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REVIEW ARTICLE

Chromium (III) Picolinate- A Review

Dhumansure Rajkumar[1], Amit Pawar[2], Tabbasum Shikalgar[2], N. S. Naikwade[2], Karnakumar V Biradar[3], K. Sreenivasa Rao[3]

[1]K.R.E.S's Karnataka college of Pharmacy, Manhalli Road, Bidar, Karnataka
[2]Appasaheb Birnale College of Pharmacy, Sangli, 416416, Maharashtra
[3]R.R.K, Societies college of Pharmacy, Naubad Bidar, Karnatka

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ABSTRACT

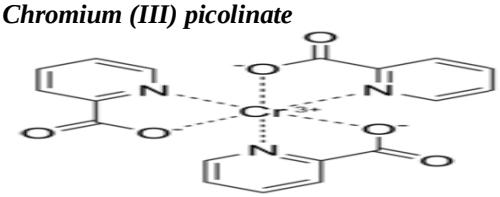
Chromium picolinate is a widely available nutritional supplement. Chromium potentiates insulin action and thus, influences carbohydrate, lipid and protein metabolism. Information on dietary intakes of chromium is limited. The suggested beneficial effects associated with increased chromium intake appear to be a result of its effect on insulin sensitivity.

Key words: Chromium picolinate, diet, insulin sensitivity.

INTRODUCTION

Chromium (III) picolinate is a chemical compound sold as a nutritional supplement to prevent or treat chromium deficiency. Another is Chromium polynicotinate, and six forms of Chromium are sold for this purpose. This bright-red coordination complex is derived from chromium (III) and picolinic acid. Small quantities of chromium are needed for glucose utilization by insulin in normal health, but deficiency is extremely rare and has only been observed in hospital patients on long-term defined diets. No biochemical basis for the human body's need for chromium has been identified. Chromium (III) picolinate has been described as a "poor choice as a nutritional supplement".

Fig 1: ***Chromium (III) picolinate***



Natural occurrence

Chromium is ubiquitous in nature, occurring in air, water, soil and biological materials over a great range of concentrations. Almost all of the sources of chromium in the earth's crust are in the trivalent state, naturally occurring chromium compounds in the hexavalent state are rare. Hexavalent chromium compounds are thus, man-made food products (WHO, 1988).

Occurrence in food, food supplements and medicines

Most of the chromium ingested with food is in the trivalent form. Early data (pre-1980) on the chromium concentration in foods are flawed, due to the difficulties encountered in contamination control during sampling, sample pre-treatment and analysis (Nordic Council, 1995). Recent data indicate that staple foods are particularly low in chromium. Processed meats, whole grain products, pulses and spices are the best sources of chromium, whilst dairy products and most fruit and vegetables, contain only small amounts. Most of the total chromium in foods derives from food processing in stainless steel containers and processors, which typically contain 18% chromium. Homogenisation of fresh meat in a food processor equipped with standard stainless steel blades almost doubles the chromium concentration of the meat (Kumpulainen *et al.*, 1980). Thus, canned and other processed foods, particularly acidic foods such as fruit juices, are clearly higher in chromium than fresh foods, with the exception of refined sugar which is very low in chromium, compared to brown sugar and molasses (Offenbacher and Pi-Sunyer, 1983). Some brands of beer are very good sources of chromium and a half pint serving may contain as much as 20 g or approximately two-thirds of the normal dietary chromium intake (Anderson and Bryden, 1983). However, some brands of beer

***Co*Corresponding Author:** Karnakumar V. Biradar**, Email:** bidarkaran@gmail.com, **Phone No:** +91- 9242302070

contain much lower concentrations of chromium and the average chromium intake per half-pint of beer is approximately 7% of the minimum suggested safe and adequate intake (National Research Council, 1989).

Drinking water

The concentration of chromium in uncontaminated waters is extremely low, <1 g/l (<0.02 mol/l). Industrial activities, such as tanning of leather, the steel industry and sites such as landfills, refuse tips and car scrap yards may cause contamination of the drinking water.

Licensed medicinal products for oral use

Six products containing chromium (and other nutrients) may be sold under the supervision of a pharmacist for use in malabsorptive states, conditions leading to hypoproteinaemia and perioperative nutritional support. The maximal daily doses specified in the licences are up to 200 g elemental chromium.

