



Potentiometric study of binary complexes of effortil hydrochloride with some divalent metal ions in aqueous medium

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ABSTRACT

The formation equilibria for the binary complexes of Effortil with Cu^{2+} , Co^{2+} , Ni^{2+} , and Zn^{2+} metal ions were investigated using potentiometric technique in aqueous medium ($t = 37^\circ\text{C}$, $I = 0.15 \text{ mol. dm}^{-3} \text{ NaNO}_3$). The formation of binary complexes was inferred from the pH-metric titration curve. The overall stability constants of the complexes formed were obtained using HYPERQUAD 2008 program using from potentiometric data. The calculated stability constants of the complexes formed have been discussed in terms of both the nature metal ions and Effortil. The stability of the complexes follows the trend $\text{Co}^{2+} < \text{Zn}^{2+} < \text{Ni}^{2+} < \text{Cu}^{2+}$, which is in agreement with the Irving-Williams order of the metal ions. The results showed the formation of ML, MHL, and ML_2 complex species. The concentration distribution of the complexes in solution was evaluated as a function of pH and discussed. Evaluation of the effect of temperature of the medium on the dissociation of ligand and the stability of binary systems has been studied. The thermodynamic parameters were calculated and discussed.

Key words: Effortil, binary complexes, Potentiometry, Speciations, and Thermodynamic parameters.

INTRODUCTION

Most pharmaceuticals, including beta-blockers, contain electron donor groups that may bind naturally occurring metal ions [1]. Essential trace metal ions such as zinc and copper are present in too low concentrations in blood plasma to significantly influence the bio availability of these drugs. The belief that beta-blockers action is related to the ability of these compounds to form complexes with metal ions has stimulated investigations of the complexing properties of β -blocker as ligands. Beta-blockers continue to be used in the treatment of hypertension. Their major advantage is a secondary protection in patients with coronary artery disease, a behavior not established for other antihypertensive drugs. The important pharmacological properties that distinguish the beta-blockers are lipid solubility, cardio-selectivity and intrinsic sympathomimetic activity [2,3]. It is known that complexation of several drugs with metal ions may cause changes in the pharmacological and physiological effects. Besides, the regulation of the arterial blood pressure is a copper- and zinc-controlled process [4]. For these reasons it is of interest to study new species where both components, ligand and metal, are related to blood pressure changes; hence, the complex formation of transition metals with Effortil compound is of fundamental interest in bioinorganic chemistry to understand the basic information on metal complexes for further research in chelation therapy, this study evaluated the complexation of Effortil with divalent metal ions (Cu^{2+} , Co^{2+} , Ni^{2+} , and Zn^{2+}). Despite a very large amount of literature data for the solution chemistry of transition metals, interactions of these metal ions in aqueous solutions with Effortil, have been little investigated [1,4,5]. Also, by scanning the literature survey reveals that there is still a possibility to work on determination of dissociation constant of Effortil and stability constants of its binary complex with metal ions under study at different temperatures where these data are scarce in the literature.

In connection with our continuing research work oriented toward the study of complexation equilibria and determination of overall stability constants of complexes of biological importance [6-10], the present work concerns a study of solution equilibria involved in the formation of binary metal complexes involving Effortil and some

divalent metal ions, as well as, investigative study of temperature dependence of Effortil and its complex process.

MATERIALS AND METHODS

Procedure and measuring techniques

3-(2-ethylamino)-1-hydroxyethyl] phenol (Effortil) was from Sopharma, Bulgaria. The metal salts were provided by BDH (England) analytical-grade products as nitrates. All materials and reagents were used as provided by the chemical companies without further purification. The purity of these reagents ranged from 98 to 99 %. Stock solutions of the metal salts were prepared in bidistilled water; the metal ion concentrations purity was checked by a standard method [11]. Carbonate-free, sodium hydroxide (titrant, was prepared by dissolving the Analar pellets in 0.15 mol dm⁻³ NaNO₃ 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. Analytical grade color-coded buffer solutions of pH= 4.0 (red) and 7.0 (green), were purchased from commercial sources. All solutions used throughout the experiments were prepared freshly in ultra pure water with resistivity of 18.3 M Ω. cm⁻¹, we boil the resultant water for sufficient time to expel the carbon dioxide. All of the aqueous solution samples were prepared gravimetrically.

The protonation and coordination equilibria were investigated by potentiometric titrations in aqueous solution at desired temperature and $I = 0.15 \text{ mol dm}^{-3} \text{ NaNO}_3$ under argon atmosphere, using an automatic titration set including a PC controlled Dosimat 665 Metrohma microburet delivery tube and a salt bridge connected with the reference cell filled with 0.1 mol dm⁻³ KCl solution in which a saturated calomel electrode was dipped, The Metrohm semimicro pH glass electrode (125 mm) was calibrated [12] via the modified Nernst Equation 1:

$$E = E_o + K \cdot \log[H^+] + J_H \cdot [H^+] + \frac{J_{OH} \cdot K_w}{[H^+]} \quad (1)$$

where J_H and J_{OH} are fitting parameters in acidic and alkaline media for the correction of experimental errors, mainly due to the liquid junction and to the alkaline and acidic errors of the glass electrode; the experiments were carried out as follows: a fixed volume of 0.10 mol dm⁻³ HCl was titrated with successive additions of 0.10 mol dm⁻³ NaOH until near neutrality in order to get parameters of E^o and J . 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. The strong acid versus alkali titrations was analyzed using the computer program (GLEE, glass-electrode evaluation) [13] which used previously [8]. For estimation of the protonation constants of Effortil, the following solutions were prepared (total volume 50 ml) and then titrated potentiometrically against a standard Carbonate-free NaOH solution (0.10 mol dm⁻³):

