The solubilization of salicylic acid by a series of non-ionic surfactants

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Solubilization may be used to increase the solubility of otherwise poorly soluble drugs. Recent work has shown that the bioavailability of solubilized drugs is not necessarily increased. Since only the unionized form of weak acids and bases is absorbed from the gastrointestinal tract, it would be useful to differentiate between the interactions of ionized drug molecules and of unionized drug molecules with surfactant micelles. The extent of drug/surfactant interactions can be conveniently expressed as a distribution ratio of the drug between micellar and non-micellar phases.

The distribution ratios of the ionized and unionized molecules of salicylic acid have been determined between water and micelles of the following polyoxyethylene (20) sorbitan esters: monolaurate (polysorbate 20); monopalmitate (polysorbate 40); monostearate (polysorbate 60) and monooleate (polysorbate 80).*

Excess salicylic acid was added to solutions of surfactant at different pH's. The solutions were shaken in a constant temperature bath for 48 h at 25° and pH was adjusted using a Radiometer pH stat. Filtered diluted samples were assayed spectrophotometrically for salicylic acid.

Plots of D_T/D_{H_2O} as a function of volume fraction, M, of polysorbate at several pH values, where D_T and D_{H_2O} are the solubilities of salicylic acid in polysorbate solutions and water respectively, are linear. The slopes, S, of these lines at each pH, plotted against the percentage of unionized salicylic acid present at that pH, are also linear. The values of S obtained by extrapolation to 0 and 100% unionized salicylic acid, are the distribution ratios K_i and K_u, of the ionized, and unionized molecules of salicylic acid respectively (Rippie, Lamb & Romig, 1964).

The distribution ratios of ionized molecules are zero indicating that the molecules do not partition into polysorbate micelles, supporting the conclusions of Hurwitz, Deluca & Kostenbauder (1963) that organic ions must have a large hydrophobic group to enable them to be solubilized by non-ionic surfactants. The distribution ratio of unionized salicylic acid increases as the alkyl chain length of the surfactant increases. It may thus be expected that the amount of unionized acid available for absorption from surfactant solutions will be dependent upon the nature of the surfactant.

REFERENCES

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   * Tween 20, 40, 60 and 80 respectively, supplied by Honeywill-Atlas Ltd.

Prediction of the micellar molecular weight and thermodynamics of micellization of mixtures of alkyltrimethylammonium salts

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Shinoda's (1954) equation for the critical micelle concentration (cmc) of a soap mixture and published data for pure surfactants were used to derive a theoretical expression for the micellar molecular weight (M) of a surfactant mixture.

$$\Sigma M_{mi}^{-\frac{1}{2\cdot303D}\frac{\omega}{(kT)}} \frac{x_i' \exp (m_i \omega/kT)}{\Sigma x_i' \exp (m_i \omega/kT)} = M_{mix}^{-\frac{1}{2\cdot303D}\frac{\omega}{(kT)}} \qquad (1)$$

where ω is the energy change per methylene radical in passing from the aqueous phase to the interior of the micelle, k is the Boltzmann constant and T is the absolute temperature. Mm_i is the micellar molecular weight of a surfactant i of chain-length m, and x is the mol fraction of the surfactant i in a state of molecular dispersion. D is the regression coefficient of the straight-line plot of log M *vs* alkyl chain-length for pure surfactants. Experimental values of M for