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Diffusion Coefficients of the Ternary System Calcium Chloride−Caffeine−Water at (25 and 37) °C

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Ternary mutual diffusion coefficients measured by the Taylor dispersion method are reported for aqueous solutions of $CaCl_2$−caffeine at carrier concentrations from (0.0025 to 0.0500) mol·dm^{-3} for each solute, respectively. The results are compared with those obtained for the binary systems H_2O−$CaCl_2$ and H_2O−caffeine, also reported here. From these data, it is possible to make conclusions about the influence of the caffeine solutes in the diffusion of calcium chloride and to contribute to a better understanding of the structure of this system.

Introduction

The interactions of metal ions with caffeine (3,7-dihydro-1,3,7-trimethyl-1*H*-purine-2,6-dione) are of major biological interest, once these systems play a dominant role in many biochemical interactions.[1−3] Among them, we are particularly interested in ternary systems involving calcium ions and caffeine, because of their role in health sciences and in physiological processes (muscle functions). In fact, some authors[3] have stated that the presence of this drug, naturally occurring in some beverages and used as a pharmacological agent, can lead to calcium deficiency, accompanied by adverse effects, osteoporosis being the most common bone metabolic disorder. The development of new and more effective treatments concerning osteoporosis, as well as optimizing the existing ones, needs knowledge on the transport process of these systems in aqueous solutions. However, we can say that the properties and behavior of such chemical systems are poorly known, even though this is a prerequisite to obtain adequate understanding to face these problems of health. In particular, our research group is especially interested in diffusion coefficients, providing these parameters with a direct measure of molecular mobility, an important factor in the preservation of biological materials in different matrices. While earlier data on diffusion coefficients of calcium chloride in aqueous solutions at (25 and 37) °C over the concentration range from (0.0000 to 0.0500) mol·dm^{-3} have been reviewed,[4] no data on mutual diffusion coefficients of Ca salts in the presence of caffeine at (25 and 37) °C, relevant data for in vivo pharmaceutical applications, have been published, as far as careful literature searches have shown. The present paper intends to fill this gap. This paper reports experimental data for differential ternary mutual diffusion coefficients (D_{11}, D_{22}, D_{12}, and D_{21}) of calcium chloride in aqueous solutions at carrier concentrations from (0.000 to 0.0500) mol·dm^{-3}, in the presence of caffeine at different concentrations (that is, from (0.000 to 0.0500) mol·dm^{-3}) using the Taylor dispersion technique at (25 and 37) °C.

Experimental Section

Materials. Calcium chloride (Sigma-Aldrich, Germany, pro analysi > 99.9 % in mass) was used without further purification. Caffeine (Sigma, pro analysi > 98.5 %) was used as received. The solutions for the diffusion measurements were prepared in calibrated volumetric flasks using bidistilled water. The solutions were freshly prepared and deaerated for about 30 min before each set of runs.

Procedure. The theory of the Taylor dispersion technique is well-described in the literature,[5−14] so the authors only indicate some relevant points concerning this method on the experimental determination of binary diffusion coefficients and ternary diffusion coefficients, respectively.

The above dispersion method is based on the dispersion of small amounts of solution injected into laminar carrier streams of solvent or solution of different compositions, flowing through a long capillary tube.[5−14] The length of the Teflon dispersion tube used in the present study was measured directly by stretching the tube in a large hall and using two high-quality theodolytes and appropriate mirrors to accurately focus on the tube ends. This technique gave a tube length of 3.2799 (± 0.0001)·10^4 mm, in agreement with less-precise control measurements using a good-quality measuring tape. The radius of the tube, 0.5570 (± 0.0003) mm, was calculated from the tube volume obtained by accurately weighing (resolution of 0.1 mg) the tube when empty and when filled with distilled water of known density.

At the start of each run, a six-port Teflon injection valve (Rheodyne, model 5020) was used to introduce 0.063 mL of solution into the laminar carrier stream of slightly different composition. A flow rate of 0.17 mL·min^{-1} was maintained by a metering pump (Gilson model Minipuls 3) to give retention times of about 1.1·10^4 s. The dispersion tube and the injection valve were kept at (298.15 and 310.15) K (± 0.01 K) in an air thermostat.

