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Chromium: Is It Essential and Is It Safe?

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Elemental chromium (Cr) was discovered in crocoite, a mineral with a deep-orange red color, by Vaquelin in 1798 [1]. Schwartz and Mertz [2] in 1959 were the first to report Cr was an essential element in rats while in 1977 Jeejebhoy et al. [3] showed it was essential in humans. Many research studies were conducted with Cr over the years [4] but the main focus was its relationship with diabetes mellitus [5]. While the evidence supporting an anti-diabetic role for Cr appeared strong it was still far from definitive [6]. The two main forms of chromium are the trivalent Cr^{III} (chromium III) and the hexavalent form Cr^{VI} (chromium VI). Of these, Cr^{III} is the most stable oxidation state found in living organisms but unable to cross cell wall membranes easily [7]. Complexing with certain organic ligands such as picolinic acid, however, allowed Cr^{III} to be readily absorbed by cell membranes [8]. A recent paper by Doddigarta and co-workers [9] showed that male Wistar rats fed a high carbohydrate diet supplemented with chromium picolinate (CrPlc) and melatonin, given individually or in combination, prevented the development of insulin resistance and type 2 diabetes. A series of studies by Anderson's group in the 1990's [10-12] used a low-Cr diet when feeding rats 55% sucrose, 15% lard, 25% casein plus vitamins, and minerals. A close examination of these studies by Bona et al. [13] questioned whether such diets were low in chromium as based on their calculations the rats were provided with 10 times higher levels of Cr per kg body weight than recommended for humans. According to National Academy of Science an adequate intake (AI) for chromium is 35 µg/day for men and 25 µg/day for women [14]. Using carefully controlled metal-free conditions (including plastic cages); Bona et al. [13] fed male Zucker lean rats over 6 months an AIN-93 G diet supplemented with 200 µg and 1000 µg Cr/kg. None of the diets, including those supplemented with Cr, had any effect on body composition, glucose metabolism or insulin sensitivity. These results raised serious concerns as to whether Cr^{III} was actually essential. A review of previous papers by Yoshida et al. [15] also questioned whether Cr was an essential trace element. The amount of Cr provided to experimental animals far exceeded the daily human intake of 20-80 µg/day and was closer to a pharmacological dose. Based on these results they also questioned whether Cr was indeed an essential trace element. After an extensive of the literature, the European Food Safety Authority determined that Cr should no longer be considered essential for humans or animals [16].

In addition to the controversy surrounding the essential status of Cr, the safety of Cr has also become an important issue. Of the two forms of Cr, the hexavalent form, Cr^{VI}, has long been known to be toxic and cancinogenic. In the 19th century, Scottish workers handling hexavalent chromium were found to develop nose cancers [17]. Later reports in Germany in the 1930's reported a high incidence of lung cancer in workers exposed to this form chromium which clearly established Cr^{VI} as a significant occupational hazard [18]. The toxicity of Cr^{VI} gained notoriety in the book and subsequent movie *Erin Brockovitch*, released in 2000, that it was a major contaminant in the drinking water of the town of Hinckley in California responsible for a cluster of illnesses and cancers. A later study by Kirpnick-sohol and co-workers in 2006 [19] reported that the both the contaminant Cr^{VI} and nutritional supplement Cr^{III} caused large scale and irreversible genome damage in yeast and mice when ingested in drinking water. A recent study in Australia by Wu and co-workers [20] raised concerns regarding the safety of nutritional supplements containing Cr^{III}. Such supplements are widely consumed for treating such metabolic disorders as insulin resistance, type 2 diabetes and also as muscle development agents. Using a combination of X-ray fluorescence microscopy (XFM) and X-ray absorption near edge structure (XANES) studies, Wu et al. [20] found that Cr^{III} injected into mice fat cells (adipocytes) was oxidized into the carcinogenic forms of chromium, Cr^{VI} and Cr^{V}. The long -latency time of Cr-induced cancers in humans makes it difficult to extrapolate from animal studies to humans. However, these researchers strongly recommended epidemiological studies be conducted to determine the cancer risk of Cr^{III} supplements. Based on the scientific data, there is clear evidence for removing chromium as an essential element for humans and animals. In addition, the ability of Cr^{III} to be converted to the toxic form of Cr^{VI} requires new regulations to protect the public from exposure to Cr.

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