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ORIGINAL ARTICLE

Solution equilibrium of metal ions-binary complexes with 3-(2-ethylamino)-1-hydroxyethyl] phenol (Effortil)

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Abstract Formation of binary complexes of Al(III), Cr(III), Fe(III), Th(IV), UO_2(II), Ce(III), La(III), and Gd(III) with 3-(2-ethylamino)-1-hydroxyethyl] phenol (Effortil) were studied potentiometrically at 37.0 °C and $I = 0.16$ mol dm^{-3} $NaNO_3$ in aqueous solution. The acid–base properties of Effortil were investigated and discussed. The order of stability of the complexes was investigated and is discussed in terms of the metal ion. The experimental pH titration data were analyzed in order to evaluate the formation constants of various intermediate species formed. The concentration distribution of various species formed in solution was evaluated.

1. Introduction

During the last two decades we have found that many drugs used in the treatment of hyper- and hypotension form stable chelate complexes with some metal ions (see e.g., Bontchev and Pantcheva, 2002; Bontchev et al., 1989, 2000, 2001). Such investigations in this field lead to the hypothesis that the complexation can modify the biological activity of the drugs by changing the homeostasis of the metalloelements and/or changing the reactivity of the medication when it is bound in the form of a metal complex (Getova et al., 2006). The essential role of transition metal ions in biological systems is well known (Eichhorn, 1975; Eichhorn and Marzilli, 1979; Martell, 1980; Sigel, 1974; Sigel and Sigel, 1990, 1996; Bertini, et al., 1992). The interest in rare earth elements results from their unique physical chemical characteristics. The entire group exists exclusively as trivalent ions in natural waters, and their ionic radius decreases by less than 20% across the fifteen member series. Group III cations exhibit an essentially similar chemical behavior in aqueous solution. Under physiological conditions these cations exist as metal complexes. They are known to bind tightly to human serum transferrin in the blood. Numerous published studies on the interactions of group III metals with transferrin are reviewed, with particular attention being given to the comparative analysis of the binding constants and to the kinetics and mechanisms of metal ion uptake and release (Harris and Messori, 2002).

In fact, little studies showing the interactions between metal ions and Effortil have been appeared in the literature (Bontchev et al., 2000). We observed that no report is concerned about the suitability of Effortil and Al(III), Cr(III), Fe(III), Th(IV), UO_2(II), Ce(III), La(III), and Gd(III) metal ions. In this context, we believed that the study of the interactions of some metal ions with Effortil may have implications on biochemical studies.

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2. Experimental

2.1. Materials and solutions

3-(2-Ethylamino)-1-hydroxyethyl] phenol (Effortil) was from Sopharma, Bulgaria. The metal salts were provided by BDH (England) analytical-grade products as nitrates. Stock solutions of the metal salts were prepared in bidistilled water; the metal ion concentration purity was checked by a standard method (Welcher, 1965). Carbonate-free sodium hydroxide (titrant, prepared in 0.10 mol dm^{-3} $NaNO_3$ solution) was standardized potentiometrically with KH phthalate (Merck AG). A nitric acid solution (0.04 mol dm^{-3}) was prepared and used after standardization. Sodium hydroxide, nitric acid, and sodium nitrate were from Merck p.a.

2.2. Apparatus

The titrimetric data were obtained using a 702 titroprocessor equipped with a 665 dosimat (Switzerland) made by Metrohm (coupled with a Metrohm combined glass electrode Ag/AgCl). The glass electrode was calibrated before each titration with two Merck standard buffer solutions in nitrate medium: first with the pH 7.0 solutions (the same as in the bulb) and then with a pH 4.0 solution. All titrations were performed at 37.0 ± 0.10 °C by coupling the titration cell with a thermostatic bath.

