# Effect of different doses of uranyl acetate on some blood parameters and hepatic enzymesin females rats.

# تأثير التراكيز المختلفة لخلات اليورانيل في بعض معايير الدم وانزيمات الكبد لإناث الجرذان

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**المستخلص**

**استهدفت الدراسة معرفة تأثير خلات اليورانيل المعطاة عن طريق الفم على بعض معطيات الدم وبعض انزيمات الكبد. استخدمت لهذا الغرض 20 جرذ من الإناث الناضجة Albino وقسمت إلى أربعة مجاميع متساوية, مجموعة السيطرة G1 وقد جرعت بالماء المقطر, ومجموعة G2 جرعت بتركيز 50ملغم/كغم/وزن الجسم من خلات اليورانيل, ومجموعة G3 جرعت بتركيز75ملغم/كغم/وزن الجسم من خلات اليورانيل, ومجموعة G4 جرعت بتركيز100ملغم/كغم/وزن الجسم من خلات اليورانيل لمدة 70يوم، جرعت الإناث لمدة 14يوم قبل التزاوج من قبل ذكور غير مجرعة وكذلك أثناء فترة الحمل 3 أسابيع وفترة الرضاعة 5 أسابيع وبعد انتهاء مدة التجربة تم سحب دم من الامهات . وقد أظهرت النتائجحصول زيادة معنوية $p<0.05$ في معدل التعداد الكلي للخلايا البيض WBC في المجاميع G4,G3,G2 مقارنة بحيوانات السيطرة G1. وحصول انخفاض معنوي $p<0.05$ في النسبة المئوية للخلايا اللمفاوية وللخلايا احادية النواة في المجموعتين G4,G3، في حين أظهرت المجموعة G2 انخفاضا غير معنويا $P>0.05$ في النسبة المئويةللخلايا اللمفاوية وللخلايا احادية النواة وحصول انخفاض معنوي $p<0.05$ في معدل خضاب الدم Hb في المجموعتين G4,G3 مقارنة بالسيطرة،في حين أظهرت المجموعة G2 انخفاضا غير معنويا $P>0.05$ في معدل خضاب الدم.كما وأظهرت االنتائج حصول أنخفاض معنوي $p<0.05$ في معدل التعداد الكلي لكريات الدم الحمر في المجاميع( G4,G3,G2 ) مقارنة بحيوانات السيطرة. وحصول إرتفاع غيرمعنوي $P>0.05$ في مستوى فعالية انزيمي الـ GOT والـ GPT في المجموعتين G3,G2 مقارنة بالسيطرة، وحصول أرتفاع معنوي $P<0.05$ في فعالية هذين الانزيمين في المجموعة G4 مقارنة بالسيطرة .في حين لوحظ حصول زيادةغير معنوية $P>0.05$ في فعالية أنزيم الـ CPK في المجاميع G4,G3,G2 مقارنة بحيوانات السيطرة.**

**الكلمات المفتاحية: خلات اليورانيل، انزيمات الكبد**

**Abstract**

**This study was carried out to investigate effects of oral administration of uranyl acetate on haematological parameters and liver enzyme. For this purpose, twenty females mature Albino rats were divided into four equal groups, control group G1 administrated distilled water, the other three groups administrated orally 50,75,100 mg/kg/b.w. /day of uranyl acetate. The route of administration was oral intubations for 10 weeks, for 14 days before mating with untreated males, as well as during pregnancy 3 weeks and lactation 5 weeks. At the end of the treatment blood samples were collected from mothers of rats. The results were obtained a significant P< 0.05 increase in the total WBC counts in groups G2,G3,G4 compared with control. A significant P<0.05 decrease in the lymphocytes and monocytes percentage in groups (G3,G4), while no significant decrease P>0.05 in G2 in the lymphocytes and monocytes percentage compared with control. And the results show significant P< 0.05 decrease in HB value in groups G3,G4, while no significant decrease P>0.05 in G2 in HB value compared with control. A significant P< 0.05 decrease was observed in total RBCs counts in groups G2,G3,G4 compared with control. No significant increase P>0.05 in GOT and GPT in groups G2 and G3 and significant P<0.05 increase in GOT and GPT activity in the serum in group G4 compared with control. No significant increase P>0.05 in CPK activity in groups G2,G3,G4 compared with control.**

