CALCIUM– AND MAGNESIUM–EDTA COMPLEXES. STABILITY CONSTANTS AND THEIR DEPENDENCE ON TEMPERATURE AND IONIC STRENGTH

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ABSTRACT

The stability constants of M^{2+}–EDTA ($M^{2+} = Ca^{2+}$ or Mg^{2+}) have been determined pH-metrically in aqueous solution. The study has been performed over a wide range of ionic strength (0.17–0.77 mole dm^{-3}) and temperature (10–45°C). Semiempirical equations have been obtained for the ionic strength dependence of formation constants.

The thermodynamic parameters for the major species have been obtained from the temperature dependence of stability constants.

The influence of the background salt is also discussed.

INTRODUCTION

Ethylenediaminetetraacetic acid (EDTA) is a ligand that forms complexes with almost all metal ions, including the alkali metal ions, the stability of which is fairly high, especially if compared with other low molecular weight ligands. Owing to its peculiar characteristic, it has been extensively studied by both inorganic and analytical chemists. Anderegg has recently published a critical survey of thermodynamic data concerning the complexation of EDTA with several metal ions and the proton [1]. EDTA has been used in medicine to remove toxic metal ions [2]; unfortunately, some inconveniences limit or make its use difficult. In fact, (a) EDTA is not selective and thus removes all blood plasma metal ions (for instance, Ca^{2+} removal, following EDTA administration aimed at the sequestration of other metal ions, can seriously damage the organism), (b) the computer simulation [3] of the conditions suitable for the removal must take into account all complexes, including those with alkali metal ions, (c) the ionic strength as well as the temperature dependence of EDTA complexes is remarkable. Hence, a good

model system should take into account all these elements.

Thus, to study EDTA sequestering characteristics, a knowledge of the dependence of the stability constants on the ionic medium and the ionic strength as well as on the temperature is of considerable interest. To this end, we here report a study on EDTA complexes with Ca^{2+} and Mg^{2+}, two of the major components of biological fluids, at various ionic strengths and temperatures, also taking into account EDTA interactions with alkali metal ions.

EXPERIMENTAL

Materials

EDTA (disodium salt, C. Erba RPE-ACS) stock solutions were standardized with zinc oxide using Eriochrom Black T as indicator, according to Flaschka [4]. Calcium and magnesium cloride (C. Erba RPE) stock solutions were standardized as recommended by Flaschka [4]. All the solutions were prepared with twice-distilled water and grade A glassware was used throughout. The ionic strength of the M^{2+}–EDTA solutions was kept at the desired value by addition of tetramethylammonium cloride (Merck).

Potentiometric measurements

E.M.F. measurements were carried out by means of two semi-automatic potentiometers (Amel 232 and Analog Devices AD 2027 B) using glass electrodes (EIL or Ingold 201 NS) and single calomels (Ingold). $E°$ was determined by titrating 20–25 cm^3 of HNO_3 (5 mmole dm^{-3}) (and tetramethylammonium cloride to keep the ionic strength at the desired value) with standard carbonate-free NaOH. Calcium and magnesium stability constants were computed from the data obtained by titrating 20–25 cm^3 of solutions containing M^{2+} and EDTA with NaOH. The pH values were reproducible within 0.007 units. All potentiometric experiments were carried out in 50 cm^3 cells at $t \pm 0.2°C$ thermostatted by means of a Colora WK4 thermostatic bath. All titrations were performed under scrubbed nitrogen previously bubbled through ampoules containing the same ionic medium at the same concentration as the solution under investigation. Magnetic stirring was employed. Some experimental details of potentiometric measurements are reported in Table 1.

H^+ and Na^+ complexes

These complexes have previously been investigated [5]. The formation constants at various ionic strengths and temperatures are reported in Table 2.

TABLE 1

Some experimental details of potentiometric measurements

M^{2+}	t (°C)	C_M [a]	C_{Me_4N} [b]	$\bar{I}$ [c]	n [d]
Ca^{2+}	10	2– 6	0.16	0.18	6
	20	2– 6	0.18	0.20	6
	25	1– 5	0.15	0.17	18
	25	5–10	0.30	0.34	6
	25	5–10	0.50	0.53	6
	25	4–10	0.75	0.76	7
	37	4– 6	0.15	0.17	8
	37	2– 6	0.32	0.35	4
	45	2– 6	0.16	0.18	6
Mg^{2+}	10	3– 7	0.16	0.18	6
	20	3– 7	0.18	0.20	7
	25	1– 5	0.15	0.17	15
	25	5–15	0.30	0.33	6
	25	5–15	0.50	0.53	6
	25	3–11	0.75	0.77	6
	37	4– 7	0.15	0.17	7
	37	3– 7	0.32	0.35	6
	45	3– 7	0.16	0.18	6

[a] Initial analytical concentrations in mmole dm^{-3}; $C_M/C_{EDTA} = 0.6$–1.1; pH < 7; titrant NaOH 0.25 mole dm^{-3}.
[b] Background concentrations in mole dm^{-3}.
[c] Mean (effective) ionic strength in mole dm^{-3}.
[d] Number of titrations.

