The CEFIC ECO16 project: Critical body residue validation for aquatic organisms exposed to chemicals causing toxicity by baseline narcosis.

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Introduction

Baseline narcosis is the result of a disturbance of biomembrane functioning caused by the presence of organic chemicals in the bilayer structure. Due to the non-specific nature of this mechanism, the membrane-disrupting potential of a single molecule is generally considered equal among all chemicals.
Therefore, chemicals that primarily exert toxicity via a narcotic mode of action may be expected to display equal critical body residues (CBRs).

In current CBR data however, a considerable variation is observed in reported values.
This may be related to the following issues:
(a) the quantity of a narcotic chemical, which caused lethality in an organism may also be present in non-lipid compartments (e.g. proteins, carbohydrates, water)
(b) storage and membrane lipids may show differential sorption behavior, resulting in dissimilar concentrations in both lipid subcompartments (Figure 1).

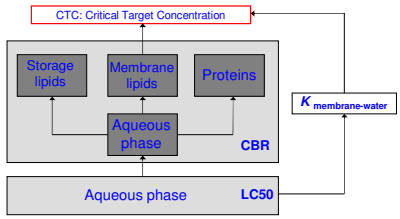

Figure 1: *Critical body residues and internal distribution.*

Research Objectives

The focus of the CEFIC ECO16 project is to get more understanding of the variation in CBR values of narcosis type chemicals. To this extent, the following three objectives have been formulated:
(1) compiling a comprehensive CBR database
(2) developing a sophisticated model to describe the process of internal distribution of narcotic toxicants and implementing it in the gathered data
(3) acquiring experimental data to provide the model with appropriate partitioning parameters and accompanying CBR data of a number of benchmark chemicals.

Approaches

(1) Existing CBR data will be selected from the Environmental Residue-Effects Database (U.S. Army Corps of Engineers & U.S. EPA), which currently comprises 15,219 distinct measurements on 419 analytes, 484 species, 15 effect classes, and 74 endpoints. Appropriate data (excluding metals, as well as reptile, bird and mammal data) will be evaluated in a newly developed tiered data quality scoring system.

Literature References

(1) Arnot, J.A. and Gobas, F.A.P.C. *Environ. Toxicol. Chem.23*, 2343-2355.
(2) Jonker, M.T.O.; Van der Heijden, S.A. *Environ. Sci. Technol.* **2007**, *41*, 7363-7369.

Acknowledgments

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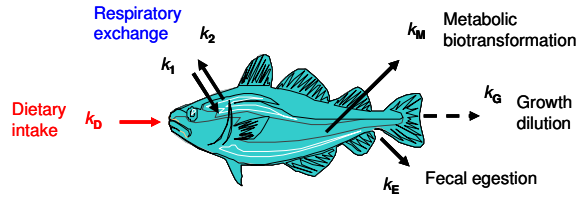
(2) A one-compartment first order kinetic model (Figure 2) will serve as basis for further model refinement. Ultimately, the model will be used to evaluate CBR data.



$$CB = ((k1 \bullet CWD) + (kD \bullet CD)) / (k2 + kE + kM + kG)$$

Figure 2: *Schematic of the one compartment first order kinetic model as described in ref. (1).*

Higher tier models will include probability of toxicity and uncertainty in toxico-kinetic model estimates as well as partitioning among the sub-compartments of the animals: aqueous phase, protein, carbohydrate, storage lipid, and membrane lipids.

(3) Partitioning data will be measured for surrogate materials representing the main biological compartments (i.e. lipids, proteins, and carbohydrates) employing a passive sampler-aided batch shake setup (see ref. *2*). Along with high quality CBR data (see conceptual setup in Figure 3) measured for 10 chemically diverse narcotic compounds and three distinct organisms (see Table 1) these data will further serve model development.

Table 1: *Selected chemicals and organisms for the experimental work.*

Test chemicals	Test organisms
-1,2,4-trichlorobenzene -1,2,3,4-tetrachlorobenzene -2,3,4-trichloroaniline -2,3,5,6-tetrachloroaniline -4-chloro-3-methylphenol -pentylbenzene -pyrene -PCB-52 -Bromophos-methyl -C12-2 linear alkylsulphonate	- *Lumbriculus variegatus* - *Asellus aquaticus* - *Poecilia reticulata*

Figure 3: *Actual passive dosing systems (left) and a conceptual CBR setup with guppy (right).*