Institute of Nuclear Chemistry and Technology

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Scandium - 47 complexes as precursors for therapeutic radiopharmaceuticals

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Sc [Ar]3d^{1}4s^2

^{44}**Sc**
^{47}**Sc**

molecular weight 44,9559 g/mol
atomic radius 164,1 pm
ionic radius 74 pm (LK=6)

LK= 6 (sometimes 4 i 8)

	IA												IIIA	IVA	VA	VIA	VIIA	VIIIA
	I																17	18
1	H 1	IIA 2															H 1	He 2
2	Li 3	Be 4											B 5	C 6	N 7	O 8	F 9	Ne 10
3	Na 11	Mg 12	IIIB 3	IVB 4	VB 5	VIB 6	VIIB 7	VIIIB 8	VIIIB 9	VIIIB 10	IB 11	IIB 12	Al 13	Si 14	P 15	S 16	Cl 17	Ar 18
4	K 19	Ca 20	Sc 21	Ti 22	V 23	Cr 24	Mn 25	Fe 26	Co 27	Ni 28	Cu 29	Zn 30	Ga 31	Ge 32	As 33	Se 34	Br 35	Kr 36
5	Rb 37	Sr 38	Y 39	Zr 40	Nb 41	Mo 42	Tc 43	Ru 44	Rh 45	Pd 46	Ag 47	Cd 48	In 49	Sn 50	Sb 51	Te 52	J 53	Xe 54
6	Cs 55	Ba 56	La 57	Hf 72	Ta 73	W 74	Re 75	Os 76	Ir 77	Pt 78	Au 79	Hg 80	Tl 81	Pb 82	Bi 83	Po 84	At 85	Rn 86
7	Fr 87	Ra 88	Ac 89	Rf 104	Db 105	Sg 106	Bh 107	Hs 108	Mt 109	110	111	112	113	114	115	116	117	118

lanthanides

actinides

Ce 58	Pr 59	Nd 60	Pm 61	Sm 62	Eu 63	Gd 64	Tb 65	Dy 66	Ho 67	Er 68	Tm 69	Yb 70	Lu 71
Th 90	Pa 91	U 92	Np 93	Pu 94	Am 95	Cm 96	Bk 97	Cf 98	Es 99	Fm 100	Md 101	No 102	Lr 103

Therapeutic radionuclides

radionuclide	$T_{1/2}$	decay mode (MeV)	max. of range
^{80m}Br	4.42 h	Auger, γ (0.037)	<10 nm
^{67}Ga	3.26 d	Auger, γ (0.09)	10 nm
^{125}I	60.0 d	Auger, γ (0.027)	10 nm
^{211}At	7.2 h	α (6.8)	65 μm
^{212}Bi	1.0 h	α (7.8), γ (0.72)	70 μm
^{169}Er	9.5 d	β (0.34)	1.0 mm
^{177}Lu	6.7 d	β (0.497), γ (0.208)	1.5 mm
^{161}Tb	6.91 d	β (0.51), γ (0.025)	1.7 mm
^{67}Cu	2.58 d	β (0.54), γ (0.185)	1.8 mm
^{105}Rh	1.48 d	β (0.57), γ (0.320)	1.9 mm
^{131}I	8.04 d	β (0.6), γ (0.364)	2.0 mm
^{77}As	1.62 d	β (0.68), γ (0.239)	2.5 mm
^{127}Te	9.4 h	β (0.7)	2.6 mm
^{153}Sm	1.95 d	β (0.8), γ (0.103)	3.0 mm
^{198}Au	2.7 d	β (0.97), γ (0.411)	4.4 mm
^{111}Ag	7.47 d	β (1.05), γ (0.34)	4.8 mm
^{149}Pm	2.21 d	β (1.07), γ (0.289)	5.0 mm
^{186}Re	3.77 d	β (1.08), γ (0.131)	5.0 mm
^{89}Sr	50.5 d	β (1.49)	8.0 mm
^{32}P	14.3 d	β (1.71)	8.7 mm
^{188}Re	16.95 h	β (2.13), γ (0.155)	11.0 mm
^{142}Pr	19.1 h	β (2.16), γ (1.6)	11.3 mm
^{90}Y	2.67 d	β (2.28)	12.0 mm

^{47}Sc 3.43 d β (0.60)

