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COMPLEX FORMATION BETWEEN RARE-EARTH ELEMENTS AND TETRACYCLINE

Maria J.C.Nastasi, F.W.Lima

Radiochemistry Division, Instituto de Energia Atômica, C.P. 11049, S.Paulo, Brasil

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Experiments based on the change of wavelength of maximum absorbance of pure tetracycline solutions, and of tetracycline plus lanthanide solutions, indicate the formation of the corresponding complexes. Extraction behaviour of the complexes in benzyl alcohol is described. The per cent extraction has been determined for rare-earth elements and for scandium, as a function of the pH of the aqueous phase. The hydrogen ion dependence of the extraction of La, Nd, Sm, Dy and Lu are presented as well as dependence of the extraction of La, Eu and Lu on the extractant.

INTRODUCTION

For about 20 years tetracycline has been used as an antibiotic agent. It has been suggested that a relationship exists between the antibacterial activity of tetracycline and its metal binding properties.[1]

Albert et al.[2,3] have shown that tetracycline forms complexes with several metal ions /Fe, Cu, Al, Co, Ni, Zn, Mn/ and they have determined the corresponding stability constants which, in some cases, are very high. Maxwell et al.[4] determined the stability constants for tetracycline and alkaline earth metals. Masters[5] made use of the complexing properties of tetracycline for the extraction of various metals and suggested an analytical application of tetracycline for the determination of ^{90}Sr in environmental grass samples.

The scope of the present work was to examine whether tetracycline is capable of forming complexes with the rare-earth elements and, if yes, to study its solvent extraction behaviour.

EXPERIMENTAL

1/ Spectrophotometric determinations

/a/ Preparation of solutions

Aqueous solutions of the rare-earth elements were prepared by dissolving their respective oxides /BDH-99.9% purity/ in hot 2N hydrochloric acid and diluting with water to obtain 10^{-3}M metal ion solutions.

Tetracycline hydrochloride /Laborterápica-Bristol/ was dissolved in water and diluted to obtain a 10^{-4}M solution.

/b/ Absorption measurements

In order to determine whether or not complex formation occurs between the rare-earth elements and tetracycline, the absorption spectra of pure aqueous solutions of tetracycline at different pH values, of pure lanthanide ions, and of the solutions of tetracycline plus lanthanide ions, were recorded. The pH of the solutions varied from 3 to 8 and the solutions were prepared as follows: 2.0 ml of a 10^{-3}M aqueous solution of the metal ion was added to 2.0 ml 10^{-4}M aqueous tetracycline, the value of the pH was adjusted with dilute HCl and NaOH and the final volume made up to 5.0 ml.

Aliquots of the solutions were transferred to silica cells and the absorption spectra recorded.

2/ Solvent extraction studies

The radioisotopes of the rare-earth elements were obtained by irradiation of their respective oxides. Two to three milligrams of each oxide were irradiated at a thermal neutron flux of 5×10^{12} $ncm^{-2}sec^{-1}$ for 30 min, and then the oxides were dissolved in hot HCl. The solutions were diluted with water to obtain 10^{-5}M metal ion solutions.

Tetracycline hydrochloride /TC/ was dissolved in slightly warm benzyl alcohol, the solution was cooled to room temperature and the final concentration made up to 10^{-2}M.

The extraction systems consisted of 5.0 ml of the organic solution, 5.0 ml of the radioactive solution of the rare-earth element and 1.0 ml of a 0.9M solution of NaCl, which was added in order to keep the ionic strength constant. The pH of the aqueous phases was adjusted to the desired value by adding dilute solutions of HCl or NaOH.

The phases were equilibrated at room temperature by shaking the system for 3 min, in a mechanical apparatus. The two phases were then separated, centrifuged and aliquots of both were withdrawn for counting. 1 ml of each phase was counted using a 2" x 1.75" well-type NaI/Tl/ detector coupled to a single-channel gamma-spectrometer.

RESULTS

The change observed in the wavelength of maximum absorbance of the pure tetracycline solution relative to that of the lanthanide-tetracycline solutions shows complex formation between the rare-earth elements and tetracycline.

TABLE 1

Wavelength /mμ/ of maximum absorbance for TC, for lanthanide-TC and for Y-TC complexes

pH	4.0	4.5	5.0	5.5	6.0	6.5	7.0
Pure TC	360	360	360	360	360	362	363
La-TC	365	372	378	384	390	392	394
Pr-TC	365	372	378	384	390	392	394
Eu-TC	383	390	394	398	400	400	400
Er-TC	384	393	402	402	402	402	402
Y -TC	383	392	400	400	400	400	400

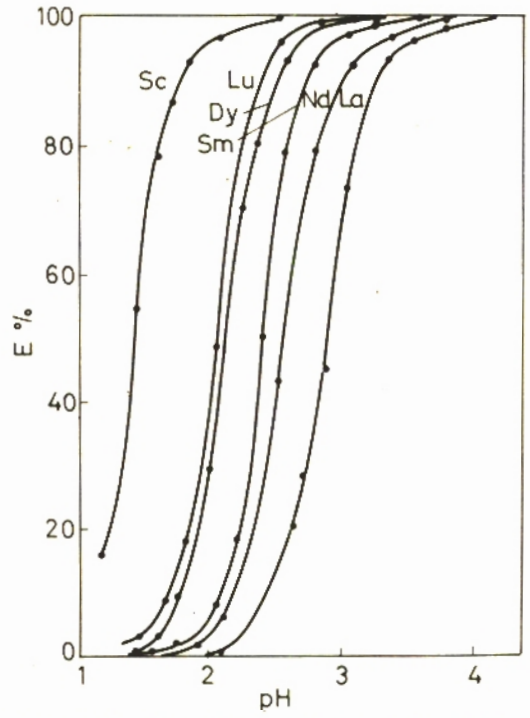

Fig.1. Variation of per cent metal extracted as a function of pH for the lanthanide-TC and scandium-TC complexes

In Table 1 are shown the wavelengths of maximum absorbance of pure aqueous tetracycline solutions and of the solutions of tetracycline plus the rare-earth ions at different pH values.

