Zinc

Zinc is an essential mineral perceived by the public today as being of "exceptional biologic and public health importance", especially regarding prenatal and postnatal development. Zinc deficiency affects about two billion people in the developing world and is associated with many diseases. In children, deficiency causes growth retardation, delayed sexual maturation, infection susceptibility, and diarrhea. Enzymes with a zinc atom in the reactive center are widespread in biochemistry, such as alcohol dehydrogenase in humans. Consumption of excess zinc can cause ataxia, lethargy and copper deficiency.

Biological role

Zinc is an essential trace element for humans and other animals, for plants and for microorganisms. Zinc is found in nearly 100 specific enzymes (other sources say 300), serves as structural ions in transcription factors and is stored and transferred in metallothioneins. It is "typically the second most abundant transition metal in organisms" after iron and it is the only metal which appears in all enzyme classes.

In proteins, Zinc ions are often coordinated to the amino acid side chains of aspartic acid, glutamic acid, cysteine and histidine. The theoretical and computational description of this zinc binding in proteins (as well as that of other transition metals) is difficult.

Between 2 and 4 grams of zinc are distributed throughout the human body. Most zinc is in the brain, muscle, bones, kidney, and liver, with the highest concentrations in the prostate and parts of the eye. Semen is particularly rich in zinc, a key factor in prostate gland function and reproductive organ growth.
In humans, the biological roles of zinc are ubiquitous. It interacts with "a wide range of organic ligands" and has roles in the metabolism of RNA and DNA, signal transduction, and gene expression. It also regulates apoptosis. A 2006 study estimated that about 10% of human proteins (2800) potentially bind zinc, in addition to hundreds more that transport and traffic zinc; a similar in silico study in the plant Arabidopsis thaliana found 2367 zinc-related proteins.

In the brain, zinc is stored in specific synaptic vesicles by glutamatergic neurons and can modulate neuronal excitability. It plays a key role in synaptic plasticity and so in learning. However, it has been called "the brain's dark horse" because it also can be a neurotoxin, suggesting zinc homeostasis plays a critical role in the functional regulation of the central nervous system. Dysregulation of zinc homeostasis in the central nervous system that results in excessive synaptic zinc concentrations is believed to induce neurotoxicity through mitochondrial oxidative stress (e.g., by disrupting certain enzymes involved in the electron transport chain, including complex I, complex III, and α-ketoglutarate dehydrogenase), the dysregulation of calcium homeostasis, glutamatergic neuronal excitotoxicity, and interference with intraneuronal signal transduction. SLC30A3 is the primary zinc transporter involved in cerebral zinc homeostasis.

### Enzymes

![Ribbon diagram of human carbonic anhydrase II, with zinc atom visible in the center](https://med.libretexts.org/Courses/Dominican_University/DU_Bio_1550%3A_Nutrition_(LoPresto)_OLD/08%3A_Water_and_…

Zinc fingers help read DNA sequences.

Zinc is an efficient Lewis acid, making it a useful catalytic agent in hydroxylation and other enzymatic reactions.
metal also has a flexible \textit{coordination geometry}, which allows proteins using it to rapidly shift \textit{conformations} to perform biological reactions.\cite{177} Two examples of zinc-containing enzymes are \textit{carbonic anhydrase} and \textit{carboxypeptidase}, which are vital to the processes of \textit{carbon dioxide} (CO2) regulation and digestion of proteins, respectively.\cite{178}

In vertebrate blood, carbonic anhydrase converts CO2 into bicarbonate and the same enzyme transforms the bicarbonate back into CO2 for exhalation through the lungs.\cite{179} Without this enzyme, this conversion would occur about one million times slower.\cite{180} at the normal blood pH of 7 or would require a pH of 10 or more.\cite{181} The non-related β-carbonic anhydrase is required in plants for leaf formation, the synthesis of indole \textit{acetic acid} (auxin) and \textit{alcoholic fermentation}.\cite{182}

Carboxypeptidase cleaves peptide linkages during digestion of proteins. A \textit{coordinate covalent bond} is formed between the terminal peptide and a C=O group attached to zinc, which gives the carbon a positive charge. This helps to create a \textit{hydrophobic} pocket on the enzyme near the zinc, which attracts the non-polar part of the protein being digested.\cite{178}

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### Other proteins

Zinc serves a purely structural role in \textit{zinc fingers}, twists and clusters.\cite{183} Zinc fingers form parts of some \textit{transcription factors}, which are proteins that recognize \textit{DNA base sequences} during the replication and transcription of \textit{DNA}. Each of the nine or ten Zn2+ ions in a zinc finger helps maintain the finger's structure by coordinately binding to four \textit{amino acids} in the transcription factor.\cite{180} The transcription factor wraps around the DNA helix and uses its fingers to accurately bind to the DNA sequence.

In \textit{blood plasma}, zinc is bound to and transported by \textit{albumin} (60%, low-affinity) and \textit{transferrin} (10%).\cite{171} Because transferrin also transports iron, excessive iron reduces zinc absorption, and vice versa. A similar antagonism exists with copper.\cite{184} The concentration of zinc in blood plasma stays relatively constant regardless of zinc intake.\cite{185} Cells in the salivary gland, prostate, immune system, and intestine use \textit{zinc signaling} to communicate with other cells.\cite{186}

Zinc may be held in \textit{metallothionein} reserves within microorganisms or in the intestines or liver of animals.\cite{187} Metallothionein in intestinal cells is capable of adjusting absorption of zinc by 15–40%.\cite{188} However, inadequate or excessive zinc intake can be harmful; excess zinc particularly impairs copper absorption because metallothionein absorbs both metals.\cite{189}