Food Intake and exposure

Information on dietary intakes of chromium is limited. Most of the chromium ingested with food is in the trivalent form. Chromium is not included in the nutrient databanks for dietary surveys. The most up to date information available is from analysis of samples from the 1997 Total Diet Study (TDS). This showed that the population average intake of chromium was 0.10 mg/day. This value is lower than that of 0.34 mg/day obtained from the 1994 Total Diet Study1 but is consistent with intakes from previous TDS prior to 1994. Chromium intake in 1994 was unexpectedly high due to relatively high concentrations in the oils and fats, milk, dairy products and nuts groups. It appears that this is unique to that year and is not part of a trend towards increasing intakes. Table 1 shows the concentration of chromium in each of the TDS food groups in 1997 and the intake from each group. Mean and upper level (97.5 percentile) chromium intake for adults has been estimated at 0.10 mg/day and 0.17 mg/day respectively using the 1997 TDS concentrations combined with consumption data from the 1986/87 Dietary and Nutritional Survey of British Adults. These figures are lower than those obtained from the 1994 TDS (0.30 mg/day and 0.52 mg/day respectively), which were unexpectedly high.

The 1997 Total Diet Study shows that the highest concentration of chromium is in the food group meat products followed by oils and fats, bread, nuts, miscellaneous cereals, fish, and sugar and preserves. The main contributors to dietary intake of chromium are beverages, bread, miscellaneous cereals and meat products. Chromium is present in a number of multi-mineral and/or vitamin food supplement products. As a single nutrient product it is available at levels between 200 and 600 g. Three different chromium salts are available: chromium chloride, chromium picolinate and chromium nicotinate (Kobla and Volpe, 2000). No purity or quality issues have been identified. Daily intake of chromium can vary widely, depending on the proportions of various food groups in the diet. Recent reports suggest that many diets in the US supply less than 50 g of chromium/day. In one study the content of the self-selected diets of 10 men and 22 women, collected by the duplicate portion method, on a daily basis for 7 consecutive days, was determined (Anderson and Kozlovsky, 1985); the daily intake for men was 33.3 g (mean,SEM) with a range of 22 - 48 g, and for the women 25 1 g with a range of 13 – 36 g. Four-day duplicate diets collected 6 times from 80 people aged over 10 years in Maryland, USA in 1995 and 1996 found chromium intakes ranged from 3.3 to 675.9 g/d with a mean of 43.9 g/d (Scanlon *et al.*, 1999). The self-selected diets of 23 apparently healthy, well-nourished elderly English volunteers supplied 24.5 g chromium/day (range 14 – 48 g) (Bunker *et al.*, 1984). MAFF conducted a duplicate diet study of vegetarian adults to assess exposures to various metals (MAFF, 2000). One hundred and one duplicate diet samples were collected over 7-day periods in 1997 and 1998. The mean dietary exposure to chromium was 0.1mg/day (minimum to maximum range, 0.03 - 0.26 mg/d). Beverages, including milk, account for approximately one fifth of the daily intake of chromium (MAFF, 1999). Normal cow's milk is reported to contain 5 to 15 ng chromium/ml and cows colostrums five-fold higher levels. Human breast milk has historically been reported to contain similar levels, but more recent reports indicate that breast milk contains approximately 0.3 – 0.4 ng/ml (Casey and Hambidge, 1984). In contrast an analysis of breast milk samples from 27 Austrian mothers found chromium concentrations ranged widely from <0.8 to 163 ng/ml with a median of 24.3 ng/ml (Krachler *et al.*, 2000). Chromium concentrations were higher in urban smoking mothers. Dietary intake of chromium in Southern Spain was recently measured by sampling duplicate diets (by electrothermal atomisation-atomic absorption spectrometry) for seven consecutive days in different population groups. A total of 161 duplicate diets from 23 subjects were analysed and mean levels of chromium intake ranged from

9.39 to 205.16 g/d, giving a mean chromium intake of 100 g/day (Garcia *et al.*, 2001).

Drinking water

The EPA has proposed an increase of the MCL for chromium to 100 g/l. The concentration of chromium in uncontaminated natural waters is extremely low, <1 g/l (<0.02 mol/l), thus its contribution to total dietary intake is negligible. The provisional guideline level, established by the WHO in 1992, for chromium in drinking water is 50 g/l. This is the limit in most developed countries, including the UK. The current maximum contaminant level for chromium in drinking water, set by the US Environmental Protection Agency (EPA), is also 50 g/l (Goldhaber and Vogt, 1989).