2.3. Procedure

The ligand concentration was varied in the range 0.001–0.006 mol dm^{-3}. Three to six different metal-to-ligand ratios, ranging from 1:1 to 1:6 for binary systems were investigated (metal:ligand). The investigated solutions were prepared (total volume 50 cm^3) and titrated potentiometrically against standard CO_2-free NaOH (0.10 mol dm^{-3}) solution. A stream of nitrogen was passed throughout the course of the experiment in order to exclude the adverse effect of atmospheric carbon dioxide. Each of the investigated solutions was thermostated at the required temperature with an accuracy of ±0.10 °C and the solutions were left to stand at this temperature for about 15 min before titration. Magnetic stirring was used during all titrations. About 100–140 experimental data points were available for evaluation in each run. Titrations were performed up to pH ≈ 11. Each set of titrations was performed at least four times and the reproducibility of the titration curves was within 0.01-pH unit throughout the whole pH range. The pH titrations were terminated when either of the pH readings became unstable, showing a downward drift. In all cases, no calculations have been performed beyond the precipitation point; hence, the hydroxyl species likely to be formed after this point could not be studied. Also, because of the rather sluggish ligand-exchange kinetics of Al(III) and the precipitation reactions when equilibration could not be reached within 10 min, the corresponding titration points were omitted from the calculations (Kiss et al., 1997). The stability constants of the binary complexes were calculated by means of computer program based on unweighted linear least squares fit (Irving et al., 1953). Standard deviations were also evaluated for the corresponding equilibrium constants. The concentration distribution of various complex species existing in solution as a function of pH was obtained using the SPECIES program (Gans and Sabatini, 1996). All solutions used throughout the experiments were prepared freshly in ultra pure water obtained from a NANO pure-ultrapure water system with resistivity of 18.30 MΩ cm. All of the aqueous solution samples were prepared gravimetrically.

2.4. Calibration of glass electrode cell

A computer program (GLEE, glass-electrode evaluation) (Gans et al., 2000) was used for the calibration of glass electrode by means of a strong acid-strong base titration. This program provided an estimate of the carbonate contamination of the base, the pseudo-Nernstian standard potential, slope of the electrode, optionally, the concentration of the base and pK_w. It used a non-linear, least-squares refinement to fit a modified Nernest Eq. (1),

$$E = E^0 + s\log[H^+] \tag{1}$$

Where E is the measured electrode potential, E^0 and s are parameters of the refinement and represent the standard electrode potential and slope, and $[H^+]$ represents the hydrogen ion concentration.

In acidic solutions the hydrogen ion concentration is obtained from the mineral acid concentration, T_H, as calculated from Eq. (2), that is, $\log[H^+] = \log(T_H)$

$$T_H = \frac{(a_H\upsilon_0 + \gamma b_H\upsilon)}{(\upsilon_0 + \upsilon_1 + \upsilon)} \tag{2}$$

a_H is the concentration, mol dm^{-3}, of acid of which υ_0 cm^3 was added to the titration vessel; b_H is the concentration, mol dm^{-3}, of base in the buret (by convention given a negative sign), υ_I is the volume, cm^3, of background electrolyte solution added to the titration vessel; and υ, cm^3, is the volume of base added from the buret; and γ is a correction factor for the base concentration, where γ is refined and the calculated base concentration is $\gamma\ b_H$.

In the alkaline solutions the effective concentration of the base is usually reduced by the presence of a small amount (preferably <1%) of carbonate contamination. The extent of this contamination can be estimated by means of a gran plot (Gans et al., 2000). Initially E^0 is estimated from the acidic region and s is taken as the ideal Nernestian slope (T/5.0399 mV). Then Eqs. (3) and (4) are fitted by linear least-squares regression.Acidic region:

$$(\upsilon_1 + \upsilon_1 + \upsilon)10^{\frac{E-E^0}{s}} = m^a\upsilon + c^a \tag{3}$$

Alkaline region:

$$(\upsilon_1 + \upsilon_1 + \upsilon)10^{\frac{E-E^0}{s} - pK_W} = m^b\upsilon + c^b \tag{4}$$

A typical Gran plot was constructed. From the slopes and intercepts of the fitted lines two estimates are obtained of the volume of base consumed at the equivalence point: $\upsilon_e^a = -c^a/m^a$ for the acidic region and $\upsilon_e^b = -c^b/m^b$ for the alkaline region. Assuming that the difference is due to carbonate, the effective base concentration is reduced by the factor $\upsilon_e^a/\upsilon_e^b$ in the alkaline region. The mineral acid concentration in the alkaline region is then given by Eq. (5).

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