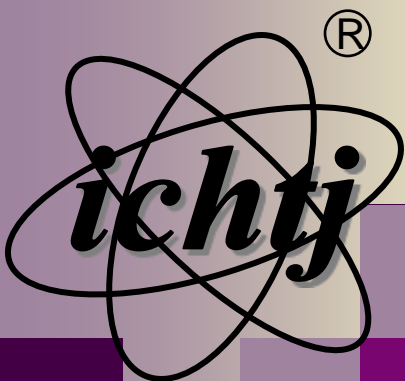


Institute of Nuclear Chemistry and Technology

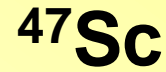
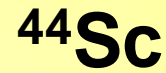
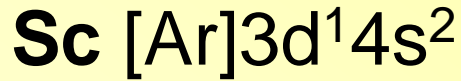


Warsaw, Poland

**Scandium - 47 complexes as
precursors for therapeutic
radiopharmaceuticals**

Agnieszka Majkowska

Aleksander Bilewicz

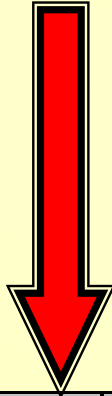


molecular weight 44,9559 g/mol

atomic radius 164,1 pm

ionic radius 74 pm (LK=6)

LK= 6 (sometimes 4 i 8)



	IA																	VIA	VIIA				
	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	VIIA 7	VIII 8	VIII 9	VIII 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		I 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														

lanthanides

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
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actinides

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
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Therapeutic radionuclides

radionuclide	$T_{1/2}$	decay mode (MeV)	max. of range
^{80}mBr	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

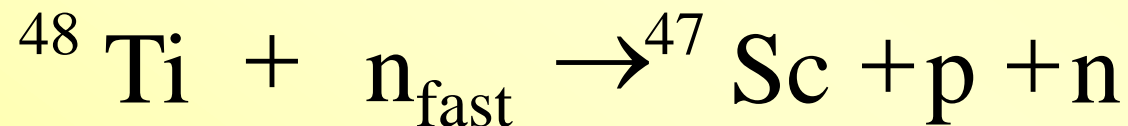
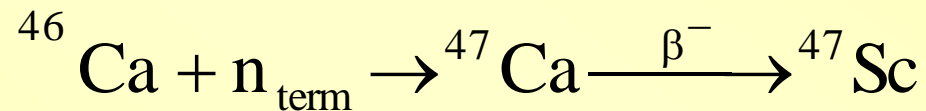
^{47}Sc 3.43 d β (0.60)

Scandium

^{47}Sc

β (0,6 MeV)

$T_{1/2} = 3,35 \text{ d}$



reactor „Maria”- Świerk

$8 \cdot 10^{13} \text{ n/s/cm}^2$

Scandium

^{47}Sc

β^- emitter

half-life

3,35 d

decay mode β^- , γ

$E_{\beta^-} = 0,4; 0,6 \text{ MeV}$

$E_{\gamma} = 159 \text{ keV}$

^{46}Sc

γ emitter

half- life

83,82 d

decay mode γ , β^-

$E_{\gamma} = 889; 1121 \text{ keV}$

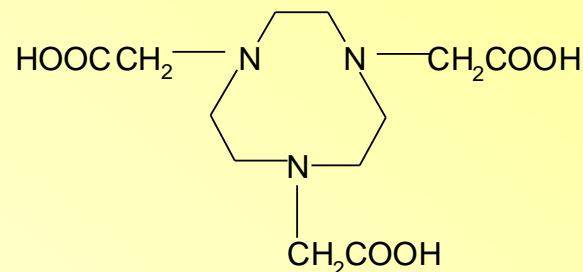
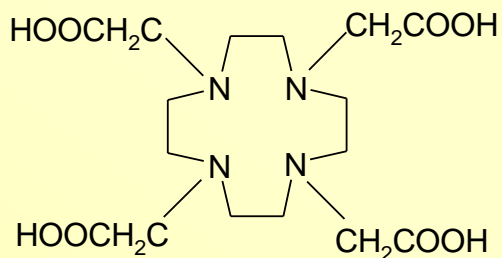
$E_{\beta^-} = 0,4 \text{ MeV}$