Scandium

^{47}Sc **β (0,6 MeV)** **$T_{1/2}$= 3,35 d**

$$^{46}\mathrm{Ca} + \mathrm{n}_{\mathrm{term}} \rightarrow {}^{47}\mathrm{Ca} \xrightarrow{\beta^-} {}^{47}\mathrm{Sc}$$

$$^{48}\mathrm{Ti} + \mathrm{n}_{\mathrm{fast}} \rightarrow {}^{47}\mathrm{Sc} + \mathrm{p} + \mathrm{n}$$

reactor „Maria”- Świerk

$8*10^{13}$ n/s/cm^2

Scandium

^{47}Sc β^- emitter half-life 3,35 d

decay mode β^-, γ E_{β^-}= 0,4; 0,6 MeV E_γ= 159 keV

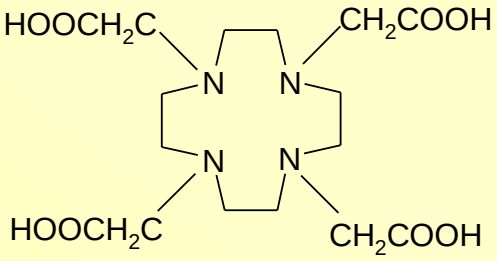
^{46}Sc γ emitter half- life 83,82 d

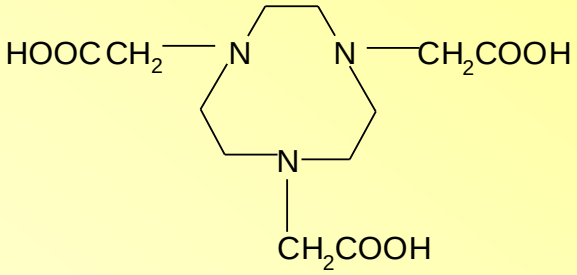
decay mode γ, β^- E_γ= 889; 1121 keV E_{β^-}= 0,4 MeV

The goal of our project

Selection of ligands for ^{47}Sc complexation

Stability constants

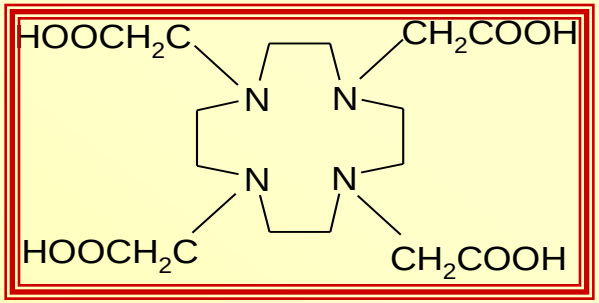




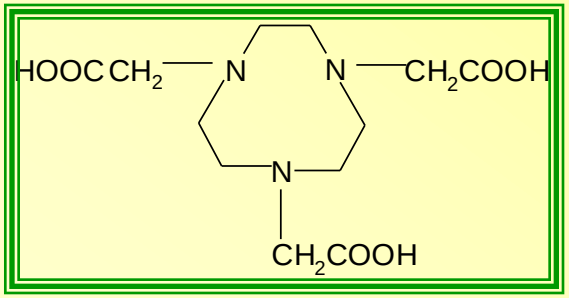
Cation	Ionic radius CN=6, [pm]	Stability constants for DOTA, **NOTA**
Lu^{3+}	86,1	23,9 **(16,1)**
Y^{3+}	90,0	24,0
Ga^{3+}	62,0	21,3 **(30,7)**
Sc^{3+}	74,5	?

