THE ELECTROPHORETIC MOBILITY OF SUSPENSIONS IN NON-POLAR MEDIA USING LASER VELOCIMETRY

D.A. Parkins[1], G. Hallworth[2], B.J. Meakin[1], Pharmaceutics Group,
School of Pharmacy and Pharmacology, University of Bath, BA2 7AY(1) and Glaxo Group Research, Ware, SG12 0DJ(2)

Whilst the physical behaviour of many aqueous pharmaceutical suspensions can be explained in terms of the DLVO theory (Matthews & Rhodes 1970), its applicability to metered dose inhalation (MDI) aerosol formulations as dispersions of microfine drug in liquefied fluorocarbon propellants is unclear. A test of the theory requires the determination of the electrophoretic mobility of the dispersed particles. Such measurements by classical microelectrophoretic techniques are not possible in pressurised aerosol systems because of the low polarity of the vehicle (relative permittivity ~2-3).

Although laser velocimetry is used to evaluate electrophoretic behaviour in aqueous media (Uzgiris 1981), there are few reports of its application to dispersions in non-polar, low conductivity solvents, because of the difficulties arising from electrohydrodynamic and space charge effects (Novotny 1982). To overcome these problems, a differential heterodyne laser velocimeter has been designed and constructed. Field strengths of $\sim 10^4 Vm^{-1}$ at reversal rates of 2-5Hz can be applied to apolar dispersions held within a narrow gap (~1.0mm) electrode assembly. A low humidity housing permits control of the suspension moisture content, an important factor in charge generation in non-aqueous dispersions (Lyklema 1968).

The technique has been validated using model systems composed of monodisperse silica spheres (diameters 3μm and 5μm) in a blend of hexane and trichloro-trifluoro-ethane (3.1:6.9 v/v) (relative permittivity = 2.25). True electrophoresis has been demonstrated through the field independence of the determined electrophoretic mobility. Values obtained were typically 1-5 x $10^{-9} m^2 s^{-1} v^{-1}$ and independent of particle size, over the range studied.

"Surfactants" are conventionally included in MDI suspensions and their effect on the electrophoretic mobility of the bronchodilator drug, salmefamol, dispersed in the propellant model, has been studied using Aerosol OT and oleic acid at concentrations up to 10^{-2}M (Figure 1). The moisture content of the dispersions, for the two surfactants, was 17ppm and 20ppm respectively. In each case the drug particles were negatively charged, demonstrating reversal of charge from the positive electrostatically charged dry powder.

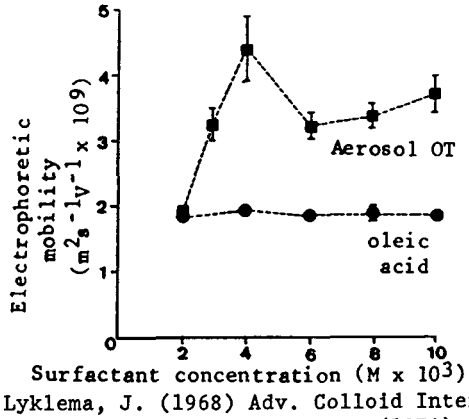

Figure 1. Variation in the measured electrophoretic mobility of salmefamol dispersions with surfactant concentration in a non-polar propellant model.
(bar indicates range of observations)

Lyklema, J. (1968) Adv. Colloid Interface Sci. 2: 65-114
Matthews, B.A., Rhodes, C.T. (1970) J. Pharm. Sci. 59: 521-525
Novotny, V. (1982) ACS Symp. Ser. 200: 281-306
Uzgiris, E.E. (1981) Prog. Surf. Sci. 10: 53-164