Aquatic Toxicity—Are Surfactant Properties Relevant?

D.W. Roberts*

Unilever Research Port Sunlight, Bebington, Wirral, CH63 3JW, United Kingdom

ABSTRACT: There are two potential approaches for quantitative structure–activity relationships modeling of aquatic toxicity of surfactants. One is to try to relate toxicity to parameters describing the surfactant properties, which can be measured or calculated. The other approach is to try to apply to surfactants parameters such as log *P* (*P* = octanol/water partition coefficient), which can also be used to relate toxicity to structure for nonsurfactants. This paper compares the two approaches and presents new data supporting the second approach as the more mechanistically relevant. Further refinements in the calculation method for log *P* are presented.

Paper no. S1162 in *JSD 3,* 309–315 (July 2000).

KEY WORDS: Anionic surfactants, log *P*, QSAR, surfactant properties.

For nonsurfactant organic chemicals, quantitative structure–activity relationships (QSAR) correlating aquatic toxicity with log *P* (*P* = octanol / water partition coefficient) are long established.

Modeling of surfactant toxicity is sometimes considered to present a different problem. Log *P* is difficult to measure for surfactants (1) and it has been argued that it is not a relevant parameter (2). However, when analyzed more closely, the arguments amount essentially to statements of the practical difficulties of measurement. This paper discusses whether log *P* or surfactant-specific parameters are more appropriate for development of surfactant toxicity QSAR.

Log P *or surfactant-specific parameters?* The tendencies of surfactants to aggregate at interfaces, to form micelles, and to act as solubilizing and emulsifying agents are sometimes quoted as arguments against the validity of log *P* for toxicity correlations.

These arguments can be countered by the following considerations (3).

Although it is experimentally difficult to measure log *P* for surfactants, because of their tendency to reside on the water / octanol interface and to solubilize octanol in water and water in octanol, there is no conceptual problem in defining a partition coefficient between octanol and water for a surfactant. *P* is simply the ratio, at equilibrium, of the concentrations of the compound in true solution in each of the two solvent phases. The fact that other equilibria exist (with concentrations at the interface and in the micellar phase if present) does not affect the definition. Surfactant in micelles is not in true solution, and the "micellar concentration" in the aqueous phase is not included in the *P* value. Although the presence of surfactant affects the solubilities of octanol and water in each other, the same phenomenon is encountered with nonsurfactant solutes and can in principle be accounted for by measuring log *P* at various concentrations and extrapolating to infinite dilution. Solubilization of octanol in the surfactant micelles will occur if the surfactant concentration is above the critical micelle concentration, but again this does not affect the definition of *P*.

There are several good reasons for using log *P* in QSAR studies of surfactants and for avoiding, where possible, the use of surfactant-specific parameters.

Firstly, surfactants and nonsurfactants form a continuum, with no clear boundary between the two. It would be universally agreed that the compound $RO(CH_2CH_2O)_nH$ is a surfactant when R is *n*-dodecyl and *n* has any positive value, and a nonsurfactant when R is ethyl and *n* has any positive value. It becomes much less clear when homologs such as R = hexyl, *n* = any positive value, or R = dodecyl, *n* = 0 are considered. By definition, surfactant-specific parameters cannot be determined for compounds which are clearly nonsurfactants, and there may be experimental difficulties in measuring them for compounds which are neither clearly surfactants nor clearly nonsurfactants.

Secondly, the use for QSAR development of the same parameter for surfactants as is used for nonsurfactants helps in clarifying whether the surfactants have the same or different mechanisms of action as compared to nonsurfactants.

Thirdly, bearing in mind that commercial surfactants are usually multicomponent mixtures, so that mixture toxicity equations need to be used, a parameter which can be calculated for each component is obviously more applicable than one which has to be measured experimentally for each component. Even though the measurement may be simple, the separation or independent synthesis of each component would be prohibitively time-consuming. Log *P* values for most surfactants, although difficult to measure, can easily be calculated from structure. Conversely, surfactant-specific parameters often can be measured readily but are difficult to calculate.

*Address correspondence at DP-PTEC, Unilever Research Port Sunlight, Quarry Road East, Bebington, Wirral, CH63 3JW, United Kingdom. E-mail: david.w.roberts@unilever.com

RESULTS AND DISCUSSION

Calculation of log P. The Leo and Hansch method (4) for calculation of log *P*, which can be done either manually or by use of commercial software, is based on the concept that the various fragments of a molecule contribute additively to its log *P* value. Log *P* is calculated by conceptually breaking the molecule down into its component fragments, summing the partial log *P* values (referred to as hydrophobic fragment values, *f*) and applying factors *F* to allow for variation in how the fragments are combined in the whole molecule. The *f* and *F* values were originally derived from experimental log *P* values for a large number of chemicals. The rules for applying them are based on mechanistic considerations of the solvation energy changes when the molecule partitions into the aqueous phase.