Chelators

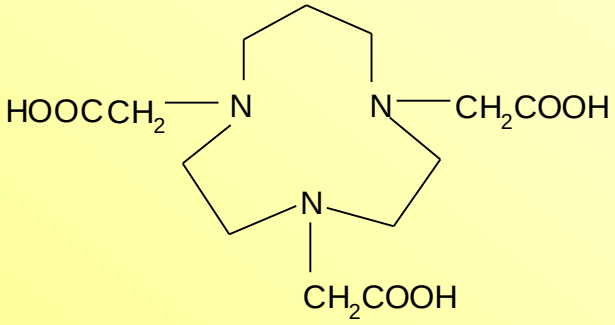
DOTA

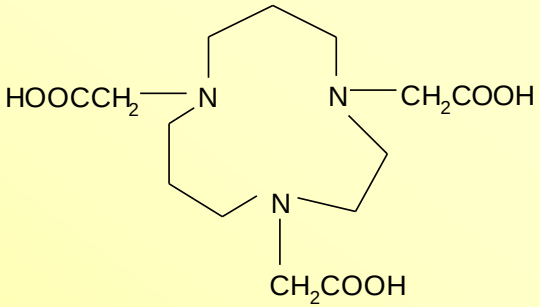


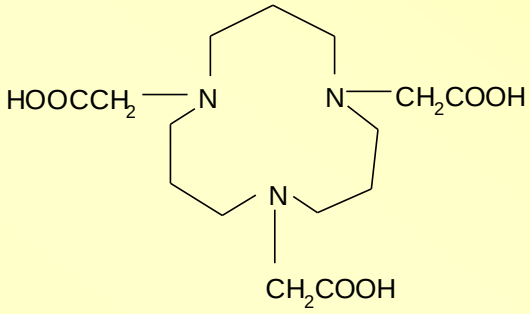
NOTA



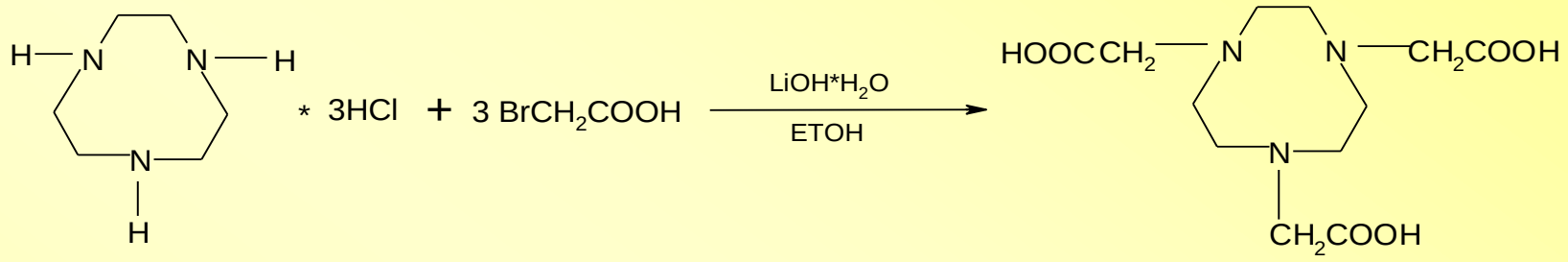
analogs of NOTA



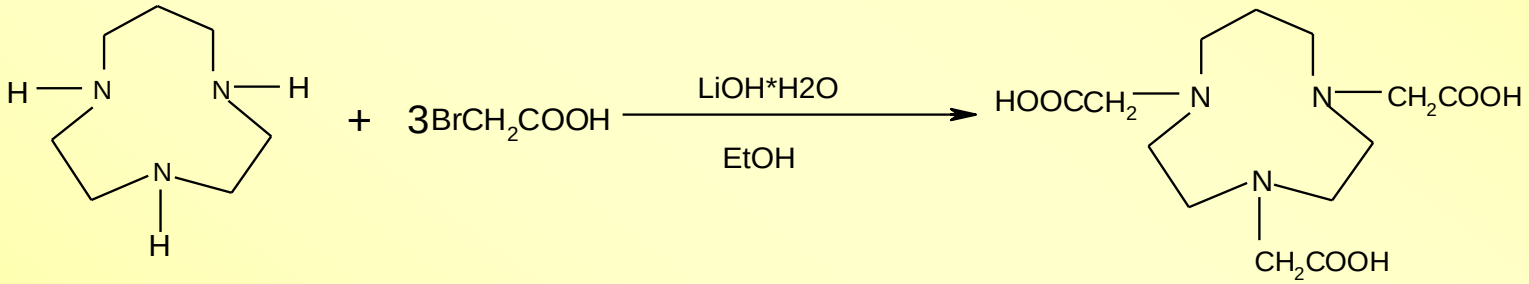




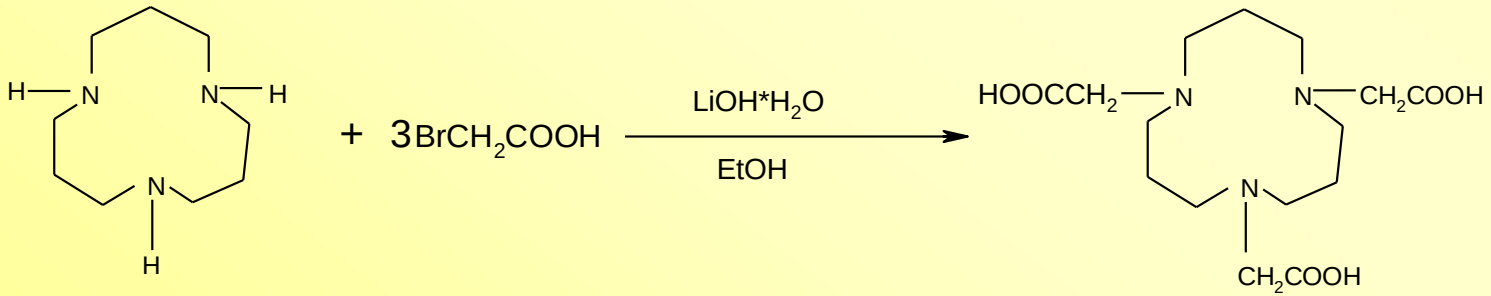
Synthesis of NOTA and its analogs



1,4,7-triazacyclononane-1,4,7-triacetic acid



1,5,8 triazacyclodecane-1,5,8-triacetic acid



