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An interfacial equilibria model for the electrokinetic properties of a fat emulsion

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Summary

A semi-empirical model is developed that may be used to describe the zeta potential behaviour of fat emulsions in complex electrolyte systems. The model encompasses specific adsorption at the interface, ionic strength effects according to the Guoy-Chapman theory and chemical speciation analysis of the bulk electrolyte using competitive thermodynamic equilibria. An example of the model is given for the competitive equilibria between calcium binding at the interface and calcium-citrate complex formation in the bulk electrolyte. Unless one uses sophisticated models patient benefit : risk ratios may be compromised through oversimplification.

Introduction

Fat emulsions prepared from vegetable oils and stabilised with egg lecithin are now widely used in intravenous nutrition regimen (Shenkin and Wretlind, 1978; Wretlind, 1981). Such emulsions are highly stable; the Kabi Nutrition product 'Intralipid 20%' is reported to have a surface potential in the range -30 to -50 mV (Washington et la., 1989; Washington, 1990) and a storage life of 1–2 years (Boberg and Hakansson, 1964; Kawilarang et al., 1980).

The stability of intravenous fat emulsions is compromised by the clinical practices of preparing 'All in One' regimen (Black and Popovich, 1981; Pamperl and Kleinberger, 1982; Burnham et al., 1983; Allwood, 1984; Whateley et al., 1984; Davis et al., 1985; Davis and Galloway, 1986; Driscoll et al., 1986). That is, the admixture of emulsions with other nutrition materials such as electrolytes, carbohydrates, amino acids, trace elements and vitamins, so that a single infusion satisfies all of the patient's nutritional requirements.

The increased use of All in One preparations has necessitated the development of predictive models to provide the clinical pharmacist with rapid stability estimates prior to formulation.

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Recently Washington (1990) has reported electrophoretic and flocculation measurements for Intralipid 20% in the presence of calcium. The resulting semi-empirical model was reported to be in good agreement with experiment but the model was limited since predictions were confined to relatively simple electrolyte systems.

We are in the process of developing predictive models for the overall stability assessment of complex intravenous fluids (Barnett et al., 1990; Duffield et al., 1991a,b; Hall et al., 1991a,b). This includes prediction of precipitation (in particular, phosphate and hydroxy solids of trace elements and electrolytes), of pH effects, osmolality, bioavailability and drug efficacy, consequences of chemical contamination, and of emulsion stability. The main technique employed is that of chemical speciation; the determination of the concentration and composition of the myriad of labile species that form in complex aqueous solutions.

Chemical speciation is achieved by considering the multitude of competitive thermodynamic equilibria in such systems (May et al., 1977; Duffield and Williams, 1986, 1989). The equilibria considered are usually too numerous to evaluate manually and so computer codes have been developed to simplify this task, PHREEQE being a typical example (Parkhurst et al., 1980). The chemical speciation approach has been used for many years in geochemical and radiological modelling (Duffield and Williams, 1986), whereby species concentrations are usually too low to allow normal analytical techniques to be employed.

This paper describes how the concept of competitive interfacial chemical speciation can be used to model the electrophoretic properties of Intralipid 20% in mixed electrolyte systems. The theory combines both an adsorption site model with the gross ionic strength effects of electrolytes (effects due to the change in the Debye double layer thickness and activity coefficients). The nature of the binding sites is described mathematically, since the specific binding sites are not necessarily known.

Interfacial charge density is used in this paper rather than zeta potential since the former is a better parameter for describing the chemistry of the interface, being the summation of ionic charge/concentration products for all interfacial species. The zeta potential is an artifact of the interfacial charge and a function of both the charge density and the electrolyte effect on the double layer thickness.

