

## Protective effect of injectable iron on cadmium-induced anemia in rats

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### الخلاصة

يسعى البحث الحالي لدراسة التأثير الوقائي للحديد من فقر الدم المحدث في الجرذان المعرضة لفترة طويلة للكاديوم. استخدم في هذه الدراسة خمسة عشرة جردي قسمت إلى ثلاثة مجاميع. أعطيت المجموعة الأولى (السيطرة) ماء الشرب فقط في حين تم إعطاء المجموعة الثانية والثالثة كلوريد الكاديوم عن طريق ماء الشرب بتركيز ٢٥ ملغم/لتر من ماء الشرب ولمدة شهر. تم حقن الجرذان في المجموعة الثالثة بالحديد (Iron Dextran) بجرعة ٥٠ ملغم/كغم في الخلب بين يوم وآخر لأربع مرات بالإضافة إلى وجود الكاديوم في ماء الشرب. وقد أظهرت النتائج انخفاضاً معنوياً في تركيز أيون الحديد في بلازما دم الجرذان المعاملة بالكاديوم لوحده مقارنة بالمجموعة المعاملة بالكاديوم والحديد سوية وكذلك مقارنة مع مجموعة السيطرة في حين كان هناك زيادة معنوية في تركيز أيون الحديد في بلازما دم الجرذان في المجموعة الثالثة المعاملة بالكاديوم والحديد سوية مقارنة بالمجموعة الثانية المعاملة بالكاديوم لوحده عند مستوى احتمال اقل من ٠.٠٥. وأدى إعطاء الكاديوم لوحده أو مع الحديد إلى إحداث زيادة معنوية في نشاط خميرة الانين امينو ترانسفيريز مقارنة مع مجموعة السيطرة في حين لم يتأثر مستوى خميرة الالكالين فوسفاتيز بتلك المعاملات. فمن هذه الدراسة نستنتج بان الحديد قد أعطى وقاية من الإصابة بفقر الدم الناتج عن التعرض للكاديوم لفترة طويلة من الزمن.

### Abstract

The current paper studied, the protective effect of iron on anemia induced by Cadmium (Cd). Fifteen male albino rats selected in this study divided into three groups, first group as control, 2<sup>nd</sup> and 3<sup>rd</sup> groups

received oral CdCl<sub>2</sub> 25mg /L mixed with drinking water for one month. Third group treated four dosage of injected iron (iron Dextran) at 50 mg/kg intraperitoneally in addition to cadmium drinking water. The result of this study showed a significant decreased of iron concentration in plasma of Cd treated group but there is a significant increase in iron concentration in 3<sup>rd</sup> group compared to 2<sup>nd</sup> group  $p < 0.05$  while there is a significant elevated with alanine aminotransferase enzyme in 2<sup>nd</sup> and 3<sup>rd</sup> group in comparing to control group. Alkaline phosphatase enzyme no change. Conclusions: this study concluded that iron supplement is prevent anemia induced by long exposure to cadmium.

### **Introduction**

Cadmium (Cd) is a wide spread industrial pollutant causing acute and chronic poisoning in human and animals .It is known to be one of the most toxic heavy metals. This toxic element can enter the metabolic pathway of some essential trace element including copper, zinc, iron, manganese, selenium and calcium by competing for ligands in biological system (1). Cd is a toxic heavy metals can enter the diet of farm animals by variety of exposure rout (diet and water) (2,3,4,5), One of the target organs which could be affected is the erythrocytes (6).

Anemia is commonly induced by chronic cadmium intoxication, which could be due to many proposed mechanisms. One of these mechanisms is intravascular hemolysis which can occur at the early stage of Cd exposure to the direct damaging effect on erythrocytes. This lead to produce a condition of microcytic hypochromic anemia and a state of iron deficiency (7). The significantly decrease of iron concentration in the body after exposure to Cd , result in decrease iron concentration in the liver, spleen and other tissues (8,9). The aim of the present study is to examine the protective effect of iron injectable in reversing the effect of cadmium induce anemia in rats.

### **Materials and Methods**

Fifteen male albino rats (10 weeks) weighing between (200-250) gm. They were housed under laboratory conditions at a temperature of  $(22 \pm 2)$  C° with a natural light/dark cycle, and food was available.

Randomly selected animals were assigned to three experimental groups (5 rats/group). The first group (control) received drinking water only, The 2<sup>nd</sup> group received cadmium - water (Cd-H<sub>2</sub>O) for 4 weeks orally. (Cd - H<sub>2</sub>O) concentrate was prepared at 6.3 ppm Cd concentration in water (25mg CdCl<sub>2</sub> in one liter H<sub>2</sub>O). The concentration of Cd depended on Petersson (10). 3<sup>rd</sup> Group was received iron at 50 mg/kg intraperitoneally during 1<sup>st</sup>, 3<sup>rd</sup>, 5<sup>th</sup>, 7<sup>th</sup> days in addition to (Cd - H<sub>2</sub>O). All experimental animal were scarified at day 30 of experiment, and blood

