., 2009).The World Health Organization (WHO) stated that the permissible daily limits for melamine amounted to 0.2 mg / kg of body weight (Ingelfinger) (2008, . The European Food Organization has recommended in the European Union that all products containing melamine greater than or equal to 2.5 mg/kg should be destroyed (Puschner et al., 2007). Which is not dangerous to humans, it amounted to 0.63 mg / kg (0Chan and Lai 2009,). Whereas, Health Canada declared the permissible daily limits for melamine to be 0.35 mg/kg body weight per day (WHO 2008,). The safety levels that apply to adults cannot be applied to children, especially infants, due to the large difference in their nutritional requirements and the composition of their organs (Chan et al., 2008; Hsieh et al. 2009). Therefore, a safety factor must be given to children compared to adults when determining the permissible amount of melamine. In food, and for this reason the amount allowed to be eaten by adults in some countries was at 0.63 mg / kg, so a safety factor of ten times must be given to children, so that the permissible amount becomes 0.063 mg / kg per day of body weight, and the European Food Organization has allowed a limit of 0.5 mg / kg per day (Chu et al. 2010,). Recently, all organizations concerned with food and health have recommended the need to destroy any food proven to contain melamine, regardless of the percentage and quality (Botha,2010).

Materials and Methods

The study was conducted in the animal house of the Department of Life Sciences - College of Education/University of Al-Qadisiyah. Male Albino Rats were used in this study, their weight ranged between 150-250 grams and their ages ranged between 3-4 months, and they were placed in special plastic cages prepared for this purpose.In this study, I used coenzyme Q10, which was obtained from one of the pharmaceutical pharmacies in the city of Diwaniyah. The dose was used 10 mg/kg of body weight of coenzyme Q10 (Samimi et al., 2019). After dissolving the full daily dose of coenzyme Q10 in the oil, each animal was dosed daily by 1 ml orally using a special wine syringe for this purpose containing Hooked needle.Melamine obtained from the laboratories of the Department of Chemistry of the College of Education/University of Al-Qadisiyah was also used in this study. The dose was 50 mg/kg body weight of melamine (Salem et al., 2018). After dissolving the full daily dose of melamine in distilled water, each animal was dosed daily by 1 ml orally using a special syringe for this purpose containing a hooked needle.In this experiment, 40 adult male white rats were used, divided randomly into four groups, each group containing 10 animals as follows:

1. Control group (C): they were dosed with physiological saline NaCl at a concentration of 0.9% for 30 days and counted as the control group.

2. The first treatment group ((T1):was dosed with melamine at a concentration of 50 mg / kg of body weight per day for 30 days.
3. The second treatment group ((T2):was dosed with coenzyme Q10 at a concentration of 10 mg/kg of body weight per day for 30 days.
4. The third treatment group ((T3): was dosed with melamine at a concentration of 50 mg/kg of body weight and coenzyme Q10 at a concentration of 10 mg/kg of body weight simultaneously daily for 30 days.

After the end of the experiment, the animals were anesthetized using chloroform, then blood was withdrawn from the heart directly using a heart stab, and 1 ml of the drawn blood was placed in blood collection tubes containing EDTA anticoagulant for the purpose of conducting analyzes of blood parameters, while placing 3 ml of the remaining blood in tubes A test free of anticoagulant, and left for 15-20 minutes at the laboratory temperature, then the samples were placed inside a centrifuge at a speed of 3000 rpm for 15 minutes for the purpose of separating the serum and for conducting hormonal and biochemical tests, and the serum was kept at a temperature of -20 °C until use .

Estimation of serum lipids

The colorimetric method for estimating the effectiveness of lipids was followed by the Cholesterol kit, the triglyceride kit, the HDL-cholesterol kit, the high-density lipoprotein measurement kit, and the analysis kit prepared by the French company Bio Merieux AS was used.

Evaluation of antioxidants in serum

Antioxidants were estimated using the colorimetric method, by using a ready-made kit prepared by the Chinese company Biosystem.

Blood CBC

The number of red blood cells, the concentration of hemoglobin, and the volume of packed cells were estimated by placing the blood sample in an EDTA tube in the

SYSMEX KX 21N automatic blood count for blood analyzes (Kobe, JAPAN), and then all the above-mentioned blood tests were recorded directly by the device.

Statistical Analysis

The results of the experiments were analyzed using the SPSS statistical program, as the Anova test was used to compare between the studied groups and the control group, and the Least Significant Difference (LSD) was calculated to test the significance of the results.

