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The combined effect of supplementary Cr(III) propionate complex and iron deficiency on the chromium and iron status in female rats

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ABSTRACT

The aim of the study was to evaluate the combined effect of supplementary chromium(III) and iron deficiency on the chromium and iron status in female rats. The study was carried out on female Wistar rats, which were divided into 6 experimental groups with different Fe levels (deficient 10% RDA and recommended (adequate) 100% RDA). Simultaneously, for six weeks their diets were supplemented with Cr(III) at doses of 1, 50 and 500 mg kg^{-1}.

The tissular chromium and iron levels were measured with the AAS method. The serum iron and TIBC were measured with colorimetric methods The serum ferritin level was measured by means of electrochemiluminescence immunoassay. The serum transferrin level was measured with the ELISA method. The haematology was measured with an automated blood analyser.

Supplementary Cr3 increased the Cr content in the tissues. This effect was weaker in the Fe-deficient groups than in those with the recommended Fe level, but it did not affect the Fe status.

Fe deficiency significantly reduced the Fe content in the tissues. Simultaneously, Cr3 supplementation mitigated the symptoms of Fe deficiency. Fe deficiency increased TIBC and transferrin levels but reduced ferritin and most haematological parameters. However, simultaneous addition of high doses of Cr3 did not deepen these adverse changes. Our results show that the trend of changes in the Fe-Cr interaction depends on the content of these elements in the body.

1. Introduction

The accumulation or deficiency of trace elements in the human body is often caused by environmental pollution, improper diet and metabolic disorders [1]. Some trace elements may be involved in the pathogenesis of diet-dependent diseases such as anaemia and diabetes.

Iron is an essential element for normal body function. It is a component of haemoglobin, myoglobin, and many enzymes used for oxygen transport and storage and for electron transport. A substantial part of the population suffers from iron deficiency, which may cause anaemia [2]. Iron deficiency is usually associated with low Fe supply, blood loss, poor absorption, diseases or increased physiological demands as in pregnancy [3].

Many studies showed that Cr(III) supplementation improved insulin sensitivity and blood glucose levels in animals and humans with impaired glucose tolerance, insulin resistance and diabetes [4,5]. Cr(III) may increase the use of energy nutrients by influencing the activity of insulin receptors and thus accelerate the loss of body weight and affect the body composition in rats [6]. However, the effect of supplementation of Cr(III) on weight loss in animals and especially in humans is controvertial. The study by Stout et al. [7] showed that chronic exposure of chromium picolinate up to 5% of the diet in male and female rodents (F344/N rats and B6C3F1 mice) for two years had no effect on body weight. Also, the mean body weights of exposed on a single dose of Cr3 2000 mg kg^{-1} b.w. Wistar rats, both sex were similar to those of the controls [8].

Nonetheless, it is suggested the treatment of Cr(III) can have a positive influence in maintain normal body weight in diabetic subjects. Sadri et al. [9] reported that Cr(III), Zn(II) and leucine (Leu) supplemenation, alone and in combination, did not change the final body weight and body weight gain in rats with type 2 diabetes. The supplementary Cr3 at dose 50 mg kg^{-1} of diet administered in the high-fat (HF) diet significantly reduced the relative body mass gain in comparison to the HF group for 5 weeks [10].

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For these reasons, in recent years Cr(III) supplements have become very popular therapeutics in diabetes and they have been used as agents aiding weight loss. Diet supplementation with pharmaceutical preparations is a deficiency prevention method. Currently the market offers a wide range of dietary supplements rich in minerals. Lately, the European Food Safety Authority (EFSA) has released a scientific opinion setting chromium (Cr) as a non-essential element for animals and humans [11]. According to this document, any physiological function assigned to Cr(III) is inappropriate in healthy subjects. In spite of this, the popularity of chromium supplements is still high all over the world. On the other hand, some authors demonstrate that the risk of type 2 diabetes is lower in adults taking chromium-containing supplements [12].

The interaction of trace elements, such as chromium, may have significant influence on the Fe status. As Fe(III) and Cr(III) are transported by the same protein − transferrin [13], they may have competitive effect on the absorption and transport to tissues [14]. However, this effect may depend on relative proportions of these elements in the diet or in the body. There are two transferrin binding sites with different affinities for Fe as a pH function. It was described that Fe(III) binding to the C-lobe was approximately 20 times stronger than Fe(III) binding to the N-lobe. Like Fe(III), trivalent chromium [Cr(III)] typically binds to the C-lobe first, followed by loading into the N-lobe [13–15].

There is a lot of data that the metabolism of several trace elements (e.g. chromium and iron) is altered in diabetes mellitus and that these nutrients might have specific roles in the pathogenesis and progress of this disease [16,17]. Consequently, there is increasing interest in the role and effectiveness of nutritional supplements in the prevention and treatment of some diseases (e.g. diabetes, anaemia).

This study investigates the combined effect of dietary Cr3 complex supplementation and Fe deficiency on the Fe and Cr status in animal model.

2. Materials and methods

2.1. Animals and diets

36 six-week-old female Wistar rats were obtained from the Department of Toxicology, Poznań University of Medical Sciences, Poland. The study was conducted at the Department of Human Nutrition and Hygiene (Poznań, Poland) and was approved by the Animals Bioethics Committee of Poznań (No. 60/2013). After adaptation to laboratory conditions, the rats were divided into six groups of approximately equal initial mean body weight, i.e. 130.5 g. The animals were housed in single cages, at controlled temperature, photoperiod and air humidity (19–22 °C, 12-h light/dark cycle, 55–60% ambient air humidity). For 6 weeks all the groups were fed semi-purified AIN–93 M diets [18] (Table 1), modified according to the two-factorial experimental design.