- (a) 0.004 mol dm⁻³ HNO₃ + 0.15 mol dm⁻³ NaNO₃,
- (b) Solution (a) + 0.001 mol dm⁻³ Effortil,

Recently, the most equilibrium studies are carried out over big ranges of reactant concentrations and concentration ratios, but when these ranges used many inevitable limitations occurs due to some reason like variations of activity coefficients for weak complexes, solubility problems, etc., and many potential applications are in composition regions outside those experimentally investigated. In our work, we used The metal-to-ligand ratios varied between 1:1-1:3 metal/ligand ratio for binary systems, and then to reach the maximum coordination number of the metal ion. The concentration of Effortil was 1.10⁻³ Mol dm⁻³ in the titrated samples has been always the same (Table 1). The pH titrations were carried out in an 80 ml commercial double walled glass vessel. Thermostated at desired temperature and left to stand for 15 minutes before titration, and the cell temperature was maintained at the required temperature by circulating thermostated water using an oil-bath setup. A magnetic stirrer was used during all titrations. Each titration was repeated at least 3 times. Typically, more than 100 pH reading (data points of potentiometric measurements) were collected into account for each titration.

Calculations

For computing the protonation constants of the Effortil and its metal complexes from pH titration data, the best equilibrium model was sought by systematically testing various pqr conditions using the advanced software program HYPERQUAD 2008 [14]. This software facilitates visual interpretation of refinements, which in turn helps greatly in obtaining the best fit. To compute stability constants from potentiometric and spectrophotometric data, many software programs such as BEST, LETAGROP, MINIQUAD, PKA, SUPERQUAD, and HYPERQUAD have been used. All of these programs use the least squares approach. Among them, HYPERQUAD 2008 is one of the most recent versions of the HYPERQUAD program to determine stability constants from potentiometric and

spectrometric data [15]. HYPERQUAD 2008 program permits the determination of formation constants from potentiometric data, especially when different equilibrium reactions take place in aqueous solution [11] for this purpose, a fitting criterion based on the minimization of the nonlinear least-squares sum defined by the difference between the calculated and the experimental data of the titration curves was used ($X^2 = \sum (E_{\text{cal}} - E_{\text{exp}})^2 / E_{\text{cal}}$). The program permits us to determination of the formation constants of different complexes, were examined. The stoichiometries and stability constants of the complexes formed were determined by trying various possible composition models. The selected model was the one that gave the best statistical fit, seemed chemically sensible, and was consistent with the titration data without giving any systematic drifts in the magnitudes of the various residuals. Good fitting between calculated curves and the experimental results confirms the validity of the obtained complexation models. In addition, the calculations were not performed for pH-regions where experimental findings showed the possibility of hydrolysis (a continuous decrease in the pH or the formation of a precipitate or when we detect any precipitation or turbidity during titration). The speciation as a function of pH using the *species* program [15].

Stability constants β_n^l are defined in terms of the equilibrium between a metal complex and its components, except that the free ligand concentration is replaced by total concentration of all ligand species not actually complexed to the metal, and the free metal ion term includes hydrolyzed metal ion and metal ion bound to other complexing species. Calculation of β_n^l can be done by:

$$\beta_n^l = \frac{\beta_n}{\alpha_M \cdot (\alpha_L)^n} \quad (2)$$

$$\alpha_M = ([M] + [MOH] + [M(OH)_2] + \dots) / [M] \quad (3)$$

Many metal ions hydrolyze to form polynuclear species so that α_M would be concentration-dependent, but in the presence of an excess strong ligand it is usually sufficient to consider only the formation of mononuclear species. Under these conditions, α_M reduced to

$$\alpha_M = 1 + 10^{(pH-pK_1)} + 10^{(2pH-pK_1-pK_2)} + \dots \quad (4)$$

where pK_1, pK_2, \dots are the successive pK_a values for the loss of a proton from a hydrated metal ion. The metal ion hydrolysis constants published in the IUPAC stability constants database and other sources have been used [16,17]. All the possible hydrolytic species resulting from the formation of the different hydroxyl complexes, including different metal ions have been taken into consideration during the calculations. Initial estimates of the stability constants of different normal and protonated binary complexes formed in solution have been refined with the computer program. The quality of the fit during this refinement was judged by the values of the sample standard deviations [14].

RESULTS AND DISCUSSION

A pH-potentiometric measurement technique was selected to evaluate the stability constant data due to its high degree of accuracy and the reliability of the proton change data obtained with a pH electrode. Before analyzing the experimental data using the HYPERQUAD program, two important issues must be resolved concerning their mode and scale of representation. Stability constants may a priori be expressed in terms of activity (true thermodynamic parameter) or concentration (stoichiometric constants) quotients. As this remark may seem of minor importance, but it nonetheless implies that comparisons between logarithmic constants are permissible for complexes of equivalent stoichiometries only. Therefore, when simulation models are used to predict the distribution of such complexes, all these considerations are implicitly taken into account in the calculations. Basically, the quality of the complexation model that can be obtained from the calculations is limited by the experimental data (potentiometric accuracy, kinetic effects, precipitation, etc.). The protonation constants of ligands are interesting and necessary for a complete understanding of the physicochemical behavior of ligands. Therefore stoichiometric protonation constants of the ligands were determined under the experimental conditions of (37 °C) and a constant ionic strength of 0.15 mol dm⁻³ NaNO₃ which were also used to determine the stability constants of the metal(II) complexes. The protonation equilibria of the ligand are defined as overall association constants. This means that for Effortil the two equilibria are expressed as:

