

## Effect of Ferrous Sulphate Intake on Absorption of Cadmium Chloride in Drinking Water in Mature Female Rabbits

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### Abstract

Cadmium is a toxic heavy metal, which is mainly absorbed by gastro intestinal tract (GIT). This absorption increases when there is a decrease in the level of iron in body stores. This study was carried to find out that the intake of ferrous sulphate affects the absorption of cadmium chloride from gastro intestinal tract (GIT) of mature rabbits exposed chronically to polluted water with cadmium chloride ( $\text{CdCl}_2$ ). Four to five months old rabbits were equally divided into three groups: Control (A), this group offered ordinary tap water, the second treated group (B), offered tap water containing 80 parts per billion (ppb)  $\text{CdCl}_2$ . The third treated group (C), offered tap water containing (80 ppb)  $\text{CdCl}_2$  with 4mg of ferrous sulphate that are given orally once a day. Cadmium concentration in serum was measured using atomic absorption instrument at the end of experiment which extended for 8 weeks. The results revealed that Cd concentration was increased significantly in the 2nd group (B) as the  $\text{CdCl}_2$  level in serum reached 2.057 ppb, while it decreases significantly in the 3rd group (C) where the level decreased to 0.455 ppb compared to control group (A). These findings concluded that the supplementing food with iron compounds led to a decrease in serum cadmium levels, where ferrous competes with the absorption of Cd.

### 1. Introduction

Cadmium is a widespread, very toxic heavy metal, which naturally exists in the earth's crust. It exists as a minor component in most zinc ores. It is a by-product of zinc production. Cadmium is utilized in the industry because of its non-corrosive properties in metal coating [1]. In 2009, 86% of global production of cadmium was used in batteries (rechargeable nickel-cadmium batteries) [2], and 6% was used in electroplating mainly in aircraft industry. In PVC, cadmium is used as heat, light, and weathering stabilizers. Also, it is used in paint pigments [3]. Cadmium levels in the environment rapidly increased during the period (1800 to 1960), predominately due to its consumption by industrialized countries and the huge increase in fossil fuel production. Non-occupationally adults and children are exposed to Cd largely through diet, with secondary exposures occurring from cigarette smoking

or second-hand tobacco smoke, house dust, and industrial emissions [4]. Cadmium has been associated with numerous adverse health problems, including impaired kidney function, diabetes, hypertension, osteoporosis, cancers in adults [5], immune suppression, neurotoxicity, and neuron developmental problems in children, [6] as well as the chronic exposure of cadmium exert profound toxic effect on activities of thyroid gland [7]. Several researchers suggested that complex of heavy metals including cadmium has a great potential for treatment of wide variety of cancers but their use is often limited due to toxic effects. Iron is an importantly essential metal and is a component of two inorganic factors, heme and Fe/s clusters. Iron deficiency is a risk factor for increasing cadmium blood and urine among never-smoking, premenopausal, non-pregnant US women [8]. Cadmium inhibits iron absorption only at low to normal levels of dietary iron [9]. Dietary Cd absorption is thought to increase when iron stores are depleted. Studies in animals have demonstrated associations between iron deficiency (ID) and increased consumption of Cd via the diet [10]. Iron plays an essential role in many biological processes and its importance is to maintain iron concentration within narrow normal range [11]. Hence, in the present study, ferrous sulphate is chosen as trace element supplement that influences on Cadmium chloride absorption from GIT and its level in serum of mature rabbits exposed chronically (8 weeks) to Cd in drinking water.

## 2. Methods and Materials

### 2.1 Chemicals

Cadmium as Cadmium chloride ( $\text{CdCl}_2$ ) was purchased from market (Dormstadt, Germany), iron as ferrous sulphate was obtained from syrup used as iron supplement (Ferrosam drop) SDI (Samara Drug, Industry) containing active ingredient, each 5ml :200mg ferrous sulphate equivalent to 40mg of elemental iron.