**Key words: uranyl acetate, hepatic enzymesin**

## Introduction

Uranium is a radioactive metallic element of high specific gravity. It is chemically classified as a heavy metal and is weakly radioactive. Uranium is found as an oxide, uraninite or mixed oxide, pitchblende or

complex salt. Occurs in nature as a mixture of three isotopes – U238 99.28%, U235 0.71% and U234 0.01%. It is ubiquitousoccurring in rocks, soil, rivers, Oceans, plants and animals. Consequently, all humans are exposed to naturally occurring uranium through ingestion, inhalation and skin contact [1]. Internalized in the body, the soluble components migrate throughout the body and uranium concentrates in the bone, kidney, and liver. The uranium content in the various tissues of the body followed a rank order lung > skeleton > liver > kidney [2], but can vary depending on the pattern and nature of exposure [1]. When the uranium enters the body, it binds with bicarbonate and proteins. This binding action helps prevent soluble uranium from interacting with most body tissues[3]. Uranium dust may consist of small, fine particles and coarse, big particles. The big particles are caught in the nose, sinuses, and upper part of the lung where they are blown out or pushed to the throat and swallowed. The small particles are inhaled down to the lower part of lung. If they do not dissolve easily, they stay there for many years and cause most of the radiation dose to lung from uranium, they may gradually dissolve and go into blood. If the particles do dissolve easily, they go into the blood more quickly [4]. Uranyl acetate is a water soluble and can be often used as stains with lead citrate for staining technique in electron microscopically examination [5]. It is one of the Uranium salts, which is most commonly associated with oxygen as the uranyl ion to form uranyl oxide (UO2). The most recent investigations considered the oral LD50 of uranyl acetate dehydrate to be 200 mg/kg /b.w. [6]and[7]. The incident of different types of cancer including blood and liver cancer has increased markedly in Iraq following the 1stGulf War 1991 as result to exposure to the different doses of radiation because using depleted uranium, uranium content in the skeleton may reflectits affinity for phosphate which is abundant in the bone has consequencesfor the bone marrow or blood forming cells. Therefore this study was come to evaluate the toxicity of different doses of uranylacetate (one of the uranium salts) on the liver function enzymes in serum and on some blood parameters in mother rat during pregnancy and lactation.

**Materials and Methods**

**1- Experimental Animals**

Thirty (10 males and 20 females) sexually mature laboratory breed males and females Sprague-Dawley Albino rats (Rattusnorvegicus) of an average body weight of 230±3.565gm and 12-15 weeks old were used in the experiment. Animals were kept under the laboratory conditions 12h light: 12h dark photoperiod, with controlled room temperature 25-28°C, good ventilation and were feed normal rodent pellets and tap water.

**2- Experimental design**

The rats were randomly divided into four groups. Female rats were mated with males 2:1 until copulation was detected. Finding of sperm in the vagina was indicated copulation and the day of detection were designated as Day 0 of gestation. Then the adult fertile females were treated with uranyl acetate dihydrate (UAD) by gavages 10 days before mating with untreated males, as well as during pregnancy and lactation for every day [8].The first group served as a control and only received drinking water .Three concentration of uranyl acetate dissolved in water were administrated by gavages to three other groups of females 50,75,100 mg/ kg/ B.W/ day. The dose of (UAD) is based on results of previous studies [9,10,11].

**3- Blood parameters and Liver enzymes**

Rats in all groups were anesthetized by diethylether. Blood samples were taken 3-5 ml from each rat by an intra-cardiac punctures in to 2 test tubes, one with EDTA anticoagulant and the other without EDTA. Blood with EDTA was used for estimation red blood corpuscles count, white blood cells counts, lymphocyte percentage, monocyte percentage and Hemoglobin concentration, were done in the same day of collection and determined by routine laboratory methods [12,13].

Blood without EDTA was centrifuge at 2500 rpm for 20 minutes to separate serum. Sera were then transferred into suitable plane tubes and preserved at -20°C. The sera were used for the estimation of various biochemical parameters Glutamic Oxaloacetic transaminase (GOT), Glutamic Pyruvic

Transaminase (GPT) and Creatine Phosphokinase (CPK)) were assayed according to the methods of [14] and [15], respectively.

**4- Statistical analysis**

The Statistical Analysis System- SAS (2004) was used to study the effect of differente treatments in the studiedparameters[16].