The role of sodium in phospholipid interfacial behaviour has been much disputed in the literature. This is best demonstrated by the studies of individual pure phospholipids (as opposed to the mixture in Intralipid 20%). Hanai et al. (1965) and McLaughlin et al. (1978) have reported that there is no evidence for binding to phosphatidylcholine vesicles in the NaCl concentration range 0.001–0.5 mol dm^{-3}. Van Dijck et al. (1978) found similar results in thermometric studies of phosphatidylserine monolayers. This supported the earlier work by Sacré and Tocanne (1977) where the effect of NaCl could be ascribed entirely to changes in the Guoy-Chapman diffuse electric-double layer. In direct contrast to these findings, Eisenberg et al. (1979) have interpreted their results for phosphatidylserine in terms of sodium binding with an equilibrium constant of 0.6 mol^{-1} dm^3, Lau et al. (1981) found the same value to be appropriate for phosphatidylglycerol. Macdonald and Seelig (1987) have since reported a value of 0.85 mol^{-1} dm^3 for sodium binding to phosphatidylglycerol-phosphatidylcholine bilayers.

If sodium binding to phospholipids occurs it would appear that an equilibrium constant in the region of 0.6 mol^{-1} dm^3 would be appropriate, thus for a 1 : 1 complex 50% binding would be expected for a sodium concentration of 1.7 mol dm^{-3}.

Washington (1990) based the requirement for sodium binding on an incorrect estimate of typical NaCl concentrations and subsequently the extent of binding; it was stated for an NaCl concentration of 0.15 mol dm^{-3} and a binding constant of 0.6 mol^{-1} dm^3 that 25% of binding sites are occupied. Simple calculation produces a figure of only 8% of sites are occupied under these conditions. Furthermore, we know of no intravenous regimen where 0.15 mol dm^{-3} NaCl is formulated together with a fat emulsion; rather an upper practical limit would appear to be 0.04–0.05 mol dm^{-3}. It is possible that quantities and concentrations have been confused, since an adult patient

may receive an NaCl dose of 0.15 mol/day but not in a 1 l solution! Further evidence for confusing quantities and concentrations is noted when the equilibrium constants are assigned units of mol^{-1} rather than $mol^{-1}\,dm^3$ in both the text and figures.

In view of the dichotomy between previous authors concerning sodium interactions, we prefer to employ the quasi-phenomenological definition of specific adsorption given by Mohliner (1965); "there is specific adsorption if the experimental data cannot be explained by the theory of the diffuse double layer". Thus, we have confined our experiments to the NaCl concentration range expected in intravenous fat emulsion regimens (i.e. 0–0.05 mol dm^{-3}) where at most less than 3% of binding sites could be expected to be occupied by sodium, if at all.

The following theoretical discussion deals only with the interactions between negatively charged emulsions and cations, since this situation is of immediate interest. The treatment for positive emulsions and anions can be shown to be of similar nature.

Theoretical

Consider the reversible equilibrium between a cation M^{n+} in solution, and a binding site B^m located at the emulsion/electrolyte interface, forming a complex $BM^{(n+m)}$ also located at the interface, where n and m represent the ionic charge of the cation and binding site, respectively.

$$B^m + M^{n+} \rightleftharpoons BM^{(n+m)} \tag{1}$$

An equilibrium constant, β_{BM}, may be used to describe the interaction

$$\beta_{BM} = \frac{c_{BM}}{c_B \cdot [M^{n+}]} \tag{2}$$

where c_B and c_{BM} are the interfacial concentrations (mol m^{-2}) of the free and complexed binding sites, and $[M^{n+}]$ is the uncomplexed cation concentration (mol dm^{-3}) in the bulk solution. The total interfacial concentration of binding sites, c_B°, is given by

$$c_B^\circ = c_B + c_{BM} \tag{3}$$

Substitution of Eqn 3 into Eqn 2 affords

$$\beta_{BM} = \frac{c_{BM}}{(c_B^\circ - c_{BM}) \cdot [M^{n+}]} \tag{4}$$

If the relative concentration of binding sites is small compared to the aqueous cation concentration then formation of the interfacial complex $BM^{(n+m)}$ will not result in a depletion of the aqueous cation concentration and thus this bulk concentration may be used throughout.