1,5,9 triazacyclododecane-1,5,9-triacetic acid

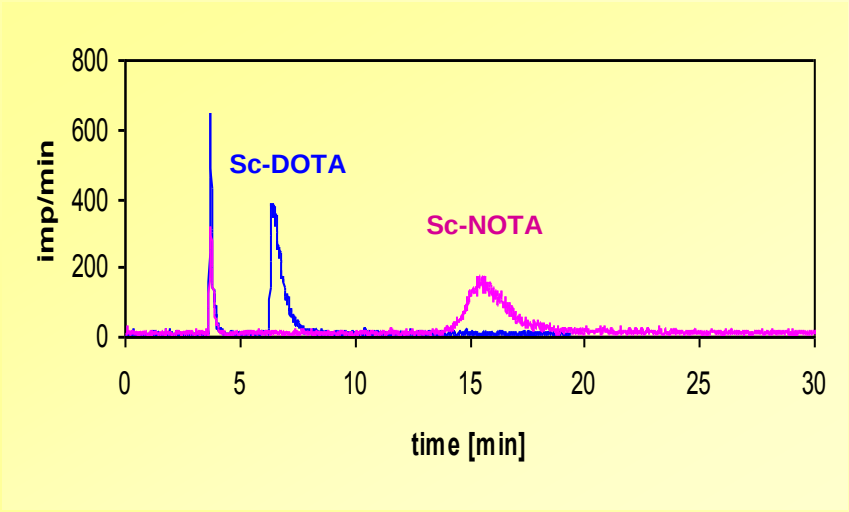
Determination of stability constants

$$K' = \frac{[^{46}ScDOTA]}{[^{46}Sc] \times [DOTA]}$$

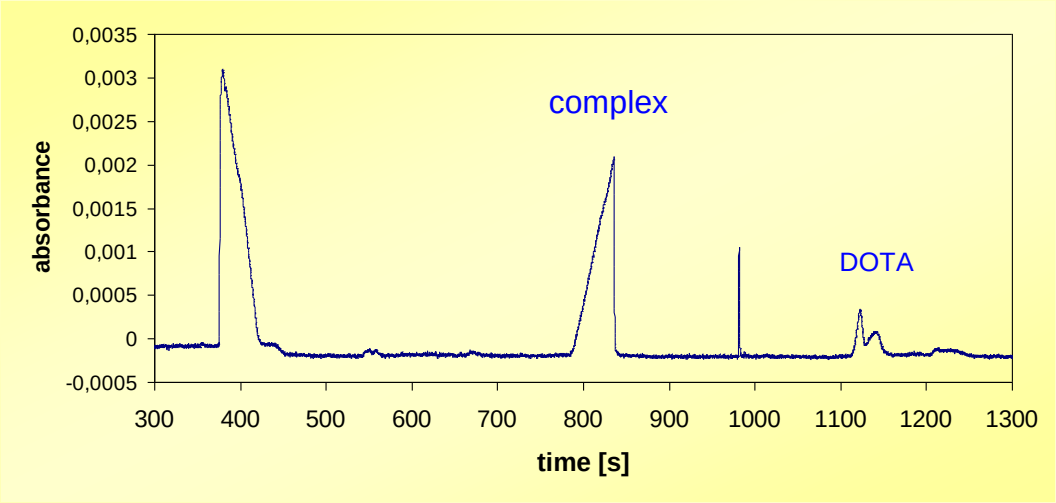
$$K = \frac{K'}{\alpha}$$

$$\alpha = \frac{Kp_1 \cdot Kp_2 \cdot Kp_3 \cdot Kp_4}{Kp_1 \cdot Kp_2 \cdot Kp_3 \cdot Kp_4 + Kp_1 \cdot Kp_2 \cdot Kp_3 \cdot [H^+] + Kp_3 \cdot Kp_4 \cdot [H^+]^2 + Kp_4 \cdot [H^+]^3 \cdot [H^+]^4}$$

