Modelling the bioavailability of trace elements

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Unit 33: Epidemiology, Biostatistics and Mathematical Modelling
Why use modelling?
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Bioavailability models for trace elements
Simulation of population absorption

Data:
Trace element chemical species
Popular co-ingested foods
Nutritional status of population

Prediction:
Estimate of actual amounts absorbed
Aid in quantifying fortification strategies
Risk assessment for under/overdosing
Simulation of Zn and Fe biofortification in Mexico

Data: Amounts of maize, wheat, beans and rice eaten, coingested foods, trace mineral contents, body reserves.

Model:
Zn: International Zinc Nutrition Consultative Group equation; total daily zinc intake and the phytate: zinc molar ratio
Fe: Bhargava Iron algorithm: promoters (vitamin C and meat), inhibitors (phytate)

Prediction: Biofortify maize with Zn to reduce ca. 50% of inadequacies. Fe inadequacy cannot be solved by biofortification.

Models of **ADME** kinetics (compartment models)

Data:
Trace element chemical variants
Concentration in food and blood

Prediction:
Quantification of
**Absorption**, **Distribution**, **Metabolism** (speciation) and **Excretion**
Physiological pathways by inference
ADME kinetics: Bioavailability of calcium ascorbate > calcium acetate

Experiment in rats with labeled $^{45}$Ca ascorbate and acetate
Data: Intake, urine, femur, fecal concentrations
Prediction:
Kinetic parameters
Ascorbate has faster uptake kinetics in 1 of 2 pathways

Study: J Cai, Q Zhang, ME Wastney, CM Weaver, Calcium Bioavailability and Kinetics of Calcium Ascorbate and Calcium Acetate in Rats, Exper Biol Med, 229, p40-45, 2004
Inorganic Selenite ($^{76}$Sel) vs Selenomethionine ($^{74}$SelMet) bioavailability human model

Data: 31 humans, 4 months feces, urine, red blood cells and plasma conc. Separate isotope tracers

Prediction:
SelMet 70% higher absorption than Sel
Experimental multiple peaks → several plasma pools
Sel turnover 213 d, SelMet turnover 430 d
50% of absorbed Se uptaken by liver for Sel & SelMet

Study: ME Wastney ME, GF Combs Jr, WK Canfield, PR Taylor, KY Patterson, AD Hill, JE Moler, BH Patterson, A human model of selenium that integrates metabolism from selenite and selenomethionine, J Nutr, 141(4) p708-17, 2011
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Kinetics of trace elements: trophic transfer

Data: Kinetic parameters for individual organisms’ ADME.

Model prediction: Estimation of the capacity of each trace element to bioaccumulate.
Kinetics of trace elements: trophic transfer

Risk assessment for biomagnification.

Non-elemental Se biomagnification is predicted and observed for most organisms.

Cd biomagnification is only predicted for filter feeders.

Cr is never expected to biomagnify.

Molecular dynamics simulation: Understanding trace element binding to biomolecules
CP Molecular dynamics simulation: probing speciation of Co and Zn bound to biomolecules

Study: C Bresson, C Lamouroux, C Sandre, C Moulin et al., An interdisciplinary approach to investigate the impact of cobalt in a human keratinocyte cell line, Biochimie, 88(11), p1619-29, 2006


Modeling Software

**WinSAAM**: Kinetic compartmental modeling software

**WinNonLin**: Pharmacokinetics software

**Charmm** and **NAMD**: Molecular dynamics simulation

**Matlab / Octave**: General purpose numerical math, many scripts available
Models of Bioavailability

A model animates a mechanism with mathematics

Bioavailability is based on a mechanism

Bioavailability models deliver more than a “single number”

Dream: couple models of trophic transfer+animal feed+human metabolism
Thank you for your attention

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