The goal of our project

Selection of ligands for ^{47}Sc complexation

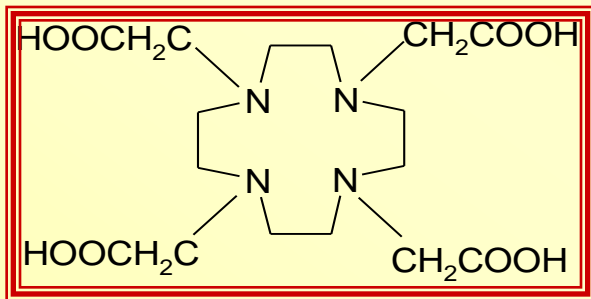
Stability constants



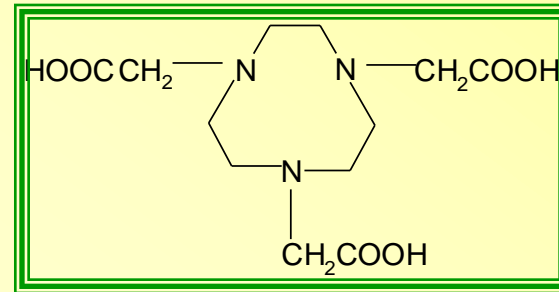
Cation	Ionic radius CN=6, [pm]	Stability constants for DOTA, NOTA
Lu ³⁺	86,1	23,9 (16,1)
Y ³⁺	90,0	24,0
Ga ³⁺	62,0	21,3 (30,7)
Sc ³⁺	74,5	?

Chelators

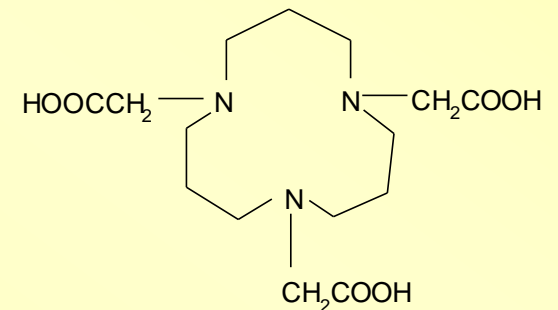
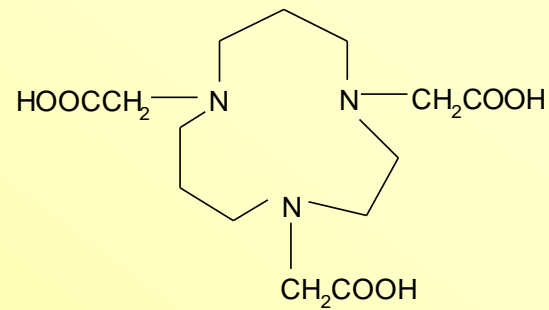
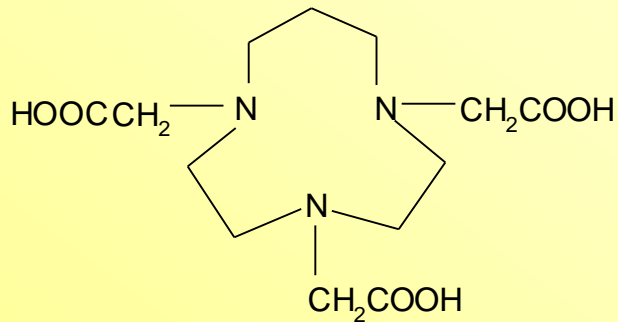
DOTA



