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8

9 Chromium

10 Introduction

11 In ionic form chromium exists in many valence states. Trivalent chromium (III) is the
 12 most stable form and the principal form of chromium found in foods and supplements.
 13 It is ubiquitous in nature, occurring in air, water, soil and biological materials. Hexa-
 14 valent chromium (VI) makes chromates and dichromates, which are strongly oxidizing
 15 and transverse biological membranes. Hexavalent chromium compounds occur only
 16 rarely in the environment and are almost always man-made. They are toxic, mutagenic
 17 and environmental contaminants.

18

19 Dietary sources and intake

20 Analysis of chromium in foods requires special sampling procedures to avoid
 21 chromium contamination from the environment (air, stainless steel, etc.). Old data on
 22 chromium contents of foods should therefore be used with care. Fish, whole grain
 23 products, nuts, pulses and spices along with processed meats, are the good sources,
 24 while most other foods have low concentrations (< 100 µg/kg). Foods high in simple
 25 sugars, such as soft drinks and table sugar, are not only low in chromium content, but
 26 also promote chromium losses (Kozlovsky et al 1986). Analysed or estimated intakes
 27 of chromium in the diet of the Nordic countries are scarce, but are in the range 20-160
 28 µg/day (Jorhem et al 1998). Many food supplements contain chromium in doses from
 29 50-100 µg per serving unit.

30

31

32 Physiology and metabolism

33 The absorption of trivalent chromium from the diet is low, 0.4-2.5 % (Lukaski et al
 34 1999). The element is mainly excreted via urine, with only small amounts being
 35 eliminated in sweat and bile. Organic chromium compounds are absorbed more
 36 efficiently but are rapidly excreted via bile. Simultaneous ascorbate administration
 37 increases chromium uptake both in humans and animals. Chromium absorption is also
 38 higher in both zinc- and iron-deficient animals.

39

40 The exact biological function of chromium has not yet been determined. Experimental
 41 chromium deficiency in animals results in reduced glucose tolerance in spite of normal
 42 insulin levels. Other deficiency signs in animals include impaired growth, elevated
 43 serum cholesterol and triglycerides, increased incidence of aortic plaques, corneal
 44 lesions and decreased fertility and sperm count.

45

46 Chromium is considered to be a cofactor for insulin, possibly through influencing
 47 membrane receptors. A low molecular weight chromium-binding substance is believed
 48 to be involved in the process (Sun et al 2000). It has also been suggested that
 49 chromium influences carbohydrate, lipid and protein metabolism via its effect on
 50 insulin action.

51 Three cases have been reported of possible chromium deficiency in humans after long-
52 term, parenteral nutrition (Jeejeebhoy et al 1977, Freund et al 1979, Brown et al 1986).
53 The symptoms observed were impaired glucose tolerance and glucose utilization,
54 weight loss, neuropathy, elevated plasma fatty acids, depressed respiratory quotient
55 and abnormalities in nitrogen metabolism. The symptoms improved after chromium
56 supplementation (200 µg/day). However, the reported concentrations of chromium in
57 blood and urine were above those considered normal even before the supplementation
58 was initiated. As with foodstuffs, analytical data on chromium concentrations in
59 biological specimens produced before approximately 1980 should be regarded with
60 caution, as possible contamination in sampling and processing may have led to
61 spuriously high values of chromium (Lukaski 1999). The lack of reliable biomarkers
62 for chromium status combined with the absence of clear-cut chromium deficiency
63 conditions are the main reason for the current uncertainties about the biological
64 significance of chromium as an essential trace element (Lukaski 1999).

