Probing toxicologically relevant interactions of inorganic pollutants in the bloodstream

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Toxic metals in blood ↔ +

- Air
- Food
- Drinking water

Cd, As, Hg

? ↔

Metal-based drugs

CDC
2010: recall of 12 million drinking glasses by McDonald’s

0.1-4.7 mg Cd/kg
5% of US population urinary Cd ≈ kidney injury
exposure-disease associations ill defined

~1.7 μg Cd/cigarette
Cd$^{2+}$ plasma protein binding erythrocyte endothelial cell

systemic toxicity

how Cd$^{2+}$ to target organ?

mechanism of Cd$^{2+}$ toxicity?

blood vessel damage

excretion

gastrointestinal tract

Dalton Trans. 39, 329-336
deadly dose: 0.5 mg

B.F. Popescu et al. (2009)
Cerebellum, 8, 340-351
human serum albumin (HSA)


HSA-Cd 1:1 complex

are small MW thiols involved in translocation?

CdCl$_2$

coinjection with Cys/GSH

↑ Cd in kidneys by 70%

add up to 1.5 mM SMW thiols to PBS-buffer

→ study their effect on stability of HSA-Cd 1:1 complex
Cys/hCys Cd complexes $\rightarrow$ target organ?


*Biochem. Pharmacol.* 1984, 33, 199-203


Hyperhomocysteinemia

analyze directly → difficult > 3700 proteins simplify if we analyze for metalloproteins

instrumental set-up:

Mobile Phase Reservoir → Rheodyne Valve → HPLC Pump → Superdex 200 HR 13 µm (250 x 1.0 cm), fractionation range: 600-10 kDa → computer terminal

…the study of a metallome

S. Mounicou, et al.
Cd$^{2+}$ displaced Zn$^{2+}$ from a metalloprotein

**conclusion**

Emerges as a versatile tool to study interactions of:

- **toxic metals** with proteins and SMW compounds **bottom up**
- **toxic metals** in whole plasma using a metallomics approach **top down**

- Fundamentally new insight to advance the toxicology of **metals** in the bloodstream
- Modulate the metabolism of **toxic metal species** by dietary additives to increase their excretion
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