The human \textit{dopamine transporter} contains a \textit{high affinity} extracellular zinc \textit{binding site} which, upon zinc binding, inhibits dopamine \textit{reuptake} and amplifies amphetamine-induced dopamine \textit{efflux in vitro}.\cite{190}\cite{191}\cite{192} The human \textit{serotonin transporter} and \textit{norepinephrine transporter} do not contain zinc binding sites.\cite{192}

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### Dietary reference intake

The Food and Nutrition Board of the U.S. Institute of Medicine updated Estimated Average Requirements (EARs) and
Recommended Dietary Allowances (RDAs) for zinc in 2001. The current EARs for women and men ages 14 and up are 6.8 mg/day and 9.4 mg/day, respectively. The RDAs are 8 and 11 mg/day. RDAs are higher than EARs so as to identify amounts that will cover people with higher than average requirements. RDA for pregnancy equals 11 mg/day. RDA for lactation equals 12 mg/day. For infants up to 12 months the RDA is 3 mg/day and for children ages 1–13 years the RDA increases with age from 3 to 8 mg/day. As for safety, the Food and Nutrition Board also sets Tolerable Upper Intake Levels (known as ULs) for vitamins and minerals when evidence is sufficient. In the case of zinc the UL is set at 40 mg/day. Collectively the EARs, RDAs and ULs are referred to as Dietary Reference Intakes.[193] The European Food Safety Authority reviewed the same safety question and set its UL at 25 mg/day.[194]

For U.S. food and dietary supplement labeling purposes the amount in a serving is expressed as a percent of Daily Value (%DV). For zinc labeling purposes 100% of the Daily Value was 15 mg, but as of May 2016 it has been revised to 11 mg. A table of the pre-change adult Daily Values is provided at Reference Daily Intake. Food and supplement companies have until July 28, 2018 to comply with the change.

### Dietary intake

![Dietary intake](https://med.libretexts.org/Courses/Dominican_University/DU_Bio_1550%3A_Nutrition_(LoPresto)_OLD/08%3A_Water_and…)

**Foods & spices** containing zinc

Animal-sourced foods (meat, fish, shellfish, fowl, eggs, dairy) provide zinc. The concentration of zinc in plants varies with the level in the soil. With adequate zinc in the soil, the food plants that contain the most zinc are wheat (germ and bran) and various seeds (sesame, poppy, alfalfa, celery, mustard).[195] Zinc is also found in beans, nuts, almonds, whole grains, pumpkin seeds, sunflower seeds and blackcurrant.[196]

Other sources include fortified food and dietary supplements in various forms. A 1998 review concluded that zinc oxide, one of the most common supplements in the United States, and zinc carbonate are nearly insoluble and poorly absorbed in the body.[197] This review cited studies that found lower plasma zinc concentrations in the subjects who consumed zinc oxide and zinc carbonate than in those who took zinc acetate and sulfate salts.[197] For fortification, however, a 2003 review recommended cereals (containing zinc oxide) as a cheap, stable source that is as easily absorbed as the more expensive forms.[198] A 2005 study found that various compounds of zinc, including oxide and sulfate, did not show
statistically significant differences in absorption when added as fortificants to maize tortillas.\[199\]

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**Deficiency**

Main article: Zinc deficiency

Zinc deficiency is usually due to insufficient dietary intake, but can be associated with malabsorption, acrodermatitis enteropathica, chronic liver disease, chronic renal disease, sickle cell disease, diabetes, malignancy, and other chronic illnesses.\[9\] Groups at risk for zinc deficiency include the elderly, children in developing countries, and those with renal dysfunction.

In the United States, a federal survey of food consumption determined that for women and men over the age of 19, average consumption was 9.7 and 14.2 mg/day, respectively. For women, 17% consumed less than the EAR, for men 11%. The percentages below EAR increased with age.\[200\] The most recent published update of the survey (NHANES 2013-2014) reported lower averages - 9.3 and 13.2 mg/day - again with intake decreasing with age.\[201\]

Symptoms of mild zinc deficiency are diverse.\[202\] Clinical outcomes include depressed growth, diarrhea, impotence and delayed sexual maturation, alopecia, eye and skin lesions, impaired appetite, altered cognition, impaired host defense properties, defects in carbohydrate utilization, and reproductive teratogenesis.\[185\] Mild zinc deficiency depresses immunity,\[203\] although excessive zinc does also.\[171\] Animals with a zinc deficiency require twice as much food to attain the same weight gain as animals with sufficient zinc.\[129\]

Despite some concerns,\[204\] western vegetarians and vegans do not suffer any more from overt zinc deficiency than meat-eaters.\[205\] Major plant sources of zinc include cooked dried beans, sea vegetables, fortified cereals, soy foods, nuts, peas, and seeds.\[204\] However, phytates in many whole-grains and fibers may interfere with zinc absorption and marginal zinc intake has poorly understood effects. The zinc chelator phytate, found in seeds and cereal bran, can contribute to zinc malabsorption.\[9\] Some evidence suggests that more than the US RDA (15 mg) of zinc daily may be needed in those whose diet is high in phytates, such as some vegetarians.\[204\] These considerations must be balanced against the paucity of adequate zinc biomarkers, and the most widely used indicator, plasma zinc, has poor sensitivity and specificity.\[206\] Diagnosing zinc deficiency is a persistent challenge.\[8\]

Nearly two billion people in the developing world are deficient in zinc.\[9\] In children, it causes an increase in infection and diarrhea and contributes to the death of about 800,000 children worldwide per year.\[8\] The World Health Organization advocates zinc supplementation for severe malnutrition and diarrhea.\[207\] Zinc supplements help prevent disease and reduce mortality, especially among children with low birth weight or stunted growth.\[207\] However, zinc supplements should not be administered alone, because many in the developing world have several deficiencies, and zinc interacts with other micronutrients.\[208\]