Using rainbow trout S9 clearance rates as first W-o-E for the biotransformation potential for surfactants

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The Cefic-ECO37 project aims to develop a bioconcentration assessment strategy for surfactants

in vitro based parameters	+	mechanistic BCF model	=	*in vivo* BCF
K_{MW} [1,2] & S9 [3,4]		*BIONIC* [5] *V3.0*		*Fish* [6,7]

ISSUE - surfactants are...

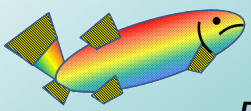
- amphiphilic chemicals: hydrophobic tail, hydrophilic head group
- bulk volume down-the-drain chemicals, difficult to assess fate
- experimentally challenging chemicals: scarce data=poor models
- often ionic, thus outside applicability domains of most QSARs
- sorbing in cell membranes (K_{MW}), so may bioaccumulate in fish
- expected (often designed) to rapidly biodegrade, but are they also biotransformed when they accumulate in exposed fish?

RESEARCH AIMS

1. can we use in vitro S9 hepatic clearance rate **($CL_{hep,S9}$)** to predict biotransformation and bioconcentration in fish ?
2. *can we use conservative partitioning data **(K_{MW})** to deduce the whole fish elimination rate from in vivo BCF data ?*
3. *can we construct surfactant specific structure-activity relationships with a systematic matrix of K_{MW} and $CL_{hep,S9}$?*

CONCEPT

in vivo
model
in vitro



fish BCF

To predict BCF: use BIONIC with K_{MW} + k_B

whole fish k_B

Aim 1. QIVIVE

Aim 2. *Deduce k_B top-down:* *in vivo BCF* *vs.* BIONIC k_B=0 BCF (K_{MW} only)

Aim 3. *Model key parameters* QSARs

Measure in vitro: K_{MW} & $CL_{hep,S9}$

CONCLUSION

BIONIC BCF model appears to capture toxicokinetics for anionic and nonionic surfactants based on S9-k_B.

For cationics, parameterization needs further refining.

ECO37 has generated:

$CL_{hep,S9}$ values for 47 surfactants. 38 showed clearance! $CL_{hep,S9}$ were < LOQ-S9 for: QACs, 1° amine cations, >C_{13} alkyl-sulfonates/-sulfates, and > C_{11}-LAS anions

K_{MW} values for 37 surfactants, making a total of ~80 K_{MW}. K_{MW} serve as key partition coefficients in BIONIC model.

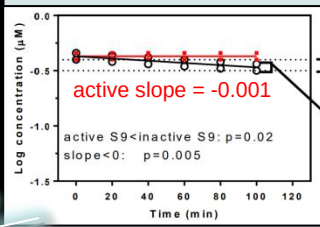
Rainbow trout $BCF_{kinetic}$ for 23 surfactants, in 3 mixtures. $BCF_{kinetic}$ range 0.01-8000 L/kg, highest for C_{16}-amines.

Refined BIONIC model to include QACs & S9-QIVIVE.

S9-evaluation

Can we use S9 to predict the biotransformation rate?

- Rapid clearance easily detected! But what if not observed?
- The lowest measurable S9 clearance = ~20% in 120 min.[3] This extrapolates to a relatively high k_B of 0.13 d^{-1} (10 g fish)
- Slower but significant clearance may go undetected.
- Other assays / metabolite formation may give further W-o-E.
- Significant S9 clearance: high biotransformation capacity Such elimination rate is likely to lower the BCF significantly.



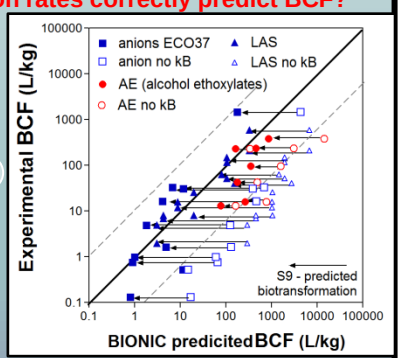
k = 0.138 h^{-1}
$CL_{hep,S9}$ = 10 mL/h/g liver

k_B = ~0.13 d^{-1} (Vd = 2.3)

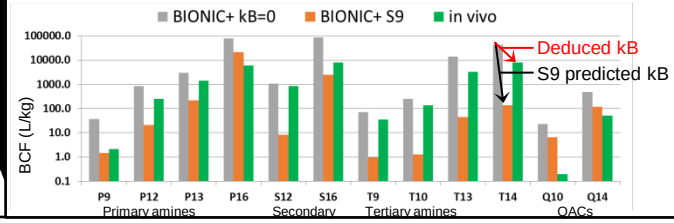
For most ionic surfactants:
Gill elimination rate (k_2) < 0.01 d^{-1}

Do S9 biotransformation rates correctly predict BCF?

- **For anionic and nonionic surfactants, in vivo BCF are closely (<10x) matched by BIONIC model predictions (incl. S9).**



- For amines (P,S,T), including S9-k_B in BIONIC underestimates in vivo BCF up to 100x. Baseline BCF (k_B=0) overestimates up to 20x: some amines are biotransformed.



ref 1: Rimmer & Droge ES&T 2017, p. 2890
ref 2: Droge ES&T 2019 p. 760
ref 3: Chen et al ES&T 2016, p. 12722
ref 4: Nichols et al. ET&C 2007 p. 1304
ref 5: Armitage et al. ET&C 2016, p. 882
ref 6: Kierkegaard et al. ES&T 2020, ASAP
ref 7: Tolls et al. ES&T 2000, P. 304