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Linking algal growth inhibition to chemical activity: A tool for identifying excess toxicity

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Introduction and objective

- Aquatic toxicity data are generally expressed on a concentration basis, e.g., as effective concentrations (EC_{50}, mg L^{-1}).
- Whereas the data are useful within regulatory risk assessment, a given EC_{50} offers no direct information on whether the compound exerts baseline toxicity or excess toxicity.

In the present study, algal growth inhibition data were expressed on a chemical activity basis with the aim to identify excess toxicity – and thereby compounds of concern.

- Chemical activity (a) quantifies the energetic level of an organic compound relative to its pure liquid [0-1, unitless], and several studies have reported that baseline toxicity requires a chemical activity of at least 0.01-0.1 [1-7].

Procedure

- Algal growth inhibition was linked to chemical activity using two approaches.

Approach 1: Algal EC_{50} values were plotted relative to a regression of sub-cooled liquid solubility, serving as visual reference for chemical activity of unity.

Approach 2: Ratios of algal EC_{50} values and (sub-cooled) liquid solubility were determine, which essentially equals the effective chemical activity (Ea_{50}).

- Toxicity well below a chemical activity of 0.01 (i.e., 1% of liquid saturation) was used to identify excess toxicity.
- Toxicity data were carefully selected from a number of algal growth inhibition tests to cover (1) a wide range of solid and liquid organic compounds, (2) several expected modes of action, MOA and (3) several algal species [8-11].

Baseline toxicity data

Data analysis

Recently, high-quality data were published on the algal growth inhibition caused by 58 polar and 50 non-polar narcotic compounds (Fig. 1, [8, 9]). Here, two different approaches were applied to analyse a total of 108 liquids and solids (including 9 miscible and 8 ionisable compounds) exerting baseline toxicity.

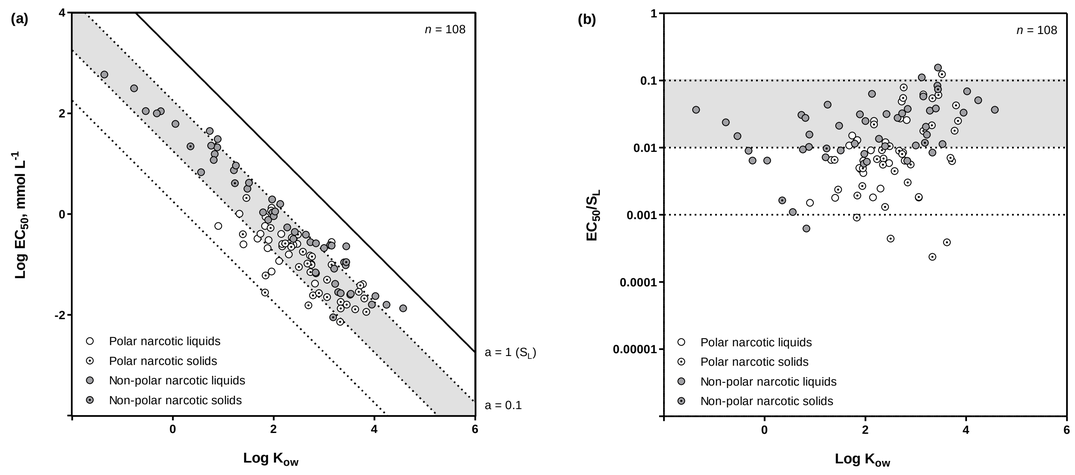

Figure 1. (a) Regression of sub-cooled liquid solubility (S_L, mmol L^{-1}, a=1) as a function of K_{ow} [12] and lines representing chemical activity levels of 0.1, 0.01 and 0.001. A total of 108 EC_{50} values (mmol L^{-1}) are plotted against their K_{ow}. (b) Ratios of the 108 EC_{50} values (mmol L^{-1}) and respective (sub-cooled) liquid solubility (S_L, mmol L^{-1}) are plotted against K_{ow}. Shaded areas are the chemical activity range 0.01 to 0.1 for baseline toxicity.

