Copper

It is an essential trace element. The daily requirement for adult is 1.5-3 mg/ day. It is seen in muscles, liver, bone marrow, brain, kidney, heart and in hair.

Sources

Meat, liver, shellfish, nuts, whole grains and green leafy vegetables are good dietary sources of Cu. Milk is very poor in copper content (Human and cow milk are poor sources of copper ; however, breast milk has a higher copper content than does cow milk. On the other hand, the copper concentration in breast milk declines with the time of lactation). Dietary deficiency is uncommon.

Typically, 30-40% of the daily copper intake is absorbed in the GI tract. Most copper is excreted through the bile, and small amount is excreted in urine.

Functions

Cu is a key component of several enzymes that play critical functions in the body. These include:

1. Ferroxidases such as the ceruloplasmin and hephaestin involved in the oxidation of ferrous iron (Fe2+) to the ferric form (Fe3+) that is required for its intracellular storage or transport through blood.
2. Lysyl oxidase: This enzyme cross-links collagen and elastin. It is responsible for forming strong and at the same time elastic tissue connections. These tissues are used, for example, for the formation of blood vessels and the heart.
3. Tyrosinase: It is necessary for (melanin synthesis).
4. Cytochrome c oxidase
5. Dopamin β hydroxylase: hydroxylates dopamine to norepinphrine.
6. Superoxide dismutase: an antioxidant enzyme responsible for detoxifying the superoxide radical.

Deficiency

 If a deficiency does develop, anemia may be seen because of the effect on Fe metabolism. Menkes syndrome is genetic causes of Cu deficiency.

Menkes syndrome

It is a genetic disorder in which diatary copper is absorbed from GIT, but cannot be transported to blood due to the absence of an intracellular copper binding ATPase (mutation in *ATP7A* gene). The copper that has entered into the cell is not able to get out, so it accumulates. Since the copper act as a cofactor to activate certain enzymes, its deficiency can cause serious side effects with time related to the function of those copper dependent enzymes that control the development of hair, brain, bone, liver and arteries. So infant is characterized by kinky hair( due to the absence of lysyl oxidase and defective cross linking of collagen and elastin), hypopigmentation and mental retardation. Parenteral administration of Cu has been used as a treatment with varying success.

Cardiovascular disease

In copper deficiency, elastin becomes abnormal, leading to weakening of walls of major blood vessels. This favors fatal rupture of aorta wall.

Melanin

Copper is present in tyrosinase which is necessary for melanin formation. Copper deficiency thus leads to hypopigmentation.

Toxicity

Toxicity from dietary sources is rare. Wilson disease is genetic causes of Cu overload.

Wilson disease

Wilson disease is a genetic disorder in which excessive amounts of copper build up in the human body. The basic defect is in ATP7B gene in the liver. This is required for normal excretion of copper from liver cells. So in its absence, copper is accumulated in the liver, leaks into the blood; and is deposited in the brain, and therefore causes liver cirrhosis and damage to the brain tissue. The damage to the brain tissue occurs mainly at the lenticular nucleus and a typical brown ring is visible around the iris (Kayser-Fleischer Ring); therefore Wilson disease is also called hepatolenticular degeneration.

Treatment

* Life-long use of chelation therapy (d-penicillamine).
* Zinc supplementation can also be used in patients with Wilson’s disease, as it prevents the renal reabsorption of copper ions and excess Zn decreases the absorption of Cu
* Liver transplant

Copper preperations:

* Topically as antifungal, astringent agent, antioxidant, promotes collagen and elastin production, and softens the appearance of fine lines and wrinkles. Copper is also an anti-inflammatory that speeds up wound healing, meaning it's great for treating scarring, pigmentation, and redness caused by inflammation.
* Orally, copper is available in many multivitamin/mineral [supplements](https://ods.od.nih.gov/factsheets/Copper-Consumer/), in supplements that contain only copper, and in other [dietary supplements](https://ods.od.nih.gov/factsheets/Copper-Consumer/).
* Parenteral nutrition (IV).

Zinc (Zn)

Zinc is an essential trace dietary mineral. The daily requirement for adult is 10 mg/ day. Approximately 60% of zinc is stored in skeletal muscle, ∼30% in bone, ∼5% in the liver and skin, and the remaining 2–3% in other tissues.