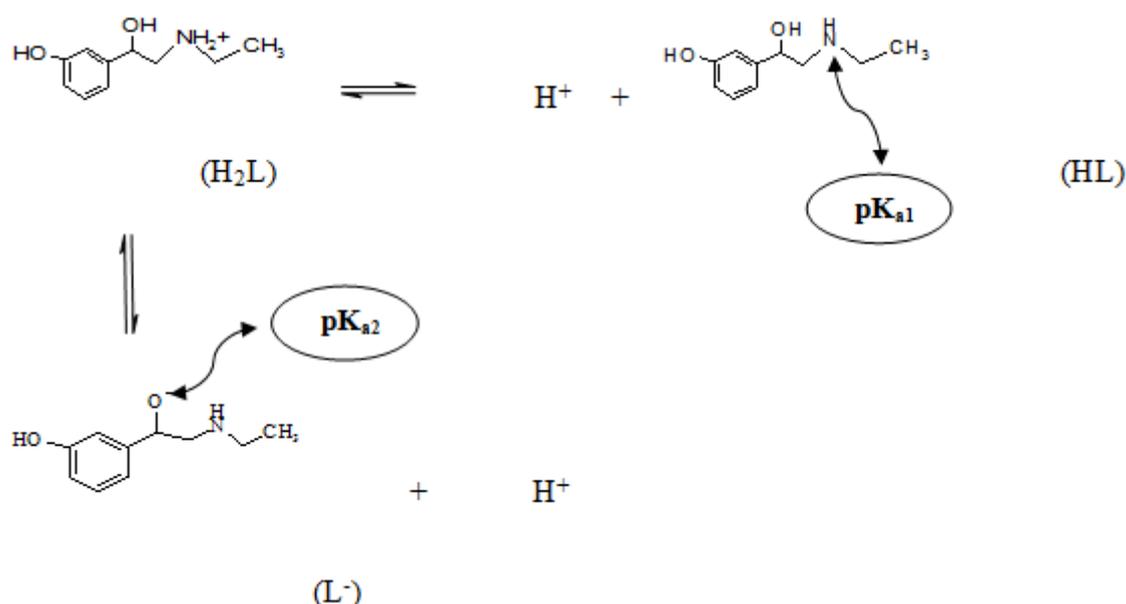




The stepwise acid dissociation constants of Effortil are defined as



It is expected to have two proton dissociation constants corresponding to the cationic NH_2^+ group and alcoholic group. It is possible that the hydroxyl group is able to form a hydrogen bond with the basic nitrogen atom and thus assist in the dissociation of ammonium hydrogen ion, since $\log_{10} \beta_1 = \text{pK}_{a2}$ and $\log_{10} \beta_2 = \text{pK}_{a1} + \text{pK}_{a2}$, (Table 2). It was established that the association of the proton is affected by strength of hydrogen bonding between the oxygen of hydroxy group and imino group. Stronger the hydrogen bond, lesser will be the dissociation and hence less is the acid character of $-\text{OH}$ group (scheme 1). Effortil reported earlier by us and others [1,4], we have redetermined the dissociation constants as it is preferable to determine the binary constants under the same experimental conditions. However, the present results agree well with those from literature [1,4]. The small differences between our value and the literature values are due to the random error, systematic errors arise in instrumental measurement and the dissociation constants are obtained with limited precision and accuracy.



Scheme 1. Show the chemical structure of the Effortil and its protonation equilibria

Binary Systems

To assess the binding abilities of $\text{M}(\text{II})$ with Effortil in aqueous solution, pH-metric studies were performed in an aqueous solution at 37°C and 0.15 mol dm^{-3} NaNO_3 ionic strength. The only system present in literature data could be found is Cu -Effortil [5], but anyhow all systems were examined in this study at same experimental conditions. Several metal ions, where their atomic number increase following the trend [18]: $\text{Co}^{2+} < \text{Ni}^{2+} < \text{Cu}^{2+} < \text{Zn}^{2+}$ were used in our study (Table 3). For the determination of the metal complex formation constants $\log \beta$ of the binary systems solution with Effortil in various molar ratios 1:1, and 1:3 (Fig. 1) were titrated against carbonate-free NaOH solution. We can see that there is a shifting of the buffer region to lower pH when metal ions are introduced into the system. The largest shifting occurred in a system containing Cu^{2+} , followed by systems containing Ni , Zn , and Co metal ions (Fig. 2). The shifting, suggests that the formation of the metal-ligand complex begins as the ligand starts to deprotonate. Several combinations of the complex species that may have occurred during complexation reaction were introduced into hyperquad 2008 program and one that best fitted the experimental titration data was chosen. The results obtained from the refinement were expressed as overall formation constants ($\log \beta_{\text{pqr}}$) and are summarized in table 4 for the systems with Effortil.

The following reactions take place during the titration of metal ion solution against the ligand solution where the equations (7) and (8) show the complexation process [18].



We can observe from the speciation diagram (Fig. 3), the system involving Effortil (L) with Cu^{2+} was able to form $[CuL]^{+}$ species in acidic pH ($pH \approx 4.36$) compared to systems with other metal ions, where, $[NiL]^{+}$, $[ZnL]^{+}$, and $[CoL]^{+}$ species were found to form at $pH \approx 6.92, 7.10,$ and 7.05 respectively. Similarly, $[CuL_2]$ species also started to form at $pH \approx 6.15$ and achieved about 93.42 % of $[ML_2]$ at $pH 8.60$, while other metals started to form $[ML_2]$ species at a higher $pH \approx 7.34, 7.41,$ and 7.45 for $[NiL_2], [ZnL_2],$ and $[CoL_2]$ respectively.

