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The incorporation of salicylic acid-dimethyl-β-cyclodextrin complex into water-in-oil microemulsions

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We have recently shown that the release of the model drug, sodium salicylate from a lecithin-based water-in-oil (w/o) microemulsion is lower than from a cosolvent system of very similar composition (Koshnevis et al., 1997). This phenomenon has obvious implications for the use of w/o microemulsions as sustained release vehicles. In order to establish whether it is possible to further control the release of drug from a w/o microemulsion we have investigated the feasibility of first complexing a model drug, salicylic acid (SA) in dimethyl-β-cyclodextrin (DM-β-CD) and then incorporating this complex into a lecithin-based microemulsion.

As a precursor to release studies, we have determined the effect of the presence of DM-β-CD, SA and SA/DM-β-CD complex on the formation of microemulsions composed of isopropyl myristate, lecithin:propanol at a mixing ratio of 1:1 and water, prepared using the method of Aboofazeli and Lawrence (1993). DM-β-CD, SA and SA/DM-β-CD complex were added to the aqueous phase used to prepared the systems. SA was added at 2.0 mg/ml, DM-β-CD at 100 mg/ml and SA/ DM-β-CD complex prepared using 100 mg./ml DM-β-CD and containing 3.5 mg/ml of SA. In all case the aqueous phase was weakly buffered at pH 2.5 using HCl, in order to ensure that the salicylic acid was solely complexed with DM-β-CD rather than interacting with the free hydroxyls on the exterior of the CD molecule.

Interestingly the use of water buffered at pH2.5 did not significantly affect the area of microemulsion existence when compared to the phase diagram obtained using unbuffered water, with a one phase clear microemulsion region being formed over a wide range of compositions. In contrast however the presence of SA, DM-β-CD or SA/ DM-β-CD in the aqueous phase each slightly reduced the area of microemulsion existence (Figure). Preliminary laser light scattering measurements at 25 wt% of total surfactant concentration showed that each of the systems exhibited the formation of microemulsion particles once a minimum concentration of aqueous phase had been reached (ie at least 9 wt%).

Similar results have been seen with β-cyclodextrin and hydroxylpropyl-β-cyclodextrin under the same experimental conditions. These results indicate that it is possible to formulate microemulsions in the presence of cyclodextrins-drug complexes. Further studies are underway to investigate the effect of complexation cyclodextrin on the release of drug from the microemulsion.

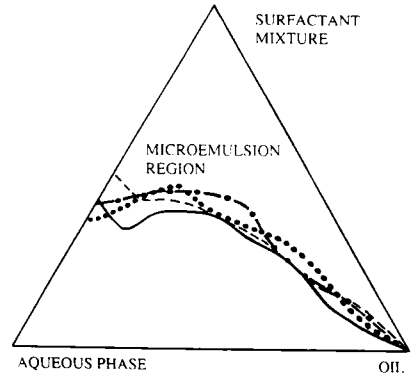

Figure: Phase diagram of quaternary phase systems containing lecithin:propanol (1:1)/aqueous phase and isopropyl myristate (solid lines: aqueous phase contains water, dashed line: aqueous phase contains salicylic acid (2.0 mg/ml) dotted/dashed line: aqueus phase contains DM-β-CD and dotted line: aqueous phase containins SA/DM-β-CD complex).

Aboofazeli R and Lawrence MJ (1993) Int. J. Pharm. 93, 161-175.
Koshnevis P, Mortazavi SA, Lawrence MJ and Aboofazeli R (997) J. Pharm. Pharmacol. 49 (suppl 4) 30.