LEARNING TOXICOLOGY THROUGH OPEN EDUCATIONAL RESOURCES

Zinc

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ZINC *(Lat. zincum, Zn)*

Zn is an ubiquitous metal (present in foodstuffs, water and air).

It is an essential trace element with less toxicity compared with other metals (e.g. As, Hg, Pb).

This element was named after the german word "zink" meaning tin.

1. Sources and uses:

Zn is present in alloys:

Metallic Zn commonly provides a protective coating for other metals (e.g. galvanizing of iron and steel). A metal alloy made of copper and zinc is **brass.**

Occupational exposure to dust and fumes of metallic Zn can occur during zinc mining and smelting. Many countries regulate workplace levels of zinc oxide fume and dust at levels between 5 and 10 mg/m^3.

Zn is used in medicine:

Zinc compounds (ZnO, $ZnSO_4$) are components of topical adstringents, dermal products, mild antiseptics, antiperspirants. Zinc gluconate and other Zn compounds are used for the treatment of severe Zn deficiency, Wilson disease (Zn helps to reduce Cu burden and to induce metallothionein). Zn is also Recommended for the prevention of blindness in age-related macular degeneration. Zinc is also suggested for improvement of quality of hair, skin and nails.

Further use of zinc:

$ZnCl_2$ is a catalyst in organic syntheses, wood preservative, in dry cell batteries, soldering fluxes in smoke bombs (powdered Zn, ZnO, $ZnCl_2$), rodenticide (zinc phosphide).

2. Zn functions in the organism:

Zn is an essential cofactor in numerous enzymes (alcohol dehydrogenase, Cu-Zn-superoxide dismutase, RNA polymerases), zinc dependent transcription factors, cofactors that catalyse the synthesis of DNA, proteins and insulin. Zn^{2+} plays an important role in various signaling pathways, is essential for cell proliferating, differentiation and apoptosis. It is necesary for normal growth and development, behavioral response, normal function of pancreas. supports immune system.

Zn deficiency is related to over-supplementation with Cu and Fe (Zn is used to treat copper accumulation associated with Wilson´s disease).

Symptoms of Zn deficiency include growth retardation, appetite loss, alopecia, diarrhea, impaired immune function, cognitive impairments, dermatitis, delayed healing of wounds.

Acrodermatitis enterohepatica is a rare genetically based, hereditary disorder of Zn deficiency due to poor intestinal absorption. This disease manifests by ulcerated skin, chronic diarrhea and alopecia.

Share video: https://www.youtube.com/watch?v=Z_IjEkvlxGA

Zinc supplementation, alone or with other micronutrients, is recommended for Zn-deficient children, especially in developing countries. The major route of Zn intake is through the diet. Zn requirement for an adult is 10 - 15 mg/day (it is increased in pregnancy and lactation).

Zn is nontoxic micronutrient at moderate supplementation levels (≤ 100 mg/day). At doses of ≥ 150 mg, Zn may cause nauzea and vomiting, and may interfere with copper absorption. At very high doses (≥ 300 mg/day), Zn may impair immune function.

Intoxications can occur in the workplace (e.g. from inhalation of $ZnCl_2$ fumes) and in population with excessive oral exposure to Zn dietary supplements or in patients hemodialyzed with water stored in galvanized steel tanks.

For more see:

http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2872358/

Effects of zinc resulting from intoxication and deficiency

3. Mechanism of toxicity:

Excessive Zn intake interferes with copper absorption: by induction of metallothionein, which has a higher affinity for copper than for zinc. Consequently, more copper is bond to MT and excreted into the feces.

$ZnCl_2$ is a corrosive agent that causes irritation of the GIT after ingestion and irritation of the respiratory tract after inhalation. Moreover, in the case of „metal fume fevere“ there is an immune response to ZnO in the pulmonary tract, Inflammation develops and cytokines release (e.g. TNFα, IL-8).

Zn^{2+} stimulate the formation of free oxygen radicals.

4. Fate in the organism:

Absorption:

The absorption of Zn from the GIT occurs in the duodenum and is homeostatically regulated. About 20-30% of ingested Zn is absorbed. Zn uptake from the intestinal lumen involves passive diffusion and carrier-mediated proces through specific Zn transportes such as ZnT-1. Intestinal absorption of Zn can be reduced

by dietary fibre, phytates, calcium and phosphorus, while amino acids, picolinic acid, and prostaglandin E_2 can increase Zn absorption.

Organically bound forms (zinc gluconate, orotate) have greater bioavailability than zinc sulfate.

On the cellular level, homeostasis of Zn is mediated by two protein families: the Zn-importer (Zip) family that transport Zn through the plasma membrane and the export proteins from Zn-transporter (ZnT) family.

Distribution:

As one of the most abundant trace elements in the body, Zn is present in all tissues and fluids in the organism. One absorbed Zn is widely distributed throughout the body.