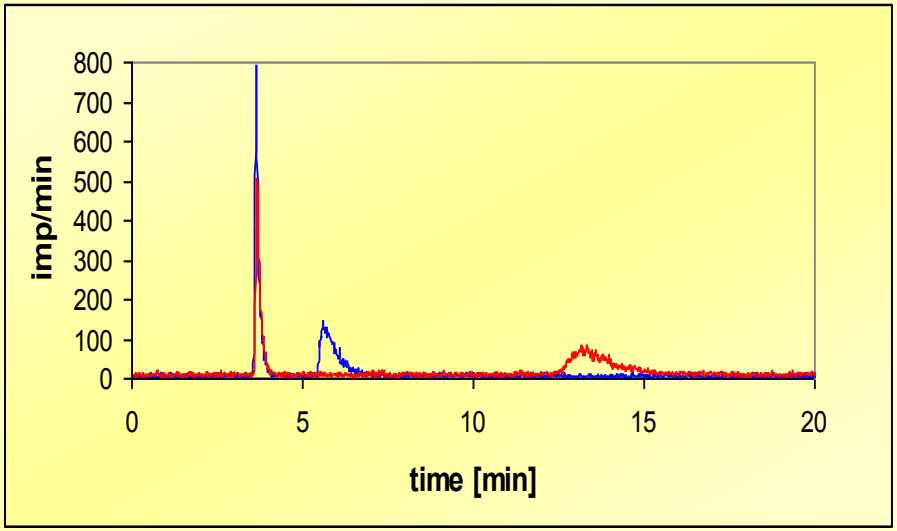
HPLC



CE



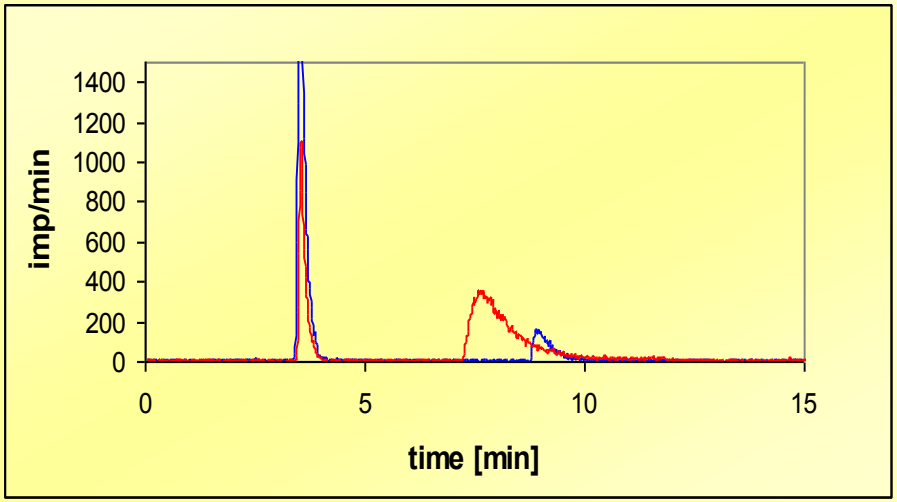
Determination of stability constants



$\log K_{Sc\text{-}DOTA} = 27,5$

$\log K_{Sc\text{-}NOTA} = 17,6$

$\log K_{Sc\text{-}10ane} = 14,8$

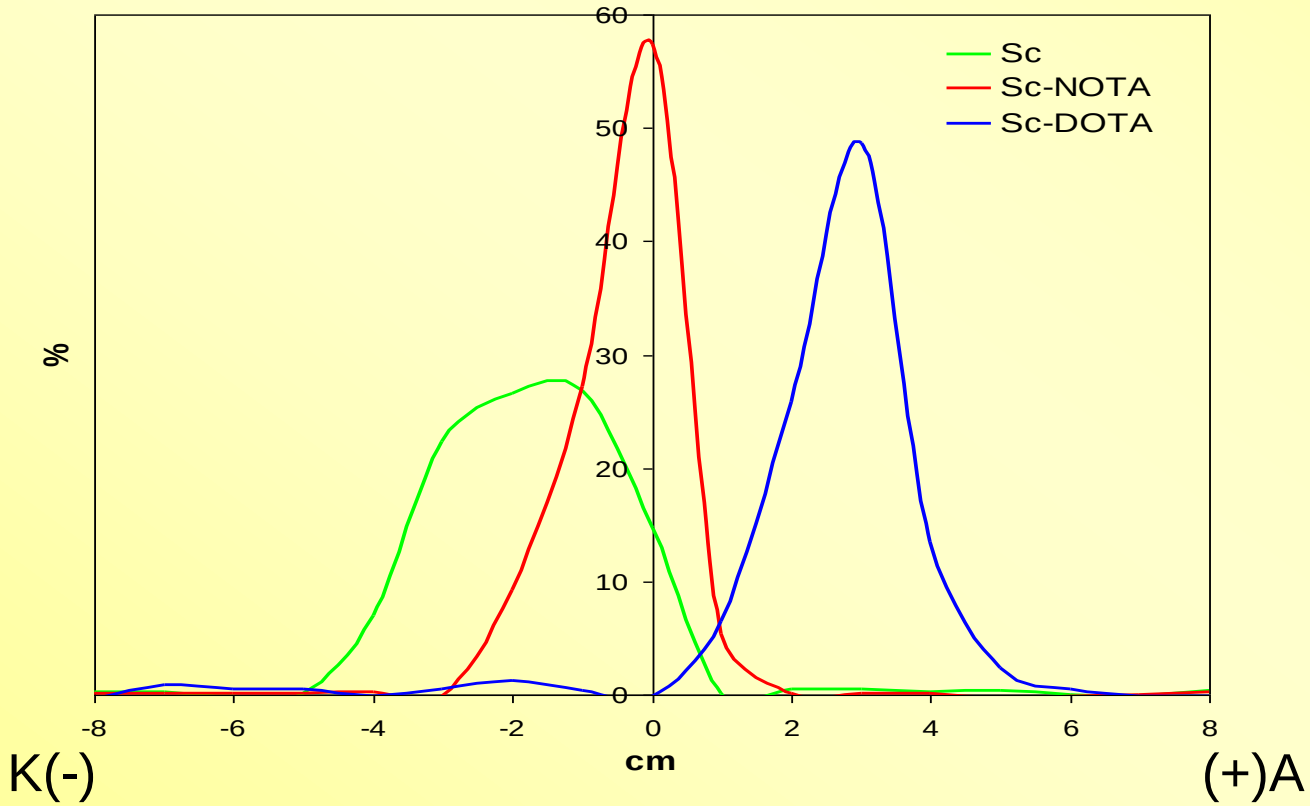


$\log K_{Lu\text{-}DOTA} = 26,7$

$\log K_{Lu\text{-}NOTA} = 15,8$