Previous publications from this laboratory have described our work in extending the Leo and Hansch log *P* calculation method to be applicable to surfactants (5–7). Although commercial software for the Leo and Hansch calculations is now widely available, the structure of most surfactants is sufficiently simple for the log *P* values to be calculated manually. For unbranched alcohol ethoxylates and their derivatives, the log *P* value is a linear function of the parent alcohol carbon number *C* and the degree of ethoxylation *E*. It follows that for any set of such surfactants, a log *P*-based QSAR can be substituted by an equivalent QSAR based on *C* and *E*. However, QSARs based on *C* and *E* are less versatile than log *P*-based QSARs since they cannot be applied to compounds having more structural diversity, and they can be misleading if applied to prediction of toxicity for branched-chain isomers and homologs.

The following guidelines for calculation of log *P* can be given.

It is important to be aware that the computerized version does not contain fragment values for anionic groupings, does not deal adequately with compounds containing several ethyleneoxy (EO) groups, and does not distinguish between different branching patterns. If using the computerized version, the best approach is as follows.

If the compound contains anionic groups, enter the structure with the anionic groups replaced by *H*. Adjust the answer manually by subtracting the fragment values for these *H* groups (0.23) and adding the bond factor (–0.12) plus the fragment values for the anionic groups as originally given by Leo and Hansch (4). Some fragment values relevant to surfactants are:

- Aliphatic $–SO_3^-$ –5.87
- Aromatic $–SO_3^-$ –4.53
- Aliphatic $–OSO_3^-$ –5.23
- Aliphatic $–CO_2^-$ –5.19
- Aliphatic ether –O– –1.82
- Aliphatic –OH –1.64
- Aliphatic ester $–CO_2–$ –1.49

The first four of these are not in the computerized version of the method. Note that all of these values are negative, indicating a hydrophilic contribution from these groups.

If the compound contains a chain of EO units, enter the structure with a single EO unit and adjust the answer manually by applying a fragment value f_{EO}, equal to –0.10 for each additional EO unit. However, this fragment value may not be universally applicable (*vide infra*).

If the compound contains branched alkyl chains, enter the structure with these replaced by linear chains with the same carbon number. Adjust the answer by applying the position-dependent branch factor (PDBF), which can be calculated as PDBF = $–1.44 \log(S + 1)$, where *S* is the carbon number of the shorter chain from the branching position. Some PDBF values are:

- Methyl branch –0.43
- Ethyl branch –0.69
- Propyl branch –0.87
- Butyl branch –1.01
- Pentyl branch –1.12
- Hexyl branch –1.22

A further recent refinement is in the way proximity factors are calculated for situations where two hydrophilic groups are close together in a molecule. The standard Leo and Hansch method, including the computerized version, has proximity factors calculated as:

- Separation by one carbon $–0.42 (f_1 + f_2)$
- Separation by two carbons $–0.26 (f_1 + f_2)$
- Separation by three carbons $–0.10 (f_1 + f_2)$

where f_1 and f_2 are the fragment values of the two hydrophilic groups; since these are negative, the proximity factors are positive. However, this method does not deal adequately with the situation where one of the two groups is much more hydrophilic than the other—a situation which arises in several common surfactants, such as ether sulfates and ester sulfonates. In work which will be published on another occasion, we have derived an approach to calculation of proximity values based on consideration of the overlap between hydration sheaths of neighboring hydrophilic groups. For example in ester sulfonates, the original method gives a proximity factor value of 3.09, which is unrealistically large (being over twice as positive as the ester group fragment value, –1.49, is negative). The new approach gives a proximity factor value of 1.49. In ether sulfates, the anionic sulfate group is separated by two carbons from an ether oxygen group. The original method gives a proximity factor value of 1.83, while the new method gives a value of 1.48.

For aquatic toxicity of nonsurfactant organic compounds, two nonspecific modes of action are recognized, each one modeled by QSAR based on log *P*: (i) general narcosis (8): $\log (1/EC_{50}) = 0.87 \log P + 1.13$; (ii) polar narcosis (9): $\log (1/EC_{50}) = 0.63 \log P + 2.52$. [$EC_{50}$ (EC = effect concentration) is the concentration (in mol/L) required to produce the toxic effect, which may be death, narcosis, immobilization, etc., depending on the test protocol, in 50% of the test population].