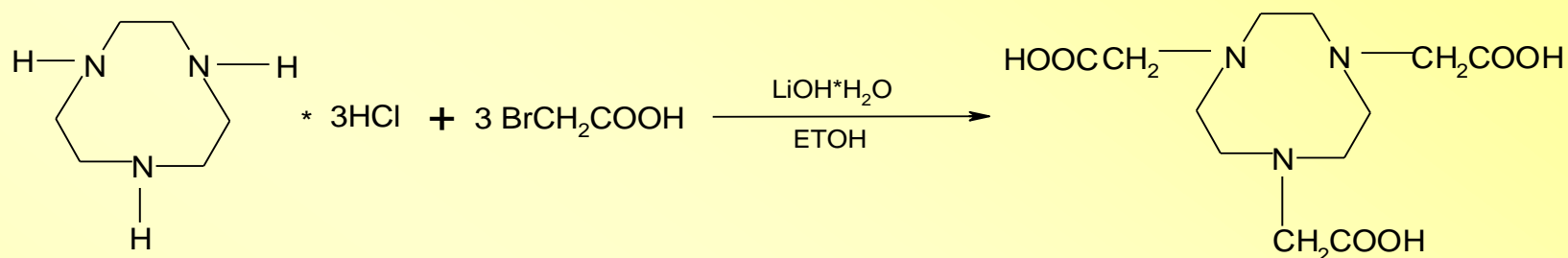
NOTA



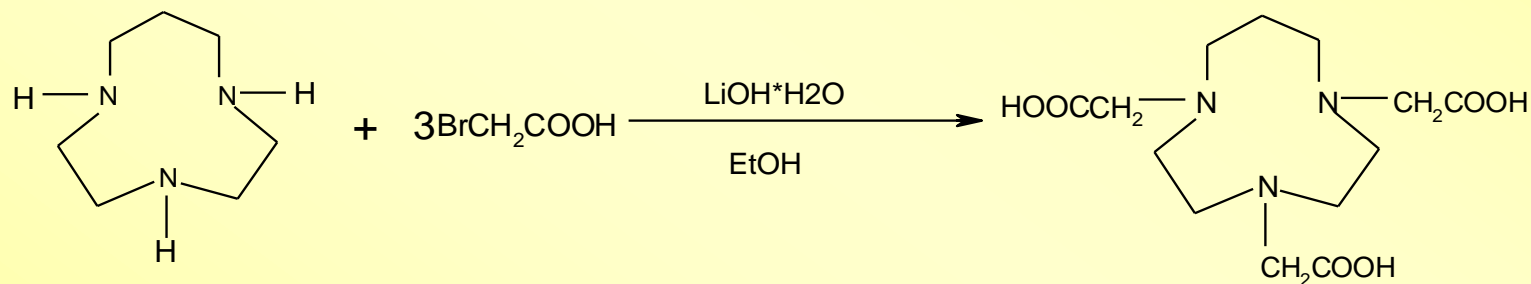
analogues of NOTA



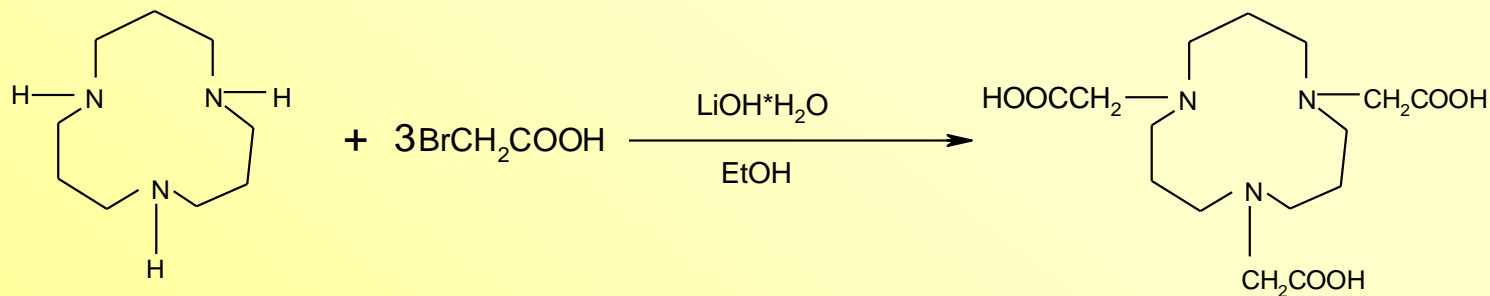
Synthesis of NOTA and its analogs



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



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



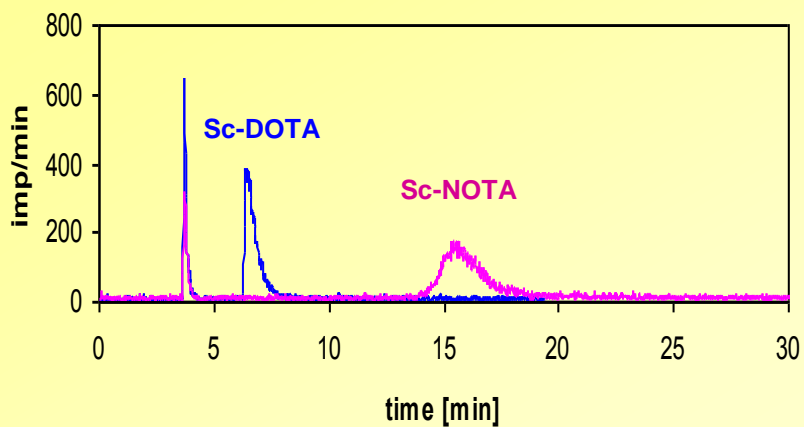
1,5,9 triazacyclododecane-1,5,9-triacetic acid

