Int. J. Chem. Sci.: 6(1), 2008, 285-290

pH METRIC STUDY OF BINARY COMPLEXES OF LANTHANIDES WITH SOME DRUGS

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ABSTRACT

Complex formation of La (III), Pr (III), Sm (III), Eu (III), Td (III) and Dy (III) with phthalyl sulphathiazole (L_1), sulphamethoxazole (L_2) and sulphadimidine (L_3) have been studied at 25 ± 0.1°C and 0.1 M ionic strength in 50% (v/v) ethanol–water mixture. The stability constants indicate the formation of 1 : 1 complexes.

Key words: Lanthanides, Drugs, Binary complexes

INTRODUCTION

The lanthanides are given a unique position in the periodic table due to their various chemical and physical characteristics[1]. Development in the coordination chemistry of lanthanides is much less as compared to the coordination chemistry of transition metals. Therefore, the study of coordination chemistry of lanthanides has attracted the attention of several workers during last two to three decades.

A tremendous amount of literature is presently available on the lanthanide complexes including a number of excellent reviews and monograph[2-8]. Some of the important reviews are those by Forsberg[9] on the complexes of oxygen donor ligands by Moeller et al.[10] on the complexes derived of non-oxygen donor[11] and by Koppikar et al. on the complexes of polyamine carboxylic acid, β-diketones and β–ketoesters have been reported[12-14]. These ligands act as anionic oxygen donors. Oximes are well known as both; anionic and neutral chelating oxygen donor ligands. Siddiqui et al.[15-16] studied the complexes of lanthanide ions with drug molecules like barbituric acid derivatives and suggested the ionic character of metal ligand bonds in the complexes. Nahendram et al[17]. also suggest the ionic nature of metal-ligand bond in the complexes of lanthanides with 2-hydroxy methyl benzimidazole. Among the numerous selective and specific complexing agents, the biologically active ligands like drug molecules have special importance in the formation of lanthanide complexes.

A search through the literature has revealed that no systematic study has been done so far on the lanthanide complexes of drug used in the present work. The objective of the present investigation is to ascertain the coordination behavaiour of these drug molecules towards lanthanide ions in 50% (v/v) ethanol–water medium.

The observed values of stability constants of these complexes have been explained on the basis of ionic size of the metal ions, basicity of ligands, gadolinium break and tetrad effect.

EXPERIMENTAL

Drugs phthalylsulphathiazole (L_1), suphamethoxazole (L_2) and sulphadimidine (L_3) were obtained from I.D.P.L., Hyderabad in pure from. All other chemicals were of AnalaR grade and were obtained from B.D.H. An Elico model LI-120 digital pH meter with combined glass electrode was used for measurement of pH value.

The experimental procedure involves potentiometric titration of (i) free $HClO_4$ (0.0135 N), (ii) free $HClO_4$ (0.0135 N) + ligand (2.00×10^{-3} M) and (iii) free $HClO_4$ (0.0135 N) + ligand (2.00×10^{-3} M) + metal ion (4×10^{-4}M) against standard 0.3676 N NaOH solution. The initial volume of each solution was taken as 50 mL. The ionic strength of all the solution was maintained constant, 0.1 M $NaClO_4$.

The titration was carried out in 100 mL Pyrex glass beaker kept in water bath maintained at constant temperature, 25 ± 0.1° C. Nitrogen gas was purged for maintaining inert atmosphere. Proton ligand stability constants and metal ligand stability constants were calculated by the following method of Irving and Rossotti[18].

The dissociation constant of ligands are presented in Table 1. The assignment of pK values of different groups in different ligands has been explained in our recent communication.

RESULTS AND DISCUSSION

The stability constants of some lanthanide complexes with drug molecule in 50% (v/v) ethanol-water medium at 25°C and $\mu = 0.1$ M ($NaClO_4$) ionic strength were determined by the some method used for transition metal complexes and are presented in Table 1.