**Results and Discussion**

Soluble uranium compounds were move into the blood within days or weeks, and will be absorbed in the blood and removed from it to other organs where theseparticles accumulate, then their different biological effect appear which depending on their solubility and their biological half-life.

1-**Effect of differentdoses uranyl acetate on some blood parameters (haematological parameters) in female rats**

The present investigation revealed a significant increase $p<0.05$ in total WBCs count of animals groups treated with uranylacetate G2,G3,G4 when compared with that of the G1 (control)group while no significant increase $P>0.05$ among treated animals Table (1).

Individuals with an elevated white blood cell count may suffer from infection, inflammation, trauma, and acute or chronic leukemia, among other conditions [17]. This increment means a sign of inflammatory response which result from alteration of many tissue organs due to the effect of uranyl acetate. The uranyl acetate chemo tactic factors that stimulate bone marrow to increase WBCs Production then elevate their level in blood [18]. Although the specific cause of higher white blood cell counts in this case was not known, this finding suggests that may be more susceptibleto the effects of uranium exposure these result were agree with study of [19]. Also the data deal with leukocyte increase in circulating blood during the lactation [20].

**Table (1):Effect of different doses uranyl acetate on some blood parameters in female rats(mean ±SE)**

| Parameters | Treatments | | | |
|---|---|---|---|---|
| | Control G1 | G2 | G3 | G4 |
| W.B.C. (x $10^3$) Cell/$mm^3$ | B 5.80 ± 1.19 | A 8.13 ± 1.81 | A 8.60 ± 2.38 | A 8.86 ± 1.27 |
| Lymphocyte % | A 83.26 ± 4.62 | A 76.63 ± 8.97 | B 61.76 ± 7.19 | B 60.03 ± 4.93 |
| Monocyte% | A 6.53 ± 3.87 | Ab 5.00 ± 1.26 | B 2.40 ± 1.04 | B 1.96 ± 1.49 |
| R.B.C. (x $10^6$) Cell/$mm^3$ | A 7.19 ± 0.51 | B 6.79 ± 0.11 | B 6.63 ± 0.25 | C 6.37 ± 1.23 |
| Hb mg/100 ml | A 13.53 ± 0.46 | B 10.20 ± 1.22 | A 13.23 ± 0.23 | Ab 12.30 ± 1.13 |

**Similar letter means no significant difference P>0.05**
**Different letters means significant differences p<0.05**

The oral administration of uranyl acetate significantly decrease lymphocyte percentage among the treated groups compared with control group except the G2 group which was not differed from control and there were no differences between the G3,G4 groups. The monocyte percentage were decreased no significantly $P>0.05$ in G2 group while they decreased significantly $p<0.05$ in G3,G4 when compared with control groupTable (1).

The decrement in lymphocyte percentage was found in animal group treated with uranyl acetate might occur because transudation and migration of the lymphocytes to sites of inflammation or because degeneration its [21],or might occur due to chromosomal aberration in lymphocyte affected with uranyl acetate which cause different lymphocyte structural alteration [22]. Since lymphocyte are made in the bone

marrow if not enough, bone marrow is produced or the activity of the bone marrow decreases, an abnormally low lymphocyte count can occur. Similar results were recorded by [23].

A monocyte is a type of white blood cell that is produced by the bone marrow and helps to protect the body from foreign invaders. When there are a decreased number of monocytes in the blood, the body is more susceptibleto illness. There can be many causes for low monocytes in the blood (monocytopenia), One cause can be from a release of toxins into the bloodstream. Another cause can be from an infectionthat affects the bone marrow by uranyl acetate these results be in agreement with previous results [19].