The amount of Zn in the adult body is about 1,3 – 3g. Most of Zn is found in muscle (60%), bone (30%), skin/hair (8%), liver (5%). Relatively high concentration of Zn are in the prostate gland, probably because of the presence of Zn-containing enzyme acid phosphatase. In the plasma Zn is bond to albumin (60-80%), which represents the metabolically active pool of Zn.

Zn is an effective inducer of metallothionein (MT) synthesis: when MT is saturated in intestinal cells, Zn absorption is decreased. MT is also an important storage depot for cellular Zn. Liver MT concentration is influenced by hormonal factors, including adrenocorticotropic hormone and pararhyroid hormone, and various stimuli that impact Zn metabolism.

Excretion:

Zn is excreted in both feces (80%) and urine (20%). Daily elimination of zinc averages about 1% of the absorbed dose.

5. Intoxication:

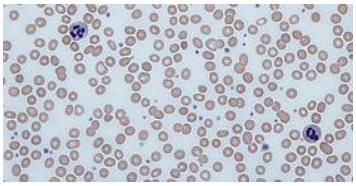
Intoxication depends on the route of entry for Zn into the organism.

Intoxication after ingestion:

Acute Zn toxicity from excessive ingestion is relatively uncommon and occurs only at high doses.

Highly corrosive compounds (such as $ZnCl_2$, in concentrations exeeding 20%) may produce within 30 minutes to 1 hour after ingestion burns of the mucosa, hemorrhagic gastroenteritis (with hematemesis, sloughing of mucous membranes, ulcer formation) and acute renal tubular necrosis and interstitial nephritis. Symptoms may rapidly progress and the patient may suffer from gastrointestinal hemorrhage, shock, and cardiovascular collapse.

Chronic, high-dose Zn supplementation interferes with the uptake of copper. Hence, many of its toxic effects are in fact due to copper deficiency (e.g. sideroblastic anemia and neutropenia).



Intoxication after inhalation:

Acute inhalation of high concentrations of $ZnCl_2$ from smoke bombs (in the military use) detonated in closed spaces results in damage to the mucous membrane including interstitial edema, pneumonitis, fibrosis.

Share video: *Zinc smoke bomb :*
https://www.youtube.com/watch?v=GOSQlnR2mFQ

Additional reading: Case report:

Accident after exposure to $ZnCl_2$ smoke during a combat exercise:
http://www.sciencedirect.com/science/article/pii/S0954611199900549

Following inhalation of ZnO and other Zn compounds (in the occupational setting) the most common effects is **„metal-fume fever“.** This syndrome resembles a flulike illness. Symptoms include fever, chills, sweating, muscular weakness, chest pain, cough and leukocytosis. Onset occurs in 4 to 6 hours, generally on the evening after exposure to fumes. Tolerance develops in workers, but may be lost over the weekend („Monday Morning fever“ MFF).

MFF can also follow exposure to fumes of copper, magnesium, aluminium, antimony, iron, manganese, and nickel in welding, galvanizing or smelting operations.

Inhalation of $ZnCl_2$ produces greater pulmonary damage compared with similar concentrations of ZnO.

The permissible exposure limit according to the OSHA limit is 1mg/m^3 for $ZnCl_2$ (fume or respirable dust fraction), and 5mg/m^3 for ZnO in workplace air during an 8-hour workday, 40-hour work week.

Share video:
https://www.youtube.com/watch?v=79UHPpbG14s&t=307s

6. Laboratory determination:

The concentration of Zn in plasma is not a sensitive indicator of Zn status and does not reflect the dose-response relationship between Zn levels in the body and effects at various target sites.

The diagnosis of Zn poisoning is confirmed by an elevated serum Zn levels (normal: 9,2 to 23 µmol/l).

7. Treatment:

Treatment of Zn poisoning is supportive.

Chelatation is very effective for reducing elevated Zn levels by increasing urinary Zn excretion.

Chelating agents:

calcium disodium EDTA, dimercaprol, D-penicillamine and N-acetylcysteine.

Calcium disodium EDTA and BAL are usually used in patients with significant Zn toxicity. EDTA is administered as the calcium salt to avoid the complication of hypocalcemia, as EDTA reacts with calcium in the same way with other metals.

8. Zinc phosphide (Zn_3P_2)

= potent rodenticide

Zinc phosphide itself is not very toxic for human, toxicity is mediated through the generation of phosphine gas (PH_3) after reaction Zn_3P_2 with water or gastric acid. Phosphine is a gas with characterictic fishy odour, used as a fumigant. This gas produces various toxic effects. Serious toxicity includes myocarditis, congestion heart failure, cardiac arrythmias, circulatory collapse, pulmonary edema. The mortality rate is high. There are no antidotes currently known.

For more see:

November, 2014: **SEVERE ZINC PHOSPHIDE POISONING IN INDIA, 15 WOMEN DIED. ZINC PHOSPHIDE FOUND IN ANTIBIOTIC TABLETS GIVEN TO WOMAN AFTER STERILISATION.**
http://uk.reuters.com/article/uk-india-health-sterilisation-idUKKCN0IZ06B20141115

Additional reading:

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