Developing Acute to Chronic Ratios (ACRs) for Understanding the Ecotoxic Effects of Surfactants

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Introduction

Surfactants are used in high volumes across various industries. Whilst their safety has been widely investigated, there are still data gaps with respect to meeting regulatory registration requirements particularly for fish chronic toxicity endpoints. Filling such data gaps would require extensive *in vivo* testing. One potential solution to this lies in the leverage of existing toxicity data, and the development of "acute-chronic ratios" (ACRs). ACRs are empirically derived ratios between the acute and chronic ecotoxicological endpoints which can be used to estimate chronic toxicity where only acute values are available. Previously they have been shown to be robust within certain (non-surfactant) substance classes and non-specific mechanisms of action [1-5].

The aim of this work is to extend this approach to surfactants, with an initial focus on anionic surfactants, as an alternative to fish chronic testing.

Methods

1. Surfactant Identification

- Identification and compilation of CAS numbers

2. Data searching

- US EPA ECOTOX
- EnviroTox
- ECHA

3. MoA

- In silico predictions
- OECD Toolbox
- ChemProp
- Sapounidou [6]
- T.E.S.T

4. ACR

- Data curation
- Acute to Chronic pairing

1. Identification and compilation of catalogue of surfactants) based on CAS number via extensive searching various database e.g. EnviroTox, US EPA ECOTOX, eChemPortal
2. Data searching for acute and chronic fish data based on CAS number.
3. In silico prediction of Mode of Action (MoA) via selected profilers to confirm their narcotic mode of ecotoxic action.
4. Data curation and ACR derivation:
   a) Data quality evaluated by Klimisch scoring [7]
   b) For acute toxicity, only LC50/EC50 values from 96 hr OECD 203 tests were used.
   c) For chronic toxicity, all data with a duration ≥14 days were used. Results from extended short-term toxicity studies reporting nominal value NOECs were omitted.
   d) If multiple acute or chronic values were available for multiple fish species, all data points were evaluated for quality and then merged by geometric mean.
   e) PFAS were excluded due to different MoAs.

Results

Derived fish ACRs for anionic surfactants

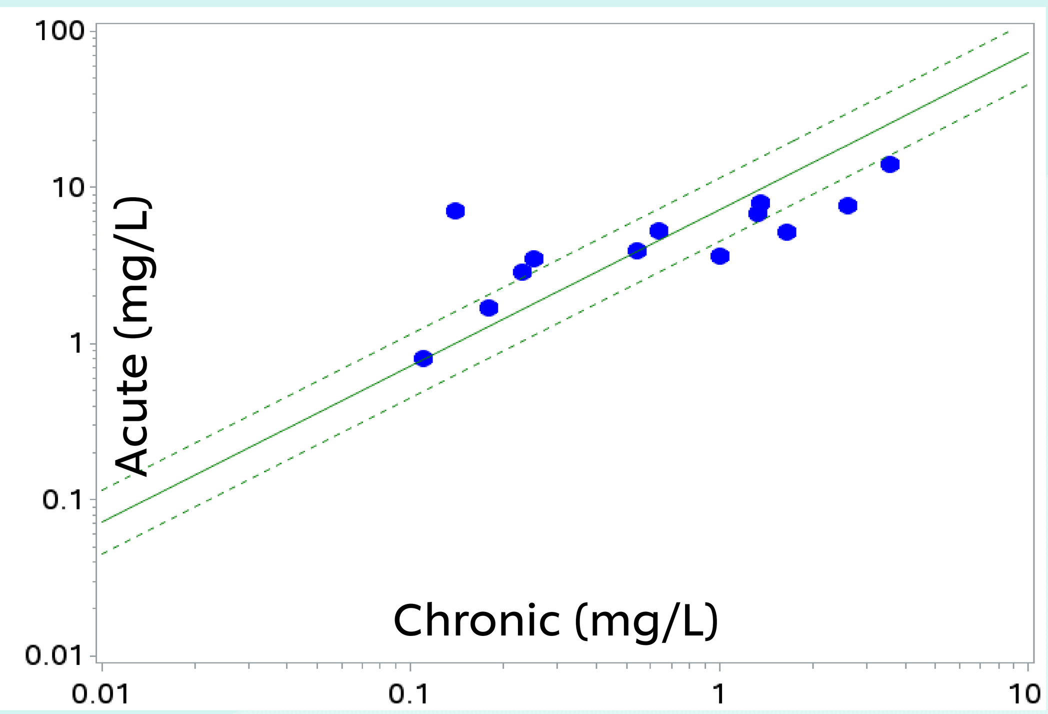

Figure 1. Derived ACR value (ACR = 7.2094), represented by the regression slope in the Log scale, with confidence intervals (4.5210, 11.4965).

