

MICELLAR PROPERTIES OF SODIUM SALTS OF URSODEOXYCHOLIC, CHENOXYCHOLIC, DEOXYCHOLIC AND CHOLIC ACIDS

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Bile acid therapy dissolves cholesterol gallstones (Danzinger et al 1972); ursodeoxycholic (UDCA) and chenodeoxycholic (CDCA) acids are of particular clinical interest. Their chemical structures differ only in the orientation of the 7 hydroxyl group on the steroid nucleus in that CDCA is the α epimer while UDCA is the β epimer. This difference gives CDCA a greater capacity to solubilise cholesterol (Carey et al 1981).

Using photon correlation spectroscopy (PCS) and surface tension (ST) measurements we investigated the properties of NaCDC and NaUDC and compared them with other common bile salts, the deoxycholate (NaDC) and cholate (NaC) - see Table 1. The PCS measurements, performed on 5% solutions, provided diffusion coefficients (D) and polydispersity indices (Q) as obtained from a quadratic fitting procedure. Hydrodynamic radii (\bar{R}_h) were calculated from values of D by using the Stokes-Einstein equation and these estimates were used to find the approximate aggregation number, Z, via the relationships proposed by Mazer et al (1979). The PCS procedure was also used to determine the critical micelle concentrations (the first time such a method has been published). The static Wilhelmy plate method for measuring surface tension provided an additional estimate of the CMC, together with values for the surface area per molecule (σ) at the interface.

We also studied the interaction of 2-phenylethanol (2PE) with bile salts by PCS, by adding increasing amounts of the aromatic alcohol to 5% w/v solutions in 0.15M NaCl, pH 10, 25°C (Fig. 1).

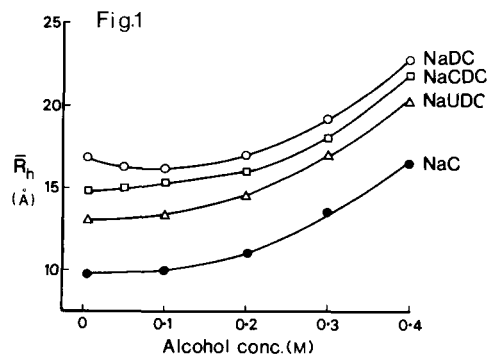
Table 1. Properties of bile salts in 0.15M NaCl, pH 10, 25°C.

Bile salt	CMC (ST) mMl ⁻¹	CMC (PCS) mMl ⁻¹	σ Å ²	\bar{R}_h^b Å	Q^c x10 ²	Z
NaUDC	6.3	7	95	13	5±2	7
NaCDC	2.7	5	97	15	5±2	10
NaDC	2.8	4	98	17	5±2	14
NaC	6.6	8	95	10	8±4	3

^a upper limit assessed

^b S.D. ± 0.5 Å

^c n = 10.



Sodium chenodeoxycholate and deoxycholate provided comparable CMCs, which were less than those of the ursodeoxycholate and cholate salts. The surface tension values at any specific concentration were in the order NaC = NaUDC > NaDC = NaCDC. This order shows that ursodeoxycholic acid is similar in hydrophilicity to the trihydroxy cholic acid, but more hydrophilic than the other dihydroxy acids, chenodeoxycholic and deoxycholic. The hydrodynamic radii and the aggregation numbers followed similar trends in that NaDC > NaCDC > NaUDC > NaC. The small differences in molecular structure are reflected by the similar σ values. The polydispersity index is not significantly different for any particular bile salt. The way in which the micellar size increases on the addition of the phenylethanol suggests that mixed micelles form or that microemulsion droplets are stabilised by the bile salt molecules.

Carey, M.C. et al (1981) *Biochemistry* 20: 3637-3648

Danzinger, R.G. et al (1972) *N. Eng. J. Med.* 286: 1-8

Mazer, N.A. et al (1979) *Biochemistry* 18: 3064-3075

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