These equations were derived for fish toxicity, but equations with very similar slopes and intercepts apply to other organisms such as *Daphnia*.

Using log *P* values calculated as described above and mixture toxicity equations where appropriate, we have derived QSARs covering a range of anionic and nonionic surfactants. In previous publications we showed that acute toxicity of nonionic surfactants is well-modeled by the general narcosis QSAR, and toxicity of anionic surfactants is well-modeled by the polar narcosis QSAR (5–7,10). In work that will be reported elsewhere, we have now carried out toxicity studies on mixtures of surfactants with nonsurfactants known to act either as general narcotics or polar narcotics. Depending on whether the two components of the mixture act by the same or different mechanisms, the mixture toxicity may or may not be additive. The findings may be summarized:

- Anionic surfactant + general narcotic — nonadditive
- Anionic surfactant + polar narcotic — additive
- Nonionic surfactant + general narcotic — additive
- Nonionic surfactant + polar narcotic — nonadditive

These findings support the view that surfactants and nonsurfactants behave similarly in their aquatic toxicity, and that log *P* is a suitable parameter for modeling surfactant toxicity.

A QSAR based on surfactant-specific parameters. A recent publication by Rosen *et al.* (2) describes a QSAR study for aquatic toxicity in river water of pure single-component anionic surfactants to the rotifer *Brachionus calciflorus*. Unlike the studies referred to above, these were chronic toxicity studies. The toxicity was correlated with a combination of two surfactant specific parameters, pC_{20} and A_{min}. The pC_{20} value is the negative log of the concentration of surfactant when the surface tension of the solution is 20 mN/m less than that of the river water, and A_{min} is the minimum cross-sectional area of the surfactant at the water surface, calculated from the slope of a surface tension/concentration plot. The toxicity values are correlated with the ratios pC_{20}/A_{min}. Table 1 shows the surfactants, their toxicities, their pC_{20} and A_{min} values, and the log *P* values calculated by the method summarized here.

Rosen *et al.* (2) argue that the pC_{20} value represents the ability of the surfactant to adsorb onto the external tissues of the organism and that A_{min}, being a function of the work required to remove the head-group hydration sheath so as to allow the molecule to pass through a membrane, is an inverse measure of the ability of the surfactant to penetrate to the interior of a cell. However, this argument seems mechanistically unsound, since it is generally considered that for chemically unreactive toxicants like these surfactants, the site of action is the external cell membrane. Nevertheless the correlation between toxicity and the pC_{20}/A_{min} parameter is good, as shown in Figure 1.

This plot, with the A_{min} value for $C_{12}SO_3$ corrected (11), is slightly better than that originally reported by Rosen *et al.* (2).

The reason for the good correlation observed may be that pC_{20} and A_{min} in combination model log *P*. If we consider that the log *P* value of any of these surfactants is composed of the contributions from the hydrophobicity of the alkyl group and the hydrophilicity of the head group, then pC_{20} largely models the former and A_{min} largely models the latter.

If this is so, then we should expect the toxicity values to be correlated with log *P* values for these surfactants. In Figure 2 log $(1/EC_{50})$ is plotted against log *P*.

Although the QSAR based on log *P* is highly significant, the statistical fit is not as good as it is for the QSAR based on pC_{20}/A_{min}. It is interesting to consider why this is so. It is possible that the pC_{20}/A_{min} values, being based on experimental measurements, predict the differences between

TABLE 1
Rotifer Toxicity of Anionic Surfactants[a]

Surfactant	$\log(1/EC_{50})$	pC_{20}	A_{min}	log *P*[b]
$C_{12}S$	5.30	3.68	0.504	1.60
$C_{12}E_2S$	5.47	4.32	0.512	2.12 (1.97)
$C_{14}S$	5.88	4.68	0.485	2.68
$C_{14}E_2S$	6.28	5.24	0.454	3.20 (3.05)
$C_{12}SO_3$	4.62	3.46	0.709[c]	0.96
$C_{12}E_4S$	5.09	4.35	0.688	1.92 (1.47)
$C_{14}E_4S$	5.85	5.51	0.569	3.00 (2.55)
$C_{15}E_4S$	6.17	5.96	0.557	3.54 (3.09)

[a] EC_{50} in mol/L. For definitions of EC_{50}, pC_{20}, and A_{min}, see text. Surfactant nomenclature: S = sulfate; SO_3 = sulfonate.
[b] Present work. Bracketed values based on $f_{EO} = -0.25$ (see text).
[c] In the paper by Rosen *et al.* (2), a value of 1.09 is given. However this seems to be a misprint and is inconsistent with the surface tension/concentration plot shown: the value given here is taken from a more recent paper by Rosen *et al.* (11) which appeared between the original submission and the revision of the present paper.