TABLE 2

Formation constants for H^+ – and Na^+ –EDTA complexes

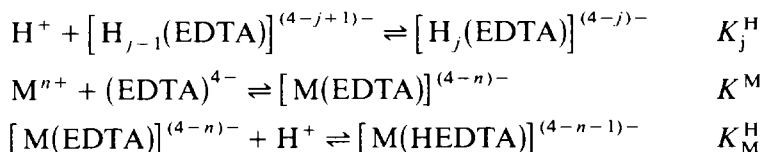|	$\log K$ ($I = 0.15$, $t = 25$°C)	C [a]	D [a]	$a \times 10^2$ [a]	$b \times 10^4$ [a]
$\log K_1^H$	10.31	2.5	– 1.7	– 1.8	2.1
$\log K_2^H$	6.11	1.6	– 0.9	– 1.1	0.8
$\log K_3^H$	2.65	0.9	– 0.4	0.35	
$\log K^{Na}$	1.70	1.9	– 1.0	– 0.4	
pK_w	13.80	0.7	– 0.2	– 3.32	1.5

[a] Parameters for the equation

$$\log K = \log K(I = 0.15, t = 25) - z^*A\left(\frac{\sqrt{I}}{1 + B\sqrt{I}} - \frac{0.3873}{1 + 0.3873\ B}\right) + C(I - 0.15) +$$

$$+ D(I^{3/2} - 0.058) + a(t - 25) + b(t - 25)^2$$

$$A = 0.5115 + 8.89 \times 10^{-4}(t - 25) + 2.95 \times 10^{-6}(t - 25)^2$$

$$B = 1.4888 + 8.77 \times 10^{-4}(t - 25) + 4.69 \times 10^{-6}(t - 25)^2$$

The formation constants of the species existing in the systems investigated are expressed as

$$H^+ + \left[H_{j-1}(EDTA) \right]^{(4-j+1)-} \rightleftharpoons \left[H_j(EDTA) \right]^{(4-j)-} \qquad K_j^H$$

$$M^{n+} + (EDTA)^{4-} \rightleftharpoons \left[M(EDTA) \right]^{(4-n)-} \qquad K^M$$

$$\left[M(EDTA) \right]^{(4-n)-} + H^+ \rightleftharpoons \left[M(HEDTA) \right]^{(4-n-1)-} \qquad K_M^H$$

The uncertainties on the parameters used are given as $> 95\%$ confidence limits throughout.

CALCULATIONS AND RESULTS

The potentiometric data were processed by means of the computer program MINIQUAD 76 A [6] in two separate steps. In the first stage, the formation constants were calculated at each ionic strength separately by taking into account four mass balance equations *, i.e. those concerning Na^+, M^{2+}, $EDTA^{4-}$ and H^+. The results obtained are listed in Table 3. Two species were taken into consideration, namely $[M(EDTA)]^{2-}$ and $[M(HEDTA)]^-$. The latter species is practically negligible under our experimental conditions; in fact, even considering the constants previously reported [1], the amount of protonated species is always less than 4%, for $C_{EDTA} < 10^{-2}$ mole dm^{-3}. At 25°C, where most of our data were obtained, it was possible to calculate the stability constants for the protonated species with an acceptable error, even at such low concentrations, as reported below.

From the values of formation constants obtained at each ionic strength, the dependence on the ionic strength can then be obtained. In previous works [7] we have shown that a semiempirical equation such as

$$\log K = \log^T K - Az^* \frac{\sqrt{I}}{1 + B\sqrt{I}} + L(I) \qquad (1)$$

where $\log^T K$ is the thermodynamic constant (at infinite dilution), A is the Debye–Huckel constant ($A = 0.5115$ at 25°C in aqueous solution), z^* is the square of the charge on each species summed over the formation reaction for the species being considered, B is an empirical parameter [$B = 1.49$ at 25°C in aqueous solution, see ref. 7 (c)], and $L(I)$ is a generic linear term can well fit the formation constants at all ionic strengths (for $I < 1$ mole dm^{-3}). By

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* It has been assumed that the tetramethylammonium ion does not significantly interact with $EDTA^{4-}$. This assumption has been previously discussed [7] and is usually agreed upon and resorted to in the literature.