The main conclusions drawn from the reported results in Table 4 about the coordination modes of Effortil in the binary systems are as follows:

- The pH titration data for M(II) with Effortil systems, It can be observed that the $\log K$ value of $[ML_2]$ species is smaller than that of $[MA]$ species, for example $\log K_{CuL_2} (5.65) < \log K_{CuL} (8.72)$. Thus, it can be concluded that the stepwise formation constant decreases with the increasing number of ligands attached to the metal ion. This phenomenon occurs possibly due to the reduction of the coordination number and the occurrence of steric effects at the metal ion after attachment of the first ligand molecule (Fig. 1)
- It is known that N, O-chelation is a characteristic coordination mode for effortil [1]. The binary formation constants so obtained are presented in Table 4. Cu(II) has greater lattice and solution energies, hence higher formation constant of complexes of Cu(II) ions is observed amongst three, Cu(II) shows higher stability as expected [5]. Co(II) complexes ($\log K_{ML_2}$) with ligand are more stable than corresponding Ni(II) complexes. This is attributed to the size of the metal ions. The successive stability constants of the binary complexes decrease in accordance with statistical expectation.
- Effortil form complexes with divalent metal ions in a similar manner. The overall result shows that the stabilities of the binary ligand–metal system in the following order: $Co^{2+} < Zn^{2+} < Ni^{2+} < Cu^{2+}$. This trend in stability constants coincides with the order in the magnitude of the buffer region shifting, shown in Fig. 2. Moreover, this stability order agrees with the Irving–William series [19], which largely reflects the changes in the heat of complex formation across the series from a combination of the influences of both the increasing polarizing ability of the metal ion [20] and the crystal-field stabilization energies [21].
- We can't calculate the stability constants of ML_3 , and this may be attributed to the fact that this Effortil forms a five membered ring that is not energetically favorable with the M(II) cation [1].
- The coordination chemistry of Cu^{2+} with ligands containing N and O donors has a significant effect on its fate, transport, and reactivity in biological and environmental systems [17]. For example of divalent metal ions, Cu^{2+} ion as a hydrated form is the predominant species in aqueous solution at $pH < 7$, while the mono- and polynuclear hydroxide complexes are formed in appreciable amounts at $pH > 7$ [17]. The Cu^{2+} hydroxide complexes in aqueous and alkaline solutions of biological and industrial importance. Generally, there are two aspects to metal hydrolysis that we need to take in considering during our calculating of the experimental data are hydrolysis of the metal ion itself and hydrolysis of a binary. From our experimental results, concentration ranges selected for the metal ions studied, the stability of metal hydroxide values are not considerably affected in the same ionic medium. However the data obtained previously at various temperatures significantly contribute to understanding the hydrolysis behavior of these metal ions. With all of these considerations, knowledge of hydrolysis constants of the metal ions in this work appears to be of primary value, and the present work may also contribute to the data collection.
- Besides $[ML]$ and $[ML_2]$ species, it was also observed that $[MLH]$ appears at lower pH. The pK_a of the protonated complex species calculated from the following equation (9): (Table 3):

$$pK_a = \log_{10} \beta_{111} - \log_{10} \beta_{110}. \quad (9)$$

The former pK_a value corresponds to -OH group which was acidified upon complex formation by 3.94, 2.64, 1.92, and 1.94 pK_a units respectively for Cu, Ni, Zn, and Co metal ions. Since the $[MLH]$ species has a significantly weaker stability than the $[ML]$ species, in the systems with less stable $[ML]$ species, particularly the $[MLHn]$ species did not appear in the early pH range [22,23].

Effect of temperature

The dissociation constants and the metal-ligand binary complexes of Effortil with $Cu^{2+}, Co^{2+}, Ni^{2+},$ and Zn^{2+} metal ions at different temperatures from 298.15-328.15 K are reported in Tables 5,6. We can see from the reported data that the calculated dissociation constants decrease as the temperature increase, which means that the acidity increase as the temperature increase [24] (Fig. 4). Stability constants $\log K_1$ decrease with increasing temperatures (Fig. 5). This may be related to the hydrolysis of metal ions [18]. The values which are recorded in Tables 5,6 were used for

calculating the thermodynamic parameter (ΔS° , ΔG° , and ΔH°) using linear regression of temperature dependence of the data [16].

$$\Delta G^\circ = -2.303RT \log K$$

$$-2.303RT \log K = \Delta H^\circ - T \Delta S^\circ$$

$$\log K = -\Delta H^\circ / 2.303RT + \Delta S^\circ / 2.303R$$

From these results we can conclude that the positive values of ΔH° indicated that the process is endothermic and follow the general trend as an ionization process of acids, the ΔG° is positive and the process are not spontaneous [25] and the ΔS° is negative values due to increase ordering as a result of solvation process and decrease the force of hydrogen bonds, also we note that the value of the entropy of the second protonation process is less positive than the first one as expected [25]. The divalent metal ions present in solution as octahedrally hydrated species the values of ΔH° and ΔS° can then be considered as the sum of two contributions; i.e., the liberation of H_2O molecules and metal–ligand bond formation. The ΔG° values were negative for the complex formation suggests the spontaneous nature of such process [25]. The ΔS values for the complexes are positive, confirming that the complex formation is entropically favorable, the positive change of entropy asserts the formation of a complex with a lower charge as compared to the initial ions and with the release of water molecules during complication; thus, complexes with a lower amount of solvation are formed. The negative values of ΔH° show that the chelation process is exothermic, indicating that the complexation reactions are favored at low temperatures. Furthermore, when a coordinate bond is formed between the ligand and the metal ion, the electron density on the metal ion generally increases. Consequently, its affinity for a subsequent ligand decreases, leading to increases in ΔG° and ΔH° of complexation. Also, generally it is noted that $-\Delta G^\circ_1 > -\Delta G^\circ_2$ and $-\Delta H^\circ_1 > -\Delta H^\circ_2$ (Table 6) which may be attributed to the steric hindrance by the interaction and entrance of a second molecule into coordination.