The interfacial charge density, σ (C m^{-2}), for any extent of binding is given by

$$\sigma = c_{BM} nF + c_B^\circ mF \tag{5}$$

which may also be equated with the zeta potential ζ

$$\sigma = \zeta \varepsilon \kappa \tag{6}$$

where ε is the permittivity of water and is taken to be 7.27×10^{-10} V^{-1} C m^{-1} at 25 °C, and κ is the inverse Debye shielding length given by

$$\kappa = \left(\frac{2e^2 LI}{\varepsilon kT} \right)^{1/2} \tag{7}$$

where e is the proton charge, L and k are the Avogadro and Boltzmann constant, and I is the electrolyte ionic strength given by

$$I = \tfrac{1}{2} \sum_i c_i z_i^2 \tag{8}$$

It is assumed in Eqn 6 that $\kappa a \gg 1$ where a is the particle radius. It is important to note that I has dimensions mol m^{-3}.

The ionic strength term inherent in Eqn 6 illustrates that the zeta potential depends both upon the concentration of the bulk electrolyte and upon specific interactions with the interface according to Eqn 5. It is for this reason that we place a greater emphasis on the use of charge density

rather than zeta potential in the description of emulsions.

The total interfacial binding site concentration, c_B^o, may be obtained from zeta potential measurements in ideal, indifferent electrolytes. In these cases $c_{BM} = 0$ since there is no specific interfacial binding and so the charge density, σ_o, is given by

$$\sigma_o = c_B^o mF \tag{9}$$

Thus σ_o and c_B^o can be evaluated for each discrete zeta potential measurement in an ideal indifferent electrolyte. Alternatively, equating Eqns 6 and 7 provides the relationship

$$\zeta^2 = \frac{\sigma_o^2 kT}{2e^2 \varepsilon LI} \tag{10}$$

Therefore, a plot of ζ^2 as a function of the inverse of the ionic strength for a range of measurements should give a slope, passing through the origin, proportional to σ_o^2.

Substitution of Eqn 9 into Eqn 5 and the resulting expression into Eqn 4 yields an expression in terms of σ and σ_o for the interfacial equilibrium constant.

$$\beta_{BM} = \frac{\sigma - \sigma_o}{\left(\sigma_o\left(1 + \frac{n}{m}\right) - \sigma\right) \cdot [M^{n+}]} \tag{11}$$

Conversely, once σ_o and β_{BM} have been evaluated for a cation interaction, then σ may be predicted for any cation concentration by rearrangement of Eqn 11.

$$\sigma = \frac{\sigma_o\left(1 + \left(1 + \frac{n}{m}\right)\beta_{BM}[M^{n+}]\right)}{1 + \beta_{BM}[M^{n+}]} \tag{12}$$

Subsequently, the electrophoretic zeta potential can be calculated using Eqn 6.

Previous authors (Eisenberg et al., 1979; Lau et al., 1981; Macdonald and Seelig, 1987; Washington, 1990) have modified the metal ion concentrations involved in interfacial equilibria according to the Boltzmann distribution

$$[M]_s = [M]_{tot} \exp(-ze^2/kT) \tag{13}$$

where $[M]_s$ is the effective metal ion concentration at the interface and $[M]_{tot}$ is the concentration in the bulk, the variation being due to repulsion or attraction to the charged interface.

The Boltzmann function describes the distribution of ions at charged conducting interfaces where the charge is assumed to be uniformly smeared over the surface. Healy et al. (1980) have observed that most emulsions consist of discrete charged sites arranged on an insulating interface for which no delocalisation can take place. Furthermore, the distance between adjacent charged sites in Intralipid 20% is shown in this paper to be several times larger than the typical Debye shielding length, thus preventing insufficient overlap of ion-charge distributions to adequately mimic a delocalised charge at a conductive interface.

It is for these reasons that we propose that the binding sites be treated as isolated species in a similar manner to ions in the bulk solution.

Solution equilibria should include consideration of activity coefficients for completeness, thus Eqn 2 becomes

$$\beta_{BM} = \frac{\gamma_{BM} c_{BM}}{\gamma_B c_B \cdot \gamma_M [M^{n+}]} \tag{14}$$

where γ_{BM}, γ_B and γ_M are the activity coefficients for the interfacial complex, free binding site and metal ion, respectively. Activity coefficients may be estimated using the Davies equation (Davies, 1938, 1967)

$$-\lg \gamma_i = 0.509 z_i^2 \cdot \left(\frac{\sqrt{I}}{1 + \sqrt{I}} - 0.30I\right) \tag{15}$$

Substitution of Eqn 14 for Eqn 2 yields activity coefficient modified expressions for Eqns 11 and 12.