TABLE 3

Formation constants for Ca^{2+} - and Mg^{2+} -EDTA complexes

M^{2+}	t (°C)	C_{Me_4N} [a] (mole dm^{-3})	I	$\log K^M$ (Exptl.)	$\log K^M$ Calcd from eqns. (5) and (6)	Δ [a]	$\log K^M$ Calcd from eqn. (7)	Δ [a]	$\log K^M$ Calcd from eqn. (10)	Δ [a]
Ca^{2+}	10	0.16	0.18	11.03					11.02	0.01
	20	0.18	0.20	10.77					10.70	0.00
	25	0.15	0.17	10.75	10.75	0.00	10.76	0.01	10.75	0.00
	25	0.30	0.34	10.61	10.53	0.08	10.53	0.08	10.56	0.05
	25	0.50	0.53	10.47	10.47	0.00	10.43	0.04	10.50	0.03
	25	0.75	0.76	10.46	10.50	0.04	10.39	0.07	10.46	0.00
	37	0.15	0.17	10.59					10.62	0.03
	37	0.31	0.35	10.49					10.42	0.07
	45	0.16	0.18	10.49					10.56	0.07
				Mean deviation		± 0.03		± 0.05		± 0.03
Mg^{2+}	10	0.16	0.18	8.86					8.86	0.00
	20	0.18	0.20	8.82					8.82	0.00
	25	0.15	0.17	8.93	8.91	0.02	8.92	0.01	8.90	0.03
	25	0.30	0.33	8.70	8.71	0.01	8.69	0.01	8.72	0.02
	25	0.50	0.53	8.67	8.66	0.01	8.59	0.08	8.67	0.00
	25	0.75	0.77	8.64	8.68	0.04	8.55	0.09	8.64	0.00
	37	0.15	0.17	8.96					9.04	0.08
	37	0.31	0.35	8.86					8.85	0.01
	45	0.16	0.18	9.15					9.18	0.03
				Mean deviation		± 0.02		± 0.05		± 0.02

[a] Δ = deviation from experimental value.

plotting the function

$$y = \log K + Az * \frac{\sqrt{I}}{1 + B\sqrt{I}} \tag{2}$$

as a function of I, one can obtain the intercept $\log^T K$, for $I \to 0$, and the form of $L(I)$. In consideration of $y(I)$ curling, one can deduce that $L(I)$ must contain more than one parameter. This is in agreement with previous findings [7g,h], according to which the linear term is expressed by the equation

$$L(I) = CI + DI^{3/2} \tag{3}$$

From eqns. (2) and (3), it follows that

$$\frac{y - y'}{I - I'} = C + D\frac{I^{3/2} - I'^{3/2}}{I - I'} \tag{4}$$

which is the equation of a straight line. C and D can be therefore obtained using eqn. (4). (I' is a reference ionic strength chosen in the I range experimentally studied.) Once C and D values are obtained, $\log^T K$ can easily be calculated from eqn. (1). At 25°C, for the two $[M(EDTA)]^{2-}$ species, it is

$$\log K^{Ca} = 12.57(\pm 0.07) - 8.184\frac{\sqrt{I}}{1 + 1.49\sqrt{I}} + 1.84\,I - 0.55\,I^{3/2} \tag{5}$$

$$\log K^{Mg} = 10.70(\pm 0.04) - 8.184\frac{\sqrt{I}}{1 + 1.49\sqrt{I}} + 2.11\,I - 0.79\,I^{3/2} \tag{6}$$

Log K^M values obtained from eqns. (5) and (6) are reported in Table 3 together with experimental $\log K^M$ values. The agreement between experimental and calculated values is good; the mean deviation is ± 0.03 and ± 0.02 log units for calcium and magnesium complexes, respectively.

