LEARNING TOXICOLOGY THROUGH OPEN EDUCATIONAL RESOURCES

Nickel

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NICKEL *(Lat. Niccolum, Ni)*

Corrosion resistant, silvery-white metal

- essential trace metal - constituent of metalloenzymes (e.g. lactate dehydrogenase, alcohol dehydrogenase)
- toxic metal

1. Sources and uses:

- steel industry (stainless steel), electroplating
- Ni alloys - coins, jewelry, buttons
- dry batteries
- catalyst for the hydrogenation of soap, fats and oils

Nickel carbonyl - $Ni(CO)_4$ - catalyst in the petroleum, plastic, rubber industries

Ni exists in three major forms:

- elemental
- inorganic compounds (water soluble and water insoluble)
- organic compounds (e.g. nickel carbonyl = nickel tetracarbonyl – a volatile liquid at 25°C, the gas is heavier than air)

2. Fate in the organism:

Absorption:

Human exposure may be by inhalation, ingestion, and dermal contact:

- Nickel (from its inorganic compounds) is poorly absorbed from the gut (< 10% of a dose)
- Ni inhaled as dust is absorbed in the lungs (35%)

- Ni is also taken up by human skin

Nickel carbonyl: because it is highly lipophilic, it readily penetrates the blood-brain barrier into the CNS.

Distribution:

- blood: Ni is bound to albumin and α_2-microglobulin and it is rapidly distributed in the body
- the highest Ni concentrations: kidneys, liver and lungs
- Ni is bound to metallothionein MT (so called nickeloplasmin)
  but Ni induces MT synthesis in liver or kidney only slightly

MT is important in the extracellular transport, intracellular binding, urinary and biliary excretion of Ni.

Excretion:

Ni taken up by ingestion is mainly excreted in the urine (90%). A small portion is eliminated in the feces, saliva and sweat.

3. Mechanism of toxicity:

Nickel exposure produces ROS, which lead to oxidative damage

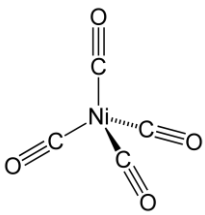
Ni readily crosses the cell membrane via Ca^{2+} channels and competes with Ca^{2+} for specific receptors.

4. Intoxication:

Acute toxicity:

The ingestion of soluble Ni salts causes gastrointestinal symptoms including nauzea, vomiting and diarrhea.

! Nickel tetracarbonyl = the most poisonous Ni compound !



Inhalation of fumes can cause serious pulmonary edema with dyspnea, cough. Death results usually from respiratory toxicity.

Chronic toxicity:

Inhalation of Ni aerosol (primarily in the steel industry): → respiratory effects: epithelial dysplasia of the nasal mucosa, sinisitis, nasal polyps, nasal septum perforation, asthma.

Skin contact: → allergic reaction:

contact eczema – „ nickel dermatitis“

For more see:
http://www.crutchfielddermatology.com/caseofthemonth/studies/I_2007_011.asp
https://www.nickelinstitute.org/en/NiPERA/HumanHealthScience/FS1-AllergicContactDermatitis/What_is_ACD.aspx

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IARC (1990) concluded that Ni and Ni compounds are **carcinogenic** to humans. Ni is a respiratory tract carcinogen in workers in the nickel-refining industry, nickel processing plants. Chronic nickel carbonyl exposure has been associated with lung cancer.

5. Laboratory determination:

The diagnosis of nickel intoxication is made on **urine or serum nickel levels**. Severity can be determinated by 8-hour urinary elimination results. Mild toxicity corresponds to a urinary nickel concentration less than 100 µg/l, moderate toxicity is seen with 100 to 500 µg/l, and severe toxicity is associated with urinary concentration exceeding 500 µg/l.

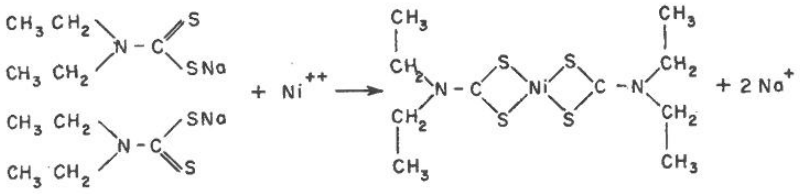
Nickel carbonyl is metabolised in the liver, liberating carbon monoxide. Carboxyhemoglobin levels may be useful.

- *Drinking water standards (EU, WHO): < 20 µg/l*
- *Workplace air limit - during an 8-hour workday, 40-hour workweek (US Occupational Safety and Health Administration, OSHA) - 1 mg/m^3*

6. Treatment: specific antidotes:

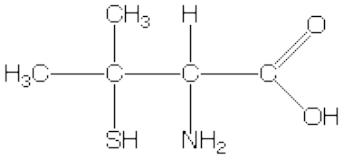
Preferred antidote:

- *sodium diethyldithiocarbamate (dithiocarb)* - this agent substantially reduced morbidity and mortality after $Ni(CO)_4$ exposure.



For more see: *Ann Clin Lab Sci.*

- *D-penicillamine*



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