$$\beta_{BM} = \left(\frac{\gamma_{BM}}{\gamma_B \gamma_M}\right) \cdot \frac{\sigma - \sigma_o}{\left(\sigma_o\left(1 + \frac{n}{m}\right) - \sigma\right) \cdot [M^{n+}]} \tag{16}$$

and

$$\sigma = \frac{\sigma_o\left(1 + \left(1 + \frac{n}{m}\right)\beta_{BM}[M^{n+}]\gamma_B\gamma_M/\gamma_{BM}\right)}{1 + \beta_{BM}[M^{n+}]\gamma_B\gamma_M/\gamma_{BM}} \tag{17}$$

The role of chemical speciation is two-fold. First, the uncomplexed cation concentration required throughout the above calculations is determined using well established aqueous thermodynamic equilibrium data. Secondly, the ionic strength, required to calculate ζ from σ in Eqn 6 and γ for each species, is determined using Eqn 8 by considering the concentration of each and every chemical species that is predicted to form in the electrolyte.

Materials and Methods

Intralipid 20% (Kabi Nutrition, Batch no. 50603-51) was obtained from the Welsh School of Pharmacy, Cardiff. Sodium and calcium chloride and trisodium citrate were Analar grade from BDH. pH measurements were made with Russell glass electrodes calibrated frequently using methods previously published (Linder et al., 1984). All aqueous solutions were purged with, and stored under, oxygen-free nitrogen. Zeta potentials were determined using a Rank Brothers Mark II Electrophoresis Apparatus equipped with a rotating prism and close circuit television monitor. Speciation calculations were performed using the code PHREEQE on a VAX mainframe, all other computation was performed on Borland Quattro spreadsheets.

Results

Fig. 1 shows the plot of the square of the zeta potential in sodium chloride as a function of the inverse ionic strength. The ionic strength is identical to the electrolyte concentration in this ideal case. The best linear fit through the origin was calculated using least-squares analysis. The slope was interpreted for σ_o using Eqn 10 and found to be -5.14 mC m^{-2}. This value was adopted for all further calculations.

Fig. 2 shows a plot of zeta potential as a function of total calcium concentration in 25 mmol dm^{-3} background NaCl. Charge reversal is observed at 3.5 mmol dm^{-3} calcium. The pH was

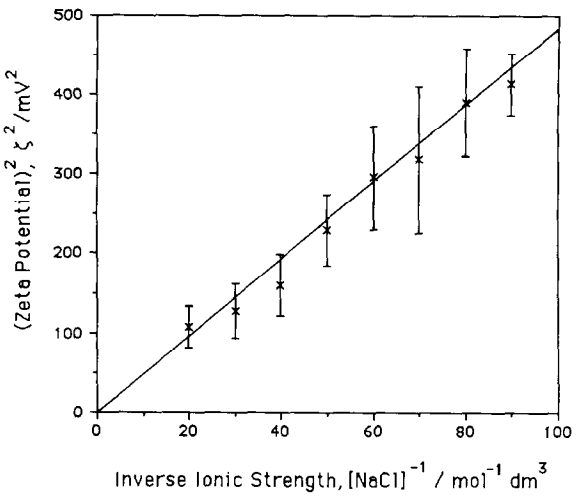

Fig. 1. The square of the zeta potential for Intralipid 20% as a function of the inverse ionic strength for sodium chloride solutions (11–50 mmol dm^{-3}). The solid line is the linear least-squares fit and analyses for $\sigma_o = -5.14$ mC m^{-2}.

measured for each calcium concentration and found to be in the range 6.8–6.9 in all cases.