Results and discussion

Hematological parameters:

The current results indicated a significant decrease ($P<0.05$) in the number of erythrocytes (RBC), hemoglobin (Hb) concentration, and average packed cell volume (PCV), with a significant increase ($P<0.05$) in the total number of white blood cells (WBC) in animals treated with melamin (T1) compared with the control group. These results agreed with the findings of (Al-sieni et al., 2013). The reason for this decrease could be due to the inhibition of iron absorption by the intestine due to the ability of melamin to bind instead of the iron absorbed by the intestine at the same binding sites in which it is absorbed and transported, which leads to a decrease in the level of iron (Tian et al.). , 2016)) and then a decrease in the concentration of hemoglobin and the number of red blood cells in rats treated with melamine. These results were also consistent with the study of Ismail and his group (2019), which indicated a significant increase in the total number of white blood cells that were treated with melamin. On the other hand, the current histological study demonstrated the effect of melanin on the histological structure of the kidney, which affects the level of the hormone Erythropoietin, as 90% of this hormone is synthesized in the kidney and works to stimulate the bone marrow to form and mature red blood cells (Jameel et al., 2021). Melamine also causes inhibition of the activity of glutathione, which is present inside the red blood cell and is responsible for removing the damage resulting from hydrogen peroxide H_2O_2, and then the free radicals will increase and H_2O_2 accumulates inside the red blood cells, causing damage to the cell membrane and its ease of breaking (Kipchumba et al., 2023)) . The decrease in the average size of packed cells may be attributed to a decrease in the number of red blood cells on the one hand and a decrease in hemoglobin concentration on the other hand (Wedward et al., 1995), where the size of the packed cells is directly proportional to the number of red blood cells, and this was confirmed by Campos and Luis (2003), indicating that the size of the packed cells increases with the increase in the number of red blood cells. In a study conducted by Strakova and his group (2014), they noted that melamine is the cause of increased fragility of blood cell membranes and rapid degradation due to inhibition of the activity of the Na^+/K^+ ATPase pump and decreased resistance to osmotic pressure, which leads to damage to the integrity of the cell membrane and its rupture. Zheng et al. (2013) also suggested that the decrease in blood parameters may reflect the toxic effect of melanin on the bone marrow. On the other hand, the results showed a significant increase ($P<0.05$) in the average number of red blood cells, hemoglobin concentration, and packed cell volume with a significant decrease in the total number of white blood cells in animals of (T3) group treated with Q10 simultaneously with melamine, compared with group (T1) Melamine treatment only. The clear improvement in the average number of erythrocytes indicates the role of Q10 in protecting unsaturated lipids, which are the main component of erythrocyte membranes, from lipid peroxidation processes, and thus will protect erythrocytes from hemolysis. Geng et al. 2004). The reason for this decrease may be due to the fact that Q10 is mainly located on the inner membranes of mitochondria: 95% of all cellular energy production depends on it and it acts as a powerful scavenger of free radicals, restricting their lethal effect and significantly reducing oxidative damage (Kristin, 2010). If it is observed that the more Q10 is available in the mitochondria, the less free radical damage. This is one reason why the highest concentrations of Q10 are found in the organs that consume the most energy: the brain, heart, liver, and kidneys (Sohal and Forster, 2007).

Table (1): shows the effect of coenzyme Q10 on some blood parameters in male ratstreated with Melamine.

PCV	Hb	RBCs	Groups
39.98 ± 0.06 A	12.72 ± 0.020 A	8.21 ±0.020 A	Control
27.97 ± 0.080 C	8.02 ± 0.026 C	4.28 ± 0.040 C	T1
41.80 ± 0.085 A	13.13 ± 0.028 A	8.91 ± 0.046 A	T2
32.83 ± 0.391 B	10.34 ± 0.130 B	6.72 ± 0.054 B	T3
2.56	2.18	1.18	LSD

The numbers represent the mean ± standard error.

The different letters indicate that there are significant differences (P<0.05) between the groups.

C: represents the control group.

T1: (the first treatment group), which was dosed with melamine at a concentration of 50 mg / kg of body weight for a period of 30 days.

T2: (the second treatment group) that was dosed with coenzyme Q10 at a concentration of 10 mg / kg of body weight daily for 30 days.

T3: (the third treatment group) which was dosed with melamine at a concentration of 50 mg/kg of body weight and coenzyme Q10 at a concentration of 10 mg/kg of body weight. Body weight daily and simultaneously for 30 days.

