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Comments on the Apparent Shape of Micelles

Keyphrases ☐ Micelles—spherical shape ☐ Surfactants—formation of spherical micelles

Sir:

In a recent communication (1), it was argued that micelles of common single-chain surfactants are probably not spherical. The argument centers on the calculation of the maximum radius, R, for the core of a spherical micelle from the length of a fully extended alkyl chain and the fact that such values are not large enough to account for spherical micelles of the sizes reported in the literature.

It was shown by geometric consideration that for a spherical micelle:

$$R = 1.772\left(\frac{zn}{d}\right)^{1/3} \qquad \text{(Eq. 1)}$$

where z is the aggregation number of the micelle, n is the number of carbon atoms in the linear alkyl moiety, and d is the core density of the micelle. It was assumed that the length of the fully extended hydrocarbon chain is equal to $1.27n$ and, therefore:

$$1.772\left(\frac{zn}{d}\right)^{1/3} \leq 1.27n \qquad \text{(Eq. 2)}$$

From this:

$$z \leq 0.368dn^2 \qquad \text{(Eq. 3)}$$

The value of 1.27 in Eq. 2 is the average bond distance in angstroms between two carbon atoms in the extended alkyl chain. There are actually $n - 1$ such bonds, plus the bond between the α-carbon and the hetero atom of the polar group. This latter bond will have a length that varies with the groups involved, usually greater than 1.27 Å. In a similar series of calculations, Tartar (2) arbitrarily chose a fraction of this bond length to include in his estimation of R, *e.g.*, 1.42 Å/2 for the C—S bond in an alkyl sulfate molecule. Actually, using $1.27n$ is no less arbitrary than this approach, while offering the possibility of calculating approximate maximum core radii without regard to molecular structure.

Table I—Calculated Values of Maximum Radius (Å)

n[a]	$1.27n$	$1.27(n-1) + 2.71$	$1.27n + 2$
10	29	40	45
12	42	55	61
14	58	73	78
16	77	94	101
18	98	118	126

[a] n is the number of carbons in the alkyl chain.

In *Reference 1*, no consideration was given to the length of the terminal C—H bond or to the van der Waals radii of the terminal hydrogens. These two factors combine to add a value[1] of about 2 Å to the length of the chain (2, 3). If this factor is taken into account, Eqs. 1 and 2 become:

$$R \leq 1.27n + 2 \qquad \text{(Eq. 4)}$$

and:

$$z \leq \frac{1.27}{1.772}n^{2/3}d^{1/3} + \frac{2}{1.772}\frac{d^{1/3}}{n^{1/3}} \qquad \text{(Eq. 5)}$$

respectively.

Since the micelle size is dependent upon the cube of the radius, the small 2 Å error in R produces a large error in aggregation number. Table I shows the results of solving Eqs. 2 and 5 for several common chain lengths.

Included also in Table I are values taken from the calculations of Tartar (2). Since his calculations depend on the specific surfactant used, these values are for a series of alkyl sulfates. For all common surfactants, Tartar's values are greater than those obtained by Schott (1) but less than those calculated according to Eq. 5.

Figure 1 is taken directly from *Reference 1*, but it also includes values calculated by the two methods just described. It is clear that a greater proportion of the aggregation numbers from the literature lie close to or below the theoretical lines when the calculation is altered. This is particularly true for the ionic surfactants. In this regard, it is interesting to note that Tartar carried out his calculations assuming the micelle to be an oblate spheroid and, in most cases, ionic surfactants in the absence of salt had ratios of the major-to-minor axes equal to or nearly unity, indicating spherical or near spherical shape.

It is further argued in *Reference 1* that spherical micelles would have to have an area of 67–70 Å^2 per head group. Since this is over twice the limiting area per

[1] The value of 2 Å is probably a minimum value. The large group volume of a terminal methyl group with respect to the volume of a methylene group is very likely associated with an increase in length along the axis of the hydrocarbon chain. The radius of a hemisphere having a volume of 32.6 Å^3 (the volume of a terminal methyl group) is 2.5 Å.