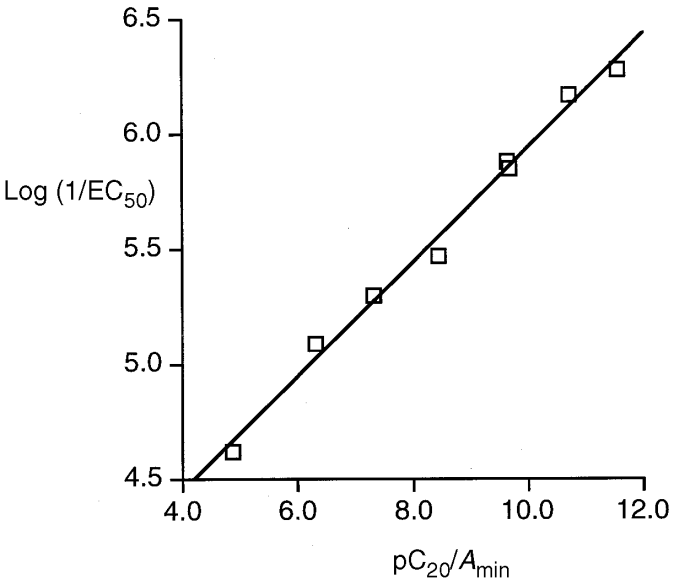

FIG.1. Log $(1/EC_{50})$ vs. pC_{20}/A_{min} [data from Rosen *et al.* (2)]. For definitions of EC_{50}, pC_{20}, and A_{min}, see text. Log $(1/EC_{50}) = 0.25\ (\pm 0.02)\ pC_{20}/A_{min} + 3.45\ (\pm 0.17)$; $n = 8$, $R^2 = 0.991$, $s = 0.06$, $F = 676$.

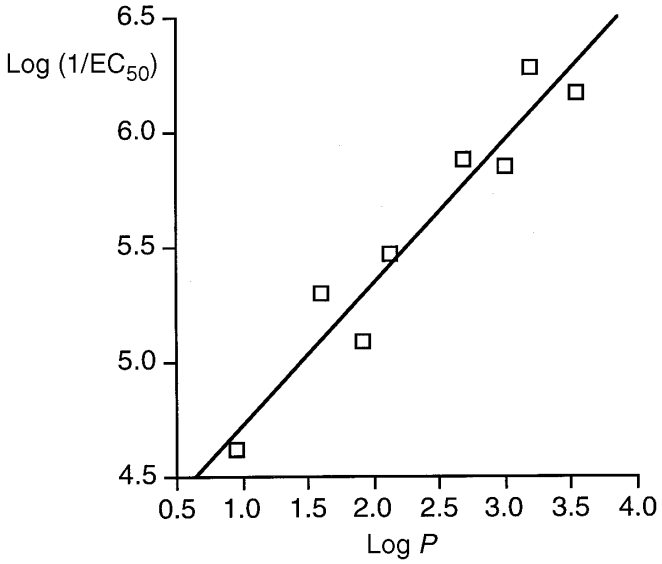

FIG. 2. Log ($1/EC_{50}$) vs. log *P* [toxicity data from Rosen *et al.* (2)]. Log ($1/EC_{50}$) = 0.62 (±0.15) log *P* + 4.11 (±0.37); $n = 8$, $R^2 = 0.924$, $s = 0.17$, $F = 73$.

the true log *P* values of the surfactants better than the calculated log *P* values do. This would imply that a further refinement of the log *P* calculation method, applicable to at least some of the surfactants discussed here, is needed.

From consideration of the underlying physical chemistry, the method of dealing with multiple EO units in the log *P* calculation may need refinement. The argument proceeds as follows.

An EO unit is more hydrophobic in a staggered conformation than in an eclipsed conformation, because of a water-sharing effect (Fig. 3). This is the basis of the well-known cloud-point phenomenon observed with ethoxylated alcohols: as the temperature of the solution is increased, the higher energy levels corresponding to the eclipsed conformations of the EO units become more populated and the hydrophilicity decreases, to the point where the surfactant comes out of solution.

A measured hydrophobic fragment value f_{EO} for an EO unit will reflect the relative contributions, at the temperature of the measurement, from the eclipsed and staggered conformers in the aqueous solution of the compound.

The f_{EO} value of –0.10 used to calculate the log *P* values shown in Table 1 was derived (10) directly from published log *P* measurements on glycols and inferentially from analysis of toxicity data for ethoxylated alkylphenols. Subsequently it has been further validated by successful application in QSAR studies on nonionic surfactants (3,6).