Table 1. Formation constants of lanthanide ion with drugs. Temp. = 25 ± 0.1°C

Lanthanide ion	Drug		
	L_1	L_2	L_3
La (III)	4.13	3.53	3.63
Pr (III)	3.90	3.57	3.96
Nd (III)	4.36	3.57	4.35
Sm (III)	4.09	4.41	4.75
Eu (III)	4.33	3.55	4.43
Gd.(III)	3.74	3.50	4.59
Td (III)	4.26	3.27	4.06
Dy (III)	4.24	3.64	4.54

Standard deviation of log K values 0.01- 0.03

The complex formation of lanthanide ions with different drug molecules was indicated by the considerable displacement of the metal titration curve from the reagent titration curve along the volume axis at pH values less then those of their hydrolysis. Turbibity appears around pH 7.5, the highest value of $\bar{n}$ obtained in this pH region was about 1.0, indicating the formation of only 1 : 1 complexes with all drug molecules. The lanthanide ions differ from each other in the number of f electron in the 4f orbitals. These orbitals are effectively shielded from interaction with the ligand orbitals by the electrons in 5s and 5p orbitals. If hybridization is to occur, it must involue normally the unoccupied higher energy orbitals like 5d, 6s and 6p, which is only expected with most strongly coordination ligands. Lanthanide ions, therefore, ordinarily from ionic compounds, which should obey the relationship given by Born for energy change on complexation of a gaseous ion of charge ‘e’ in a medium of dielectric constant D as –

$$E = e^2/2r^* (1 - 1/D)$$

Since the stability constants are related directly to this energy, it is expected that the log K values for various rare earths should increase linearity with $e^2/2r$. Such a relationship has been tested for rare earth complexes[19-21].

Moeller et al.[22] have observed in general a regular increase in stabilities with an increase in atomic number or with decrease in crystal radius from La to Eu with a discontinuity at Gd (gadolinium break). For the ions beyond galolinium, two distinct type of behaviours have been observed.

(i) A normal increase in stabilities with decrease in radius in complexes of NTA and EDTA[20-23].

(ii) An essential constancy or occasional maxima or minima in the plot of log K vs $e^2/2r$ in the complexes of IMDA, HEDTA and DTPA[24-26.]

The shielding of 4f electrons is exhibited in the stability constant of the present rare earth complexes with drug molecules. The plot of log K vs 1/r for the chelates of drug molecule distinctly shows a regular increase in stability constants from lanthanum with a discontinuity at gadolinium, which is co mmonly known as gadolinium break. Stability constant increases and then decreases, in all the systems studied; thus, showing minima and maxima after gadolinium break. The gadolinium break, which is observed, may be corrected to discontinuity in crystal radii of gadolinium. In all the cases, Gd (II) complexes have lower values of log K in relation to those of Eu (III) and Tb (III) complexes. As we proceed through the lanthanide series, the nuclear charge and the number of 4f electron increases by one at each step. The shielding of the 4f electron by another is quite imperfect owing to the shift of orbitals, so that at each increase the effective nuclear charge experienced by each 4f electron increases; thus causing a reduction in the size of the entire 4f shell. The lowering in log K value in the Gd (III) chelates in relation to the corresponding Eu (III) chelates may be due to the fact that progressively smaller radii impose increasingly steric hindrance on the ligand on account of metal ligand interactions.

Tetrad effect

Among various interesting features of the 4f shell revealed so far, the regularities or periodicity in the physico-chemical properties of lanthanide ions and even their compounds have earned an important position. Klemm[27] put forward the 'diad' grouping while Noddack[28] proposed the 'triad, classification of lanthanide. The tetradic classification of lanthanides was suggested first by Enders[29].

The definition of the phenomenon of periodicity in the properties of lanthanides was attempted by Peppard and coworkers[30-31] who introduced the term "tetrad effect". A number of properties of the lanthanides ions that relate to the thermodynamic stabilities of their complexes show a tetrad effect, when related to the atomic number. This effect is generalized as "in systems involving lanthanide ions", the point on a plot of the logarithm of a suitable numerical measure of a given property of these elements against atomic number may be grouped through the use of smooth curve without infection, into four tetrads with the gadolinium point being common to the second and third tetrads and extended smooth curves intersecting additionally in the[60,61 and 67, 68] regions. "A differential plot method"[33-34] has been used to examine the presence of tetrad effect. The discontinuities are occurring in the plot of the ratio of the change of property under study to that of the change in atomic number. The plot of d (ΔG) against atomic number shows a better demonstration of the occurrence of discontinuities at ½ Gd, ¼ Pr-Nd and ¾ Ho-Er filled stages of the 4f shell. The tetrad effect is exhibited by the lanthanides chelates of drug.

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Accepted: 17.09.2007