Zinc is excreted primarily through the gastrointestinal tract, with minor loss through urinary excretion.

Sources

Food rich in zinc include meat, milk, fish, egg, nuts, and legumes. Patients with malnutritions, alcoholism, inflammatory bowel disease, and malabsorption syndromes are at increased risk of zinc deficiency. Zinc from animal foods like red meat, fish, and poultry is more readily absorbed by the body than zinc from plant foods. Person on a vegetable diet may not receive adequate amount of zinc because phytic acid (phosphate storage molecules in some plant products), found in vegetable protein such as soybean, combines with zinc and decreases its absorption.

 Note: Phytates may also bind Ca2+ and nonheme Fe. Several drugs (for example, penicillamine) chelate metals, and their use may cause Zn deficiency.

Function:

 Zinc ions are important for a variety of biological processes. It plays key roles as a structural, catalytic, and signaling component.

* Structural

Zinc finger motif is a three dimentional structural motif present in many proteins (ex: transcription proteins that interact with DNA or RNA) that binds zinc ions and forms a finger like structure in order to stabilize the protein folds.

* Catalytic

Carboanhydrase (CA), carboxypeptidase and superoxide dismutase are some examples for well-studied zinc-containing enzymes.

Ex: Carboanhydrase (CA)

 CAs are enzymes that catalyse the hydrolysis of carbon dioxide.

**H2O+CO2 ↔ HCO3− +H+**

The human CA consists of 259 amino acids. The catalytic site contains a Zn2+ ion which is coordinated by three neutral histidine (His) residues and a water molecule. The water molecule is believed to be important for structural reasons and enzymatic functionality.



* Signaling component

 Zinc is acting as a signaling mediator. For example: in the central nervous system, zinc, which is released from presynaptic neurons upon excitation into synaptic clefts, modulates synaptic transmission by binding to various transporters and receptor channels on postsynaptic neurons.

Uses:

1. Barrier creams. Zinc is present in barrier creams, for example, in creams used against nappy rash, often formulated with paraffin and cod-liver oil. Calamine lotion and creams are indicated for the treatment of pruritus, and both contain zinc oxide.
2. Treatment option for Wilson disease. Zinc is one treatment option for Wilson disease, as the zinc supplementation prevents the absorption of copper. It is important to note that zinc treatment has a slow onset time, which is crucial to take into account when switching from another therapy such as chelation therapy. Zinc acetate is usually offered to the market in an oral delivery form, mainly in capsules.
3. For the stabilization of the structure and shape of insulin.
4. To treat zinc deficiency and acrodermatitis enteropathica.
5. Zinc supplementation in humans has the potential to decrease diarrhea mortality in children as well as the incidence of infections and to improve immune functions.

### Immune-booster as in common cold

1. Sexual impotence: zinc may [increase testosterone levels](https://www.hims.com/blog/how-to-increase-testosterone), [improve blood flow to the genital area](https://www.hims.com/blog/the-best-ways-to-improve-blood-flow-to-your-penis) and enhance sexual function and satisfaction in both men and women.

Zinc deficiency

many symptoms caused by zinc deficiency have been described, including growth retardation, hypogonadism, skin abnormalities, and mental lethargy persistent diarrhea, alopecia, taste disorders, immune insufficiency, brain dysfunctions, impairment of wound healing, loss of appetite, chronic inflammation, liver disease, and neuropsychological changes such as emotional instability, irritability, and depression.

Note: Severe deficiency is seen with a defect in the intestinal transporter for Zn that results in the malabsorption disorder acrodermatitis enteropathica (inherited form of zinc deficiency results in improper enteral zinc absorption). Symptoms include rashes, slowed growth and development, diarrhea, and immune deficiencies. Vision problems may also occur because Zn is needed in the metabolism of vitamin A. Treatment: Zinc supplement.

Zinc toxicity

Continuous zinc supplementation is generally safe, however higher doses should be limited to short term use due to an increased risk of gastrointestinal adverse effects, copper deficiency, reduced immunity, anemia, and genitourinary complications with long term use.

Treatment:

* dimercaprol.
* d-pencillamine
* Chelation with calcium disodium edetate (CaNa2EDTA)