Molybdenum

Molybdaenum, from Ancient Greek Μόλυβδος *molybdos*, meaning *lead*), is a Group 6 chemical element with the symbol *Mo* and atomic number 42. The free element, which is a silvery metal, has the sixth-highest melting point of any element. It readily forms hard, stable carbides, and for this reason it is often used in high-strength steel alloys. Molybdenum does not occur as the free metal in nature, but rather in various oxidation states in minerals. Industrially molybdenum compounds are used in high pressure and high temperature applications, as pigments and catalysts.

Most molybdenum compounds have low water solubility, but the molybdate ion MoO_4^{2-} is soluble and will form if molybdenum-containing minerals are in contact with oxygen and water. Recent theories suggest that the release of oxygen by early life was important in removing molybdenum from minerals into a soluble form in the early oceans, where it was used as a catalyst by single-celled organisms. This sequence may have been important in the history of life, because molybdenum-containing enzymes then became the most important catalysts used by some bacteria to break into atoms the atmospheric molecular nitrogen, allowing biological nitrogen fixation. This, in turn allowed biologically driven nitrogen-fertilization of the oceans, and thus the development of more complex organisms.

At least 50 molybdenum-containing enzymes are now known in bacteria and animals, though only the bacterial and cyanobacterial enzymes are involved in nitrogen fixation. Due to the diverse functions of the remainder of the enzymes, molybdenum is a required element for life in higher organisms (eukariotes), though not in all bacteria.

The most important use of the molybdenum in living organisms is as a metal heteroatom at the active site in certain enzymes. In nitrogen fixation in certain bacteria, the nitrogenase enzyme, which is involved in the terminal step of reducing molecular nitrogen, usually contains

molybdenum in the active site (though replacement of Mo with iron or vanadium is also known). The structure of the catalytic center of the enzyme is similar to that in iron-sulfur proteins, it incorporates a Fe_4S_3 and $MoFe_3S_3$ clusters.

In 2008, evidence was reported that a scarcity of molybdenum in the Earth's early oceans was a limiting factor in the further evolution of eukaryotic life (which includes all plants and animals) as eukaryotes cannot fix nitrogen and must acquire it from prokaryotic bacteria. The scarcity of molybdenum resulted from the relative lack of oxygen in the early ocean. Oxygen dissolved in seawater helps dissolve molybdenum from minerals on the sea bottom. However, although oxygen may promote nitrogen fixation via making molybdenum available in water, it also directly poisons these nitrogenase enzymes, so that organisms which continued to fix nitrogen in aerobic conditions were required to isolate their nitrogen-fixing enzymes in heterocysts, or similar structures.

Though molybdenum forms compounds with various organic molecules, including carbohydrates and amino acids, it is transported throughout the human body as MoO2−4.At least 50 molybdenum-containing enzymes were known by 2002, mostly in bacteria, and their number is increasing with every year; those enzymes include aldehyde oxidase, sulfite oxidase and xanthine oxidase. In some animals, and in humans, the oxidation of xanthine to uric acid, a process of purine catabolism, is catalyzed by xanthine oxidase, a molybdenum-containing enzyme. The activity of xanthine oxidase is directly proportional to the amount of molybdenum in the body. However, an extremely high concentration of molybdenum reverses the trend and can act as an inhibitor in both purine catabolism and other processes. Molybdenum concentrations also affect protein synthesis, metabolism and growth.

In animals and plants these enzymes use molybdenum bound at the active site in a tricyclic molybdenum cofactor. All molybdenum-using enzymes so far identified in nature use this cofactor, save for the

phylogenetically ancient nitrogenases, which fix nitrogen in some bacteria and cyanobacteria. Molybdenum enzymes in plants and animals catalyze the oxidation and sometimes reduction of certain small molecules, as part of the regulation of nitrogen, sulfur and carbon cycles.

