On the Similarity Between Micelles of Nonionic Detergents and Globular Proteins

Sir: The purpose of this communication is to point out quantitative similarities in certain physical properties of globular proteins dissolved in water at pH values near their isoelectric points, and micelles of nonionic detergents. These similarities are interesting because the two classes of particles differ so widely in chemical composition and in origin. A recent compilation (H. Schott, J. Colloid Interface Sci. *24,* 193, 1967) of properties of micelles of nonionic detergents in aqueous solution at 25 C brought their similarity to solutions of globular proteins to the writer's attention.

Hydrophobic bonding plays a crucial role in the formation of nonionic micelles (Poland and Scheraga, J. Phys. Chem. *69,* 2431, 1965) and in the configuration of globular proteins (Scheraga et al., J. Biol. Chem. *237,* 2506, 1962). Both classes of particles are compact, approximately spherical and nearly monodisperse (H. Schott, loc. cit; C. Tanford, Physical Chemistry of Macromolecules, John Wiley & Sons, Inc., New York, 1963). Small excluded volumes plus the lack of electrostatic repulsion owing to the almost complete absence of net charges result in second virial coefficients close to zero. Moreover, intrinsic viscosities are only slightly larger than Einstein's theoretical 2.5 value for noninteracting, rigid spherical particles. Most properties of nonionic micelles and globular proteins in aqueous solution are scarcely affected by added electrolytes even at fairly high concentrations.

Some parameters characterizing globular proteins (C. Tanford, loc. cit.) and micelles of representative nonionic detergents (H. Schott, loc. cit; Elworthy and McDonald, Kolloid-Z.u.Z. Polymere *195,* 16, 1964) are assembled in Table I. All globular proteins for which these data could be found are listed. Among the methods used to determine the molecular weights of the proteins were osmotic pressure, sedimentation equilibrium and velocity, and light scattering, while sedimentation velocity, light scattering, and dye solubilization (H. Schott, J. Phys. Chem. *70,* 2966, 1966; *71,* 3611, 1967) were used to determine micellar molecular weights. The radii of the hydrated particles were calculated from sedimentation and diffusion constants combined with partial specific volumes, from intrinsic viscosities and dry particle weights, or from dry particle weights and hydration values combined with partial specific volumes.

Monodispersity is indicated by the agreement between number-average molecular weights determined by osmometry or dye solubilization and weight-average molecular weights determined by turbidity or sedimentation techniques. Hydration values δ_1, representing grams of water per gram of anhydrous solid, were calculated as the difference between anhydrous molecular weights and measurements of the size of the kinetic unit comprising particle plus solvent associated with it, assuming spherical shape. The latter measurements include intrinsic viscosity or sedimentation constant combined with partial specific volume and, for the proteins, with diffusion constant as well (H. Schott, J. Colloid Interface Sci. loc. cit.; C. Tanford loc. cit.).

It is the presence of both hydrophilic and hydrophobic portions in the molecules of globular proteins and of nonionic detergents which causes them to form small and compact particles in aqueous solution yet renders these particles stable against coacervation. The hydrophobic portions form the core of the particles, the hydrophilic, hydrated portions are largely in an outer shell (H. Schott, J. Colloid Interface Sci. loc. cit.; C. Tanford, loc. cit.). As can be seen from Table I, the proteins and micelles have very nearly the same hydration and intrinsic viscosity values. By comparison, most solutions of flexible-chain polymers of comparable molecular weights have intrinsic viscosities and δ_1 values one or two orders of magnitude larger.