$\log K_{Lu\text{-}10ane} = 12,7$

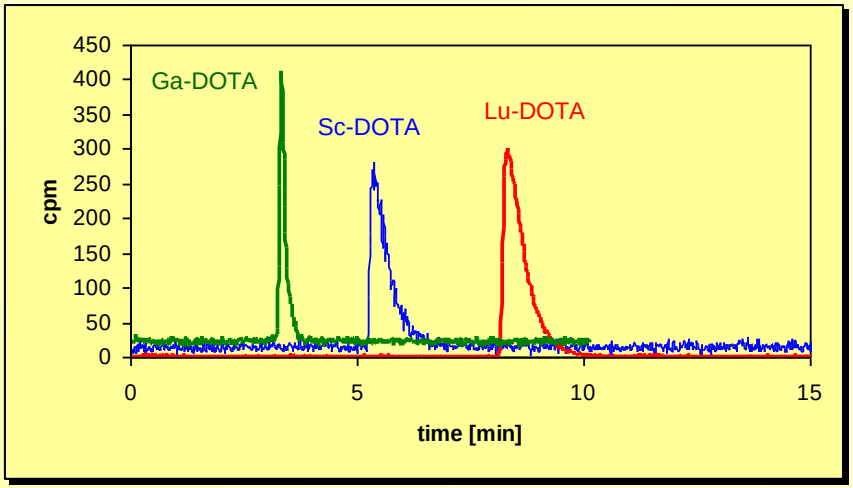
Paper electrophoresis

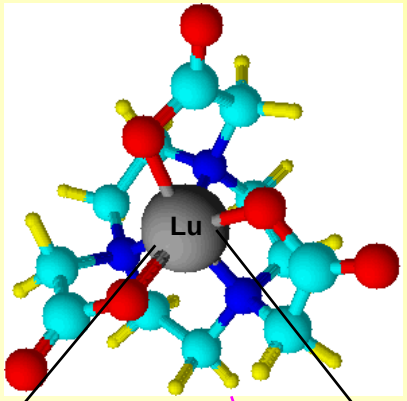


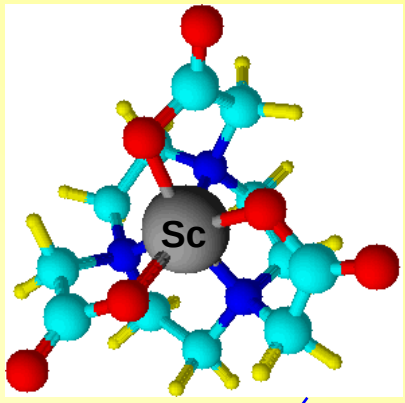
Adsorption on cation and anion exchangers

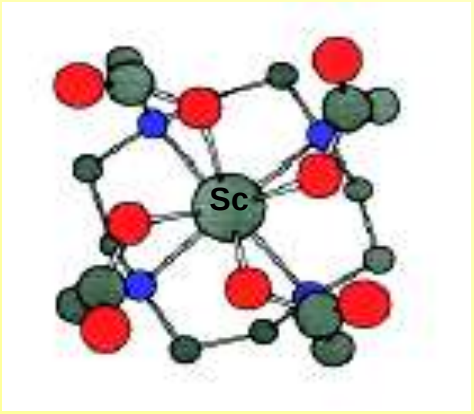
	Sc(DOTA)	Sc(NOTA)	Lu(DOTA)
cationit Dowex 50	–	+	–
anionit Dowex 1	+	+	+
complex charge	-	0	-

