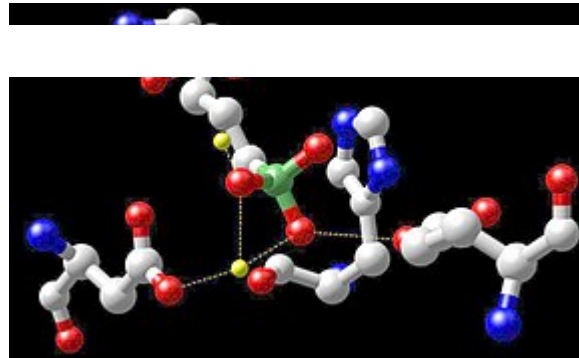


Biological role

Biochemistry

The classes of enzymes that have manganese cofactors is large and



Reactive center of arginase with boronic acid inhibitor – the manganese atoms are shown in yellow.

includes oxidoreductases, transferases, hydrolases, lyases, isomerases, ligases, lectins, and integrins. The reverse transcriptases of many retroviruses (though not lentiviruses such as HIV) contain manganese. The best-known manganese-containing polypeptides may be arginase, the diphtheria toxin, and Mn-containing superoxide dismutase (Mn-SOD).^[57]

Biological role in humans

Manganese is an essential human dietary element. It is present as a coenzyme in several biological processes, which include macronutrient metabolism, bone formation, and free radical defense systems. It is a critical component in dozens of proteins and enzymes.^[58] The human body contains about 12 mg of manganese, mostly in the bones. The soft tissue remainder is concentrated in the liver and kidneys.^[25] In the human brain, the manganese is bound to manganese metalloproteins, most notably glutamine synthetase in astrocytes.^[59]

Toxicity

Excessive exposure or intake may lead to a condition known as manganism, a neurodegenerative disorder that causes dopaminergic neuronal death and symptoms similar to Parkinson's disease.^{[25][60]}

Nutrition

Dietary recommendations

The U.S. Institute of Medicine (IOM) updated Estimated Average Requirements (EARs) and Recommended Dietary Allowances (RDAs) for minerals in 2001. For manganese there was not sufficient information to set EARs and RDAs, so needs are described as estimates for Adequate Intakes(AIs). As for safety, the IOM sets Tolerable upper intake levels (ULs) for vitamins and minerals when evidence is sufficient. In the case of manganese the adult UL is set at 11 mg/day. Collectively the EARs, RDAs, AIs and ULs are referred to as Dietary Reference Intakes (DRIs).^[61] Manganese deficiency is rare.^[62]

The European Food Safety Authority (EFSA) refers to the collective set of information as Dietary Reference Values, with Population Reference Intake (PRI) instead of RDA, and Average Requirement instead of EAR. AI and UL defined the same as in United States. For people ages 15 and older the AI is set at 3.0 mg/day. AIs for pregnancy and lactation is 3.0 mg/day. For children ages 1–14 years the AIs increase with age from 0.5 to 2.0 mg/day. The adult AIs are higher than the U.S. RDAs.^[63] The EFSA reviewed the same safety question and decided that there was insufficient information to set a UL.^[64]

Current AIs of Mn by age group and sex^[61]

Males		Females	
Age	AI (mg/day)	Age	AI (mg/day)
1–3	1.2	1–3	1.2
4–8	1.5	4–8	1.5
9–13	1.9	9–13	1.6
14–18	2.2	14–18	1.6
19+	2.3	19+	1.8
			pregnant: 2
			lactating: 2.6

For U.S. food and dietary supplement labeling purposes the amount in a serving is expressed as a percent of Daily Value (%DV). For manganese labeling purposes 100% of the Daily Value was 2.0 mg, but as of May 27, 2016 it was revised to 2.3 mg to bring it into agreement with the RDA.^{[65][66]} Compliance with the updated labeling regulations was required by 1 January 2020, for manufacturers with \$10 million or more in annual food sales, and by 1 January 2021, for manufacturers with less than \$10 million in annual food sales.^{[67][68][69]} During the first six months following the 1 January 2020 compliance date, the FDA plans to work cooperatively with manufacturers to meet the new Nutrition Facts label requirements and will not focus on enforcement actions regarding these requirements during that time.^[67] A table of the old and new adult Daily Values is provided at Reference Daily Intake.

Biological role in bacteria

Mn-SOD is the type of SOD present in eukaryotic mitochondria, and also in most bacteria (this fact is in keeping with the bacterial-origin theory of mitochondria). The Mn-SOD enzyme is probably one of the most ancient, for nearly all organisms living in the presence of oxygen use it to deal with the toxic effects of superoxide (O_2^-), formed from the 1-electron reduction of dioxygen. The exceptions, which are all bacteria, include *Lactobacillus plantarum* and related lactobacilli, which use a different nonenzymatic mechanism with manganese (Mn^{2+}) ions complexed with polyphosphate, suggesting a path of evolution for this function in aerobic life.

Biological role in plants

Manganese is also important in photosynthetic oxygen evolution in chloroplasts in plants. The oxygen-evolving complex(OEC) is a part of photosystem II contained in the thylakoid membranes of chloroplasts; it is responsible for the terminal photooxidation of water during the light reactions of photosynthesis, and has a metalloenzyme core containing four atoms of manganese.^{[70][71]} To fulfill this requirement, most broad-spectrum plant fertilizers contain manganese.

Precautions

Manganese compounds are less toxic than those of other widespread metals, such as nickel and copper.^[73] However, exposure to manganese dusts and fumes should not exceed the ceiling value of 5 mg/m³ even for short periods because of its toxicity level.^[74] Manganese poisoning has been linked to impaired motor skills and cognitive disorders.^[75]

Permanganate exhibits a higher toxicity than manganese(II) compounds. The fatal dose is about 10 g, and several fatal intoxications have occurred. The strong oxidative effect leads to necrosis of the mucous membrane. For example, the esophagus is affected if the permanganate is swallowed. Only a limited amount is absorbed by the intestines, but this small amount shows severe effects on the kidneys and on the liver.^{[76][77]}

Manganese

Hazards	
GHS hazard statements	H401
GHS precautionary statements	P273, P501 ^[72]
NFPA 704 (fire diamond) 