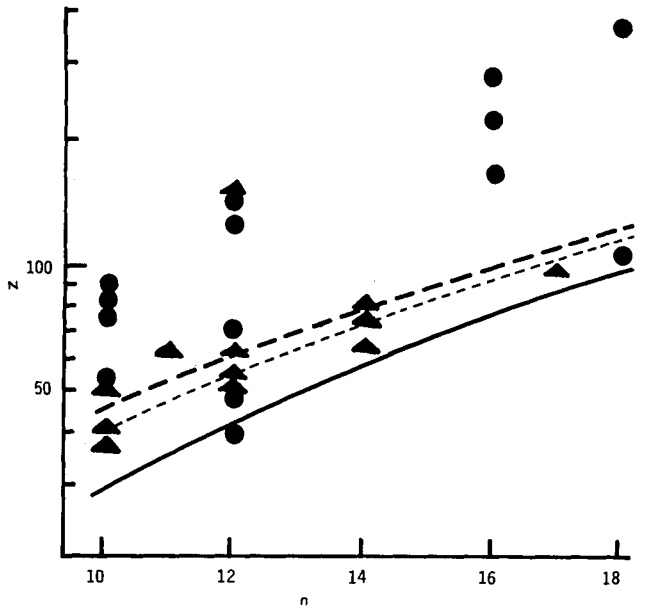

Figure 1—*Aggregation numbers* (z) *of surfactants* versus *the number* (n) *of carbon atoms in the normal alkyl moiety. Key:* ▲, *ionic surfactants;* ●, *nonionic surfactants;* —, *Eq. 2;* – –, *Eq. 5; and* - - -, *values for sodium alkyl sulfates determined using Tartar's calculations. The points below each of the lines are consistent with spherical micelles. (This graph was made from a Xerox enlargement of Fig. 1 of* Reference 1.)

molecule for surfactants such as sodium dodecyl sulfate at the air–water interface, this was felt to be unlikely because of the large hydrocarbon area that would be exposed to the aqueous solution. These large values for area per molecule, however, are in good agreement with values obtained for pure surfactants at their point of maximum adsorption at the air–water or oil–water interface (50–70 Å^2) (4–8). Limiting surface areas approaching closest packing would only be attained when significant external force is applied to overcome the electrical repulsion, hydration, and counter-ion penetration of the polar groups. Indeed, determination of surface potentials of micelles by acid–base titration (9, 10) and by electrophoresis (11) give charge densities and, hence, molecular areas which are similar to saturation adsorption values. In fact, surface potential determinations combined with a spherical micelle model have enabled the calculation of micelle weights in agreement with independent experimentally determined values (10).

In conclusion, the exact shape of micelles is still an open question, but, in general, arguments against spherical micelles presented earlier (1) do not seem valid. Until more definitive evidence is available, a spherical or near-spherical micelle model can be considered useful in the estimation of molecular area and other micelle dimensions. This is especially true for single alkyl chain ionic surfactants, where independent evidence such as light scattering and hydrodynamic data are consistent with a spherical micelle.

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In Vitro Binding of Pentylenetetrazol to Plasma Proteins

Keyphrases ☐ Pentylenetetrazol—*in vitro* binding to plasma proteins, GLC analysis, rabbits ☐ Drug–protein plasma binding, *in vitro*—pentylenetetrazol, rabbits ☐ GLC—analysis, pentylenetetrazol binding to rabbit plasma proteins

Sir:

Pentylenetetrazol has been used extensively in clinical medicine and pharmacology for its CNS stimulating actions. For this reason, it is pertinent to study the distribution and factors influencing the drug's rate of metabolism and elimination. The fact that many conflicting and incomplete conclusions have been postulated about pentylenetetrazol's fate in the body (1, 2) illustrates the need for more investigations into some of its physiochemical parameters, among which is its binding behavior to plasma proteins.

The possibility of pentylenetetrazol being bound to plasma proteins was discovered in this laboratory during a series of studies with the drug. No data concerning binding of pentylenetetrazol have been reported in the literature. It, therefore, became necessary to perform some preliminary *in vitro* binding studies with pentylenetetrazol.

Equilibrium dialysis conditions were used for determining the fraction of pentylenetetrazol bound to plasma proteins (3). A mixture of 5.0 ml. of rabbit whole plasma[1], 1 ml. of pH 7.4 0.067 *M* Sorensen buffer, and 0.1 ml. of a standard pentylenetetrazol solution was placed in cellophane dialysis bags. The bags were incubated at 37° for 36 hr. in 17 ml. of Sorensen buffer con-

[1] New Zealand white male rabbits from Cherokee Labs, Atlanta, Ga.