Function

Chromium is an essential nutrient that potentiates insulin action and thus, influences carbohydrate, lipid and protein metabolism. However, the nature of the relationship between chromium and insulin function has not been clearly defined. Mertz *et al.* (1974) suggested that the biologically active form of chromium (glucose tolerance factor) is a complex of chromium, nicotinic acid and possibly the amino acids glycine, cysteine and glutamic acid. Many attempts have been made to isolate or synthesise the glucose tolerance factor; none has been successful. Thus, the precise structure of the glucose tolerance factor and whether it is the biologically active form of chromium, remain uncertain. 24. Low-molecular-weight chromuim-binding substance (LMWCr) is a naturally occuring oligopeptide which has recently been proposed as the biologically active form of chromium. Its primary function is proposed to be the activation of insulin receptor tyrosine kinase in response to insulin. Chromium is essential for LMWCr to perform this function. (Vincent, 2000.) Chromium may have a biochemical function that affects the ability of the insulin receptor to interact with insulin. For example, it has been found that *in vitro*, RNA synthesis directed by free DNA is enhanced by the binding of chromium to template (Okada *et al.*, 1981); this suggests that chromium may act similarly to zinc in regulating gene expression, so it may be regulating the synthesis of a molecule that potentiates insulin action. This suggestion is supported by the finding that there is a four-hour lag period between the administration of biologically active chromium and its optimal effect on insulin action *in vivo* (Tuman and Doisy, 1977).

Deficiency

Gross chromium deficiency has not been seen in humans, although signs of chromium deficiency have been found in patients receiving long-term parenteral nutrition with infusates low in chromium. Jeejeebhoy *et al.* (1977) reported on a patient receiving long-term parenteral nutrition for three and a half years, exhibiting impaired glucose tolerance and glucose utilisation, weight loss, neuropathy, elevated plasma fatty acids, depressed respiratory quotient and abnormalities in nitrogen metabolism. A woman given total parenteral nutrition low in chromium for five months developed severe glucose intolerance, weight loss and a metabolic encephalopathy-like state (Freund *et al.*, 1979). Both were alleviated by chromium supplementation. Brown *et al.* (1986) reported that chromium supplementation reversed the development of unexplained hyperglycaemia and glycosuria, during administration of a total parenteral nutrition regime of several months duration. All subjects in these studies exhibited impaired glucose tolerance or hyperglycaemia, with glycosuria and a refractiveness to insulin. These symptoms, it is suggested, should therefore be considered as signs of chromium deficiency.

Overview of reported beneficial effects

Extravagant claims about the benefits of chromium have been made. The suggested beneficial effects associated with increased chromium intake appear to be a result of its effect on insulin sensitivity and include muscle and strength enhancing properties, aiding weight and fat loss, delaying ageing and treating diabetes (Nielsen, 1996). Clinical studies in diabetics have shown that supplementing the diet with chromium can decrease fasting blood glucose levels, improve glucose tolerance, lower insulin levels and decrease total cholesterol and triglyceride levels while increasing HDL-cholesterol levels (Mooradian *et al.*, 1994). In a double-blind, placebocontrolled, randomised trial in China, Anderson *et al.* (1997a) supplemented adults with type II diabetes with placebo, 200 g chromium or 1000 g chromium. Over 4 months there were pronounced and significant decreases in fasting blood glucose and insulin and 2-hour blood glucose and insulin in the 1000 g group. Evidence relating to the other claims is equivocal (Nielsen, 1996) but it has been suggested that initial chromium status of study participants may be an important mediating factor and benefits will only be seen in those who have marginal or poor chromium status (Vincent, 2000).

Interactions

Chromium interacts with iron in binding to transferrin. Consequently, chromium has been shown to impair iron metabolism and storage. Significant reductions in serum iron, total iron-binding capacity, ferritin and haemoglobin have been reported (Ani and Moshtaguie, 1992). Haemochromatosis, is a pathological condition characterised by an overly high gastrointestinal absorption of dietary iron, leading to saturation of transferrin with iron and iron accumulation in the liver. In this condition, transferrin cannot bind absorbed chromium (III) (Lim *et al.*, 1983). However, there is no evidence of haemochromatosis causing any ill health effects due to low circulating chromium levels.

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