In the sulfated ethoxylated alcohols, the chain of EO units is terminated by a relatively heavier atom, sulfur, which in turn carries three oxygen atoms. Consequently the inertial forces tending to stretch the EO chain toward its maximum length (i.e., all staggered conformation) are stronger in alcohol ethoxy sulfates (AES) than in ethoxylated alcohols. This implies that, at the same temperature, the proportional contribution of the more hydrophilic staggered EO units will be greater in AES than in ethoxylated alcohols. It follows that a more negative value than –0.10 would be appropriate for f_{EO} when applied to AES. Modified log *P* values for the AES compounds in Table 1 were therefore calculated using an f_{EO} value of –0.25 (arbitrarily chosen on the basis of visual inspection of Fig. 2) for each EO unit after the first. The modified log *P* values, shown in brackets in Table 1, are 0.15 lower than those for the E_2 compounds and 0.45 lower for the E_4 compounds. Figure 4 shows a plot of log ($1/EC_{50}$) against log *P*, using the modified log *P* values for the AES compounds.

The statistical quality of this QSAR is comparable to that of the QSAR based on pC_{20}/A_{min}, and better than that of

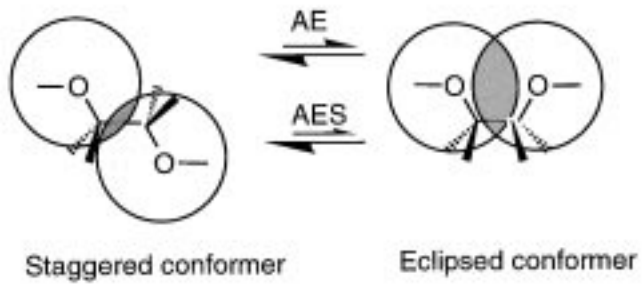

FIG. 3. Hydration of ethyleneoxy (EO) units. The circles represent the hydration sheaths of low energy (relative to bulk water) water molecules surrounding the oxygen atoms. AE, alcohol ethoxylate; AES alcohol ethoxy sulfate. Water molecules in the overlap volumes are shared between the two oxygen atoms. The greater the overlap, the more low-energy molecules are shared, the lower the total number of low-energy water molecules solvating the oxygen atoms, the lower the total hydrophilicity. The overlap volume is greater in the eclipsed conformer than in the staggered conformer, so the latter is more hydrophilic. The more the equilibrium lies on the staggered side, the more negative the contribution of the EO unit to log *P*.

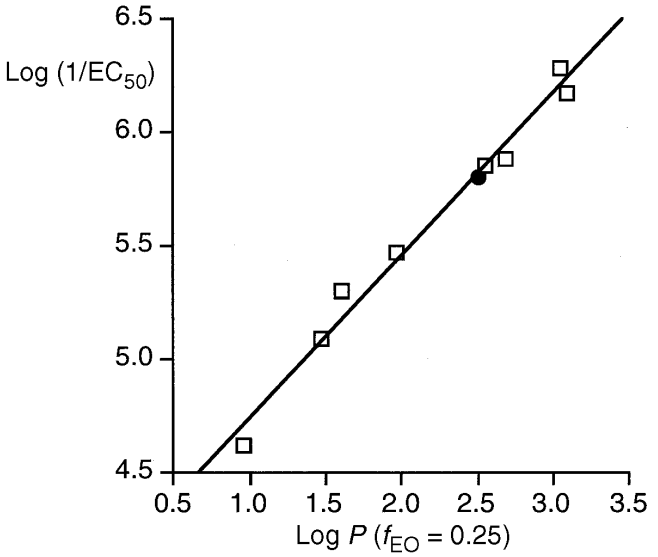

FIG. 4. Log ($1/EC_{50}$) vs. log *P* ($f_{EO} = –0.25$). Log ($1/EC_{50}$) = 0.71 (±0.08) log *P* + 4.03 (±0.18); $n = 8$, $R^2 = 0.982$, $s = 0.08$, $F = 330$. ●, $C_{13}E_2S$ (not included in regression).

the QSAR based on $f_{EO} = -0.10$ for log *P* of AES. This finding supports the argument made above, and now more work needs to be done to validate this modification of the log *P* calculation and to arrive at a more accurate f_{EO} value for use with AES and similar compounds.

