## P.46 Surfactants and aqueous solubility enhancement of drugs: importance of the hydrophilic "head group"

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Micellar solubilisation is an attractive way of increasing the apparent aqueous solubility of poorly-water soluble drugs. While the effect of increasing the alkyl chain length of a surfactant (SAA) on solubilisation is well understood, very little is known about the effect of changing the nature of the hydrophilic head group. Accordingly, we report here on systematic studies performed to determine the solubilisation capacity of micelles formed by a range of $C_{12}$ chain surfactants (SAAs) with varying head groups, namely the cationic dimethylammonium bromide (TAB), the anionic sodium sulphate (SS), the zwitterionic dimethylamminopropanesulphonate (DAPS), the phosphocholine (PC), the dimethylamine-N-oxide (DAO) for the poorly-water soluble drug, testosterone propionate (TP).

The solubilisation capacity of the various micelles for TP was correlated with the structure of the micelles. Micelle structure, in the absence and presence of saturation amounts of TP, was determined using small angle neutron scattering (SANS) in combination with contrast variation. For the micellar systems tested, three 'contrasts' namely, protiated SAA (h-SAA) in $D_2O$, chain-deuterated SAA (d-SAA) in $H_2O$ and d-SAA in $D_2O$ were studied. The critical micelle concentration (CMC) of the SAAs was determined by surface tensiometry. As the CMC of the SAAs are very low in comparison to the concentrations used for the solubilisation and SANS studies, their contribution to the measurements were assumed to be negligible. Furthermore, as the aqueous solubility of TP is only 0.0009 %w/w, any increase in the apparent solubility of TP in the presence of micelles assumes that the TP is present in the surfactant micelles.

The studies show that the SAA head group plays a significant role both on the structure of the micelles and their capacity to solubilise TP. For example, the SANS studies showed that, at saturation, the charged surfactants, particularly $C_{12}$SS, exhibited the greatest capacity for TP, and the non-ionic micelles the least, with the micelle formed by the zwitterionic surfactants being intermediate. Furthermore, regardless of head group, all micelles were prolate in shape and became even more elongated in shape in the presence of TP. This study suggests that surfactant charge is important in solubilising TP, even though TP is neutral. Further studies (MD simulations and neutron reflectivity) are underway to determine the precise location and/or orientation of TP within the micellar systems above.