The existence of the lanthanide-tetracycline complexes was also demonstrated by extraction experiments. Fig.1 shows

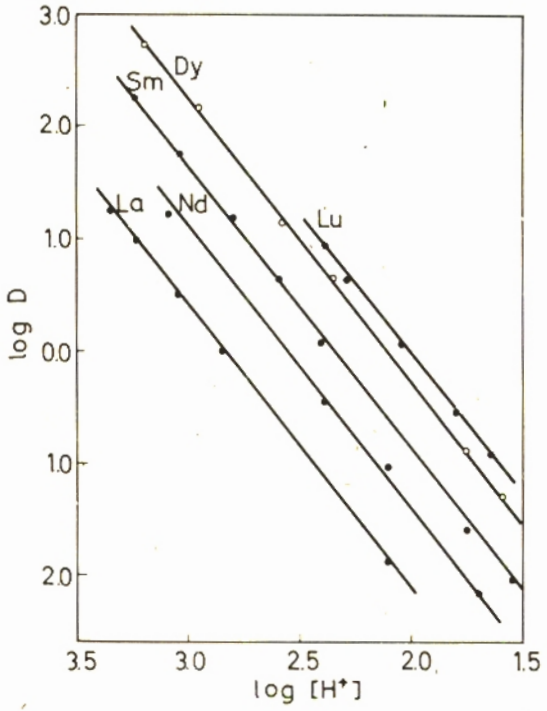

Fig.2. Hydrogen ion dependence of the extraction of lanthanide ions into tetracycline-benzyl alcohol. Concentration of TC solution 10^{-2}M; of lanthanide ions, 10^{-5}M

the variation of per cent metal extracted as a function of pH, for some of the lanthanide elements and also for scandium.

To show that the metal present in the organic phase is bonded to the tetracycline molecule, the radioactive lanthanide solution has been contacted with pure benzyl alcohol at various pH values. No activity was detected in the organic phase /benzyl

alcohol only/ showing that the extractable species was the lanthanide-tetracycline complex.

In Fig.2 the hydrogen ion dependence of the extraction of La, Nd, Sm, Dy and Lu is shown. The slopes of the lines are equal to 2.5 in all cases.

The dependence on the extractant concentration is shown in Fig.3. The slopes of the lines are 2.4 for La and Lu, and 2.7 for Eu.

It can be seen in Fig.1 that, although no complete separation between the lanthanides can be achieved in a single

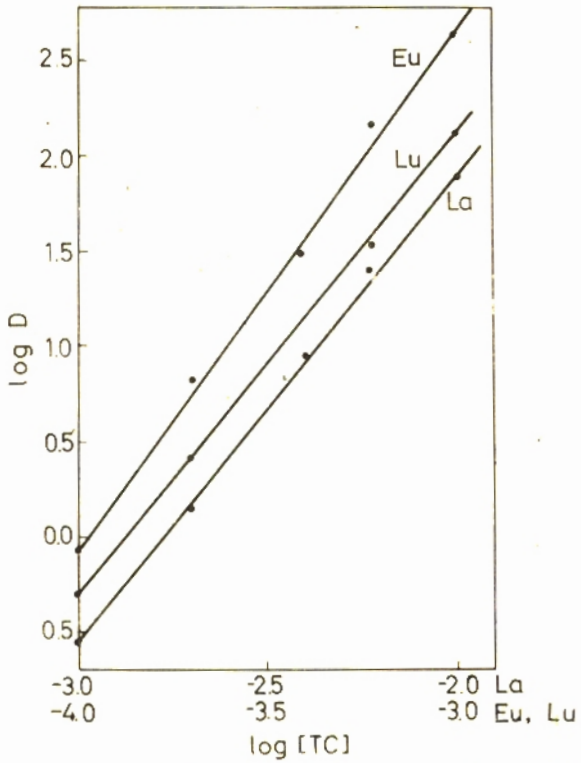

Fig.3. Extractant dependence of the extraction of lanthanide ions into tetracycline-benzyl alcohol at pH 4.0 for La and Lu, and at pH 4.4 for Eu

separation step, it is possible to have an enrichment in one of the constituents of a mixture of lanthanides by choosing the appropriate pH value. The enrichment of lutetium in a mixture containing lanthanum and lutetium has been examined; in an experiment carried out at a pH of 2.60, 97.2% of the lutetium and 29.4% of the lanthanum initially present were found in the organic phase, with one single extraction step.

In accordance with Stary[6], the lower slope of the distribution curves relative to the value corresponding to the metal ion change can be explained by hydrolysis and/or stepwise formation of the extractable complex.

The presence of another anionic ligand would also lead to a slope with a value smaller than 3.0 for the tripositive lanthanide ions in accordance with Marcus and Kertes.[7] The only anionic ligand that might be responsible for some coextraction in the present work is Cl^- from the NaCl used to keep the ionic strength constant. In order to verify if Cl^- might be acting as coextractant, an experiment was carried out with ^{36}Cl as a tracer in the form of $H^{36}Cl$. After equilibration of tetracycline, lanthanides and the tracer solutions, no activity due to ^{36}Cl was found in the organic phase showing that chlorine is not bonded to the lanthanide-tetracycline molecule present in that phase.

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