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Development of acute toxicity quantitative structure activity relationships (QSAR) and their use in linear alkylbenzene sulfonate species sensitivity distributions

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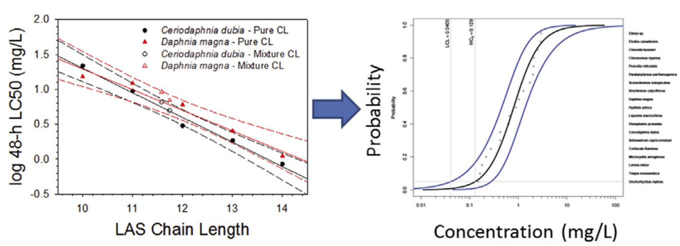
HIGHLIGHTS

- New single species QSARs for the anionic surfactant LAS are developed and verified.
- The new QSARs are applied to normalize diverse chronic toxicity data to relevant hazard assessment scenarios.
- Single Species Sensitivity Distributions (SSDs) are determined and compared to mesocosm findings.
- SSDs are somewhat conservative compared to robust stream mesocosm results.
- Integrated use of QSARs, normalization and SSD formulation provides a flexible method for environmental hazard determination.

GRAPHICAL ABSTRACT



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ABSTRACT

Linear Alkylbenzene Sulfonate (LAS) is high tonnage and widely dispersed anionic surfactant used by the consumer products sector. A range of homologous structures are used in laundry applications that differ primarily on the length of the hydrophobic alkyl chain. This research summarizes the development of a set of acute toxicity QSARs (Quantitative Structure Activity Relationships) for fathead minnows (*Pimephales promelas*) and daphnids (*Daphnia magna*, *Ceriodaphnia dubia*) using accepted test guideline approaches. A series of studies on pure chain length LAS from C10 to C14 were used to develop the QSARs and the robustness of the QSARs was tested by evaluation of two technical mixtures of differing compositions. All QSARs were high quality (R^2 were 0.965–0.997, $p < 0.0001$). Toxicity normalization employing QSARs is used to interpret a broader array of tests on LAS chain length materials to a diverse group of test organisms with the objective of developing Species Sensitivity Distributions (SSDs) for various chain lengths of interest. Mixtures include environmental distributions measured from exposure monitoring surveys of wastewater effluents, various commercial mixtures, or specific chain lengths. SSD 5th percentile hazardous concentrations (HC5s) ranged from 0.129 to 0.254 mg/L for wastewater effluents containing an average of 11.26–12 alkyl carbons. The SSDs are considered highly robust given the breadth of species ($n = 19$), use of most sensitive endpoints from true chronic studies and the quality of

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the underlying statistical properties of the SSD itself. The data continue to indicate a low hazard to the environment relative to expected environmental concentrations.

1. Introduction

Environmental fate and effects of LAS (linear alkylbenzene sulfonate) have been intensively evaluated since the 1960's when the ready biodegradable LAS replaced the non-biodegradable branched alkyl benzene sulfonate (Hanna et al., 1964). Because LAS is used at such high volumes globally, in a wide range of consumer product and industrial applications, LAS is considered a high priority chemical for environmental assessment and has been assessed for potential risk to the environment in many chemical management programs over the past two decades (Cowan et al., 2014).

Key aspects of LAS physical chemistry, ecotoxicity in various environmental compartments, and exposures in those compartments are known. Cowan et al. (2014) provided a recent review of LAS environmental risk assessment, along with other anionic surfactants, in North America summarizing these key attributes. Depending on the scientific or regulatory assessment and jurisdiction, aquatic toxicity evaluations of LAS have included anywhere from ~10 to as many as 60 individual studies of chronic responses to LAS (van de Plassche et al., 1999; HERA, 2009; REACH dossier at http://echa.europa.eu/substance-information/-/substanceinfo/100.063.721, ECHA, 2010). The rich data set for LAS has been needed to address environmental safety due to the high tonnage with wide-dispersive use of the compound, general range of chronic ecotoxicity (between 250 and 10,000 μg/L depending on the species), moderate sorptivity (Kd in the range of 3000 L/kg), and bioaccumulation potential (BCF, <1000 L/kg) (Cowan et al., 2014). In addition to the large amount of single species chronic aquatic toxicity data, LAS has been assessed in detail in realistic stream mesocosm studies. Belanger et al. (2002) developed the most comprehensive assessment of this type using a system of 12-m long stream channels that were exposed to 56 days to C12 (12 alkyl carbons)-LAS concentrations that spanned the range of anticipated no effects to substantial effects (roughly 126–2978 μg/L). Periphytic, invertebrate and fish responses to LAS exposure were assessed frequently during the study to develop an understanding of response patterns. The ecosystem level No-Observed-Effect-Concentrations (NOEC) for LAS to this system was 268 μg/L soluble LAS driven by responses of blue-green algae and key invertebrate mayfly, stonefly, and caddisfly fauna.