Table (1) showed no significant decreased in Hb valuein the treated animals as comparing with control group except G2 group which was decreased significantly $p<0.05$ comparing with control group and also showed that the oral administration of uranylacetate were affected the total RBCs count of female rats in G2,G3,G4 respectively. Total RBCs count showed significant decrease at $P<0.05$ in treated compared with untreated animals (control group), uranium has the potential to exert toxic effects on several important physiological processes including kidney function, bone development, and hematopoiesis [1]. Uranium accumulation in the bone directly affects its structure and metabolism [24]. Because erythrocyte originates in bone marrow, uranium sequestered in bone has the potential to alter hematopoiesis. Erythrocyte production is regulated by the hormone erythropoietin, which is produced in the peritubular cells of the kidney [25]. Uranium also is nephrotoxic, and can compromise kidney function by disturbing renal proximal tubule reabsorption[26]. Thus, uranium may not only affect hematologic parameters directly via irradiation of bone marrow, but also indirectly by acting on the kidneys and potentially reducing erythropoietin production. Of the few animal and population-based studies that have examined this relationship, some have observed alterations in hematologic measures in association with uranium exposure[27,28]. Dygert exposed rats to ammonium diuranate dusts containing 6.8 mg uranium/m3 for 6 hours/day for 30 days and observed decreases in red blood cell counts. Another study of uranium miners with <5 up to 20 years of work experience had small but significant decreases in hemoglobin concentration[29].

Three hypotheses could explain RBC decrease: reduced erythropoiesis, increased erythrocyte degradation for iron recycling or renal dysfunction (Anemia).

The blood draw from female rats during lactation when plasma volume is increase during lactation lead the red cell become less concentration compared with volume of plasma and leads to Haemodilution then the blood flow in small vessel evaluate[30]. Reduced rate is attributable hemoglobin in dairy animals to higher requirements mammary gland upsurge in simultaneous needs blood circulation [31].

Previous records of hematological parameters after chronic exposure to uranium and proved to be contradictory .For instance by [32] were study hemoglobin and RBC content in sheep fed on pasture from areas which bombs containing depleted uranium remained within the normal ranges, whereas surveyed residents living around nuclear plant area revealed increases in these hematological parameters [28]. Similarly to the present work [19] who injection the experimental rabbits with 1mg/Kg uranyl acetate This discrepancy between these studies may be due to a difference in the exposure pathway, in the physical-chemical form of uranium, in the received doses, in the duration of exposure and the time post-exposure, as well as in the occurrence of exposure in these different cases of uranium exposure.

**2-Effect of different doses uranyl acetate on hepatic enzymes**

Table (2) showed no significant increment $P>0.05$ in GOT and GPT in the serum of G2,G3 groups comparing with control group except G4 group which was increased significantly $p<0.05$ comparing with control group.

As a general rule, however, damage to liver function is characterized by an increase in plasma levels of GOT and GPT, indicating considerable parenchymal cell damage.This may be due to the degeneration of hepatocytes by necrosis and cell cytolysis which causes leakage of these enzymes into blood circulation

[33] which gives an indication on the hepatotoxic effect of uranyl acetate, this observation corroborates the findings of [34]who had observed after high level of subcutaneous DU administration and [11]when he give rats intragastrically 75mg / kg / b.w Uranylnitrat. The results in this study contrasted to the results of [35] who had observed decrease in plasma levels of GOT and GPT when he exposed rats to depleted uranium in their drinking water These contradictory results are probably due to the quantity of uranium used and the duration of contamination.

**Table (2): Effect of different doses uranyl acetate on hepatic enzymes activity in serum of female rats (mean ± SE)**

| Parameters | Treatments | | | |
|---|---|---|---|---|
| | G1 | G2 | G3 | G4 |
| GOT (In/ml) | B 194.42 ± 3.57 | Ab 203.89 ± 6.31 | Ab 208.18 ± 5.46 | A 211.32 ± 4.73 |
| GPT (In/ml) | B 66.36 ± 1.38 | Ab 73.77 ± 2.55 | Ab 72.86 ± 3.00 | A 74.40 ± 1.57 |
| CPK (mg/dl) | A 67.62 ± 5.63 | A 69.94 ± 1.75 | A 73.19 ± 6.44 | A 74.25 ± 2.46 |

**Similar letter means no significant difference P>0.05**

**Different letters means significant differences p<0.05**

Increase was in CPK activity in serum of treated animals, but this Increase did not reach the significant levels comparison with control group.

Because CPK is mainly metabolized by the liver macrophages [36] the of CPK plasma increases in severe liver insufficiency. Consequently, an accumulation of CPK activity in plasma is to be expected in this case and due to the massivehepatocellular destruction occurring in hepatocallular as primary effect of hepatic necrosis[37] therefore, there is a leakage CPK into the circulation, CPK considered as a good indicative of myocardial damage [38] so its appearance in sera of treated animals the presence reflect of massive myocardial damage which affected by uranyl acetateTable(2) [39].

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