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Scandium-DOTA complexe for a new PET/3γ camera for medical applications and radio labeling studies

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Abstract - The aim of this paper is to report the stability constant value for Sc^{3+} complexes with polyaminopolycaroxylates ligands and their behaviour in serum conditions as well as for in vivo conditions for PET imaging with 44Sc and radio-immunotherapy with 47Sc.

Keywords – PET / RIT / Scandium / Chelates

I. INTRODUCTION

A new nuclear medical imaging technique based on the measurement of the emitter location in the three dimensions with a few mm spatial resolution using β+/γ emitters, has been developed by our team [1]. Such measurement could be realized thanks to a new kind of radio-nuclides which emit a γ-ray quasi-simultaneously with the β+ decay whose the most interesting radio-nuclide candidate is ^{44}Sc. In addition to this, ^{47}Sc is planned by the nuclear medicine teams for its potential interest for the β- radio-immunotherapy RIT [2]. Such applications strictly demand that metallic radionuclide remain intimately associated to the targeting protein to minimize the toxicity derived from the dissociation and the delivery of radiation to normal, non targeted body tissues. Owing to their structural features, tetraazamacrocyclic derivatives form metal complexes with the required properties for these applications. The high affinity shown by some polyaminocarboxylic acids has been exploited to form very stable complexes (log K_{ML} > 20) [3].

The chelating ligand DOTA has been shown to bind transition metals and rare-earths with extreme stability under physiological conditions, leading to its use in vivo [4]. A DOTA derivative (NBD) was tested with lanthanides and Sc3+ for its complexation properties and with the monoclonal antibody 2D12.5 [4]. Nevertheless, it was showed that the NBD-Sc chelate bound the 2D12.5 antibody with a much lower affinity than the strongest binding rare earth complexe, perhaps because Sc^{3+} has a much smaller ionic radius [5]

II. RESULTS

Only results on DOTA are presented here. The protonation constants of DOTA have been obtained from potentiometric data by means of the least-squares program HYPERQUAD [6] Table 1 gives the protonation constants determined together with values obtained previously [6] and shows that our values are in excellent agreement with those obtained at 298 K and for different background solutions reported in a critical compilation of equilibrium constants.

The pKa values determined previously for DOTA were fixed and only the stability constant of Sc-DOTA was fitted. From literature [6], it was shown that the stoichiometry of the complex is 1:1 described by the following equilibrium.

$$L^{4-}_{aq} + Sc^{3+} \rightarrow [LSc]^{-}_{aq} \qquad \log \beta = 20{,}8$$

The formation of complexes is kinetically slow, which prevents certain uses as radiopharmaceuticals. In order to get information on the kinetics and on the structural modifications as a function of time, fluorescence measurements were conducted with Eu since this element could be used as a structural probe, whose chemistry is close to the element of interest Sc. From TRLFS kinetics experiment, it was deduced that the equilibrium of Eu^{3+} complexation with DOTA was reached after 5 hrs (Fig. 1). This seems to be too long for radiopharmaceutical applications. Thus, the stability constants and the kinetics properties of others tetraazamacrocyclic ligands (DTPA, TETA …) better suited for the smaller ionic radius of Sc will be tested.

TABLE I. Protonation constants of DOTA

	Literature data			**This work**
	0,1 Me_4NCl	0,1 Me_4NCl	0,1 Me_4NNO_3	$NaClO_4$ 0,1M
Log K_1	11,74	11,73	12,09	11,54
Log K_2	9,76	9,40	9,68	9,14
Log K_3	4,68	4,50	4,55	4,58
Log K_4	4.11	4,19	4,13	4,34
Log K_5	2.37			

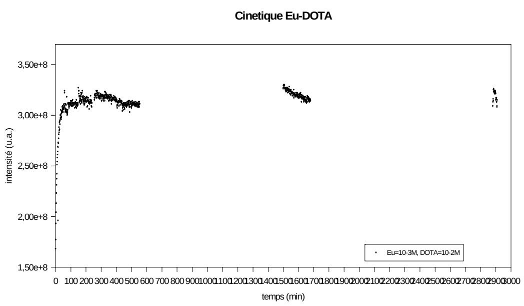

Fig. 1. TRLFS kinetics of Eu^{3+} complexation with DOTA

[1] C. GRIGNON, J. BARBET, M. BARDIES, T. CARLIER, J.F. CHATAL, O. COUTURIER, J.P. CUSSONEAU, A. FAIVRE-CHAUVET, L. FERRER, S. GIRAULT, T. HARUYAMA, P. LE RAY, L. LUQUIN, S. LUPONE, V. METIVIER, E. MORTEAU, N. SERVAGEANT and D. THERS., Nuclear Instruments and Methods in Physics Research Section A: Accelerators, Spectrometers, Detectors and Associated Equipment 571 (1-2), 142-145, (2007)

[2] L.F. MAUSNER K.L. KOLSKY, V. JOSHI and S.C. SRIVASTAVA, Appl. Radiat. Isot., 49, 285 (1998).

[3] R. DELGADO, J. COSTA, K.P. GUERRA and L.M.P. LIMA, Pure Appl. Chem, 77 (3), 569-579 (2005).

[4] T.M. CORNEILLIE, P.A. WHESTONE, A.J. FISHER and C.F. MEARES, JACS, 125, 3436-3437 (2003).

[5] T.M. CORNEILLIE, A.J. FISHER and C.F. MEARES, JACS, 125, 15039-15048, (2003).

[6] A.C. FERRAND. Thesis, Lausanne, Switzerland (2004).