Determination of stability constants

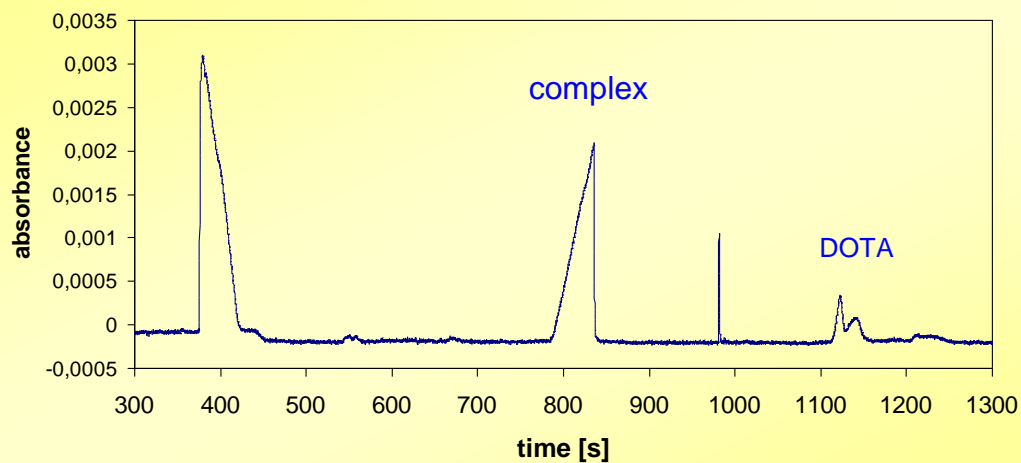
$$K' = \frac{[{}^{46}\text{ScDOTA}]}{[{}^{46}\text{Sc}] \times [\text{DOTA}]}$$

$$K = \frac{K'}{\alpha} \quad \alpha = \frac{K_{p1} \cdot K_{p2} \cdot K_{p3} \cdot K_{p4}}{K_{p1} \cdot K_{p2} \cdot K_{p3} \cdot K_{p4} + K_{p1} \cdot K_{p2} \cdot K_{p3} \cdot [\text{H}^+] + K_{p3} \cdot K_{p4} \cdot [\text{H}^+]^2 + K_{p4} \cdot [\text{H}^+]^3 \cdot [\text{H}^+]^4}$$

