LEARNING TOXICOLOGY THROUGH OPEN EDUCATIONAL RESOURCES

Heavy metals

Marie Vopršalová
Department of Pharmacology and Toxicology
Faculty of Pharmacy in Hradec Králové, Charles University,
Heyrovského 1203, 500 05 Hradec Králové, Czech Republic

e-mail: marie.voprsalova@faf.cuni.cz

Heavy metals (HM) – although the term has never been defined by any authoritative body such as International Union of Pure and Applied Chemistry (IUPAC), refers to any metal that has a density greater than 5 $g.cm^{-3}$ (= greater than Fe). Examples of HM include metals such as Cd, Hg, Pb, Cr, Ni, Cu, Zn and also semimetals (= metalloids), such as As.

Toxicity of heavy metals depends on several factors

- Dose
- Chemical compound
- Route of exposure
- Age, gender, genetics
- Nutritional status of exposed organism

Some HM **in the trace concentrations** are necessary to maintain the metabolism (e.g. essential micronutrients Zn, Cu).
However, they can lead to poisoning **in higher concentrations**.

Mechanisms of heavy metals toxicity

There are several mechanisms by which heavy metals (or their compounds containing them) exert their toxic effects. There is no uniform mechanism for all toxic metals.
Here is the list of known mechanisms:

- Interaction with sulfhydryl (-SH) groups of metalloenzymes and proteins → decreasing enzyme activity
- High affinity for other ligands: amine $–NH_2$, phosphoryl $–PO_3$, carboxy –COOH groups → damage to biomolecules with impairment of their functions
- Mimicry - heavy metal (e.g. As) binds to physiological sites for chemically related essential metals → this disrupts a variety of important cellular functions, e.g. signaling and transport proceses

- Production of reactive oxidative species
- Formation of DNA adducts and induction an array of aberant gene expression → carcinogenesis. Some heavy metals are classified as human carcinogens according to the International Agency for Research on Cancer (IARC).

*The word "**cancer**" originates from Greek Word καρκίνος - karkinos (= carb or crayfish), which was used to describe tumors and its surrounding vessels by a physician Hippocrates)*

The cellular mechanisms of heavy metal toxicity are mutiple → they induce multiple organ damage.

HM poisoning is generally treated by the administration of **chelating agents**.

Chelation

= proces by which organic molecules incorporate metal ions into their molecule structure by the means of chemical groups called ligands.
→ ideally a stable and biologically inert metal complex is formed

> ***„Chelate“*** *is derived from chele, χηλή (Greek word)*
> *= crabś claw*
> *The term was first used in 1920 by researchers:*
> *Morgan, G., T. and Drew, H. D. K.: LCXII - researches on residual affinity and co-ordination. Part II. Acetylacetones of selenium and tellurium.* J. Chem. Soc., Trans. 1920, 117, 1456.

Heavy metals classification

- **As, Pb, Hg, Cd**

metals of major public health significance (according to the World Health Organization).

They induce multiple organ damage, even at lower levels of exposure. They are dangerous because they tend to accumulate in the organism.

Accumulation *= an increase of concentration in a organism after repeated exposure*

- **Cr, Ni, Zn, Cu, Fe**

essential metals but with high potential for toxicity in higher exposure

References:

- Klaassen, C D..: Casarett and Doull's toxicology: The Basic Science of Poisons, 7th ed., McGraw-Hill: New York, 2008, 931-980
- Shannon, M.W., Borron, S.W., Burns, M. J.: Haddad and Winchester's Clinical Management of Poisoning and Drug Overdose, 4th ed., Sunders/Elsevier: Philadelphia, 2007,1111-1170
- Swaran, J.S.F., Vidhu, P.: Chelation in Metal Intoxication. Int J Environ Res Public Health. 2010 Jul, 7(7), 2745–2788

https://toxoer.com

Project coordinator: Ana I. Morales
Headquarters office in Salamanca.
Dept. Building, Campus Miguel de Unamuno, 37007.
Contact Phone: +34 663 056 665