the Cobalt Development Institute

Essentiality of Cobalt Compounds

Provided to ECHA through Public Consultation (15th June to 14th September 2011) Regarding Prioritisation of Cobalt Salts

NOTE: this document is a working draft and should therefore be treated accordingly

Overview: Cobalt Essentiality Human and Non-Human Animals

Introduction

Cobalt is a natural metallic element found in combination with other naturally occurring metallic and mineral elements. Therefore cobalt is present in airborne dust, seawater, and soil. It is emitted into the environment from natural events such as volcanic eruptions and forest fires, and from anthropogenic sources such as burning fossil fuels or processing cobalt ores and compounds in refining facilities. The main source of exposure to cobalt for the general population is through their diet and most of the cobalt ingested is inorganic. Although there is variability depending on the type of diet, humans ingest 0.1-1.0 µg Co/kg body weight on a daily basis. Relatively high levels of cobalt are found in shellfish, animal livers, vegetables, dried fruits, and nuts. Ingestion of cobalt within normal dietary ranges has not been associated with adverse health consequences. While elemental cobalt in ionic form is essential for some plants and animals, it is the cobalt-containing Vitamin B_{12} (cobalamin) that is required by humans and non-ruminant animals. Cobalt has also been identified in at least eight other non-vitamin B_{12} enzymes that are essential for vital biochemical processes in both plant and animal species (Kobayashi and Shimizu (1999).

Vitamin B_{12} is Essential for Humans

Humans and other non-ruminant mammals are unable to synthesize significant quantities of Vitamin B_{12}. In the human diet, Vitamin B_{12} is obtained mainly from animal products where it accumulates from bacterial synthesis in the animal gut and is subsequently absorbed. For humans, Vitamin B_{12} is an essential cofactor in the synthesis of red blood cells and nucleic acids, and in enzymatic pathways that lead to the degradation of fatty acids and amino acids. Vitamin B_{12} deficiency in humans is manifested by macrocytic megaloblastic anaemia and neurological deficits due to demyelination of nerve tracts in the central and peripheral nervous system. The estimated total body content of Vitamin B_{12} is believed to be between 2.0-2.5 mg. Cobalt composes about 4.3% of the weight of Vitamin $B_{12,}$ so the body burden of cobalt contributed by Vitamin B_{12} is about 0.11mg. The recommended daily dietary allowance of Vitamin B_{12} for adults is 2 µg/day. Vitamin B_{12} has no observable adverse effect from intake when consumed parenterally at 1000 µg twice weekly for three years. There is considerable experience and clinical evidence of safety with oral intakes of 3000 µg per day. However, no clear health benefit has been reported for non-deficient humans ingesting these large amounts.

Elemental Cobalt is Essential for Some Plant and Animal Species

Non-human mammals also are unable to synthesize their own Vitamin B_{12}. Thus non-ruminant animals have a dietary requirement for Vitamin B_{12}. Ruminant animals rely on the bacteria living in the rumen to synthesize Vitamin $B_{12,}$ from inorganic cobalt which the animal then absorbs. Horses, rabbits and fowl are able to absorb Vitamin B_{12} from bacteria living in their hindgut. Ruminants, horses, rabbits, and fowl have a dietary requirement for inorganic cobalt. Ruminal

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biosynthesis of Vitamin B_{12} can be inefficient and is dependent on the amount of cobalt in the diet. Supplementation of dietary intake with inorganic forms of cobalt that are easily solubilized in the rumen increases the synthesis of Vitamin B_{12}. Cobalt oxides appear to have less nutritive value than do the more soluble salts $CoCO_3$ and $CoSO_4$. Cobalt deficiency in the diet of ruminants, horses rabbits, and fowl is manifested by a concomitant Vitamin B_{12} deficiency. The health effects include infertility, increased perinatal mortality, anaemia, fatty liver, and decreased ability to fight disease. Cobalt toxicity in animals is reported to be rare, most likely because the levels of dietary exposure, even with supplementation, is well below toxic levels.

Cobalt deficiencies have been shown to result in reduced growth and/or blood related effects in a variety of fish species including salmon (Halver 1957), brown trout (Phillips et al. 1964) and channel catfish (Dupree 1966). Japanese eels were also found to require cobalt (vitamin B_{12}) for normal growth (Arai et al. 1972). Cobalt, in the form of Vitamin B_{12}, is frequently added to fish feeds as part of a multivitamin premix.

Cobalt has also been shown to be essential for nitrogen fixation by free-living bacteria and blue-green algae. Unicellular green algal species have also been shown to require cobalt and cobalt is included as a micronutrient in the OECD method 201 standard algal culture medium (OECD 1984). In higher plants, cobalt has also been shown to be an essential element required for nitrogen fixation in legumes and is often added to soils in the form of inorganic fertilizers.

Deficiency versus Toxicity

While humans require Vitamin B_{12} rather than inorganic cobalt it is clear that cobalt ingested in low levels such as from food sources is not associated with adverse health outcomes. That humans are continuously exposed to bioavailable (absorbable) cobalt is confirmed through bio-monitoring studies that show a range of measurable amounts (0.2-2 µg Co/L) are consistently present in urine. The total body pool of cobalt is about 1.5mg and cobalt does not tend to bioaccumulate. High repetitive oral doses of cobalt can be associated with effects on red blood cells, thyroid, and heart. These effects indicate that systemic exposures to cobalt have thresholds below which toxicity is not expected. While low levels of Vitamin B_{12} intake can be associated with diseases of deficiency (see discussion above) the ingestion of large amounts of Vitamin B_{12} has not been reported to be toxic to humans.

For ruminants, rabbits, horses, and fowl insufficient levels of cobalt in their diets results in Vitamin B_{12} deficiency. Cobalt toxicity in these animals is rare because concentrations of cobalt normally present in animal diets are lower than those needed to cause toxicity and maximum tolerable levels (for diet) are set to avoid toxicity. Characteristic signs of chronic overexposure to cobalt for most species are reduced feed intake and body weight, emaciation, anaemia, hyperchromemia, debility, increased liver cobalt and increased disease susceptibility.
Considering dietary exposure, veterinary and agricultural experience with animals, as well as, experience with the general human population, indicates cobalt toxicity/or deficiency is based on a threshold level.

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