Dispersion of the injected samples was monitored using a differential refractometer (Waters model 2410) at the outlet of

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the dispersion tube. Detector voltages, $V(t)$, were measured at accurate 5 s intervals with a digital voltmeter (Agilent 34401 A) with an IEEE interface. Binary diffusion coefficients were evaluated by fitting the dispersion equation

$$V(t) = V_0 + V_1 t + V_{\max}(t_R/t)^{1/2} \exp[-12D(t - t_R)^2/r^2 t] \tag{1}$$

to the detector voltages, where r is the internal radius of our Teflon dispersion tube. The additional fitting parameters were the mean sample retention time t_R, peak height $V_{\max}$, baseline voltage V_0, and baseline slope V_1.

Diffusion in a ternary solution is described by the diffusion equations (eqs 2 and 3),

$$-(J_1) = (D_{11})_\nu \frac{\partial c_1}{\partial x} + (D_{12})_\nu \frac{\partial c_2}{\partial x} \tag{2}$$

$$-(J_2) = (D_{21})_\nu \frac{\partial c_1}{\partial x} + (D_{22})_\nu \frac{\partial c_2}{\partial x} \tag{3}$$

whereJ_1, J_2, $(\partial c_1)/(\partial x)$, and $(\partial c_2)/(\partial x)$ are the molar fluxes and the gradients in the concentrations of solute 1 and 2, respectively. The index ν represents the volume-fixed frame of the reference used in these measurements. Main diffusion coefficients give the flux of each solute produced by its own concentration gradient. Cross diffusion coefficients D_{12} and D_{21} give the coupled flux of each solute driven by a concentration gradient in the other solute. A positive D_{ik} cross coefficient (i ≠ k) indicates cocurrent coupled transport of solute i from regions of higher to lower concentrations of solute k. However, a negative D_{ik} coefficient indicates counter-current coupled transport of solute i from regions of lower to higher concentration of solute k.

Extensions of the Taylor technique have been used to measure ternary mutual diffusion coefficients (D_{ik}) for multicomponent solutions. These D_{ik} coefficients, defined by eqs 2 and 3, were evaluated by fitting the ternary dispersion equation (eq 4) to two or more replicate pairs of peaks for each carrier stream.

$$V(t) = V_0 + V_1 t + V_{\max}(t_R/t)^{1/2} \left[W_1 \exp\left(-\frac{12D_1(t - t_R)^2}{r^2 t}\right) + (1 - W_1)\exp\left(-\frac{12D_2(t - t_R)^2}{r^2 t}\right)\right] \tag{4}$$

Two pairs of refractive-index profiles, D_1 and D_2, are the eigenvalues of the matrix of the ternary D_{ik} coefficients. W_1 and $(1 - W_1)$ are the normalized pre-exponential factors.

In these experiments, small volumes, ΔV, of the solution, of composition $\bar{c}_1 + \Delta\bar{c}_1$, $\bar{c}_2 + \Delta\bar{c}_2$ are injected into carrier solutions of composition, $\bar{c}_1$ and $\bar{c}_2$ at time $t = 0$.

Results and Discussion

The diffusion coefficient values for the ternary system $CaCl_2$ + caffeine + water at (25 and 37) °C, D_{11}, D_{12}, D_{21}, and D_{22}, are summarized in Tables 1 and 2. These results are the average of four experiments. Good reproducibility was observed, as seen by the small standard deviations of the mean, S_{Dav}. Previous papers reporting data obtained with this technique have shown that the error limits of our results should be close to the imprecision, therefore giving an experimental uncertainty of (1 to 3) %.[9−14]

The main coefficients D_{11} and D_{22}, giving the molar fluxes of the $CaCl_2$ (1) and caffeine (2) components driven by their own concentration gradient, are compared with those obtained for binary systems at the same temperatures and with the same technique (Tables 1 and 2), that is, for $CaCl_2$[4,15] and caffeine[16] in aqueous solutions, respectively. In general, these coefficients are lower than the binary diffusion coefficients of aqueous $CaCl_2$ and caffeine for both temperatures (deviations between 1 % and 6 %). However, in general, at the concentrations used in this study, we verify that added caffeine produces relatively minor changes in D_{11} for $CaCl_2$, while added $CaCl_2$ produces major changes in D_{22} for caffeine. From these results, it is evident that the $CaCl_2$ species exerts an influence on the diffusion of caffeine in aqueous solution (that is, in general, for [$CaCl_2$]/[caffeine]/[ratio values ≥ 0.5), increasing this effect with the increase of these ratios. Some calcium ions can be present in