The plot of charge density as a function of free calcium concentration is displayed in Fig. 3. The uncomplexed calcium concentration for each measurement was determined using PHREEQE (Parkhurst et al., 1980) together with the equi-

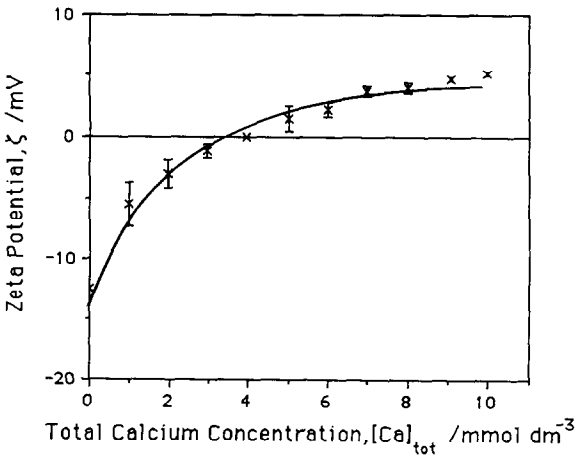

Fig. 2. Zeta potential of Intralipid 20% as a function of total calcium concentration for calcium chloride solutions (0–10 mmol dm^{-3}) with 25 mmol dm^{-3} background sodium chloride. The solid line is the theoretical line described by Eqn 17 where $\beta_{BCa} = 610$ mol^{-1} dm^3 and $\sigma_o = -5.14$ mC m^{-2}.

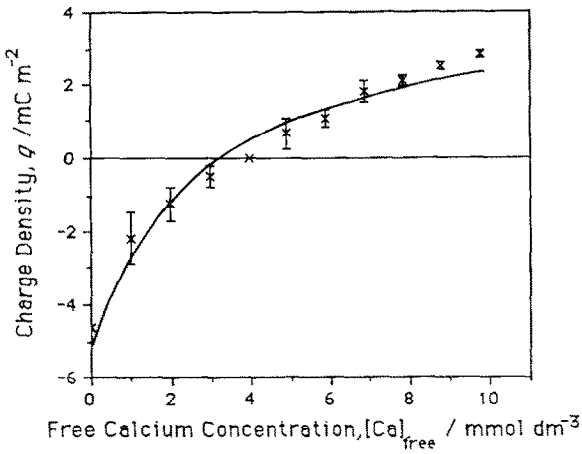

Fig. 3. Charge density of Intralipid 20% as a function of uncomplexed calcium concentration for calcium chloride solutions (0–10 mmol dm^{-3}) with 25 mmol dm^{-3} background sodium chloride. The solid line is the theoretical line described by Eqn 17 where $\beta_{BCa} = 610$ mol^{-1} dm^3 and $\sigma_o = -5.14$ mC m^{-2}.

librium constants listed in Table 1. A summary of the speciation calculations is provided in Table 2. The interfacial charge density for each measurement was calculated using the ionic strength values determined by PHREEQE and Eqns 6 and 7. The equilibrium constant β_{BCa} was determined to be 610 mol^{-1} dm^3 using least-squares optimisation on Eqn 17, assuming $m = -1$, for each data point in Fig. 3, the value for σ_o having been determined from Fig. 1. The predicted relationship between interfacial charge density and free calcium concentration is represented by the solid curve in Fig. 3. This relationship is also depicted as a solid curve in Fig. 2 upon transformation of charge density data to zeta potential using Eqn 6.

TABLE 1

Thermodynamic equilibrium constants used in Intralipid-calcium studies

Species	lg β	Ref.
OH^-	−13.997	Baes and Mesmer, 1976
HCl	−6.10	Truesdell and Singers, 1974
$CaOH^+$	−12.85	Baes and Mesmer, 1976
$CaCl^+$	0.08	Elgquist and Wedborg, 1975
NaOH	−13.80	Baes and Mesmer, 1976
NaCl	−0.90	Benson and Teague, 1980

TABLE 2

Chemical speciation summary and electrophoretic data for Intralipid-calcium studies

$[CaCl_2]$	$[Ca^{2+}]$ (mmol dm^{-3})	I	ζ (mV)
0.00	0.00	24.9	−12.56
1.00	0.98	27.9	−5.58
2.00	1.96	30.9	−3.01
3.00	2.94	33.8	−1.10
4.00	3.92	36.8	0.00
5.00	4.90	39.7	1.44
6.00	5.87	42.7	2.22
7.00	6.85	45.6	3.64
8.00	7.82	48.6	4.06
9.00	8.79	51.5	4.71
10.00	9.76	54.4	5.18

Fig. 4 shows the plot of zeta potential as a function of total calcium concentration in 25 mmol dm^{-3} background NaCl in the presence of varying concentrations of citrate, a ligand which complexes Ca^{2+}. The position of charge reversal is found at greater calcium concentrations than in Fig. 2.