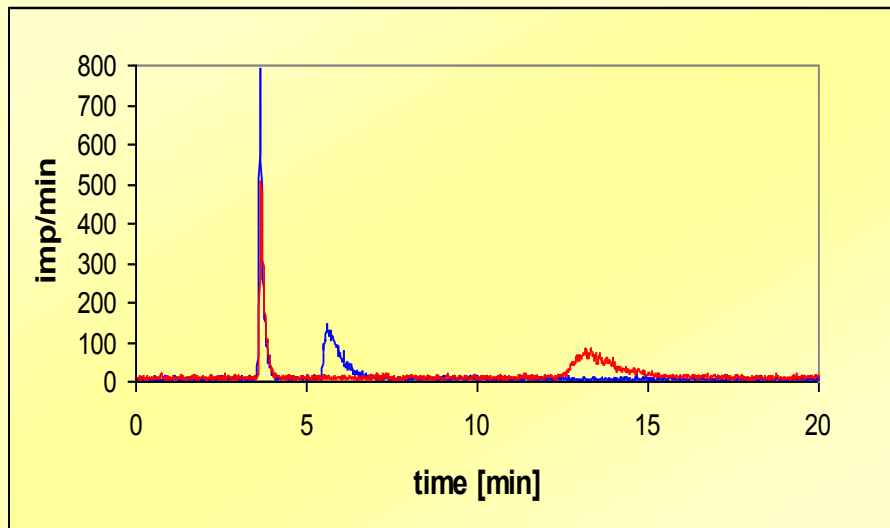
HPLC



CE



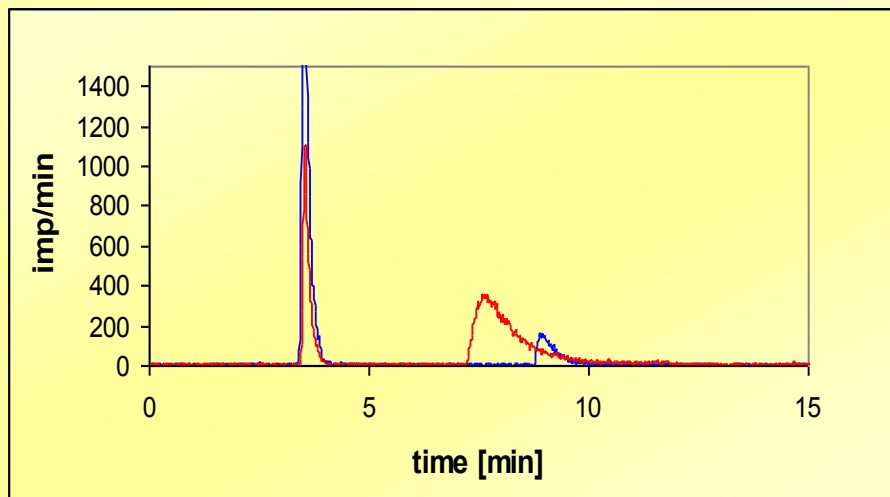
Determination of stability constants



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

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

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

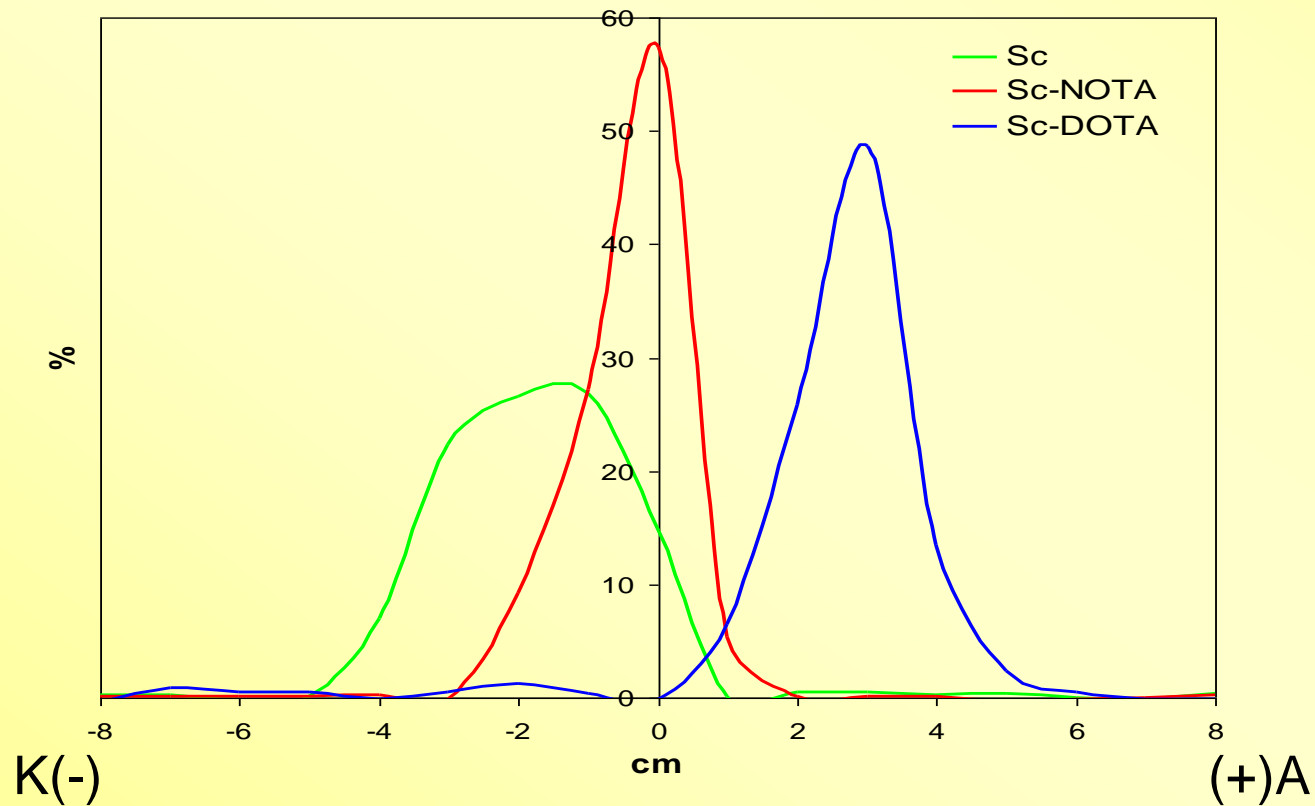


$$\log K_{\text{Lu-DOTA}} = 26,7$$

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