The predictive ability of this QSAR can be tested using data for a further anionic surfactant, $C_{13}E_2S$, for which a toxicity value determined in the same test system has been reported by Versteeg *et al.* (12). pC_{20} and A_{min} values are not reported, so it is not possible to use the QSAR established by Rosen *et al.* (2) to predict the toxicity. However the log *P* value is easily calculated as 2.51 (based on $f_{EO} = -0.25$). Applying the log *P*-based QSAR equation gives a predicted log $(1/EC_{50})$ value of 5.81. The observed value for log $(1/EC_{50})$ is 5.80 (EC_{50} in mol/L). The experimental log $(1/EC_{50})$ and the calculated log *P* are plotted as a filled circle in Figure 4. The very good agreement between calculated and observed toxicity demonstrates the predictive capability of the log *P*-based QSAR.

Application of QSAR to multicomponent surfactants. Many commercial surfactants are mixtures of homologs and isomers, and the toxicity of such a surfactant results from the combined action of all the components. There are several approaches for dealing with this situation. In discussing these approaches, it is assumed that the QSAR equation has the general form:

$$\log (!/EC_{50}) = aF(X) + b \quad [1]$$

where *a* and *b* are constants and *F* (*X*) is some mathematical function of *X*, a measured or calculated physical property value, or combination of physical property values.

Method 1. Mixture toxicity equations. The most rigorous method, applicable when an existing QSAR is to be used for prediction of toxicity, is to calculate the toxicity for each component and apply a mixture toxicity equation. The general mixture toxicity equation for EC_{50}, applicable when all components act by the same toxic mechanism, is:

$$1/EC_{50}\,(\text{mixture}) = f_1/EC_{50_1} + f_2/EC_{50_2} + \cdots \quad [2]$$

where f_1, f_2 etc., are the mole fractions of components 1, 2, etc., EC_{50} values being in molar concentration units. Application of this method requires that the composition of the surfactant mixture is known, and that X values are known or can be calculated for each component of the mixture.

Method 2. Weighted average physical parameters. Another method is to use *F* (weighted average *X*) for example if *F* (*X*) is log *P*, then *F* (weighted average *X*) is given by log $(f_1P_1 + f_2P_2 + \cdots)$, and the toxicity of the mixture would be calculated as:

$$\log (!/EC_{50})\,(\text{mixture}) = \text{antilog}\,(f_1P_1 + f_2P_2 + \cdots) + b \quad [3]$$

This is an approximate method, and will not give a result identical to the more reliable estimate from the mixture toxicity method. There is a systematic mathematical error in the estimate of log $(1/EC_{50})$: for a QSAR based on log *P* this is equal to:

$$\log [(f_1P_1 + f_2P_2 + \cdots)^a - (f_1P_1{}^a + f_2P_2{}^a + \cdots)] \quad [4]$$

This is the best method to use when toxicological data on a multicomponent substance are to be used in developing a QSAR. Note that this method is applicable irrespective of whether or not the true *X* value of the mixture is given by the weighted average *X* value of the components. For a QSAR based on pC_{20}/A_{min} the toxicity of the mixture would be calculated as:

$$a\,[-\log (f_1C_{20_1} + f_2C_{20_2} + \cdots)]/(f_1A_{min_1} + f_2A_{min_2} + \cdots) + b \quad [5]$$

Method 3. Measured physical parameters for the mixture. The toxicity is calculated from the measured physical parameter *X* of the mixture, as:

$$\log (1/EC_{50})\,(\text{mixture}) = aF\,[X\,(\text{mixture})] + b \quad [6]$$

This method is equivalent to method 2, but is only applicable if the *X* value of the mixture really is equal to the weighted average *X* value of the components. If this can be demonstrated to be the case, the method may be useful for estimating toxicity from a physical measurement, or for using data on a multicomponent substance in developing a QSAR. This is the case when *X* is the octanol/water partition coefficient *P*, although in practice it is simpler to use calculated *P* values and apply method 1 or method 2.

It remains to be established whether or not this method would be applicable for a QSAR based on the pC_{20}/A_{min} parameter. If so, measurement of pC_{20}/A_{min} would be a convenient and rapid empirical means of estimating toxicity for multicomponent surfactants. It seems reasonable to expect that pC_{20} would be additive, i.e.,

$$pC_{20}\,(\text{mixture}) = -\log (f_1C_{20_1} + f_2C_{20_2} + \cdots) \quad [7]$$

but it is much less clear whether the same applies to A_{min}:

$$A_{min}\,(\text{mixture}) = f_1A_{min_1} + f_2A_{min_2} + \cdots\,? \quad [8]$$

On the basis of the information currently available, it is not possible to state whether pC_{20} and A_{min} determined for a mixture would give a good prediction of EC_{50} using the QSAR based on pC_{20}/A_{min}. Rotifer chronic toxicity and surface tension/concentration studies for commercial mixtures such as linear alkylbenzene sulfonate (LAS) and partly branched AES would be useful in this context.