Multiple MOA data

Data analysis

The chemical activity concept was applied to two large datasets, including a wide range of compounds and multiple MOA. The selected data were based on growth rate inhibition and originated from 48 and 72-h toxicity tests with different freshwater green algae.

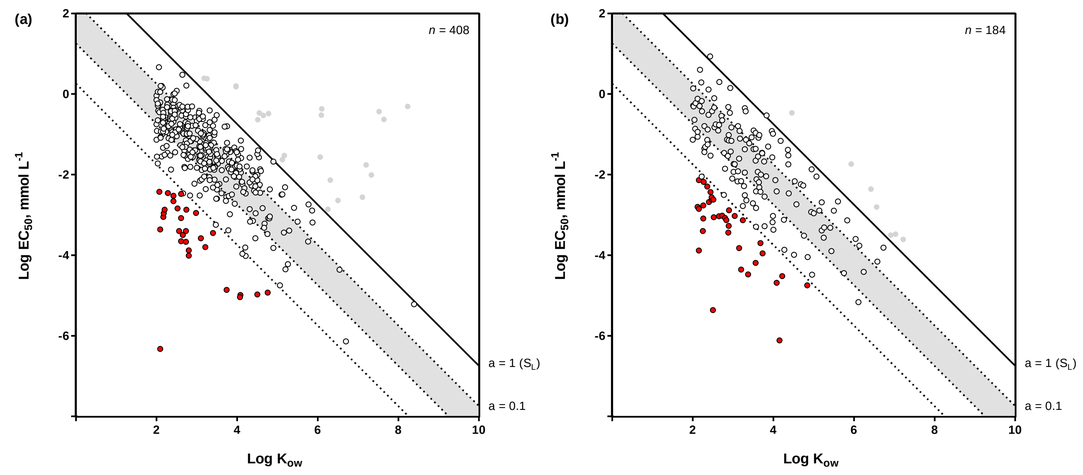

Figure 2. Regression of sub-cooled liquid solubility (S_L, mmol L^{-1}, a=1) as a function of K_{ow} [12] and lines representing chemical activity levels of 0.1, 0.01 and 0.001. Data (mmol L^{-1}) (a) reviewed by Fu et al [10] and (b) used for the Danish EPA Q-SAR for algal toxicity [11] are plotted against their K_{ow}. Grey circles: questionable data; red circles: compounds indicating excess toxicity. Shaded areas are the activity range 0.01 to 0.1.

Result and Conclusions

- Approach 1 (Fig. 1a): the majority of data were within the activity range 0.01 to 0.1, in good agreement with baseline toxicity. Approach 2 (Fig. 1b): data were more scattered, and four data points were below the activity of 0.001.
- Compounds characterised as polar narcotics (MOA 2, [8]) generally exerted toxicity at lower activities compared to non-polar narcotics (MOA 1, [9]).
- Challenges: Approach 1 relies on a generic relationship between sub-cooled liquid solubility and Log K_{ow}, whereas approach 2 relies on accurate physicochemical properties to estimate (sub-cooled) liquid solubilities.
- Based on these results, approach 1 was used for the first data analyses of two large datasets, including a wide range of compounds and multiple MOA (Fig. 2).

Preliminary Results and Next Steps

- For the dataset compiled from Fu et al (Fig. 2a), the vast majority of compounds were within the baseline toxicity range. A total of 29 compounds (7.1%) indicated excess toxicity and are studied further. Also, 22 compounds (5.4%) had EC_{50} above (sub-cooled) liquid solubility and the data were thus found questionable.
- For the dataset by Kusk et al (Fig. 2b) the overall picture is similar with the majority of compounds within the baseline toxicity range, 19.0% indicating excess toxicity and 3.8% of the data found questionable (Ea_{50} >1).
- Further analysis will look into: (1) the compounds indicating excess toxicity, (2) current knowledge on MOA of selected compounds,(3) the distribution of liquids and solids and (4) potential differences between algal species.

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