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

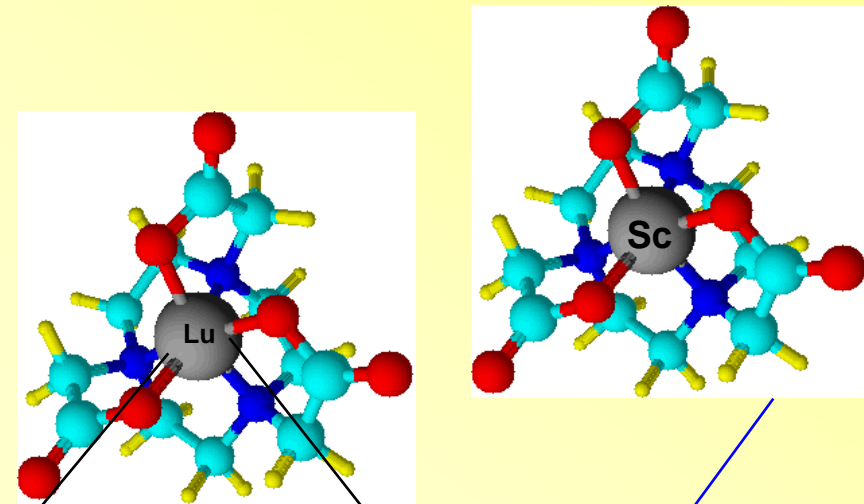
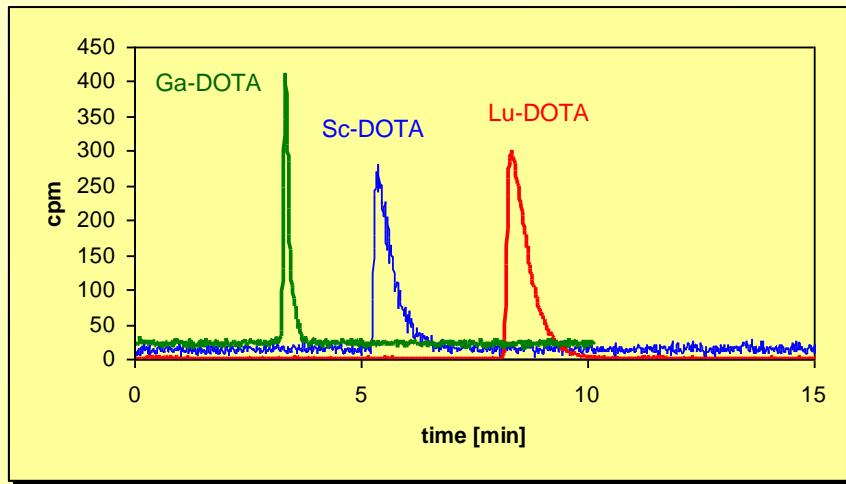
Paper electrophoresis



Adsorption on cation and anion exchangers

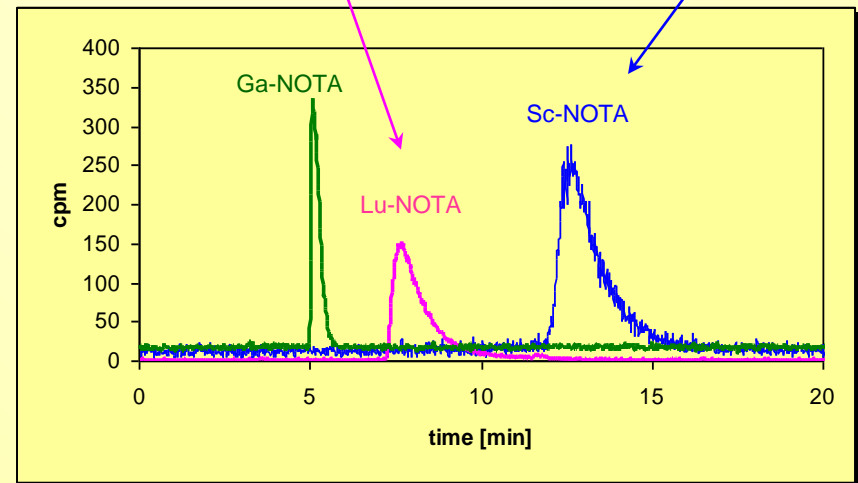
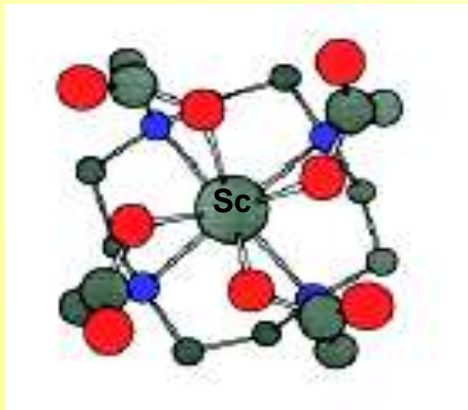
	Sc(DOTA)	Sc(NOTA)	Lu(DOTA)
cationit Dowex 50	—	+	—
anionit Dowex 1	+	+	+
complex charge	-	0	-