In the second stage, the potentiometric data obtained at different ionic strengths were processed together by means of a modified version of the computer program MINIQUAD 76 A [7b,8], refining simultaneously both the formation constants and the ionic strength dependence parameters (i.e. C and D). Interestingly, both calcium and magnesium formation constants were found to have practically the same dependence on the ionic strength. In fact, we obtain $C = 2.11$ and $D = -0.95$ for calcium and $C = 2.16$ and $D = -0.93$ for magnesium. Hence, for both calcium and magnesium, the equation expressing the ionic strength dependence (at 25°C) may be written as

$$\log K^M = \log K^M(I = 0.15) - 8.184\left(\frac{\sqrt{I}}{1 + 1.49\sqrt{I}} - 0.2456\right)$$

$$+ 2.1(I - 0.15) - (I^{3/2} - 0.058) \tag{7}$$

where $\log K^{Ca}\ (I = 0.15) = 10.81 \pm 0.02$ and $\log K^{Mg}(I = 0.15) = 8.97 \pm$

TABLE 4

Thermodynamic parameters for the formation of Ca^{2+} - and Mg^{2+} -EDTA complexes, at 25°C and $I = 0.16$ mole dm^{-3}

M^{2+}	ΔG (kcal mole^{-1})	ΔH (kcal mole^{-1})	ΔS (cal mole^{-1} deg^{-1})
Ca^{2+}	14.69 ± 0.03	−6.0 ± 0.3	29 ± 2
	(14.4)[a]	(−6.55)	(27)
Mg^{2+}	12.17 ± 0.03	2.9 ± 0.3	51 ± 2
	(11.60)	(3.49)	(51)

[a] Anderegg [1], $I = 0.1$ (KNO_3), $t = 20$°C.

0.02. The values, at the different ionic strengths investigated, calculated by using eqn. (7) are listed in Table 3.

Finally, all formation constant values obtained at different ionic strengths and temperatures were fitted by means of the empirical equation

$$\log K_{t,I}^M = \log K_{25,0.16}^M + \sum c_{ij}(t - 25)^i(\sqrt{I} - 0.4)^j \qquad (8)$$

thus obtaining for calcium and magnesium complexes the following values

	Ca	Mg	
$\log K_{25,0.16}^M$	10.77	8.92	
c_{01}	− 1.86	− 1.84	
c_{02}	4.75	4.76	(9)
c_{03}	− 4.67	− 4.44	
c_{10}	− 0.0147	0.00718	
c_{20}	0.00033	0.00040	

with an error, as a function of t and I, given by

$$\epsilon\left(\log K^M\right) = 0.02 + 0.003|t - 25| + 0.11|\sqrt{I} - 0.4| \qquad (10)$$

Log K^M values calculated by means of eqn. (8) using the values listed in (9) are reported in the last column of Table 3.

At 25°C, it was also possible to calculate the formation constants for the protonated species as well as their dependence on ionic strength. For the constant K_M^H one obtains *

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* In this case, owing to the larger error affecting the formation constant value, the term $DI^{3/2}$ cannot be determined. On the other hand, on the basis of the data previously obtained for the dependence of the formation constants on the ionic strength [7], for the protonation of the species $[M(EDTA)]^{2-}$ $DI^{3/2} < 0.13$ within the range $0 \leqslant I \leqslant 0.75$. This implies an error in $\log K_M^H$ smaller than 0.1, since the term $DI^{3/2}$ is partially contained in CI. This error, being smaller than the experimental error can be neglected.

$$\log K_{Ca}^{H} = 3.5(\pm 0.1) - 2.05 \frac{\sqrt{I}}{1 + 1.49\sqrt{I}} + 0.7\,I \tag{11}$$

$$\log K_{Mg}^{H} = 4.4(\pm 0.1) - 2.05 \frac{\sqrt{I}}{1 + 1.49\sqrt{I}} + 0.5\,I \tag{12}$$

The enthalpy changes accompanying the complexation of calcium and magnesium with EDTA can be obtained from eqn. (8).

$$\Delta H(t = 25°C, I = 0.16) = c_{01}\ln 10\,RT^2 = c_{01}\,407\,(\text{kcal mole}^{-1}) \tag{13}$$

The values of the thermodynamic parameters for $[Ca(EDTA)]^{2-}$ and $[Mg(EDTA)]^{2-}$ are reported in Table 4.

DISCUSSION AND CONCLUSIONS

The formation constant values of calcium–and magnesium–EDTA complexes reported here show the following peculiarities.