Table 1. Ternary Diffusion Coefficients, D_{11}, D_{12}, D_{21}, and D_{22}, for Aqueous Calcium Chloride (1) + Caffeine (2) Solutions and the Respective Standard Deviations, S_D, at 25 °C

c_1[a]	c_2[a]	R[b]	$D_{11} \pm S_D$ $10^{-9}\ \mathrm{m^2 \cdot s^{-1}}$	$D_{12} \pm S_D$ $10^{-9}\ \mathrm{m^2 \cdot s^{-1}}$	$D_{21} \pm S_D$ $10^{-9}\ \mathrm{m^2 \cdot s^{-1}}$	$D_{22} \pm S_D$ $10^{-9}\ \mathrm{m^2 \cdot s^{-1}}$	D_{12}/D_{22}[c]	D_{21}/D_{11}[d]
0.000	0.0025					0.749[e]		
0.000	0.0050					0.738[e]		
0.000	0.0100					0.703[e]		
0.000	0.0500					0.594[e]		
0.0025	0.0000		1.270[f]					
0.0050	0.000		1.260[f]					
0.0100	0.000		1.215[f]					
0.0500	0.000		1.115[f]					
0.0025	0.0050	0.5	1.258 ± 0.012 (−0.9 %)[g]	0.062 ± 0.011	−0.042 ± 0.004	0.701 ± 0.010 (−5.0 %)[h]	0.088	−0.033
0.0050	0.0025	2	1.212 ± 0.004 (−3.8 %)[g]	0.056 ± 0.007	−0.041 ± 0.006	0.711 ± 0.012 (−5.1 %)[h]	0.079	−0.034
0.0050	0.0050	1	1.191 ± 0.006 (−5.5 %)[g]	0.116 ± 0.003	−0.158 ± 0.008	0.635 ± 0.009 (−13.9 %)[h]	0.183	−0.133
0.0100	0.0100	1	1.215 ± 0.006 (−0.0 %)[g]	0.016 ± 0.002	−0.071 ± 0.011	0.698 ± 0.006 (0.7 %)[h]	0.023	−0.058
0.0500	0.0500	1	1.162 ± 0.013 (+4.2 %)[g]	0.082 ± 0.028	−0.197 ± 0.028	0.582 ± 0.002 (−2.0 %)[h]	0.141	−0.170

[a] c_1 and c_2 in units of $\mathrm{mol \cdot dm^{-3}}$. [b] $R = c_1/c_2$ for ternary systems. [c] D_{12}/D_{22} gives the number of moles of $CaCl_2$ cotransported per mole of caffeine. [d] D_{21}/D_{11} gives the number of moles of caffeine counter-transported per mole of $CaCl_2$. [e] Taylor binary D values for aqueous caffeine (Leaist and Hui, 1990).[15] [f] Our experimental binary D values for aqueous $CaCl_2$ (Ribeiro et al.[4]). [g] These values indicated in parentheses represent the relative deviations between the experimental values of D_{11} and the binary values for the same concentration, D (see note e). [h] These values indicated in parentheses represent the relative deviations between the experimental values of D_{22} and the binary values for the same concentration, D (see note f).

Table 2. Ternary Diffusion Coefficients, D_{11}, D_{12}, D_{21}, and D_{22}, for Aqueous Calcium Chloride (1) + Caffeine (2) Solutions and the Respective Standard Deviations, S_D, at 37 °C