65

66 A number of chromium supplementation studies have been published investigating
67 effects on insulin and blood glucose levels. (Althuis et al. 2002, Balk et al. 2007). In
68 20 randomized controlled trials (RCTs) included in a meta-analysis from 2002 (Althuis
69 et al. 2002), no effect of chromium on glucose or insulin concentrations was seen in
70 non-diabetic subjects. Although some studies suggest beneficial effects of chromium
71 supplementation in individuals with type 2 diabetes (Balk et al. 2007), the results are
72 yet inconclusive, and further studies are needed in order to make any claims about
73 chromium supplementation in this group (Althuis et al. 2002, Balk et al. 2007, Mullee
74 et al. 2012)

75

76 There are also quite a few studies looking at chromium supplementation in relation to
77 body composition and lipid metabolism (Mullee et al. 2012) Possible benefits to total
78 and LDL cholesterol concentrations at supplementation of 200 to 240 µg
79 chromium/day have been suggested (Mullee et al. 2012). However, the number of
80 studies in this area is still limited and the studies which the suggestion is based on are
81 defined as being at high risk of bias (Mullee et al. 2012). The effects of chromium
82 supplementation on body composition therefore remain inconclusive (Mullee et al.
83 2012).

84

85 **Requirements and recommended intake**

86 As described above, the role of chromium as an essential nutrient is still unclear. If
87 chromium is an essential trace element it must have a specific role in an enzyme
88 cofactor, and a deficiency should produce a disease or impairment of function.
89 Methods for evaluating chromium status are missing. Furthermore, there is still
90 uncertainty about how chromium deficiency in humans manifests itself, and the
91 requirement for chromium is accordingly not known.

92

93 The EU SCF (1993) stated that “Since data on the essentiality and metabolism of
94 chromium are so sparse, the Committee is unable to specify any requirements”.
95 The UK Committee on Medical Aspects of Food Policy (1991) calculated a theoretical
96 requirement for adults from balance studies of 23 µg/day by using regression equations
97 and mentioned that a safe and adequate level of intake is believed to lie above 25
98 µg/day for adults.

99

100 The US Food and Nutrition Board (2001) estimated Adequate Intakes (AI) for
101 chromium for different age groups based on calculations of well-balanced diets: for
102 men (19-50 years) 35 µg/day and for women 25 µg/day.

103

104 Authors of a scientific report submitted to EFSA in 2012 came to the conclusion that
105 evidence was still inadequate for setting dietary reference values for chromium
106 (Mullee et al. 2012). The conclusion was based on a systematic review including
107 relevant publications from January 1990 to September/October 2011.

108

109 The Nordic Recommendations of 2004 did not include recommendations for
110 chromium intake. As very few relevant new human studies have been conducted since
111 then, requirements are also impossible to establish this time and accordingly,
112 recommendations have not been set for any age group. Data are also lacking on the
113 requirements during pregnancy. The US Food and Nutrition Board (1991) suggests an
114 increase of 5 µg/day during pregnancy.

115

116 Within Europe, chromium concentration of human milk range between 0.09 to 19.8
117 µg/L, (Mullee et al. 2012). The chromium concentration seems to be independent of
118 maternal chromium intake (Anderson et al 1993, Wappelhorst et al. 2002,
119 Mohamedshah et al 1998). A study on lactating Finnish mothers found an average
120 concentration of 0.4 µg/L (range 0.2-0.7) (Kumpulainen and Vuori 1980).

121

122 **Upper intake levels and toxicity**

123 Chromium III has low toxicity, no adverse effects were observed at intakes of 1000-
124 2000 µg/day. Due to the lack of adequate data, the EU Scientific Committee for Food
125 (2003) has not suggested a Tolerable Upper Intake Level (UL) for chromium (III)
126 salts. The same conclusion was reached by the US Food and Nutrition Board (2001)
127 and the UK Expert Group on Vitamins and Minerals (2003).

128

129 Chromium picolinate, a trivalent chromium compound popular in many food
130 supplements, is being discussed because of possible adverse health effects. It may
131 influence the central nervous system and thus behaviour (Reading 1996). One study
132 has suggested kidney damage as a result of high doses of chromium supplementation
133 (Cerulli et al 1998). Potential clasterogenicity is being discussed (Bagchi et al 2002). It
134 is still unclear whether these effects are due to the picolinate fraction or to the higher
135 extent of chromium absorption. The UK Food Standards Agency (2003) advises
136 people not to take chromium picolinate and has consulted on a proposal to ban the use
137 of this form of chromium in the manufacture of food supplements because there is a
138 chance that it could cause cancer. A paper from 2004 (Berner et al) evaluated one
139 particular brand of chromium picolinate and found it safe.

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