The study was carried out on 36 healthy female Wistar rats, which were divided into 6 experimental groups (six animals in each) with different Fe level (deficient 5 mg kg^{-1} − 10% RDA, recommended (adequate) 45 mg kg^{-1} − 100% RDA). Simultaneously, their diets were supplemented with Cr(III) at doses of 1, 50 and 500 mg kg^{-1}, given as $[Cr_3O(O_2CCH_2CH_3)_6(H_2O)_3]\cdot NO_3$, also known as Cr3: the control group (C1) − Fe 45 mg kg^{-1}, Cr 1 mg kg^{-1} (ca. Fe; group C50 − Fe 45 mg kg^{-1}, Cr 50 mg kg^{-1}; group C500 − Fe 45 mg kg^{-1}, Cr 500 mg kg^{-1}; group D1- Fe 5 mg kg^{-1}, Cr 1 mg kg^{-1}; group D50 − Fe 5 mg kg^{-1}, Cr 50 mg kg^{-1}, group D500 − Fe 5 mg kg^{-1}, Cr 500 mg kg^{-1}. Female rats consumed an average of 15 g diet per day, equivalent to ~0.22 mg kg^{-1} b.w. (D groups) and ~4 mg kg^{-1} b.w. (C groups) per day of Fe and 0.1; 3.3; 30 mg kg body weight (b.w.) day^{-1} for Cr(III).

The rats were allowed free access to food and distilled water throughout the whole experiment. The feed intake was measured daily, while body weight gains were monitored weekly.

2.2. Test chemicals

Iron(III) citrate (reagent grade, 16.6% Fe) was purchased from Sigma-Aldrich, Poland. The chromium(III) complex with propionic acid (Cr3), in the form of nitrate salt (chemical formula $[Cr_3O(O_2CCH_2CH_3)_6(H_2O)_3]NO_3$ was synthesised in a laboratory at the Department of Technology and Instrumental Analysis, Poznań University of Economics, Poland, applying the method described by Earnshaw et al. (1966). The Cr3 complex was found to contain 21% of elemental Cr. The content was determined with the AAS method (AAS-3 spectrometer with BC correction, Zeiss, Germany).

2.3. Data collection

At the end of the experiment, after 12-h starvation, the rats were euthanised by asphyxiation with CO_2. Blood was collected into tubes, tissue samples (liver, kidneys, heart, spleen, pancreas, ovaries) were harvested, weighed, and frozen at −20 °C.

2.4. Laboratory analyses

2.4.1. Blood morphology

The haemoglobin (Hb) and haematocrit (HCT) were measured with an automated blood analyser (Sysmex K-1000, TAO Medical Electronics Co., Kobe, Japan). The red blood cell count (RBC) and other blood morphology indices [mean corpuscular volume (MCV), mean corpuscular haemoglobin (MCH), mean corpuscular haemoglobin concentration (MCHC), white blood cell count (WBC), platelets (PLT),

Table 1
The chemical composition of experimental diets (mean ± SD).

Component	Unit	Content of compound in experimental diets					
		C1	C50	C500	D1	D50	D500
Energy	MJ 100 g^{-1}	1.82 ± 0.00	1.83 ± 0.03	1.89 ± 0.06	1.92 ± 0.05	1.80 ± 0.04	1.87 ± 0.03
Fat	%	7.46 ± 0.05	7.22 ± 0.08	7.26 ± 0.31	7.36 ± 0.24	6.62 ± 0.29	7.19 ± 0.10
Protein	%	17.12 ± 0.10	17.17 ± 0.14	17.27 ± 0.24	17.64 ± 0.35	17.90 ± 0.13	17.22 ± 0.16
Carbohydrates	%	63.46	63.67	63.45	63.55	64.12	63.78
Dry mass	%	90.47 ± 0.05	90.54 ± 0.22	90.26 ± 0.08	90.14 ± 0.26	89.40 ± 0.03	89.70 ± 0.14
Ash	%	2.47 ± 0.04	2.48 ± 0.11	2.32 ± 0.50	2.45 ± 0.08	2.77 ± 0.05	2.63 ± 0.12
Ca	g kg^{-1}	4.96 ± 0.13	5.16 ± 0.13	5.02 ± 0.11	5.00 ± 0.19	5.10 ± 0.11	5.02 ± 0.37
Mg	mg kg^{-1}	441.42 ± 8.99	473.12 ± 1.44	511.73 ± 17.55	478.69 ± 15.46	473.73 ± 56.11	529.95 ± 13.13
Fe	mg kg^{-1}	58.05 ± 0.70	57.09 ± 2.83	59.13 ± 1.98	3.43 ± 0.38	3.30 ± 1.08	3.03 ± 0.59
Zn	mg kg^{-1}	52.51 ± 1.60	50.71 ± 1.90	52.41 ± 2.02	49.26 ± 9.70	45.90 ± 7.51	44.41 ± 5.66
Cu	mg kg^{-1}	5.45 ± 0.94	4.43 ± 0.15	5.93 ± 0.79	5.11 ± 0.88	5.53 ± 0.90	5.51 ± 0.60
Cr	mg kg^{-1}	1.24 ± 0.23	50.04 ± 6.48	425.14 ± 10.28	1.69 ± 0.12	48.89 ± 2.00	459.14 ± 24.42