Biochemical parameters

Lipid profile

The present results indicated that the treatment with melamine led to a significant increase (P<0.05) in the levels of total cholesterol, triglycerides, LDL and VLDL in the blood with a significant decrease in the level of HDL compared with the control group. These results were consistent with what was reported by (Chen*et al.*, 2009). These results were also consistent with the study of Puschner and his group (2007), where they noted that giving mice melamine caused an increase in cholesterol levels, triglycerides, LDL, and VLDL, with a decrease in the level of HDL due to an increase in the level of peroxide as a result of the delayed emptying of food from the stomach due to the accumulation of fat in the small intestine. Compared to the time needed for healthy digestion, which affects the antioxidant defense mechanism causing oxidative stress. On the other hand, melamine leads to an imbalance in the transport of cholesterol to and from the liver, causing a disturbance in the metabolism and thus an increase in the level of total cholesterol (Liong& Shah, 2006). Also, Higashikawa and his group (2009) noticed that when treating mice with melamine, the level of triglycerides, which is the main component of VLDL lipoproteins, increased, which causes an increase in the level of VLDL.

On the other hand, the current results showed a significant decrease($P<0.05$) in the level of lipids andincrease ($P<0.05$) inHDL in the blood of animals that dosed Q10 with melamin compared with animals that received melamin only. These results were consistent with what was mentioned by (Liu *et al.* , 2023) that showed the effectiveness of Q10 in reducing the level of total cholesterol and triglycerides in the blood. The reason for the decrease in the level of triglycerides in the blood may be attributed to the antioxidant activity of Q10, as it suppresses free radicals and reduces lipid peroxidation, thus preventing lipolysis (Kipchumba *et al*., 2023). Q10 is very safe and has the least harmful effects, as one of the effective treatments for lowering blood triglyceride levels in people with metabolic diseases (Sharifi *et al*., 2018) and (El-Houseiny *et al*., 2022) found that a mixture of red yeast rice, berberineBerberine, policosanol, astaxanthin, Q10, and folic acid significantly reduced plasma triglyceride and LDL cholesterol levels.

Table (3): The effect of coenzyme Q10 on lipid profiles in male albino ratstreatment with Melamine.

VLDL	LDL	HDL	TG	Cholesterol	Groups
8.74 ± 0.32 C	18.29 ± 0.17 C	43.93 ± 0.09 B	43.72 ± 0.52 C	70.96 ± 0.14 C	Control
15.22 ± 0.11	72.04 ± 0.21	25.96 ± 0.18	76.13 ± 0.44	113.22 ± 0.5	T1

A	**A**	**D**	**A**	**A**	
7.22 ± 0.41 D	**8.04 ± 0.11 D**	**49.2 ± 0.20 A**	**36.14 ± 0.22 D**	**64.46 ± 0.38 D**	**T2**
11.76 ± 0.23 B	**39.02 ± 0.34 B**	**36.07 ± 0.22 C**	**58.82 ± 0.30 B**	**86.85 ± 0.48 B**	**T3**
0.56	**1.77**	**2.57**	**2.69**	**3.85**	**LSD**

The numbers represent the mean ± standard error.

The different letters indicate that there are significant differences (P<0.05) between the groups.

C: represents the control group.

T1: (the first treatment group), which was dosed with melamine at a concentration of 50 mg / kg of body weight for a period of 30 days.

T2: (the second treatment group) that was dosed with coenzyme Q10 at a concentration of 10 mg / kg of body weight daily for 30 days.

T3: (the third treatment group) which was dosed with melamine at a concentration of 50 mg/kg of body weight and coenzyme Q10 at a concentration of 10 mg/kg of body weight. Body weight daily and simultaneously for 30 days.

