Determining Acute to Chronic Ratios in Aquatic Toxicity

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INTRODUCTION

- Various studies have considered Acute to Chronic ratios (ACR) which may vary from a factor of 2 to a factor of 10.
- A better understanding of ACRs would allow a more appropriate selection of uncertainty factors in risk assessment.
- 6 main Classes of Mechanisms of toxic Action have been characterised for organic chemicals using the MechoA scheme, and these can be categorised into dozens of sub-classes on the basis of chemical structure (Bauer *et al.,* 2018).
- For several MechoA Classes (notably 1, 2 and 3), we have found quantifiable relationships which are MechoA sub-class and species specific

METHODS

- For each endpoint (fish acute, fish chronic etc), MechoAs which are hydrophobicity-driven have been linked to dedicated QSAR models for the prediction of aquatic toxicity to quantify the toxicity of a chemical substance.
- Thus, mathematical models are obtained by simple linear regression of both acute and chronic fish toxicity studies versus their hydrophobicity.
- Comparing the trend lines for both acute and chronic endpoints, it is possible to consider ACR for each MechoA sub-Class and for each species and to take into account the relative ACR for chemical substances with different hydrophobicity.

1. iSafeRat® MechoA
   - Internally developed structural alert scheme
   - Based on hundreds of substances
   - Each assay result is validated

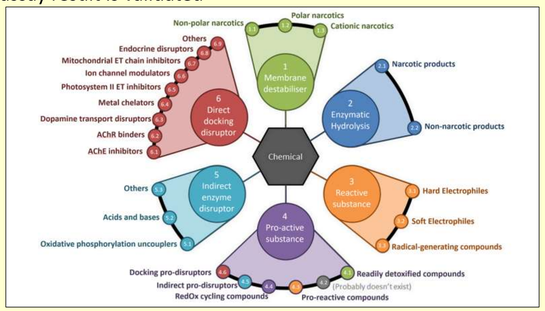

Figure 1: MechoA Scheme

2. iSafeRat® models for acute and chronic toxicity for fish, daphnids and algae:
   - Internally validated based on quality experimental studies
   - Visual representations of regressions are presented for a selected set of MechoAs to demonstrate a variety of possible options with tentative mechanistic explanations.

There is no "one factor fits all" for Acute to Chronic ratios (ACRs)! Everything depends on the Mechanism of Toxic Action (MechoA)

And each MechoA has it's own ACR

⇒ MechoA dictates the relative level of acute and chronic toxicity

=> Hydrophobicity dictates the potential and degree of acute and chronic toxicity

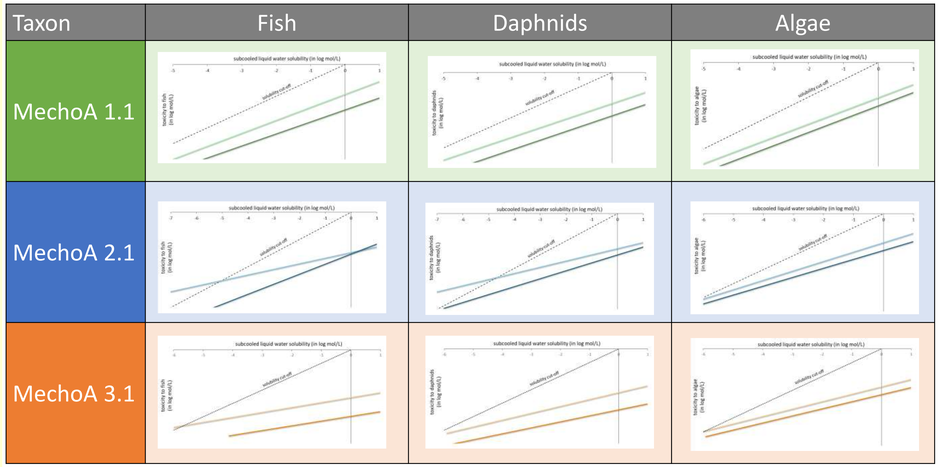

Figure 2: Comparison of the models predicting acute and chronic toxicity to fish, daphnids and algae for three MechoA sub-classes

Table 1: ACR comparison for fish, daphnids and algae for three MechoA sub-classes

	Fish	Daphnids	Algae
MechoA 1.1	ACR = 5	ACR = 7	ACR = 3
MechoA 2.1	ACR = [1;57]*	ACR = [3;17]*	ACR = 3
MechoA 3.1	ACR = 24	ACR = [8;19]*	ACR = 3

*Hydrophobicity dependent

DISCUSSION

If the ACR range between 2 and 10 found in the literature is observed for MechoA 1.1, it is interesting to notice it dramatically changes for other MechoA. So, for ester compounds acting through a MechoA 2.1 (*i.e.* enzymatic hydrolysis), the ACR is very influenced by metabolism. Indeed it is expected fish and daphnids have different capacities to metabolise these compounds while algae can't. For algae, the ratio between EC50 and NOEC seem always equal to 3.

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