### 2.2 Animals

A total of eighteen mature rabbits with average weight of 800 to 1000 g of local breed were acclimated to holding for one week prior to commencements of dosing. Animals were housed in clear stainless steel cages in conditioned room (23-27 °C) with controlled lightening. They were equally divided into three groups and treated for 2 months in winter as follows:

Group (A), six rabbits in this group received tap water and served as control group, the group (B) received 80 ppb of cadmium chloride in drinking water, while the animals of group (C) received 80 ppb cadmium chloride in addition, receiving a daily dose of 4mg ferrous sulphate by mouth [12].

Fasting blood samples (3 mL) were collected from all animals before treatment, weekly and at the end of the experiment (8th weeks) via cardiac puncture technique, then serum was separated and frozen at -20 °C for further chemical analysis.

### 2.3 Chemical Analysis

**Preparation of samples [13]:** We used (High performance microwave digestion system, ETHOSE ONE, Millstone USA) to eliminate any biological materials presented in the serum and prevailing only the chemical elements. For measuring the cadmium in serum samples, we used atomic absorption, (Analytic jena Model nov AA 400 P Germany).

### 2.4 Statistical Analysis

Statistical analyses of data were performed on the basis of a two-way analysis of variance (ANOVA) using significant level of ( $P < 0.05$ ).

## 3. Results

The effect of adding 80 ppb of  $\text{CdCl}_2$  to drinking water on the level of cadmium in group (B) serum was shown in Table (1). The level of Cd was significantly increased ( $p < 0.05$ ) at the end of treatment period. Its levels were elevated during all of the eight weeks compared to respective levels in the control group. After supplementation with ferrous to treated rabbits, cadmium levels decrease significantly ( $p < 0.05$ ) in the serum of animals in group (C) at the end of treatment period as compared to pre-treatment values (group B in Table 2). The levels were decreased during all of the eight weeks compared with levels of cadmium chloride in serum of animals of group (B).

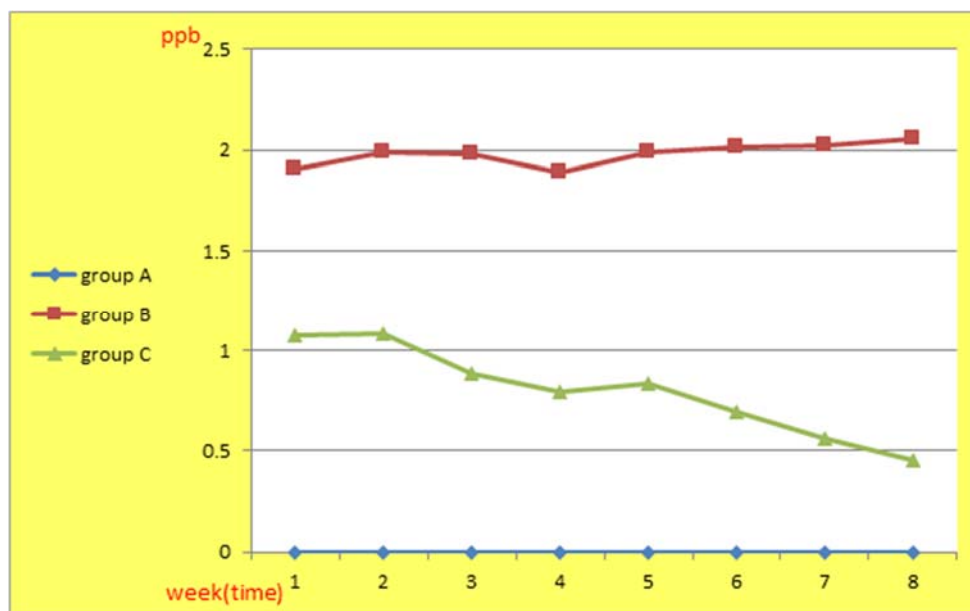
Figure (1) shows the levels of cadmium in the serum of the tested animals during the eight weeks compared to control group and the statement of the effect of iron intake on the level of cadmium in the serum of treated animals (group C).