The free calcium concentrations were calculated as for Fig. 3 using PHREEQE together with

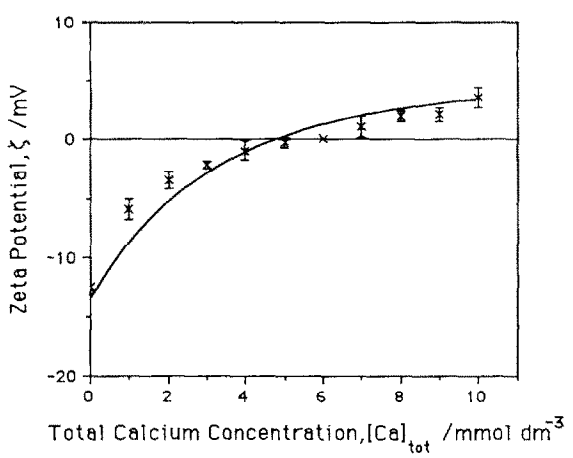

Fig. 4. Zeta potential of Intralipid 20% as a function of total calcium concentration for calcium chloride solutions (0–10 mmol dm^{-3}) with trisodium citrate (0–2.5 mmol dm^{-3}) and 25 mmol dm^{-3} background sodium chloride. The solid line is the theoretical line described by Eqn 17 where $\beta_{BCa} = 610$ mol^{-1} dm^3 and $\sigma_o = -5.14$ mC m^{-2}.

TABLE 3

Thermodynamic equilibrium constants used in Intralipid-calcium-citrate studies

Species	lg β	Ref.
$HCTA^{2-}$	6.28	Raymond, 1987
H_2CTA^{1-}	11.02	Raymond, 1987
H_3CTA	14.14	Raymond, 1987
$CaCTA^{1-}$	4.83	Raymond, 1987
CaHCTA	9.33	Raymond, 1987
$CaCTA_2^{4-}$	5.86	Raymond, 1987
$Ca_2CTA(OH)$	1.94	Raymond, 1987
$NaCTA^{2-}$	1.33	Rechnitz and Zamochnick, 1964

TABLE 4

Chemical speciation summary and electrophoretic data for Intralipid-calcium-citrate studies

$[CaCl_2]$	$[Na_3CTA]$ (mmol dm^{-3})	$[Ca^{2+}]$	I	ζ (mV)
0.00	0.00	0.00	24.9	−12.56
1.00	0.25	0.75	28.0	−5.99
2.00	0.50	1.47	31.0	−3.40
3.00	0.75	2.18	33.0	−2.16
4.00	1.00	2.88	36.8	−0.92
5.00	1.25	3.58	39.7	−0.19
6.00	1.50	4.27	42.5	0.00
7.00	1.75	4.96	45.4	1.04
8.00	2.00	5.65	48.2	1.95
9.00	2.25	6.34	51.1	2.05
10.00	2.50	7.02	53.9	3.60

the equilibrium data in Table 1 and the calcium-citrate constants listed in Table 3. A summary of the pertinent speciation predictions are listed in Table 4. The plot of charge density as a function of free calcium is shown in Fig. 5. The solid curves in Figs 4 and 5 are the predicted relationships using the value for β_{BCa} determined from Fig. 3.

Discussion

The linear relationship in Fig. 1 of ζ^2 with $[NaCl]^{-1}$, for which this paper is the first publication, confirms the ideality of this salt and the absence of any significant evidence for specific