Relationships between the properties of central metal ion and stability of complexes

In an attempt to explain why a given ligand prefers binding to one metal rather than another, it is necessary to correlate the stability constants with characteristic Properties of the metal ions such as the ionic radius, ionization energy, electronegativity and the atomic number. We have discussed the relationships between the properties of central metal ions [25] reported in Table 3, and the stability constants of the complexes. The formation constants of M^{2+} -complexes of bivalent 3d transition metal ions with Effortil are in the order: $Co < Zn < Ni < Cu$ in accordance with the Irving–Williams order [19]. The correlation between $\log K_1$ and the reciprocal ionic radii ($1/r$) of the studied bivalent transition metal ions was found to be almost linear. Also, a good linear correlation has been obtained between $\log K_1$ and the electronegativities of the metal ions under study. This is in accordance with the fact that the increasing electronegativity of the metal ions (Table 3) will decrease the electronegativity difference between the metal atom and the donor atom of the ligand. Thus, the metal–ligand bond will have more covalent character, which may lead to greater stability of the metal chelates. A good linear relationship has been obtained between $\log K_1$ and the second ionization potential of the bivalent metal ions under study. In general, it is noted that the stability constant of the Cu^{2+} -complex is quite large compared to the other metals. The ligand field will give Cu^{2+} some extra stabilization due to tetragonal distortion of the octahedral symmetry [26]. Thus, the $\log K$ value of the Cu^{2+} complex deviates significantly when $\log K_1$ values of metal chelates are shown in Table 4.

Table 1 Summary of experimental parameters for the potentiometric measurements

Solution Composition	[ligand] range 1×10^{-3} , metal/ligand ratio ranging from 1:1-1:3 for binary system, at different different temperatures and $I = 0.15 \text{ mol dm}^{-3} \text{ NaNO}_3$.
T (°C)	(25-55) °C for the dissociation of Effortil and for its binary complex systems with M^{2+} (Cu, Co, Ni, and Zn) metal ions
n_{tot}^a	80-250
n_{tit}^b	3-6

^a Number of titration points per titration. ^b Number of titrations per titration curve.

Table 2. Protonation constants (Log β and pKa) of Effortil at 37 °C and 0.15 mol dm⁻³ (NaNO₃) in aqueous medium, with standard deviations in parentheses and ^a Sum of squares of residuals

System	Equilibrium	Log β	pKa	Proton released from
Effortil. HCL	$H_2L^+ \rightleftharpoons H^+ + HL^+$	7.39(0.01)	7.39 [4]	-NH ₂ ⁺ - Immino group
	$HL^+ \rightleftharpoons H^+ + L^2$	16.63(0.03)	9.24 [4]	-OH Alcoholic group
S ^a	3.5×10^{-7}	2.7×10^{-6}	3.8×10^{-7}	

Table 3. Atomic number, ionic radius, electronegativity, and ionization potential of the investigated bivalent metal ions ^a

Metal ion	Co(II)	Ni(II)	Cu(II)	Zn(II)
Atomic number	27	28	29	30
Ionic radius (pm)	79	72	71	74
Electronegativity	1.88	1.910	2.000	1.650
Second ionization energy (kJ/mol)	1646	1753	1958	1733

^a values were taken from Ref. [18]Table 4. Overall formation constants of the metal complexes of Effortil at $I = 0.15 \text{ mol dm}^{-3}$ (NaNO_3), $t = 37^\circ\text{C}$ in aqueous medium, with standard deviations in parentheses, and ^a Sum of squares of residuals

System	M	L	H ⁺	Cu ²⁺	Co ²⁺	Ni ²⁺	Zn ²⁺
$\text{M}^{2+} + \text{L} \rightleftharpoons \text{ML}^+$	1	1	0	8.72(0.01)	3.76(0.02)	3.90(0.01)	3.87(0.01)
$\text{M}^{2+} + 2\text{L} \rightleftharpoons \text{ML}_2$	1	2	0	14.37(0.04)	7.34(0.03)	7.42(0.05)	7.35(0.02)
$\text{M}^{2+} + \text{HL} \rightleftharpoons \text{MLH}^+$	1	1	1	12.66(0.01)	5.34(0.02)	6.54(0.01)	5.90(0.03)
Log K ₁				8.72, 8.46 [5]	3.76	3.90	3.87
Log K ₂				5.65, 5.03 [1]	3.58	3.52	3.48
ΔlogK				-3.07	-0.18	-0.38	-0.39
S ^a				3.2×10^{-7}	2.5×10^{-6}	4×10^{-7}	1.6×10^{-7}

Table 5 Thermodynamic parameters of the dissociation process of Effortil at 0.15 mol dm^{-3} (NaNO_3) at different temperatures in aqueous medium with standard deviations in parentheses