(a) $[M(EDTA)]^{2-}$ complexes show $\log K^M$ values that are significantly higher than those reported in the literature [1]. This is ascribed to the fact that the constants previously determined had been obtained in ionic media containing alkali metal ions which form complexes, the stabilities of which are not negligible, mainly as far as the sodium complex is concerned. Moreover, whilst our constants are given at a real I value, those reported in the literature are obtained at an ionic strength that can significantly differ from the background concentration, generally referred to as the only contribution to the ionic strength. In fact, even when considering relatively low M^{2+} and $EDTA^{4-}$ concentrations, given the high charge of the reagents, their contribution to the ionic strength is large. For example, when $C_{Ca} = C_{EDTA} = 3$ mmole dm^{-3}, the contribution of the reactants only to the ionic strength is on the average higher than 20 mmole dm^{-3}, which, in terms of $\log K^M$, means ca. 0.05 log units at $I \sim 0.15$ mole dm^{-3}.

(b) The constants pertinent to the protonation equilibria of $[M(EDTA)]^{2-}$ complexes ($\log K_{Ca}^{H} = 3.1$, $\log K_{Mg}^{H} = 4.0$ at 25°C and $I = 0.1$ mole dm^{-3}) are very close to those reported by Schwarzenbach and Ackermann [9] ($\log K_{Ca}^{H} = 3.15$ and $\log K_{Mg}^{H} = 3.82$ at 20°C and $I = 0.1(KNO_3)$ mole dm^{-3}). This, what is more, for a hardly determinable species, could at first sight seem casual. On the contrary, this accordance is due to the fact that the above equilibrium does not depend on the complexation of EDTA with alkali metal ions and is less influenced by the ionic strength (the limiting slope is, in this case, 2.05 whilst it is 8.18 for the formation of $[M(EDTA)]^{2-}$).

Log K^M values at infinite dilution are probably the only reliable values so far reported and are $\log^T K^{Ca} = 12.57 \pm 0.08$ and $\log^T K^{Mg} = 10.71 \pm 0.05$. Though they have been obtained by extrapolation, they are to be considered correct since they have been obtained from different functions; the error is

understandably higher than that affecting the constants determined within the experimental ionic strength range.

As to the dependence on the ionic strength, one must stress the importance of the availability of log K^M values over a large range of ionic strength (i.e. owing to EDTA sequestering properties, they can be used to obtain model systems for fluids having dissimilar ionic strengths, such as blood plasma or sea water, the ionic strengths of which are 0.15 and 0.7 mole dm^{-3}, respectively). Moreover, once again it must be pointed out that, having considered the so-called secondary interactions of the background with the ligand, the dependence on the ionic strength is, at least up to $I = 0.75$ mole dm^{-3}, the same for complexes of different nature but having the same charge, as can be seen from a comparison of eqns. (5) and (6), from c_{01}, c_{02} and c_{03} values of (9), and as far as concerns the protonated species, from the comparison of eqns. (11) and (12). Finally, the effect of the background on the log K^M values must be taken into account. Some numerical examples can stress this point. If K^{M_1} is the constant obtained disregarding the background effect, log K^M is given by

$$\log K^M = \log K^{M_1} - \log \alpha \tag{13}$$

where $\alpha = (1 + K^{Na}C_{Na})$ or $\alpha = (1 + K^K C_K)$, which, performing the appropriate calculations, gives

C_{M^+}	$\log \alpha$
0.15 K^+	0.2
0.15 Na^+	0.9
0.45 K^+	0.4
0.45 Na^+	1.4

This demonstrates that an improper use of the formation constants can misrepresent the model systems based on these constants and render meaningless the comparisons between constants obtained in different ionic media.

ΔH and ΔS values reported in Table 4 are in relatively good agreement with those found by Anderegg through direct calorimetry [1], also reported in Table 4. It must be pointed out that the differences in ΔG and ΔH, due in part to the different experimental conditions, cancel out in ΔS. This is in agreement with the suggestion of Yatsimirskii and Karacheva [10], according to whom the ΔS of the species $[Ca(EDTA)]^{2-}$ is practically independent of the ionic strength as well as the background ($\Delta S = 30$ cal $mole^{-1}$ deg^{-1} for $0.06 \leqslant I \leqslant 1.6$ mole dm^{-3} and with a variable concentration of Na^+).

Equation (8) allows the speciation in natural fluids in which calcium, magnesium and EDTA are present within the ranges $0 \leqslant I \leqslant 0.8$ mole dm^{-3} and $10 \leqslant t \leqslant 45°C$; it must be borne in mind that the constants so obtained are affected by an error that, though still acceptable. increases significantly

when moving away from the "standard" values (i.e. $t = 25°C$ and $I = 0.16$ mole dm^{-3}).

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