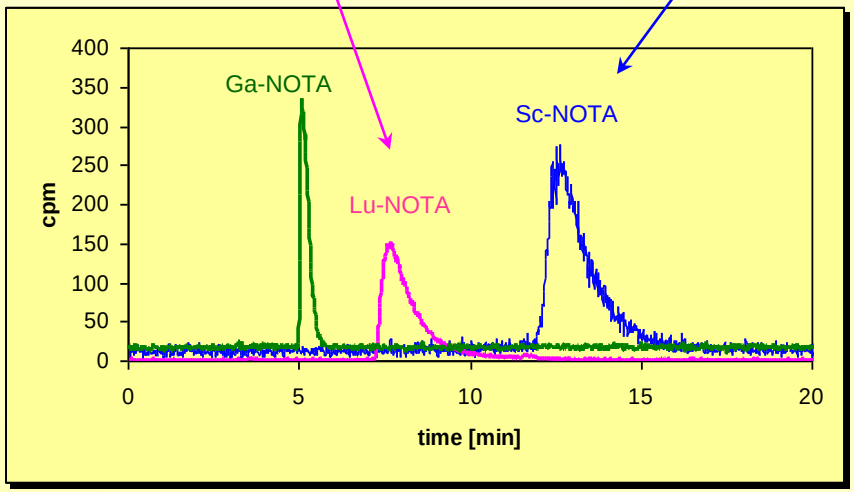
Chromatographs of HPLC











Complexes in different molar ratio

pH=6,0 t=20^{0}C ITLC after 24h

[Sc^{3+}] = 164nmol

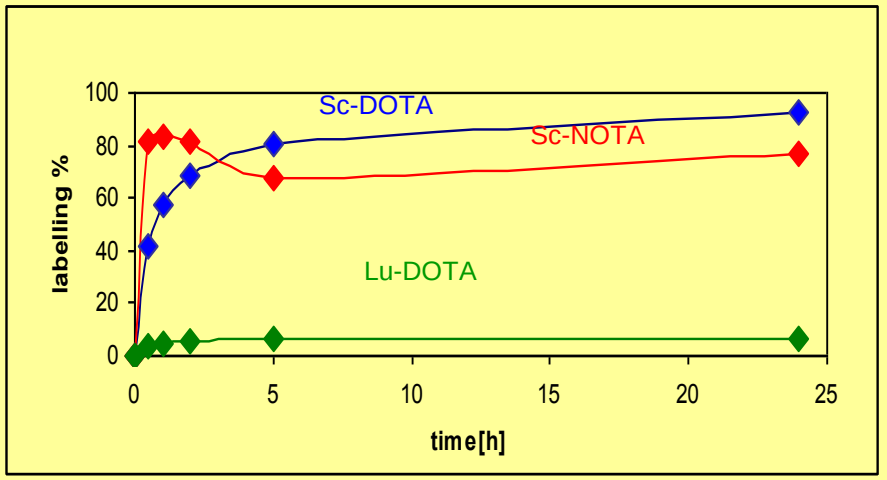
Sc-DOTA

metal:ligand	labelling %
1:1	89.6
1:2	99.4
1:5	99.4
1:10	99.3
1:20	99.3

Sc-NOTA

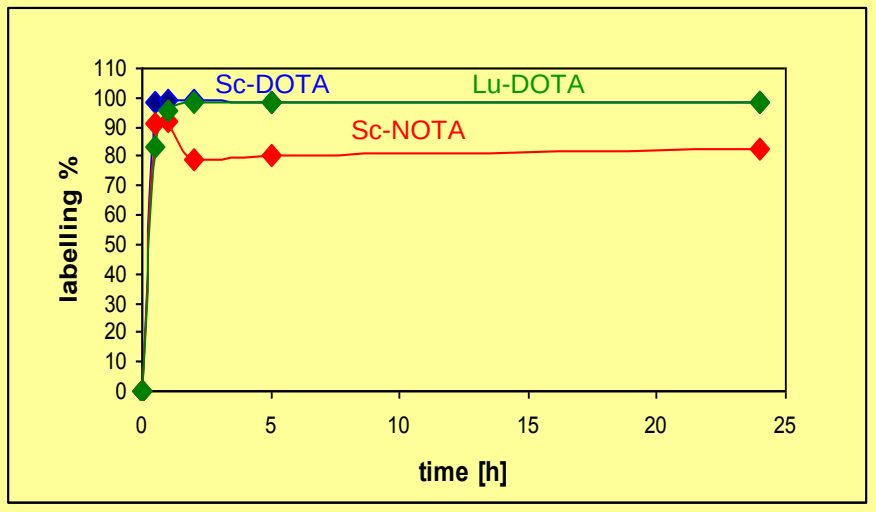
metal:ligand	labelling %
1:1	88.3
1:2	98.3
1:5	98.2
1:10	98.8
1:20	99.1