Chromatographs of HPLC



H₂O

H₂O



Complexes in different molar ratio

pH=6,0 t=20°C ITLC after 24h

[Sc³⁺] = 164nmol

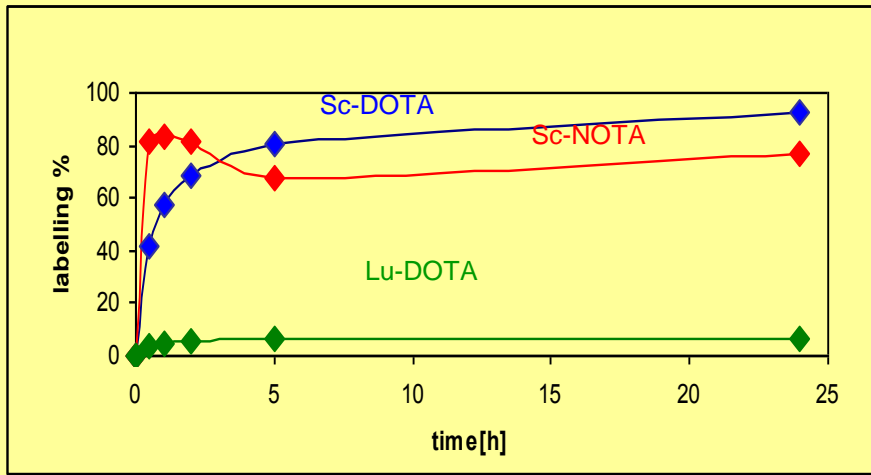
Sc-DOTA

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

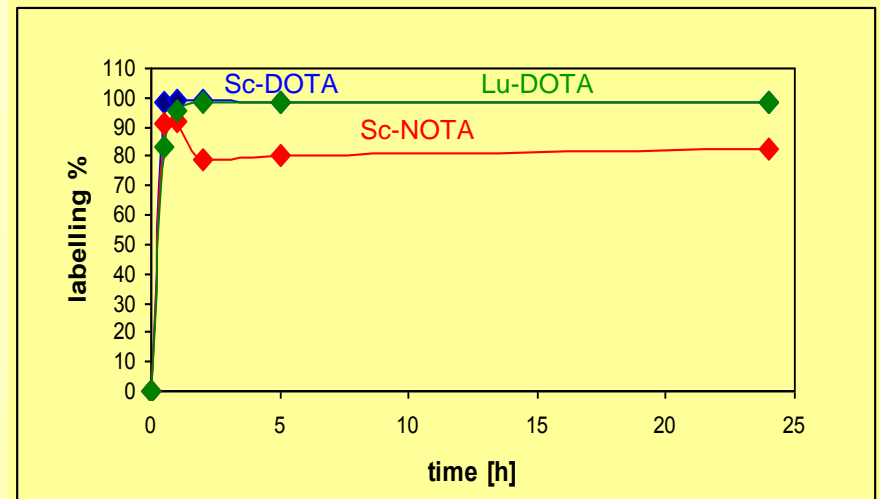
metal:ligand	labelling %
1:1	88.3
1:2	98.3
1:5	98.2
1:10	98.8
1:20	99.1

Kinetics



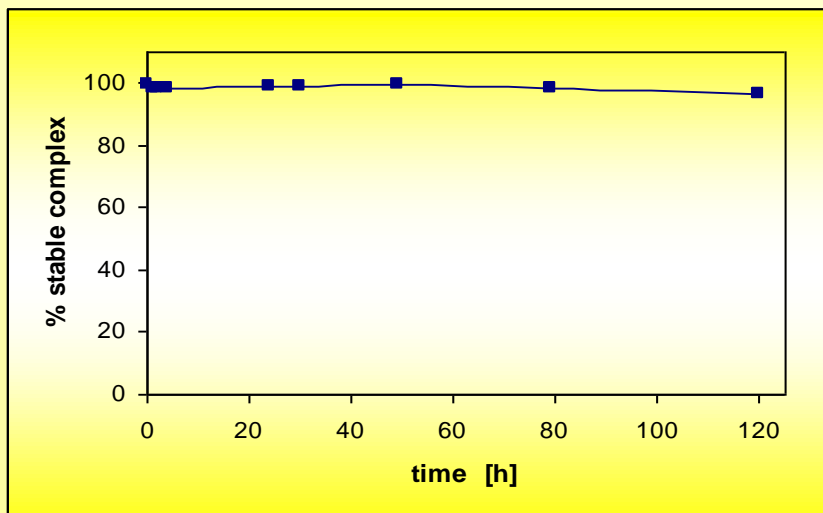
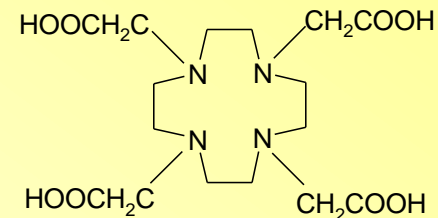
$T=20^{\circ}\text{C}$, $\text{pH}=1,5$

