

## FLOCCULATION OF MODEL AEROSOL SUSPENSIONS BY SURFACTANT MIXTURES

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The volatile nature of aerosol formulations at room temperature requires that measurement of suspension stability be carried out under pressure in sealed vessels. The experimental complications involved have caused the stability of aerosol mixtures to be less well understood than the stability of colloids in nonvolatile aqueous systems. In order to simplify the study of colloid stability in chlorofluorocarbon solvents, we have investigated the flocculation of a model aerosol suspension, that of the hydrophilic material lactose in the model CFC solvent 1,1,2 trichloro-1,2,2 trifluoroethane (TCTFE, b.p. 47°C). The behaviour of this system was compared with that of the same material in propellant 11 (b.p. 23°C).

Lactose BP was reduced to a mean particle diameter of 3  $\mu\text{m}$  in a fluid energy mill. Varying amounts of this material were dispersed in the solvent using an ultrasonic probe. The effects of varying amounts of the surfactant lecithin (Lipoid E80) was also investigated. After 1 hour the mixtures were investigated microscopically for the presence of particle aggregates and visually for gross creaming and floc formation. Partial phase diagrams showing the regions in which the systems were flocculated were constructed. These are shown in Figs. 1 (TCTFE) and 2 (propellant 11).

In the absence of surfactants, the lactose formed coarse flocs above a phase volume of 0.1% in both solvents. In propellant 11, low concentrations of lecithin was sufficient to stabilise the system at all phase volumes of lactose studied. However, in TCTFE, higher concentrations of lecithin acted as weak flocculants, resulting in formation of small flocs and creaming of the suspensions. It is surprising that such different behaviour is seen in solvents with similar chemistry, and this emphasises the importance of the propellant mixture in the stabilization of aerosol suspensions. It thus appears that suspension stability cannot be directly inferred from the behaviour of mixtures in less volatile solvents.

Figure 1

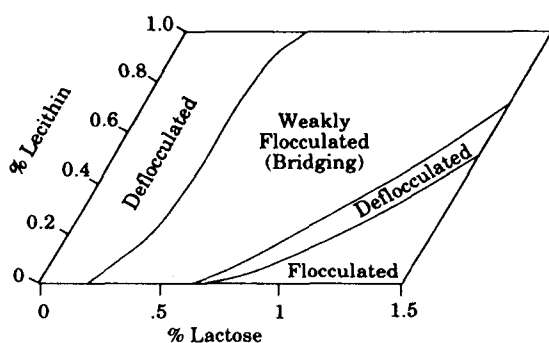
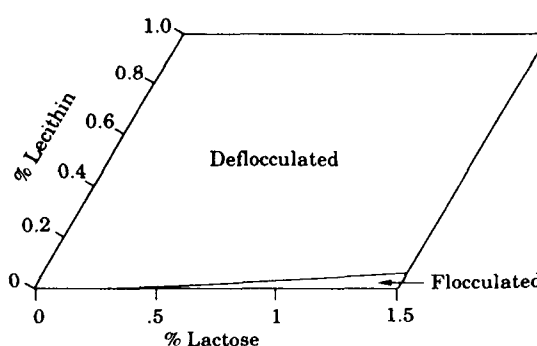


Figure 2



The observation of flocculation at high surfactant concentrations is not surprising since solvency of hydrocarbons in non-aqueous systems is poor, and the desolvation energy of the hydrophobic surfactant chains probably has little associated enthalpy. The hydrophobic chains would produce flocculation by bridging under these conditions. Any steric contribution to the stabilization of the colloid by the surfactant is probably entropy driven, suggesting that the flocculation may be strongly temperature dependent.

Microscopic examination showed that the critical flocculation concentrations were ill-defined, since small aggregates were formed over a wide range of low concentrations. This is probably due to the high polydispersity of the lactose used and suggests that further studies will have to use material that has been classified into a narrower range of sizes.

Hallworth G.W. (1987) in Ganderton & Jones (eds), Drug delivery to the respiratory tract, Ellis-Horwood, Ch. 9, 87-118.