TABLE I

Solution Properties of Globular Proteins and Micelles of Nonionic Detergents[a]

Species	$M^b \times 10^{-3}$	R[c]	$R/\sqrt{M/N}$[d]	δ_1[e]	$[\eta]^f_\Phi$	s_0[g]
ribonuclease	13	19	1293	0.59	4.6	1.64
lysozyme	14	21	1352	0.89	....	1.87
chymotrypsinogen	23	23	1151	0.52	4.6	2.54
β-lactoglobulin	35	27	1120	0.72	4.5	2.83
ovalbumin	45	28	1010	0.45	4.6	3.55
serum albumin	65	35	1065	1.07	5.0	4.31
hemoglobin	68	32	982	0.69	4.8	4.31
catalase	250	52	810	0.70	5.3	11.3
urease	480	62	693	0.53	....	18.6
Branched nonylphenol(EO)$_{15}$	70	42	1226	1.65	5	1.4
branched *octylphenol*(EO)$_{10}$	90	43	1107	1.26	5.6	3.80
n-dodecanol(EO)$_{14}$	100	43	1045	0.975	5.0	1.0
n-dodecanol(EO)$_{28}$	82	39	1054	0.835	4.7	1.62
n-hexadecanol(EO)$_9$ (15 C)	135	45	946	0.69	4.0	.....
n-hexadecanol(EO)$_9$ (25 C)	140	46	948	0.71	4.2	.....
n-hexadecanol(EO)$_9$ (35 C)	158	48	937	0.77	4.4	.....
n-hexadecanol(EO)$_9$[h] (45 C)	176	51	944	0.83	4.55	.....

[a] Unless otherwise stated, the data refer to 20–25C.
[b] Weight of dry particle.
[c] Radius (A) of fully hydrated particle, assuming spherical shape.
[d] cm $g^{-1/2}$; N is Avogadro's number.
[e] Hydration, grams of water per gram of dry particle.
[f] Intrinsic viscosity based on volume fraction Φ.
[g] Sedimentation constant at infinite dilution, Svedbergs.
[h] Cloud point of *n*-hexadecanol(EO)$_9$ is 75C.

The molecular weights M of the proteins span a 37-fold range which includes the micellar molecular weights of the detergents. Sedimentation constants s_0 of both classes of particles are of the same order of magnitude but, since they depend on particle size, those of the proteins cover a wide range (see Table I). In order to compare the compactness of the particles, an empirical parameter, $R/(M/N)^{1/2}$, was calculated; R is the radius of the hydrated particles and N is Avogadro's number. Since two different classes of compounds are being compared, the analogy to the ratio radius of gyration to square root of molecular weight, which is used to characterize polymer molecules in solution, is only formal. The value of this empirical dimensional parameter varied by merely $\pm 30\%$ for the proteins and by $\pm 15\%$ for the micelles. The average value (1,053) for the 9 proteins is almost identical to the average value of 1,026 for the micelles. These values are several-fold smaller than those calculated for solutions of common vinyl polymers because globular proteins and nonionic micelles are nearly spherical and unusually compact, with little or no solvation in the core. For instance, the $R/(M/N)^{1/2}$ values for polystyrene dissolved in cyclohexane and in butanone are between 2,200 and 3,000 $cm/g^{1/2}$ (C. Tanford, loc. cit.).

Heating solutions of nonionic detergents and globular proteins eventually results in phase changes. Hydration and molecular weight of detergent micelles remain relatively unaffected by rising temperature (see Table I) until the cloud point is approached. At about 25 C below the cloud point, intrinsic viscosity and micellar molecular weight begin to increase very rapidly, while the hydration begins to drop, but less rapidly, with further temperature increase (Elworthy and McDonald, loc. cit.). At the cloud point, phase separation occurs. This process is reversible, whereas denaturation by heat of the solutions of most globular proteins is irreversible (C. Tanford, loc. cit.). Of course, the data for the nonionic detergents listed in Table I were obtained at temperatures well below their cloud points.

The differences between globular proteins and nonionic micelles are well known. The resemblance in shape, compactness, degree of hydration, and intrinsic viscosity of solutions of globular proteins near their isoelectric point and of nonionic detergent micelles is remarkable, especially in view of the considerable difference in composition, structure and origin.

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• *Addendum*

JAOCS *45*, 547–548, 1968, P. B. Moseley and J. B. Stanley: "Chromatographic Determination of Neutrals in Tall Oil Fatty Acids, Gum and Wood Rosin."

On page 548, Table I and II, under the heading "Sample," Pamak-I should read: Pamak-4.