The Fate of Chiral Organochlorine Compounds and Selected Metabolites in Intraperitoneally Exposed Arctic Char

(SALVELINUS ALPINUS)

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Chiral Compounds
α-Hexachlorocyclohexane (α-HCH)

$\text{cis}$-chlordane

$^{13}\text{C}_4$-heptachlor
Atropisomeric PCBs

Mirror Plane
Arctic char
(Salvelinus alpinus)

Contaminants in peanut oil
~200 ng of each per g fish
Sampling

- Control cohort
- 1 week \((n=3)\)
- 2 weeks \((n=3)\)
- 5 weeks \((n=4)\)

50 liter flow-through aquaria
aerated water at +10°C
14 h light:10 h dark cycle

Muscle and liver samples
Extraction and Clean Up

Mixing with Na$_2$SO$_4$

Column extraction
acetone:hexane 2.5:1
hexane:diethylether 9:1

Fat removal
semi-permeable membrane devices (SPMD)
cyclopentane

Florisil chromatography
Instrumental analysis

- **GC-MS**
  - EI+ and ECNI
  - SIM and full-scan

- **GC-ECD**

- **SP-5 (Supelco®)**
  - 30 m, 0.32 mm, 0.25 μm

- **Chirasil Dex (Varian, Inc.)**
  - 30 m, 0.25 mm, 0.25 μm
Metabolites

Heptachlor → Heptachlor-exo-epoxide (HEPX)
Muscle samples

\[ \alpha\text{-HCH was eliminated} \]

\[ \text{HEPX was formed} \]

The PCBs were assimilated differently
Increasing concentration

PCB-174  PCB-136  PCB-149  PCB-132

Decreasing $K_{ow}$

PCB-174  PCB-95

Peanut oil

Fish
Assimilation of PCBs

$C_{\text{max}}$ vs $1/K_{\text{ow}} \times 10^7$

Steric effect coefficients (SECs)

Shaw and Connell, ES&T 18:18-23, 1984

PCB-95
PCB-149
0.74

PCB-132
0.65

PCB-174
0.58

PCB-136
0.54

Increasing steric hindrance
Assimilation of PCBs

Oil

Fish

ng/g muscle tissue

SEC/K_{ow} \times 10^7

C_{max}

SEC/K_{ow} \times 10^7

CB-95  CB-132  CB-149  CB-136  CB-174

0  10  20  30  40  50  60  70  80  90

0  1  2  3  4  5  6  7

0  10  20  30  40  50  60  70  80  90
Average $C_{\text{max}}$ vs $\text{SEC/K}_{\text{ow}}$

- $r^2=0.86$
- $p=0.023$

Graph showing a linear relationship between $\text{SEC/K}_{\text{ow}}$ and ng/g muscle tissue for compounds CB-174, CB-132, CB-136, and CB-95.
Half-lives 8-10 days for all compounds. 

Primarily other clearance than biotransformation.

**Liver samples**

- **Elimination**
- **HEPX was formed**

### Compound Concentrations

#### a-HCH
- PCB#95
- PCB#136
- PCB#149
- PCB#132
- PCB#174

#### op-DDT
- cCHL

#### HEPX
- Liver samples

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Enantiomeric composition

Reference standards were racemic.
Did it change during the experiment?
Indication of that biotransformation occurred.

Enantiomeric Fraction (EF)

EF = Area of (+)/Area of (+) and (–)
EF = 0.50 means racemic
EF > 0.5 means excess of (+)
EF < 0.5 means excess of (–)
Chiral results

Excess of (+) $\rightarrow \alpha$-HCH

1-week 2-weeks

0.47 0.48 0.49 0.50 0.51

STDs

Muscle Liver

5-weeks

Enantioselective biotransformation
Chiral results

cis-Chlordane

Assimilation seems to be non-enantioselective
Chiral results

Muscle Formation resulted in a racemic mixture
Chiral results

**o,p’-DDT**

QA- Two different ionization techniques.
Different trends in liver and muscle.
Chiral results PCBs

- PCBs 95, 149 and 174, no apparent enantioselective biotransformation.

- PCB 132 increasing proportion of (+) in muscle.

- PCB 136 increasing proportion of (+) in muscle and liver.
Assimilation

- The contaminants were assimilated.
- The assimilation appeared to be non-enantioselective.
- $K_{ow}$ and steric effects seem to influence assimilation.

Elimination

- Slow elimination in muscle with exception of $\alpha$-HCH.
- Fast and similar elimination in liver of all compounds – indicate primarily other clearance than biotransformation.
Summary 2(2)

**Biotransformation?**
- HEPX was formed - racemic mixtures.
- Chiral time trends for some compounds.

**Species specific differences?**
- Enantiomeric excess vary among species.
- Enantioselective biotransformation seems to be species specific.
Thanks to:

- **My co-authors:**
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  Håkan Berg, University of Texas, USA
  Per-Erik Olsson, Örebro University, Sweden

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Thank you for the attention!