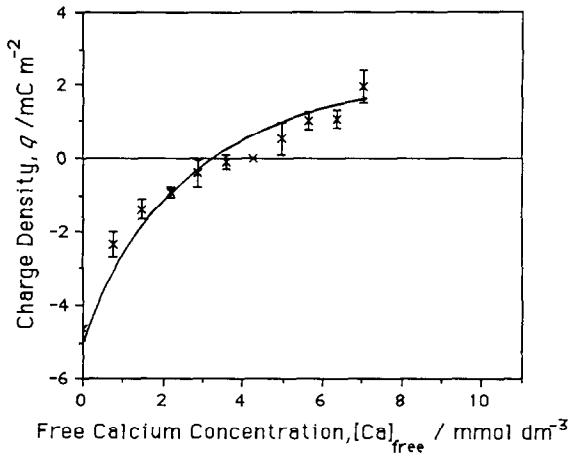

Fig. 5. Charge density of Intralipid 20% as a function of uncomplexed calcium concentration for calcium chloride solutions (0–10 mmol dm^{-3}) with trisodium citrate (0–2.5 mmol dm^{-3}) and 25 mmol dm^{-3} background sodium chloride. The solid line is the theoretical line described by Eqn 17 where $\beta_{BCa} = 610$ mol^{-1} dm^3 and $\sigma_o = -5.14$ mC m^{-2}.

interaction between the electrolyte constituents and the interface. Had such specific interactions occurred in the NaCl concentration range explored, then a curvilinear relationship would be expected below the drawn line. The use of many electrophoretic data in determining the interfacial charge density in this manner is superior to single measurement approaches.

The value for σ_o calculated from Fig. 1 is equivalent to an average area of 3100 Å^2 for each charge at the interface and corresponds to an intercharge spacing of 56 Å. In comparison, the Debye length is usually much less than this distance and ranges from 14 to 31 Å for the data in Fig. 1. We have taken this as supportive evidence that the binding sites should be treated as point charges at the interface with minimal Debye shielding overlap.

Fig. 1 also demonstrates our conviction that the common literature practice of quoting zeta potentials is meaningless in the absence of specific data concerning the electrolyte ionic strength. Furthermore, the ionic strength for non-ideal electrolytes must be obtained using chemical speciation techniques rather than simplistic calculations involving total ion concentrations.

The specific nature of the surfactant material in Intralipid 20% is not reported in the literature and must be treated empirically. This is in contrast to the well-defined aqueous chemistry which is available to speciation chemists. In the present model it is assumed that there is only one type of binding site at the interface which may form a 1 : 1 complex with a metal cation. The charge valence, m, of the binding site is not directly measurable and must be inferred from experimental data. This is an essential step prior to the evaluation of β_{BM} with Eqns 16 and 17.

Fig. 3 clearly shows that the charge density undergoes a change in sign and tends towards the same value – but of opposite sign – to that for σ_o. Inspection of Eqn 5 indicates that this is possible only if $m = -1$, when $n = +2$, as is the case for calcium. The value for β_{BCa} was found to be 610 mol^{-1} dm^3 (lg $\beta_{BCa} = 2.79$) and of similar order to that for Ca(glycerol 1-phosphate)$^+$; lg $\beta = 1.66$ (Schwarzenbach and Anderegg, 1957) and $CaHPO_4$; lg $\beta = 2.74$ (Nancollas and Reddy, 1974).

The success of the interfacial charge density-chemical speciation approach is illustrated in Figs 4 and 5. The calcium complexing ligand citrate was included as the trisodium salt (i.e. an indifferent cation), at a constant ratio to calcium, to the otherwise identical electrolyte to that used in Figs 2 and 3. Washington's (1990) model could not have predicted any change in the plot of ζ vs total calcium. Comparison of the data presented in Fig. 4 with that in Fig. 2 shows that the charge reversal is, however, shifted from 3.50 mmol dm^{-3} to 4.75 mmol dm^{-3} in the presence of citrate. The solid curve of good fit to the experimental data in Fig. 4 is the predicted relationship using Eqn 17 together with the values for σ_o and β_{BCa} determined in the previous experiment, and the free calcium concentrations listed in Table 4. Examination of the free calcium concentration data and Fig. 5 provides an explanation for the change in the ζ vs calcium plot – approx. 30% of the calcium at each concentration is complexed to citrate and this decreases the free calcium concentration available for interfacial equilibria. This is an example of the concept of competitive equilibria and stresses the necessity for using this approach in any comprehensive model which considers benefit : risk ratios for patients. As expected the plot of σ vs $[Ca^{2+}]$ in the presence of citrate in Fig. 5 is superimposable with that in Fig. 3 in the absence of citrate in accordance with Eqn 17.