$T=70^{\circ}\text{C}$, $\text{pH}=1,5$

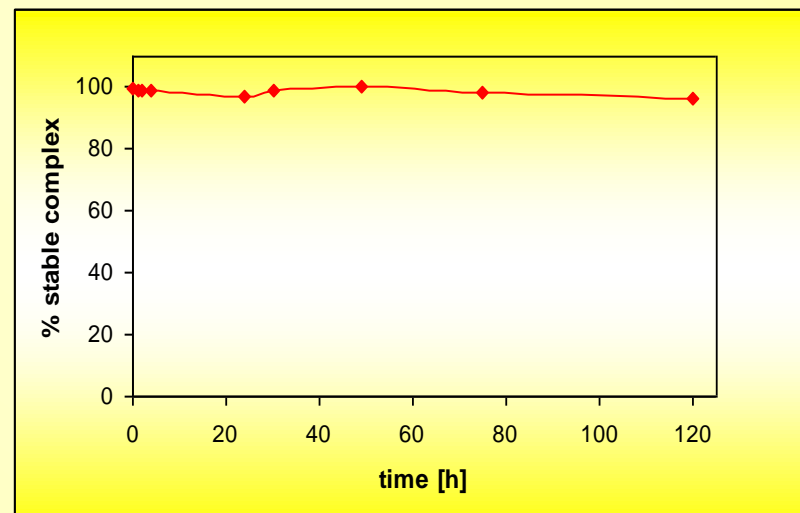


Examination of stability

Sc-DOTA

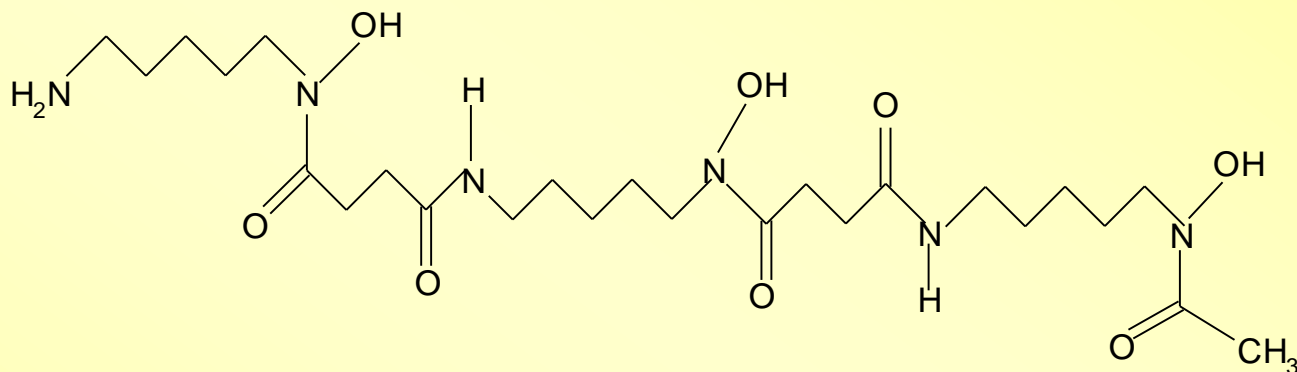


SERUM

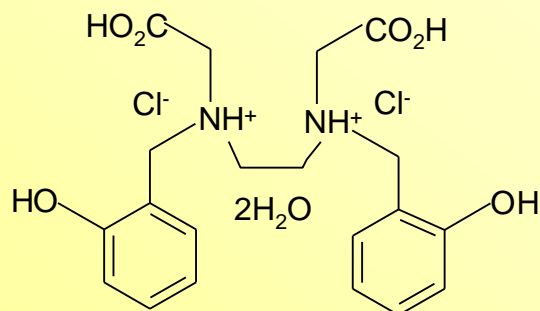


PBS

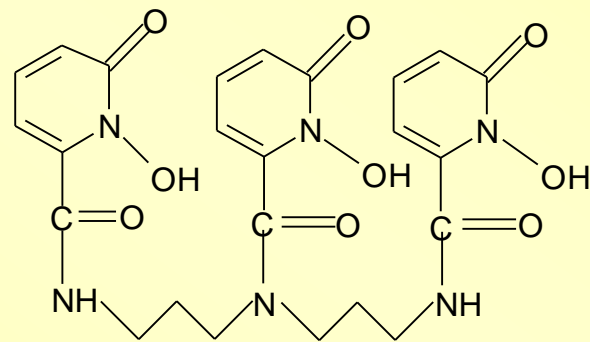
Alternative acyclic ligands



desferrioxamine (DFO)



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



LICAM



Thank you for
your attention