Ligand	T(K)	Dissociation constants		Free energy change (kJ.mol ⁻¹)		Enthalpy change (kJ.mol ⁻¹)		Entropy change (J.mol ⁻¹ K ⁻¹)	
		pKa ₁	pKa ₂	ΔG ₁	ΔG ₂	ΔH ₁	ΔH ₂	ΔS ₁	ΔS ₂
Effortil	298	8.60(0.01), 8.83 [1]	9.75(0.02)	164.67	186.68	145.61	66.46	325.12	36.84
	310	7.39[5]	9.24 [5]	141.50	176.92				
	318	7.32(0.01)	9.12(0.03)	140.16	174.62				
	328	7.03(0.03)	9.05(0.01)	134.60	173.28				

Table 6 Formation constants and thermodynamic parameters of the binary systems at Effortil at 0.15 mol dm^{-3} (NaNO_3) at different temperatures in aqueous medium with standard deviations in parentheses

System	T(K)	LogK	Thermodynamic parameters		
			ΔG°(kJ.mol ⁻¹)	ΔH°(kJ.mol ⁻¹)	ΔS°(JmolK ⁻¹)
Cu ²⁺ -(Effortil)	298	8.88(0.01), 8.46 [13]	-50.67	-23.13	92.33
	310	8.72(0.02)	-51.76		
	318	8.62(0.04)	-52.49		
	328	8.51(0.01)	-53.45		
Cu ²⁺ -(Effortil) ₂	298	5.74(0.02), 5.03 [1]	-32.75	-13.92	63.19
	310	5.65(0.01)	-33.54		
	318	5.58(0.05)	-33.98		
	328	5.52(0.01)	-34.67		
Ni ²⁺ -(Effortil)	298	4.02(0.03)	-22.94	-15.39	25.24
	310	3.90(0.01)	-23.15		
	318	3.85(0.04)	-23.44		
	328	3.77(0.02)	-23.68		
Ni ²⁺ -(Effortil) ₂	298	3.61(0.01)	-20.60	-12.27	27.92
	310	3.52(0.02)	-20.89		
	318	3.48(0.03)	-21.19		
	328	3.41(0.01)	-21.42		
Zn ²⁺ -(Effortil)	298	3.95(0.01)	-22.54	-11.2968	37.66
	310	3.87(0.03)	-22.97		
	318	3.82(0.01)	-23.26		
	328	3.77(0.03)	-23.68		
Zn ²⁺ -(Effortil) ₂	298	3.55(0.01)	-20.26	-10.686	32.11
	310	3.48(0.02)	-20.66		
	318	3.43(0.04)	-20.88		
	328	3.38(0.02)	-21.23		
Co ²⁺ -(Effortil)	298	3.81(0.01)	-21.74	-8.18	44.75
	310	3.76(0.03)	-22.32		
	318	3.72(0.03)	-22.65		
	328	3.68(0.02)	-23.11		
Co ²⁺ -(Effortil) ₂	298	3.62(0.02)	-20.66	-7.02	45.78
	310	3.58(0.03)	-21.25		
	318	3.54(0.01)	-21.55		
	328	3.51(0.04)	-22.04		