**Table (1).** The effect of cadmium chloride absorbed by GIT on the cadmium level (ppb) in rabbit's serum.

| Weeks<br>groups      | Pretreatment<br>Serum Cd<br>Concentration<br>(ppb) |        | Treatment Serum Cd Concentration (ppb) |        |        |        |        |        |        |        |
|----------------------|----------------------------------------------------|--------|----------------------------------------|--------|--------|--------|--------|--------|--------|--------|
|                      | 1                                                  | 2      | 1                                      | 2      | 3      | 4      | 5      | 6      | 7      | 8      |
| Control              | 0.0001                                             | 0.0001 | 0.0001                                 | 0.0001 | 0.0002 | 0.0001 | 0.0001 | 0.0001 | 0.0001 | 0.0002 |
| Treated<br>Group (B) | 0.0002                                             | 0.0001 | 1.903                                  | 1.988  | 1.983  | 1.892  | 1.990  | 2.015  | 2.025  | 2.057  |

**Table (2).** The effect of ferrous sulphate (4 mg/kg bw) on the cadmium level of cadmium in rabbits' serum.

| Weeks<br>Groups | Treatment Serum Cd Concentration (ppb) |       |       |       |       |       |       |       |
|-----------------|----------------------------------------|-------|-------|-------|-------|-------|-------|-------|
|                 | 1                                      | 2     | 3     | 4     | 5     | 6     | 7     | 8     |
| <b>B</b>        | 1.903                                  | 1.988 | 1.983 | 1.892 | 1.990 | 2.015 | 2.025 | 2.057 |
| <b>C</b>        | 1.079                                  | 1.083 | 0.882 | 0.795 | 0.835 | 0.693 | 0.56  | 0.455 |



**Figure (1).** Levels of Cd in the serum of the test animals' groups (B & C) compared with control group (A).

#### 4. Discussion

Cadmium is an environment toxic pollutant affecting various tissues. Data of the present study showed that 80 ppb of  $\text{CdCl}_2$  in drinking water for 8 weeks significantly increased the levels of cadmium in the serum of rabbits. Cadmium absorption by GIT is influenced by diet composition and nutritional factors, e.g., dietary intake of iron, where there may be an interaction between anemia and blood levels of Cadmium [13].

Osuala et al, 2013 suggested that Cadmium caused erythrocyte destruction which probably led to release of  $K^+$ . Hyperkalemia has reported to arise in condition characterized by excess destruction of cells with redistribution of  $K^+$  from intracellular to extracellular compartment as massive hemolysis [14].

Many mechanistic studies found that the intestinal transporter for non heme iron, Divalent Metal Transporter 1 (DMT1) mediates the transport of Pb and Cd. DMT1 is regulated, in part, by dietary iron, and chemical species of Cd and Pb that are transported by DMT1 and would be made available through digestion and are also found in plasma. Accordingly, the involvement of DMT1 in metal uptake offers a mechanistic explanation for why an iron-deficient diet is a risk factor for Pb and Cd poisoning. It also suggests that diets rich in iron containing food could be protective against heavy metals poisoning [15].

The DMT1 protein is likely regulated in the small intestine at the mRNA level by body iron depletion and increases Cd uptake from the gastrointestinal tract with subsequent transfer of Cd to the circulation and body tissues [16].

## 5. Conclusions

The administration of cadmium chloride over the experimental period has established the fact of its increment in the blood but the administration of iron leads to decrease in its level, and its toxic effects on various tissues. Accordingly, we recommend conducting experiments on the use of doses of iron worker and their effects on cadmium levels, heavy smoker peoples, workers in batteries, dyes factories, and pitmen. In addition, pregnant women suffering from anemia should take at least 80-120 mg of ferrous sulphate and this proven in most pharmaceutical constitution take at least 80-120 mg of ferrous sulphate daily to minimize the effects of cadmium, and prevent its accumulation.

The persistence of cadmium in the environment requires a long-term approach to minimize human exposure through environmental management and maintenance of lower cadmium levels wherever possible.

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