Kinetics



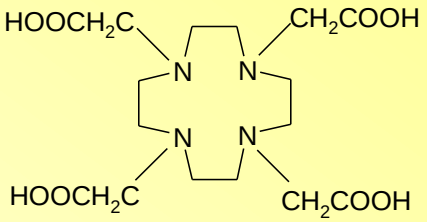
T=20^{0}C, pH=1,5

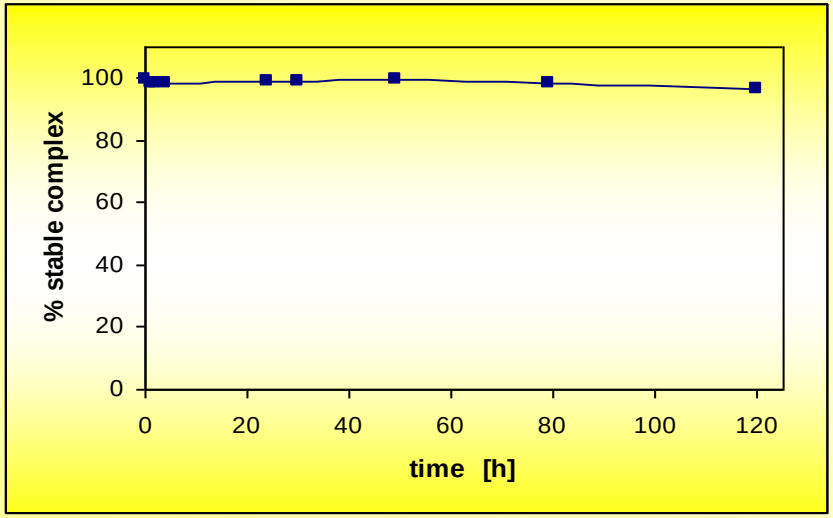
T=70^{0}C, pH=1,5



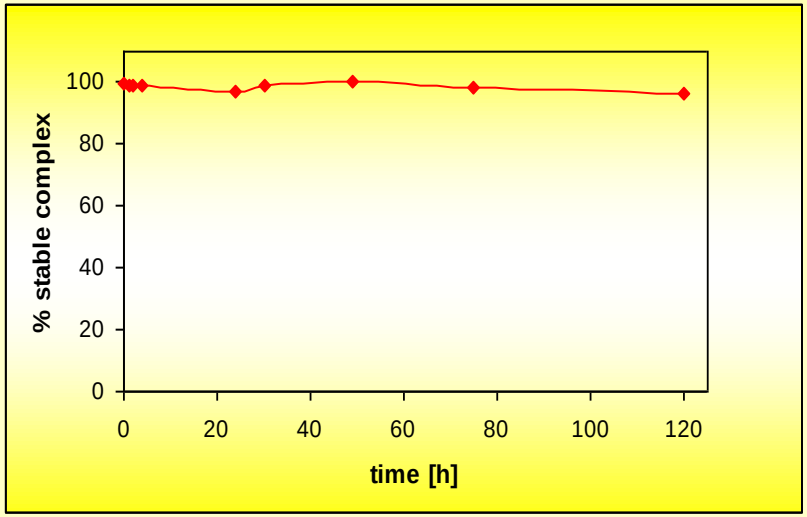
Examination of stability

Sc-DOTA



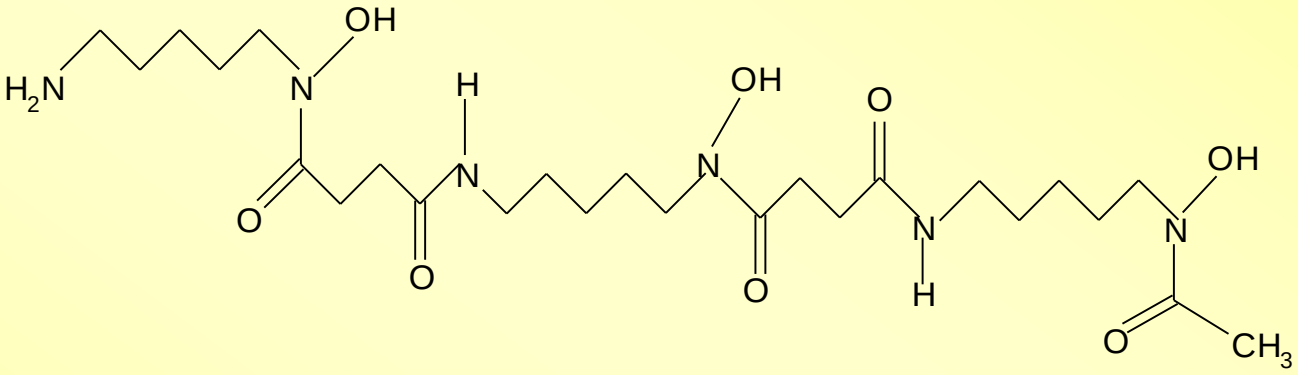


SERUM

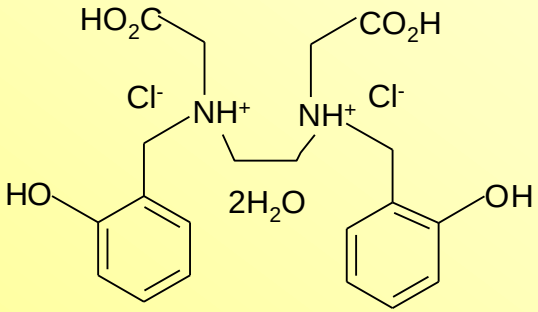


PBS

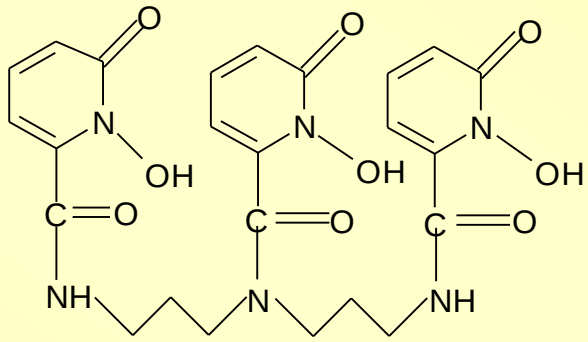
Alternative acyclic ligands



desferrioxamine (DFO)



N,N'-bis-(2-hydroxybenzyl) ethylenediamine-N,N'-diacetic acid dihydrochloride dihydrate (HBED)



LICAM

Thank you for your attention