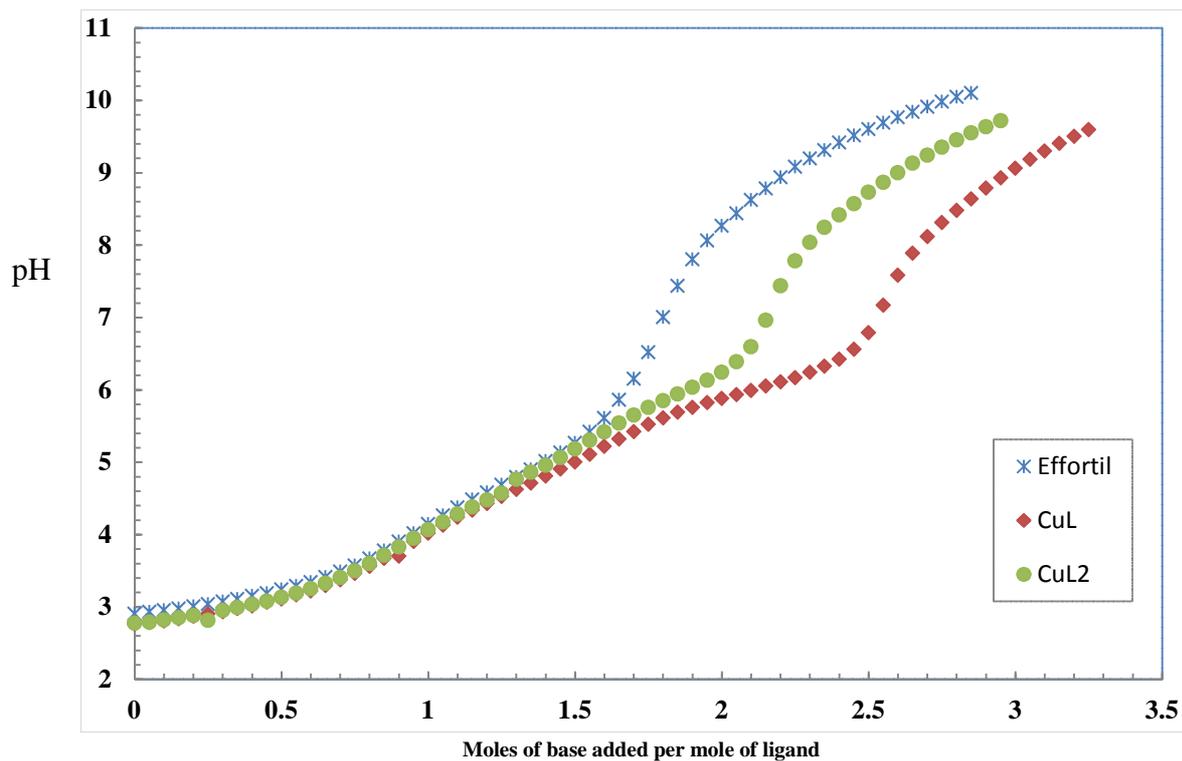


Fig. 1. Potentiometric *pH*-titration curves for the Effortil e and for the Cu(II)-Effortil system at 37°C, $I = 0.15 \text{ mol dm}^{-3} \text{ NaNO}_3$ and $C_{\text{Effortil}} = 1 \times 10^{-3} \text{ mol dm}^{-3}$

Moles of base added per mole of ligand

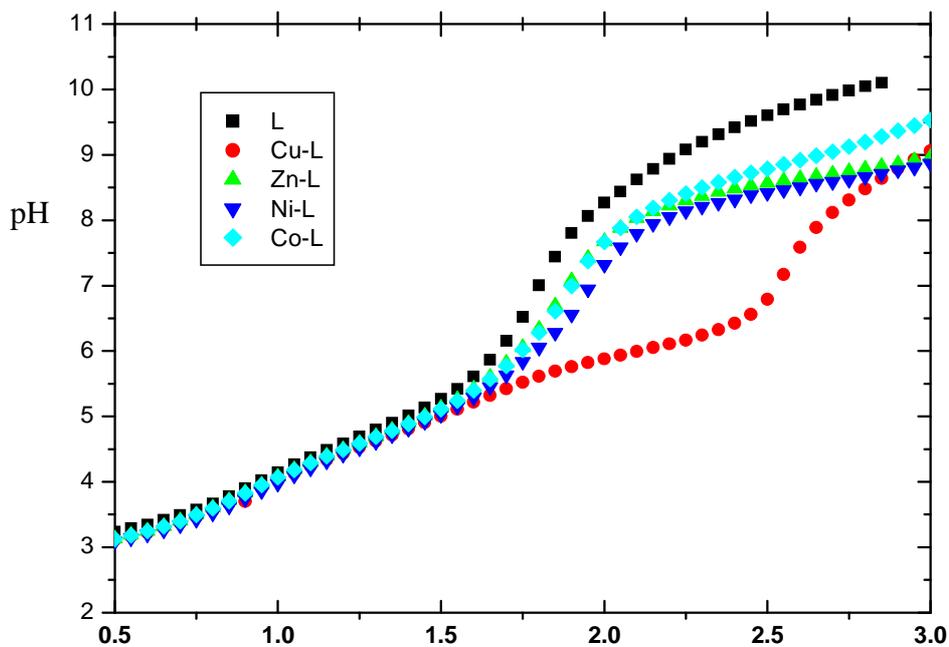


Fig. 2. Experimental curves of the binary system containing: Effortil (L) and divalent metal ions at 37°C, $I = 0.15 \text{ mol dm}^{-3} \text{ NaNO}_3$ and $C_{\text{Effortil}} = 1 \times 10^{-3} \text{ mol dm}^{-3}$