c_1[a]	c_2[a]	R[b]	$D_{11} \pm S_D$ 10^{-9} $m^2 \cdot s^{-1}$	$D_{12} \pm S_D$ 10^{-9} $m^2 \cdot s^{-1}$	$D_{21} \pm S_D$ 10^{-9} $m^2 \cdot s^{-1}$	$D_{22} \pm S_D$ 10^{-9} $m^2 \cdot s^{-1}$	D_{12}/D_{22}[c]	D_{21}/D_{11}[d]
0.000	0.0025					1.021[e]		
0.000	0.0050					0.980[e]		
0.000	0.0100					0.944[e]		
0.000	0.0500					0.822[e]		
0.0025	0.0000		1.602[f]					
0.0050	0.0000		1.601[f]					
0.0100	0.000		1.590[f]					
0.0500	0.000		1.530[f]					
0.0025	0.0050	0.5	1.581 ± 0.005 (−1.3 %)[g]	0.016 ± 0.007	−0.030 ± 0.008	0.987 ± 0.001 (0.71 %)[h]	0.016	−0.019
0.0050	0.0025	2	1.558 ± 0.001 (−2.7 %)[g]	0.018 ± 0.005	−0.091 ± 0.007	0.943 ± 0.012 (−7.6 %)[h]	0.019	−0.058
0.0050	0.0050	1	1.605 ± 0.001 (0.25 %)[g]	0.051 ± 0.009	−0.070 ± 0.004	0.959 ± 0.006 (−2.1 %)[h]	0.053	−0.044
0.0100	0.0100	1	1.565 ± 0.008 (−1.6 %)[g]	0.040 ± 0.004	−0.055 ± 0.016	0.947 ± 0.005 (+0.32 %)[h]	0.042	−0.035
0.0500	0.0500	1	1.482 ± 0.003 (−3.1 %)[g]	0.029 ± 0.005	−0.015 ± 0.007	0.788 ± 0.009 (−4.1 %)[h]	0.037	−0.010

[a] c_1 and c_2 in units of $mol \cdot dm^{-3}$. [b] $R = c_1/c_2$ for ternary systems. [c] D_{12}/D_{22} gives the number of moles of $CaCl_2$ cotransported per mole of caffeine. [d] D_{21}/D_{11} gives the number of moles of caffeine counter-transported per mole of $CaCl_2$. [e] Our experimental Taylor binary D values for aqueous caffeine.[15] [f] Our experimental binary D values for aqueous $CaCl_2$ (Ribeiro et al.[4]). [g] These values indicated in parentheses represent the relative deviations between the experimental values of D_{11} and the binary values for the same concentration, D (see note e). [h] These values indicated in parentheses represent the relative deviations between the experimental values of D_{22} and the binary values for the same concentration, D (see note f).

solution as aggregates; consequently, they will have less mobility, and they can be responsible for relatively large decreases in D_{22}. This effect is less relevant when we consider the effect of caffeine on transport of $CaCl_2$, probably due to the similarity of the mobilities of caffeine-free species and eventual aggregates of $CaCl_2$ and caffeine.

The limiting values for infinitesimal concentration of cross-coefficients D_{12} and D_{21} should be zero within the experimental error. However, at finite concentrations, the cross coefficients D_{12} and D_{21} values different from zero may be used to understand the influence of these solutes in diffusion of solution components. In our case, the gradient in the concentration of $CaCl_2$ produces counter-current coupled flows of caffeine, while the gradient in the concentration of caffeine produces cocurrent coupled flows of $CaCl_2$. Considering that D_{12}/D_{22} gives the number of moles of $CaCl_2$ cotransported per mole of caffeine, we may say that, at the concentrations used, a mole of diffusing caffeine cotransports at most 0.02 mol of $CaCl_2$, increasing the cotransport with the increase of its concentration. Through D_{21}/D_{11} values, at the same concentrations, we can expect that a mole of diffusing $CaCl_2$ counter-transports at most 0.03 mol of caffeine. Similarly, at 310.15 K, the number of moles of of $CaCl_2$ cotransported per mole of caffeine, $D_{12}/D_{22,}$ is at most 0.02 mol, while the number of moles of caffeine counter-transported per mole of calcium chloride, D_{21}/D_{11}, is at most 0.02 mol.

Conclusion

From the ternary diffusion measurements, we can conclude that, for infinitesimal concentration, the solutes are not interacting. However, from the cross coefficients D_{21} and D_{21} values different from zero at finite concentrations, having in mind that the main coefficients D_{11} and D_{22} are not identical to the binary diffusion coefficients of aqueous $CaCl_2$ and caffeine, we can conclude that the diffusion of $CaCl_2$ in aqueous solutions at both temperatures, (25 and 37) °C, may be affected by the eventual presence of new different species resulting from various equilibria.

Diffusion coefficients measured for aqueous solutions of $CaCl_2$ and caffeine provide transport data necessary to model the diffusion for various chemical and pharmaceutical applications.

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