The mesocosm NOEC has routinely been compared to Species Sensitivity Distribution (SSD) summaries of LAS in terms of the HC5 or the fifth percentile Hazardous Concentration (the concentration that is expected to protect 95% of species at the NOEC level) (van de Plassche et al., 1999; Versteeg et al., 1999; Cowan et al., 2014). LAS is often tested as a technical mixture of chain lengths that range from C10 to C14 (where 10 to 14 indicate the range of alkyl carbons present). Chain length averages for LAS used in detergents that go down the drain to wastewater treatment plants typically range from C11.6 (Europe) to C11.9 (US). By industry voluntary agreement, average chain lengths in commercial detergents do not exceed C12 (SDA, 1996; HERA, 2009; Cowan et al., 2014) and have been in place since the 1990s. Limits to chain lengths below C12 were imposed due to aquatic toxicity considerations. Thus, the database for LAS toxicity is a mixture of materials tested as pure compounds (a single chain length) and technical mixtures that range from predominant C11 to C12 averages. To make things somewhat more complex, the technical mixtures tested in the laboratory do not reflect those that enter the environment. Longer chain lengths are preferentially removed in waste treatment and what enters waste treatment is a combination of all the various laundry products for all manufacturers, each of which may differ in the technical mixture used in a given product for performance or cost reasons. Ecotoxicity is known to be driven by chain length being roughly correlated to hydrophobicity (Fendinger et al., 1994 and many others). To rationally utilize the available chronic toxicity data, and place these studies into a proper hazard assessment context for environmentally-released LAS, the process of aquatic toxicity normalization was developed by van de Plassche et al. (1999) for several detergent surfactant classes and further refined by Boeije et al. (2006) for nonionic alcohol ethoxylate surfactants, Belanger et al. (2009) for aliphatic alcohols, Dyer et al. (2000) for alcohol ethoxysulfate anionic surfactants and Sanderson et al. (2009) for alkyl dimethyl amine oxide zwitterionic surfactants. The process of normalization utilizes the following approach that includes use of the initial empirical result and high quality QSARs to adjust the measured toxicity to a hypothetical target (for example, an environmental mixture or a particular commercial distribution of interest):

$$\text{Normalized toxicity (target CL specified)} = \text{Measured toxicity of tested CL} \times \left[\frac{\text{QSAR prediction for target CL}}{\text{QSAR prediction for tested CL}}\right] \quad (1)$$

CL in the above equation refers to Chain Length of the hydrophobe moiety. The normalization of aquatic toxicity data is central to producing a high quality SSD (van de Plassche et al., 1999) and depends greatly on the QSAR used for predictions. Various QSARs have been used in the development of LAS-normalized chronic toxicity data sets (Table 1) including generic acute QSARs (van de Plassche et al., 1999; Cowan et al., 2014) and acute anionic surfactant QSARs (Versteeg et al., 1999). These have resulted in the development of a variety of LAS Species Sensitivity Distributions summarized in Table 2. In an ideal situation, the QSARS used would be high quality, appropriate for predicting chronic toxicity and minimally trophic level specific (e.g., algae, *Daphnia*, and fish). In addition, the previous normalizations utilized log Kow as a surrogate for hydrophobicity. CL is also a reasonable surrogate for hydrophobicity with longer alkyl chains having great hydrophobic effect on toxicity. Using CL has some advantages to Kow as the experimental determination of surfactant octanol-water partitioning is technically challenging. AE and alcohol toxicity normalizations were able to include trophic-level specific chronic toxicity QSARs because the data was available (Boeije et al., 2006; Belanger et al., 2009). However, the use of trophic level specific chronic toxicity QSARs is very infrequent, even for such a well-studied class of anionic surfactants such as LAS. The combination of using the various QSARs along with differing input data sets has resulted in SSD HC5's that range from 0.15 to 0.48 mg/L.

In the research presented here we develop new trophic-level specific acute QSARs for LAS based on pure chain length compounds and modern analytical techniques, verify the predictions of the resulting QSARs with commercial mixtures and use these as