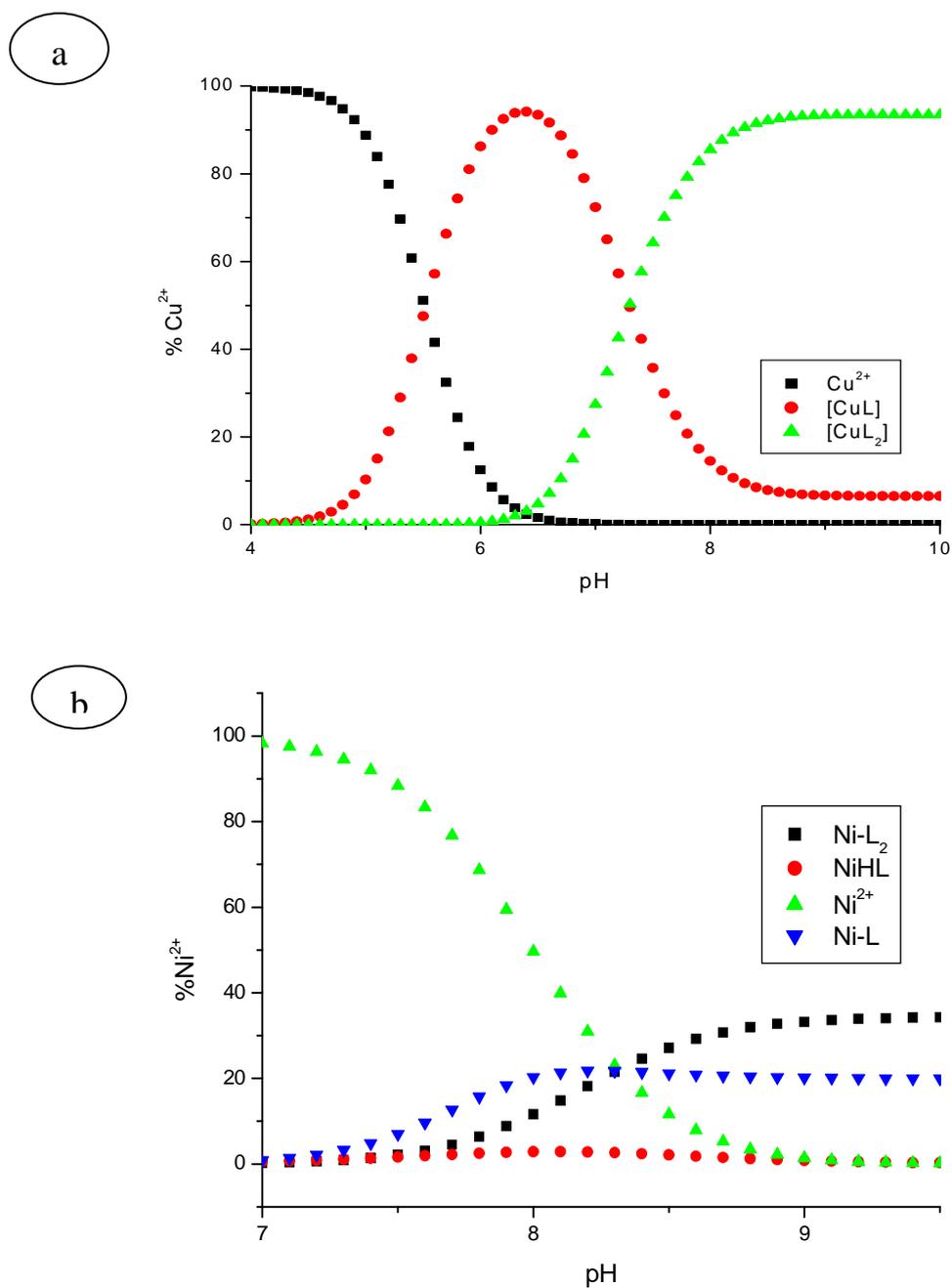


Fig. 3. Species distributions for the binary systems of Effortil (L) and the metal(II) ions: (a) Cu^{2+} ; and (b) Ni^{2+} ; at a 1:2 metal to ligand ratio, $T = 37 \pm 0.1 \text{ C}$ and $I = 0.15 \text{ mol dm}^{-3} \text{ NaNO}_3$

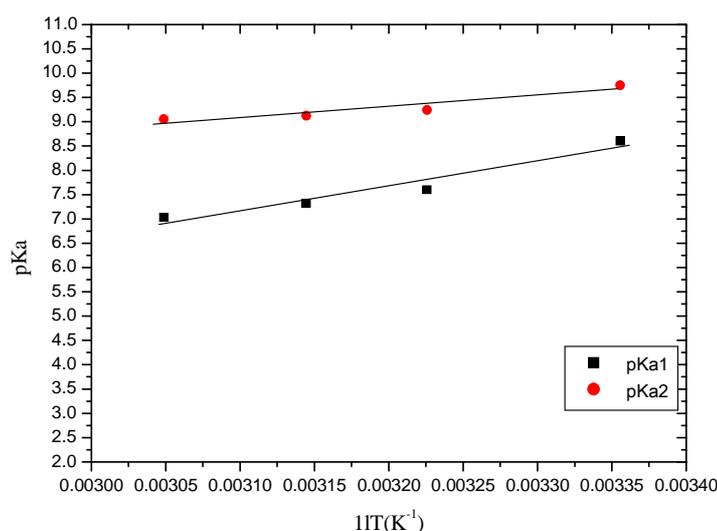


Fig. 4 Plot of pK_1 and pK_2 values of the Effortil versus $1/T$ (K) at $0.15 \text{ mol dm}^{-3} \text{ NaNO}_3$ aqueous medium

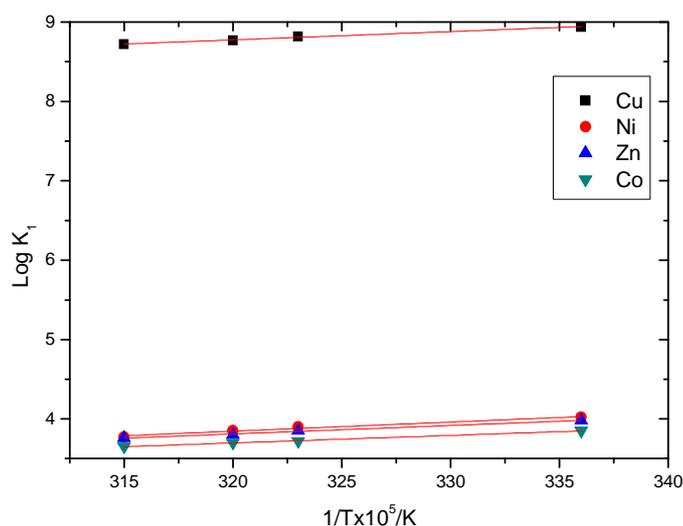


Fig. 5 plot of $\log K_1$ of M^{2+} -Effortil complexes versus $1/T$ (K) at $0.15 \text{ mol dm}^{-3} \text{ NaNO}_3$ aqueous medium

CONCLUSION

In conclusion, the study of $M(\text{II})$: Cu^{2+} , Co^{2+} , Ni^{2+} , and Zn^{2+} metal ions with Effortil in aqueous solutions by potentiometry were investigated. The results shows that the formation of binary compound with composition ML and ML_2 . The dissociation constants and the formation equilibria of Effortil with metal ions are investigated potentiometrically in aqueous solution in the temperature range of 298–328 K, and the values of the thermodynamic parameters were calculated and discussed. It would be possible to calculate the equilibrium distribution of the metal species in biological fluids. Which may form a clear basis for understanding the interaction of such metal complex species under physiological conditions. The ligand and complexes may have interesting biological activity and that need specially designed research conducted by specialized biologists.

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