Characterisation of human exposure pathways to perfluorinated compounds - comparing exposure estimates with biomarkers of exposure

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Perfluorinated compounds (PFCs)

Perfluoroalkyl sulfonates (PFSAs)

Perfluoroalkyl carboxylates (PFCAs)

Precursors of PFCs
- Fluortelomer alcohols (FTOHs)
- Perfluoralkyl sulfonamides (FOSAs)
- Perfluoroalkyl sulfonamidoethanol (FOSEs)
Toxicokinetics

- Readily absorbed (oral, inhalation)
- Associated to proteins (e.g. serum albumin)
- Highest concentrations in blood and liver
- Not metabolised
- Excreted primarily via urine
- Long elimination half-lives in humans (2-7 years)

PFCs have been found in human blood world-wide
Toxicity – animal studies

- hepatotoxicity
- immunotoxicity
- developmental toxicity
- neonatal mortality
- hormonal effects
Adverse health effects - in humans

• Several epidemiological studies conducted
• For example: diabetes, cardiovascular diseases, cholesterol level, thyroid function, immune function, liver and kidney function, reproductive and developmental outcomes
• Findings are not consistent
• Need for more studies!
Do to their toxicokinetic properties and the observed adverse effects, PFCs are of concern.
Risk assessment

How frequent and to what extent are we exposed to PFCs?
Exposure pathways to PFCs

- Air
- Breast milk
- Diet
- In utero
- Dust
- Dermal contact
Exposure

Precursors to PFOA

Metabolism of precursors of PFOA

Degradation in the environment

PFOA
Exposure assessment - external dose

- Measuring concentrations in delivering media, e.g. food and dust
- Combine with exposure factors (e.g. food consumption or inhalation rate)
- Calculate total intake
- Compare different exposure pathways
- Important for selecting appropriate actions
Exposure assessment - internal dose

- Measure chemicals in biological matrices such as blood, breast milk, urine (biomonitoring)
- Combine with knowledge on distribution in the body
- Calculate body burden (total amount in the body)
- Integrated exposure over time
- Take individual differences into consideration (e.g. age and gender)

Distribution
Half-life
Principal objective

To characterise different human exposure pathways of PFCs by comparing estimates of exposure from diet, indoor air and house dust with biomarkers of exposure.

Internal dose
BROFLEX study

questionnaire  dust  beverages  questionnaire

air  n = 41  food

blood  breast milk
**Studies**

**BROFLEX study**

**Time trends:**
pools of serum, males, 40-50 years, 1977-2006

**Levels in food:**
pools, 21 types of food and beverages

**Which food and predictors:**
175 serum samples, FFQ

**Levels in breast milk:**
longitudinal samples, up to 12 months, 10 mothers

**Levels in cord blood:**
plasma from mother at birth and cord plasma, 123 pairs
Methods for PFCs in plasma/serum and breast milk

blood/breast milk +
internal standard +
methanol/acetonitrile

mixing +
centrifugation +
dilution

Column switching LC-MS/MS
Summary of method validation

- High sensitivity
- High repeatability and accuracy
- Suitable for large sample series:
  - Low sample volume 150 - 200 µl
  - High capacity (100 samples per week)
  - Low operational costs

Haug et al., J. Chromatogr A. 1216 (2009), 385-393
Results

• Internal dose
  – Levels in blood and breast milk

• External dose
  – Adults
  – 6 months old infants

• Comparison of external and internal doses
  – Associations
  – PK modeling
Time trends - blood

In utero exposure

n=123 pairs

In utero exposure

Blood vs breast milk

Haug et al. Environ. Int. (2011) 37, 687-693

Blood

Breast milk

PFOA: ca 3%

PFOS: ca 1.5%

n=19
Blood vs breast milk

Haug et al. Environ. Int. (2011) 37, 687-693
Breast feeding period

Decrease (1 year):
- PFOA: 94%
- PFOS: 37%

Internal dose

- PFCs are found in blood
- PFCs are transferred to the fetus through the placenta
- PFCs are found in breast milk
PFCs in indoor air vs house dust

- FOSA/FOSEs in air were significantly correlated to PFSAs in dust
- No significant correlations between FTOHs in air and PFCAs in dust

Predictors of PFCs in indoor air/house dust

Levels in food and beverages

Intake of PFCs from the diet

Intake of PFCs from the diet

Intakes of PFOA/PFOS

- Absorption assumed to be 100%
- Food - questionnaire
- Drinking water - 1.41 L/day
- Dust – 50, 100 or 200 mg/day
- Indoor air – 3 biotransformation factors for precursors
  - FTOHs to PFOA 0.02, 0.5 or 1.7%
  - FOSAs/FOSEs to PFOS 1, 20 or 100%
  - Inhalation rates of 13.3 m³/day (adults), 6.8 m³/day (infants)
- Consumption of breast milk assumed to be 700 mL/day
Median of intakes; infants

Haug et al. Environ. Int. (2011) 37, 687-693
Individual intakes - women

Haug et al. Environ. Int. (2011) 37, 687-693
Individual intakes - women

Scenario 1

PFOA

Scenario 3

Haug et al. Environ. Int. (2011) 37, 687-693
Food is generally the major source of exposure for adults, however the relative importance of the indoor environment vary a lot and contribute considerably for several individuals.

Breast milk is the major source of exposure for breast-fed infants.

The major contributors to dietary intake were fish and shellfish.
Internal vs external dose

Serum concentration of PFOS, ng/ml

Estimated intake of PFOS divided in quartiles
Concentrations of PFCs in serum, ng/mL

Haug et al. Environ. Int. (2011) 37, 687-693
Comparing internal and external dose

• Significant associations between intakes and blood levels were seen

• PK modelling showed that the intakes calculated are reasonable
Future perspectives

- “New” compounds
- Larger studies and more environments
- Sampling strategy
- Products - environment
- Exposure factors
- Young children
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