The present model makes good predictions of the experimental measurements previously reported by Washington (1990); namely that the calcium concentration for charge reversal increases with increasing NaCl present. Washington interpreted this in terms of a sodium binding constant of value 15 mol^{-1} dm^3, which is large compared to the values of 0.6–0.85 mol^{-1} dm^3 reported in single phospholipid studies (Eisenberg et al., 1979; Lau et al., 1981; Macdonald and Seelig, 1986).

Fig. 6 shows the predicted relationship for zeta potential with calcium for three different NaCl concentration; 0 and 40 mmol dm^{-3} for comparison with Washington's (1990) measurements and 25 mmol dm^{-3} from the present work. The synthetic relationships were calculated using Eqs 15 and 17 with $\beta_{BCa} = 610$ mol^{-1} dm^3 and speciation calculations determining the free calcium concentrations and ionic strength. Our predicted relationships agree well with the zeta potential measurements reported by Washington (1990) and

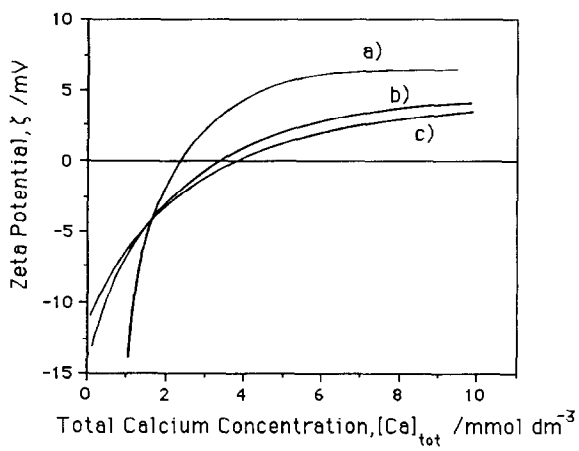

Fig. 6. Predicted relationship between zeta potential and calcium for various sodium chloride concentrations; (a) 0 mmol dm^{-3}, (b) 25 mmol dm^{-3} and (c) 40 mmol dm^{-3}. The equation for each line is given by Eqn 17 where $\beta_{BCa} = 610$ mol^{-1} dm^3 and $\sigma_o = -5.14$ mC m^{-2}, the ionic strength and free calcium concentrations are those calculated using PHREEQE.

indeed the point of charge reversal is predicted by this model to increase from 2 mmol dm^{-3} calcium in the absence of NaCl to 4 mmol dm^{-3} calcium in 40 mmol dm^{-3} NaCl.

Furthermore, these predictions rely upon only a single optimised parameter; the equilibrium constant β_{BCa} in contrast to the four optimised parameters required by Washington's (1990) model; i.e. ζ_{Na}, K_{Na}, ζ_{Ca} and K_{Ca}. The parameters ζ_{Na} and ζ_{Ca} are conceptual only in nature, since they refer to the theoretical zeta potential at 100% binding of the metal concerned at some unstated ionic strength.

The present model may be further developed to account for the competitive interfacial binding of several cations by including extra concentration terms in Eqn 3, charge terms in Eqn 5 and thus also in Eqns 16 and 17. The equilibrium constants for each are measured in the absence of competitive cations in a similar manner to that described for calcium above. Such experiments are currently in progress and will be reported upon completion.

We may already account for the effect of competitive aqueous ligands for the cations, using the existing speciation computer programs and the vast thermodynamic database that has been assembled by past and present researchers (Hall and Williams, 1990).

The ultimate objective is to incorporate the interfacial equilibria expressions with the existing aqueous thermodynamic data to provide a single computer code to model intravenous emulsions.

We have neither confirmed nor dispelled sodium binding to Intralipid 20% but have shown that it is not necessary to include this in a model appropriate for intravenous formulations.

In conclusion, the most important aspects of this work may be summarised as follows – charge density is superior to zeta potential in describing interfacial chemistry; the plot of ζ^2 vs I^{-1} is useful in evaluating the interfacial charge density; chemical speciation analysis is mandatory before electrokinetic data can be interpreted for interfacial equilibria; and the resulting equilibria in combination with chemical speciation and activity coefficient evaluation may be successfully used to predict zeta potentials for Intralipid 20% in the presence of calcium and a competing ligand.

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