Oxidative indicators and antioxidants

The results of the current study showed a significant decrease in the level of glutathione (GSH) and catalase (CAT), accompanied by a significant increase in the level of malondialdehyde (MDA) in the group of animals treated with melamine only (T1) when compared with the control group. These results are consistent with the findings of (Fouad &Jresat, 2012). These results are also consistent with the study of Jameel and his group (2021), which indicated a decrease in the level of CAT and GSH with an increase in the level of MDA in the liver, kidneys, and heart of rats treated with melamine, and this may be due to Oxidative damage caused by melamine in those organs. Chang and his group (2021) also indicated a decrease in the level of GSH, CAT and SOD with an increase in the level of lipids in the serum and livers of rats treated with melamine for a period of thirty days. The reason for this was explained by an imbalance between oxidants and antioxidants, etc. As a result, oxidative stress leads to the generation of large amounts of active oxygen species ROS, which increases the rate of consumption of glutathione, which is the most important non-enzymatic antioxidant in removing free radicals and their products, and then turns into its inactive oxidized form GSSG (Rabey et al., 2019). The mechanism of action of GSH is to prevent oxidation and reduce oxidative stress, either through the removal of free radicals directly, or through enzymes that are included in its composition, such as glutathione peroxidase (GPX), thus contributing to the reduction of oxidative stress and thus its level decreases (Suleyman et al. , 2003). The main target of free radical interactions is the polyunsaturated fatty acids of the cellular membranes because they have double bonds, and as a result of the oxidation of these fatty acids by the action of free radicals, MDA results as a final product of the Peruvian process of fat oxidation (Carocho& Ferreira, 2013). The compatibility between the low level of GSH and the high level of MDA results from the process of stimulating the activity of the Fatty acyl-CoA oxidase enzyme and starting the oxidation of fatty acids, which leads to an increase in the production of hydrogen peroxide H2O2, which stimulates the production of lipid peroxides, as it works to change the permeability of cellular membranes, causing damage to cells, which results in Elevated MDA level (Basha&Sovers, 1996). Kuol et al. 2013 also indicated that melamin increases inflammation and oxidative stress by activating the NF-κB/cox-2 and NOX/ROS pathways. Guo and co-workers (2012) also noted that melamine has an important role in activating NOX to produce ROS, suggesting that NOX inhibitors may be clinically useful for reducing melamine nephrotoxicity. Melamine activates the NF-κB pathway, thereby activating NOX to produce ROS, which in turn stimulates the NF-κB pathway. As a result, inflammation occurs (Guo et al., 2012). In addition, the present results showed that concomitant administration of Q10 with melamine to animals decreased the level of MDA and increased the level of GSH and CAT compared to the animals given only melamine. This may be due to the role of Q10 in curbing free radicals resulting from oxidative stress, as Q10 is one of the most powerful antioxidants that scavenge free radicals and then protect cells from the harmful effect caused by these radicals (Jorat et al., 2018) and thus reduce From the consumption of GSH, and Q10 reduces Peruvian fat oxidation and protects cellular membranes from the negative effects of free radicals, as well as increases cell defenses against these radicals through some enzymes that play an antioxidant role, including CAT, SOD (Fouad &Jresat, 2012; Sharifi et al. ., 2018). These results were consistent with the study (Liu et al., 2023) on the role of Q10 by raising the level of GSH, SOD, GPx, and CAT with a decrease in the level of MDA. These results may explain the role of Q10 in lowering the level of cholesterol, triglycerides VLDL and LDL with a high level of HDL and thus reducing the level of lipids in the blood, which is the main cause of oxidative stress by virtue of the positive relationship between the concentration of lipids in plasma and the generation of free radicals that cause Peruvian fat oxidation. Polyunsaturated fatty acids present in the cell membranes and thus affect their permeability, which results in an increase in the level of CAT and GSH and a decrease in the level of MDA (Amiya, 2016). He explained why because it is a lipid-soluble molecule and is a natural antioxidant synthesized endogenously in all humans and animals, Q10 has the potential to be an antioxidant, scavenging free radicals and thus inhibiting lipid and protein synthesis (Gürkan, 2005). through the conversion of an alpha-tocopheroxyl radical to alphatocopherol (Begum, 2009). Q10 works by affecting antioxidants, such as vitamin E, and can prevent and remove free radicals either directly or by stimulating vitamin E (Pobezhimova&Voinikov, 2000). It was found that Q10 is the only endogenously synthesized lipid antioxidant, and it can effectively protect not only lipids from peroxidation but also proteins from oxidation by reducing free radicals and preventing their proliferation. It can also interfere with the oxidation of DNA, especially mitochondrial DNA. (Bentinger et al., 2007).

SOD	GSH	CAT	MDA	Groups
2.17 ±0.004 B	2.5 ± 0.007 B	0.636 ± 0.004 B	1.60 ± 0.003 C	Control
1.59 ± 0.015 D	1.63 ± 0.010 D	0.332 ± 0.005 D	3.31 ± 0.026 A	T1
2.51 ± 0.039 A	2.95 ± 0.024 A	0.859 ± 0.001 A	1.04 ± 0.002 D	T2
1.91 ± 0.014 C	2.01 ± 0.007 C	0.543 ± 0.009 C	1.99 ± 0.013 B	T3
0.031	0.033	0.02	0.06	LSD

The numbers represent the mean ± standard error.

The different letters indicate that there are significant differences ($P<0.05$) between the groups.

C: represents the control group.

T1: (the first treatment group), which was dosed with melamine at a concentration of 50 mg / kg of body weight for a period of 30 days.

T2: (the second treatment group) that was dosed with coenzyme Q10 at a concentration of 10 mg / kg of body weight daily for 30 days.

T3: (the third treatment group) which was dosed with melamine at a concentration of 50 mg/kg of body weight and coenzyme Q10 at a concentration of 10 mg/kg of body weight. Body weight daily and simultaneously for 30 days

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