Method 4. Calculated physical parameters for the average molecular structure. This method is simplest to apply when the QSAR is based on log *P*. For example a 2:1 molar mixture of $C_{12}S$ and $C_{14}S$ has an average structure of $C_{12.67}S$, and the log *P* value can be calculated as:

$$\log P = \log P\,(C_{12.67}S) + 0.67 \times (\text{increment for } CH_2)$$

$$= 1.60 + 0.67 \times 0.54 = 1.96 \quad [9]$$

This method is applicable when all the components are isomers or homologs of each other but cannot be applied to mixtures of different surfactant types, for example LAS and AES. The systematic mathematical error in the estimate of log $(1/EC_{50})$ by this method using a QSAR based on log *P* is equal to:

$$a[f_1 \log P_1 + f_2 \log P_2 + \cdots] - \log[f_1 P_1^{\,a} + f_2 P_2^{\,a} + \cdots] \qquad [10]$$

To apply this method with a QSAR based on pC_{20} and A_{min} would require a method for estimating these parameters from structure. Currently this is not possible, but if a wider-ranging set of pC_{20} and A_{min} data were generated regression analysis could be used to develop calculation methods based on structural descriptors such as surfactant type (AS, AES, ...), alkyl chain length, and degree of ethoxylation.

In Table 2 methods 1, 2, and 4 are applied to prediction of rotifer chronic toxicity for two multicomponent surfactants: coco AS, treated as a 2:1 molar mixture of $C_{12}S$ and $C_{14}S$, and coco AES-1, treated as a six-component mixture with C_{12} and C_{14} in 2:1 molar proportion and E-0, E-1, and E-2 in 1:1:1 molar proportion.

Interpretation of the log P *based QSAR.* It is highly revealing to compare the regression equation for the log *P*-based rotifer chronic toxicity plot shown in Figure 4 with that reported for acute aquatic toxicity to *Daphnia* in hard water of LAS and ester sulfonates, which have been shown to act as polar narcotics (7):

rotifer chronic toxicity

$$\log (1/EC_{50}) = 0.71\ (\pm 0.08) \log P + 4.03\ (\pm 0.18) \qquad [11]$$

Daphnia acute toxicity

$$\log (1/EC_{50}) = 0.70\ (\pm 0.08) \log P + 2.54\ (\pm 0.21) \qquad [12]$$

TABLE 2
Calculated Log $(1/EC_{50})$ Values for Multicomponent Surfactants[a]

Method	Coco AS	Coco AES-1
Log *P* QSAR		
Mixture toxicity	5.58	5.85
W.a. parameter[b]	5.64	5.92
W.a. structure	5.42	5.86
pC_{20}/A_{min} QSAR		
Mixture toxicity	5.57	6.07
W.a. parameter	5.38	5.66

[a]Log $(1/EC_{50})$ values are based on 0.71 log *P* + 4.03 or on 0.25 pC_{20}/A_{min} + 3.45. For $C_{12}E_1S$ and $C_{14}E_1S$ components of coco alcohol ethoxy sulfate (AES)-1, pC_{20} and A_{min} values are estimated by linear extrapolation from the values (shown in Table 1) for the corresponding E_2 and E_4 ethoxamers: $C_{12}E_1S$, pC_{20} = 4.035, A_{min} = 0.424; $C_{14}E_1S$, pC_{20} = 5.105, A_{min} = 0.3965. The average formulae of coco AS and coco AES-1 are $C_{12.67}S$ and $C_{12.67}E_1S$, respectively. For application of the average structure method, the log *P* values for these hypothetical compounds are calculated by adding 0.36 (= 0.67 × 0.54, 0.54 being the log *P* increment for a methylene group) to the log *P* value of the C_{12} homolog.

[b]W.a. (weighted average) parameter entries are calculated from log $(f_1P_1 + f_2P_2 + \cdots)$ or from –log $(f_1C_{20_1} + f_2C_{20_2} + \cdots)$ and $(f_1A_{min_1} + f_2A_{min_2} + \cdots)$. For definitions of *P*, QSAR, p_{20}, and A_{min} see text.