- The average ACR was derived using the Univariate procedure in SAS 9.4
- This estimated the mean difference between the log-transformed acute toxicity and the log-transformed chronic toxicity along with the 95% confidence interval.
- Back calculating by taking the exponential gives the ACR estimate

Results (contd)

Table 1. Summary of ACR analyses for anionic surfactants

	ACRs
Number of substances	13
50th percentile (median)	**7.21**
90th percentile	**13.71**
Min value	2.92
Max value	50.71

Based on the albeit limited dataset of only 13 unique chemicals an ACR of **7.21** for the prediction of chronic fish toxicity of anionic surfactants has been derived.

This value is in line with the recommended value for anionic surfactants from ECOSAR of 6.5 [8].

The most accurate ACRs are derived when the acute and chronic toxicity values are measured in the same study with the same species, using the same batch of chemicals, and under similar test conditions. However, this is rarely the case, so uncertainties are recognised within this study.

Additionally, we assumed that the same CAS number reflects the same substance was tested in both acute and chronic tests, regardless of the exact composition.

In order to account for the uncertainty, the ACR value of **13.71 (90th percentile)** could be adopted as a precautionary measure and used to support a reduction in the current requirement for testing of vertebrates as part of a Weight of Evidence approach.

Further Work

The work presented here is focussed entirely on acute to chronic extrapolations for anionic surfactants in fish.

However, in order to fully leverage this approach, it is our aim to extend this analysis to include all surfactant classes i.e. anionics, cationics, non-ionics, and zwitterionics and include all trophic levels.

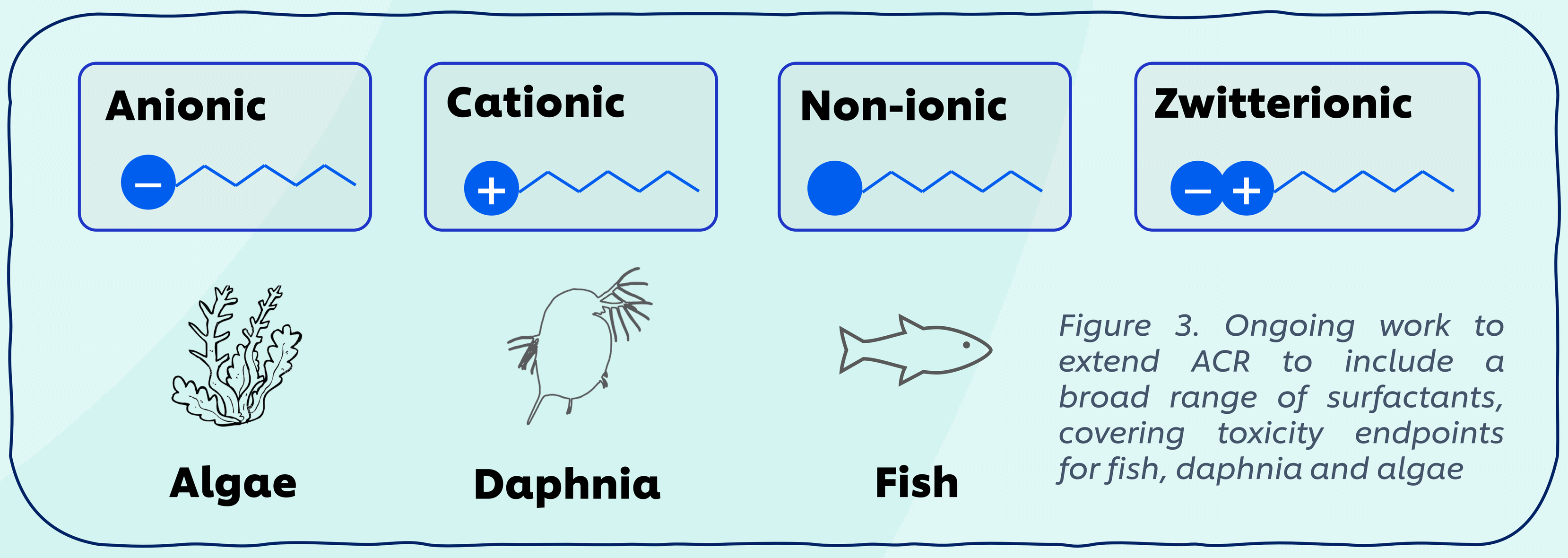

Figure 3. Ongoing work to extend ACR to include a broad range of surfactants, covering toxicity endpoints for fish, daphnia and algae

Using a similar approach to that described in Methods, the dataset has been expanded to over 1000 different surfactants. Aquatic data have been subsequently retrieved for approx. 200 substances indicating the challenges in data availability.

This dataset is currently undergoing an extensive data curation step prior to analysis.

Preliminary results indicate that the resulting surfactant ACRs for each trophic level are likely to be in the same order of magnitude as seen here, however, further work is required to address the current uncertainties around potential outliers.

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