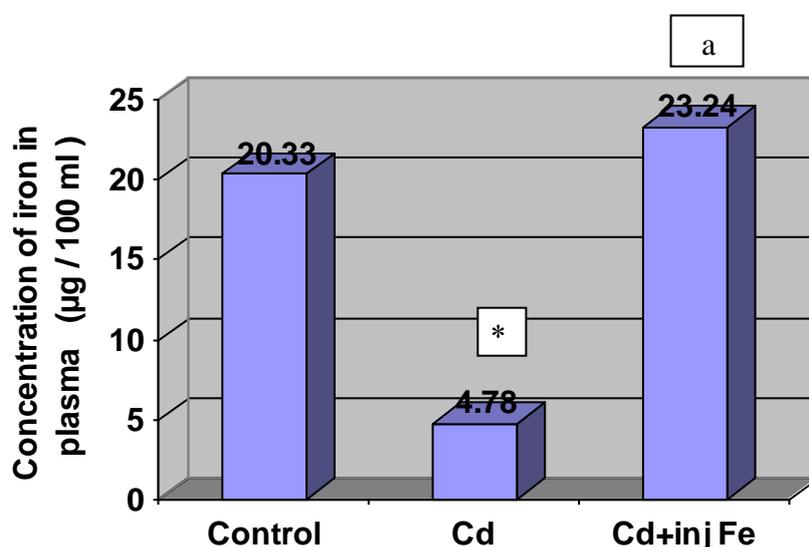
sample were collected in heparinized tube, plasma were obtained and used for assay iron by (Iron colorimetric kit, Biomaghreb), alanine aminotransferase enzyme (ALT kit, Bio Merieuxsa, France) and alkaline phosphatase enzyme (ALP kit, Syrbio, Syria).

The data were expressed as mean  $\pm$  SE, difference between three experimental groups were statistically analyzed by analysis of variance followed by the least significant difference test. The level of significance was at  $p < 0.05$ .

## Results

In the present study exposure to Cd in drinking water for one month had lead to a significant decrease in iron concentration of plasma in 2<sup>nd</sup> group compared to control group (figure 1). The administration of iron at 50 mg/kg with Cd was significantly increase the concentration of iron in 3<sup>rd</sup> group compared with 2<sup>nd</sup> group which treated by Cd alone. Non significant difference was found between control and 3<sup>rd</sup> groups (figure 1).

The alanine aminotransferase enzyme activity was significantly increased in 2<sup>nd</sup> and 3<sup>rd</sup> group in comparison to control group but alkaline phosphatase enzyme was non significantly affected by cadmium (table 1).



Figure(1): Effect of Cd , (Cd + iron ) combination on iron concentration in the plasma of rats after one month of treatment

- value are mean  $\pm$  SE 5 rats /group .
- \* Significantly different from the control group.  $P < 0.05$  .
- a. Significantly different from Cd alone treated.  $P < 0.05$

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**Table (1): Effect of Cd, (Cd + iron) combination on alanine aminotransferase enzyme and alkaline phosphatase enzyme in plasma of rats after one month of treatment**

	Treatment		
	Control	Cd	Cd + Fe
ALT ( unit /liter)	9.2 $\pm$ 1.3	16.9 $\pm$ 1.8 *	18.6 $\pm$ 0.7 *
ALP (unit/liter)	179.9 $\pm$ 17.3	189.4 $\pm$ 9.7	180.1 $\pm$ 12.9

- value are mean  $\pm$ SE 5 rats /group .

\* Significantly different from the control group. P < 0.05 .

ALT: alanine aminotransferase enzyme.

ALP: alkaline phosphatase enzyme.

### Discussion

In the present study rats exposed to cadmium showed decrease in iron concentration of blood. Iron depletion has been recognized as one of the mechanism of Cd – induce anemia (7,10) because Cd accumulate in erythrocytes affected membrane cytoskeleton and decreases cell deformability, and these cells are trapped and destroyed in spleen. Iron deficiency can be detected in animals after an oral exposure to Cd, which compete with iron for absorption in the intestines then cadmium bind with membrane of red blood cells (11). Cd distribution to the liver and subsequently stimulate the synthesis of metallothionin (MT) which binds Cd forming Cd- MT complex and reactive oxygen species (12,13,14). The Cd- MT is transport to the blood and cause destruction of the red blood cell and this lead to anemia (15,16).

In the present study, injectable iron intraperitoneal in first week of exposure to Cd cause significantly increase in iron concentration in group 3<sup>rd</sup> in comparison to group 2<sup>nd</sup> and the value of iron was return to normal value. This result was in agreement with other studies that suggested adequate dietary iron supplement reduce Cd retention in the body. Iron and Cd compete on same sensitive site in the gastrointestinal tract, or may be due to Cd inhibit absorption of iron at low to the normal levels of dietary intake iron but in high levels supplement of iron, Cd are absorb by other non competitive mechanism (17,18).

In 2<sup>nd</sup> and 3<sup>rd</sup> group showed that the alanine aminotransferase enzyme was increased probably due to Cd induce liver injury and damage. This finding is in agreement with other studies that suggest the administration of Cd increase the level of alanine aminotransferase enzyme. (19, 20). It was suggested that Cd causes liver injury and damage (21, 22). because Cd distribution to the liver and stimulate to synthesis of Cd-MT complex and increase the level of alanine aminotransferase in the blood (12,13). Alkaline phosphatase enzyme was not affected by Cd exposure.

### Conclusion

From this results the Parental administration of iron intraperitoneally for rats exposure to Cadmium for long period in drinking water produced a protective effect from anemia induce by Cadmium. Iron supplementary found to be an essential to overcome anemia induced by Cadmium toxicity.

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