Human dietary intake and deficiency

The human body contains about 0.07 mg of molybdenum per kilogram of weight. It occurs in higher concentrations in the liver and kidneys and in lower concentrations in the vertebrae. Molybdenum is also present within human tooth enamel and may help preventing its decay. Pork, lamb and beef liver each have approximately 1.5 parts per million of molybdenum. Other significant dietary sources include green beans, eggs, sunflower seeds, wheat flour, lentils and cereal grain.

The average daily intake of molybdenum varies between 0.12 and 0.24 mg, but it depends on the molybdenum content of the food. Acute toxicity has not been seen in humans, and the toxicity depends strongly on the chemical state. Studies on rats show a median lethal dose (LD_{50}) as low as 180 mg/kg for some Mo compounds. Although human toxicity data is unavailable, animal studies have shown that chronic ingestion of more than 10 mg/day of molybdenum can cause diarrhea, growth retardation, infertility, low birth weight and gout; it can also affect the lungs, kidneys and liver. Sodium tungstate is a competitive inhibitor of molybdenum. Dietary tungsten reduces the concentration of molybdenum in tissues.

Dietary molybdenum deficiency from low soil concentration of molybdenum has been associated with increased rates of esophageal cancer in a geographical band from northern China to Iran. Compared to the United States, which has a greater supply of molybdenum in the soil, people living in these areas have about 16 times greater risk for esophageal squamous cell carcinoma.

Molybdenum deficiency has also been reported as a consequence of non-molybdenum supplemented total parenteral nutrition (complete intravenous feeding) for long periods of time. It results in high blood levels of sulfite and urate, in much the same way as molybdenum cofactor deficiency. However, presumably since pure molybdenum deficiency from this mechanism is seen primarily in adults, the neurological consequences have not been as marked as for the congenital cofactor deficiency.

Related diseases

A congenital molybdenum cofactor deficiency disease, seen in infants, results in interference with the ability of the body to use molybdenum in enzymes. It causes high levels of sulphite and urate, and neurological damage.. The cause is inability of the body to synthesize molybdenum cofactor, a heterocyclic molecule which binds molybdenum at the active site in all known human enzymes which use molybdenum.

Copper-molybdenum antagonism

High levels of molybdenum can interfere with the body's uptake of copper, producing copper deficiency. Molybdenum prevents plasma proteins from binding to copper, and it also increases the amount of copper that is excreted in urine. Ruminants that consume high amounts of molybdenum develop symptoms including diarrhea, stunted growth, anemia and achromotrichia (loss of hair pigment). These symptoms can be alleviated by the administration of more copper into the system, both in dietary form and by injection. The condition can be aggravated by excess sulfur. Copper reduction or deficiency can also be deliberately induced for therapeutic purposes by the compound ammonium tetrathiomolybdate, in which the bright red anion *tetrathiomolybdate* is the copper-chelating agent.

Tetrathiomolybdate was first used therapeutically in the treatment of copper toxicosis in animals. It was then introduced as a treatment in Wilson's disease, a hereditary copper metabolism disorder in humans;

it acts both by competing with copper absorption in the bowel and by increasing excretion. It has also been found to have an inhibitory effect on angiogenesis, potentially via the inhibition of copper ion dependent membrane translocation process involving a non-classical secretion pathway. This makes it an interesting investigatory treatment for cancer, age-related macular degeneration, and other diseases featuring excessive blood vessel deposition.

Precautions

Molybdenum dusts and fumes, as can be generated by mining or metalworking, can be toxic, especially if ingested (including dust trapped in the sinuses and later swallowed). Low levels of prolonged exposure can cause irritation to the eyes and skin. Direct inhalation or ingestion of molybdenum and its oxides should be avoided. OSHA regulations specify the maximum permissible molybdenum exposure in an 8-hour day as 5 mg/m^3. Chronic exposure to 60 to 600 mg/m^3 can cause symptoms including fatigue, headaches and joint pains.