The slopes are identical within the error limits, having a value of about 0.71 which is very close to that established for nonsurfactant polar narcotics. The intercept for the rotifer QSAR is about 1.5 log units larger than that for the LAS and ester sulfonates acute toxicity polar narcosis QSAR. Thus the anionic surfactants shown in Table 1 are about 30 times more toxic in the chronic rotifer test than they would be in an acute fish or *Daphnia* test. This ratio is in the range of general experience that chronic EC_{50} values can be up to two orders of magnitude lower than acute EC_{50} values. The implication is that anionic surfactants act as polar narcotics in chronic toxicity as well as acute toxicity. There is no evidence for enhanced toxicity (as compared with nonsurfactants) arising from their surfactant properties.

Good reasons have been demonstrated here why log *P* should be the parameter of first choice for surfactant QSAR. The fact that it is easily calculated from structure makes it more rapidly and widely applicable than surfactant-specific parameters, which need to be measured, which is particularly important because commercial surfactants are usually mixtures.

It has been demonstrated how a QSAR based on surfactant-specific parameters can be reformulated as a log *P*-based QSAR. This having been done, a further advantage of the log *P* parameter becomes apparent: from the log *P*-based QSAR it is immediately evident that the toxicities of the anionic surfactants are consistent with what would be expected based on the polar narcosis QSAR established for nonsurfactants.

Overall, this study provides further evidence that in aquatic toxicity, surfactants do not constitute a special class of chemicals.

REFERENCES

1. Morrall, S.W., R.R. Herzog, P. Kloepper-Sams, and M.J. Rosen, Octanol/Water Partitioning of Surfactants and Its Relevance to Toxicity and Environmental Behaviour, *Fourth World Surfactants Congress Proceedings*, Barcelona, A.E.P.S.A.T., Barcelona, Spain, Vol. 3, 1996, p. 220.
2. Rosen, M.J., Y. P. Zhu, S.W. Morrall, D.J. Versteeg, and S.D. Dyer, Estimation of Surfactant Environmental Behaviour from Physical Chemical Parameters, *Fourth World Surfactants Congress Proceedings*, Barcelona, A.E.P.S.A.T., Barcelona, Spain, Vol. 3, 1996, p. 304.
3. Roberts, D.W., and S.J. Marshall, Applications of Hydrophobicity Parameters to Prediction of the Acute Aquatic Toxicity of Commercial Surfactant Mixtures, *SAR and QSAR in Environ. Res. 4*:167 (1995).
4. Leo, A.J., and C. Hansch, *Substituent Constants for Correlation Analysis in Chemistry and Biology*, Wiley, New York, 1979.
5. Roberts, D.W., Aquatic Toxicity of Linear Alkyl Benzene Sulphonates (LAS) – A QSAR Analysis, *Jorn. Com. Esp. Deterg. 20*:35 (1989).
6. Roberts, D.W., M.T. García, I. Ribosa, and W. Hreczuch, QSAR Analysis of Aquatic Toxicity of Ethoxylated Alcohols, *Ibid. 27*:53 (1997).
7. Roberts, D.W., S.J. Marshall, and G. Hodges, Quantitative Structure–Activity Relationships for Acute Aquatic Toxicity

of Surfactants, *Fourth World Surfactants Congress Proceedings*, Barcelona, A.E.P.S.A.T., Barcelona, Spain, Vol. 4, 1996, p. 340.
8. Könemann, H., Quantitative Structure Activity Relationships in Fish Toxicity Studies. 1. Relationship for 50 Industrial Pollutants, *Toxicology 19*:209 (1981).
9. Saarikoski, J., and M. Viluksela, Relation Between Physicochemical Properties of Phenols and Their Toxicity and Accumulation in Fish, *Ecotoxicol. Environ. Saf. 6*:501 (1982).
10. Roberts, D.W., QSAR Issues in Aquatic Toxicity of Surfactants, *Sci. Tot. Environ. 109/110*:557 (1991).
11. Rosen, M.J., L. Fei, Y.-P. Zhu, and S.W. Morrall, The Relationship of the Environmental Effect of Surfactants to Their Interfacial Properties, *J. Surfact. Deterg. 2*:343 (1999).
12. Versteeg, D.J., D.T. Stanton, M. A. Pence, and C. Cowan, Effects of Surfactants on the Rotifer, *Brachionus calyciflorus*, in a Chronic Toxicity Test and in the Development of QSARs, *Environ. Toxicol. Chem. 16*:1051 (1997).

[Received July 8, 1999; accepted March 8, 2000]

Dr. David W. Roberts received his B.Sc. (1962) and Ph.D. (1965) degrees in chemistry from the University of Manchester Institute of Science and Technology. He began working with Unilever Research in 1967 and currently is a surfactant manufacturing and toxicological chemistry specialist in the Laundry Manufacturing and Supply Chain Technology unit. He has published about 100 research papers and patents in these subjects.