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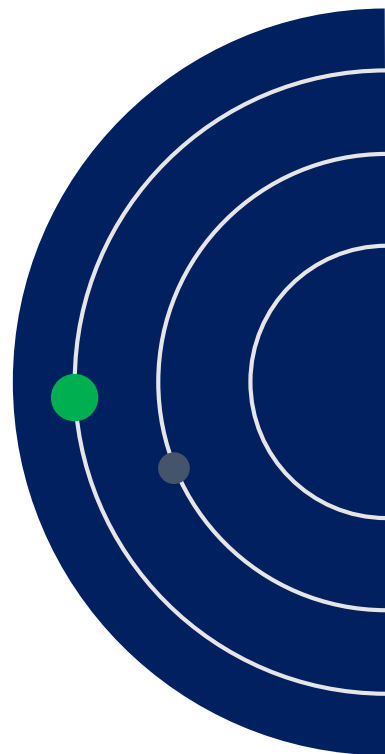
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# Optimization of the Separating Resin for establishing a $^{103}\text{Ru}/^{103\text{m}}\text{Rh}$ Generator

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# Optimization of the Separating Resin for establishing a $^{103}\text{Ru}/^{103\text{m}}\text{Rh}$ Generator

## I – Context

- A- Auger electron for Targeted Radionuclide Therapy
- B-  $^{103\text{m}}\text{Rh}$  : potential candidate for Auger therapy
- C-  $^{103\text{m}}\text{Rh}$  : production via generator

## II – Evaluation of Ru/Rh separation with chelating resin

- A- Literature review
- B- Retention Evaluation : Batch experiments
- C- Column tests : generator simulation
- D- Column tests :  $\text{Ru}^{\text{III}}$  retention evaluation

## III – Conclusion and outlooks

# I – Context

## Auger electron for Targeted Radionuclide Therapy

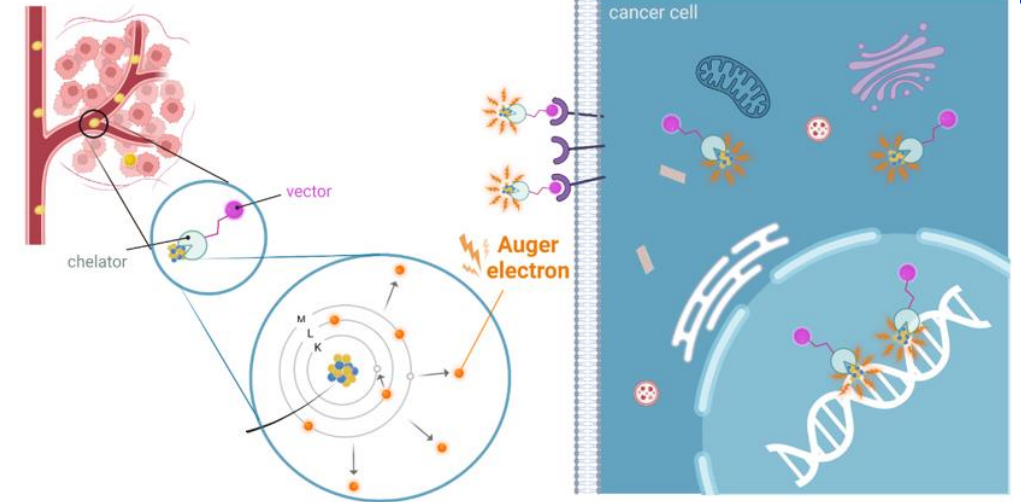
Auger and conversion emission can be applied for Targeted Radionuclide Therapy

→ Very selective treatment on the level of individual cell

		<ul style="list-style-type: none"> <li style="margin-right: 10px;"><span style="color: red;">●</span> PET</li> <li style="margin-right: 10px;"><span style="color: blue;">●</span> Beta Therapy</li> <li style="margin-right: 10px;"><span style="color: green;">●</span> SPECT</li> <li style="margin-right: 10px;"><span style="color: yellow;">●</span> Alpha Therapy</li> <li style="margin-right: 10px;"><span style="color: purple;">●</span> Auger e<sup>-</sup> Therapy</li> </ul>																																	
1	H																	2	He																
3	Li	4	Be																	10	Ne														
11	Na	12	Mg																	18	Ar														
19	K	20	Ca	21	Sc	22	Ti	23	V	24	Cr	25	Mn	26	Fe	27	Co	28	Ni	29	Cu	30	Zn	31	Ga	32	Ge	33	As	34	Se	35	Br	36	Kr
37	Rb	38	Sr	39	Y	40	Zr	41	Nb	42	Mo	43	Tc	44	Ru	45	Rh	46	Pd	47	Ag	48	Cd	49	In	50	Sn	51	Sb	52	Te	53	I	54	Xe
55	Cs	56	Ba	57-71	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		
87	Fr	88	Ra	89-103	Rf	Db	Sg	Bh	Hs	Mt	Ds	Rg	Cn	Nh	Fl	Mc	Lv	Ts	Og																

*Lanthanoids	57	58	59	60	61	62	63	64	65	66	67	68	69	70	71
	La	Ce	Pr	Nd	Pm	Sm	Eu	Gd	Tb	Dy	Ho	Er	Tm	Yb	Lu
**Actinoids	89	90	91	92	93	94	95	96	97	98	99	100	101	102	103
	Ac	Th	Pa	U	Np	Pu	Am	Cm	Bk	Cf	Es	Fm	Md	No	Lr

[2] T. I. Kostelnik and C. Orvig, *Chem. Rev.*, 2019, **119**, 902–956.



[1] J. Bolcaen and al., *JNudMed.*, 2023

### Criteria for potent candidates

**Dosimetry consideration** : high level of electrons with energy less than 50 keV

**Half-life**

**Availability of the radionuclide/Production**

**Chemical procedure for the radiopharmaceutical preparation**

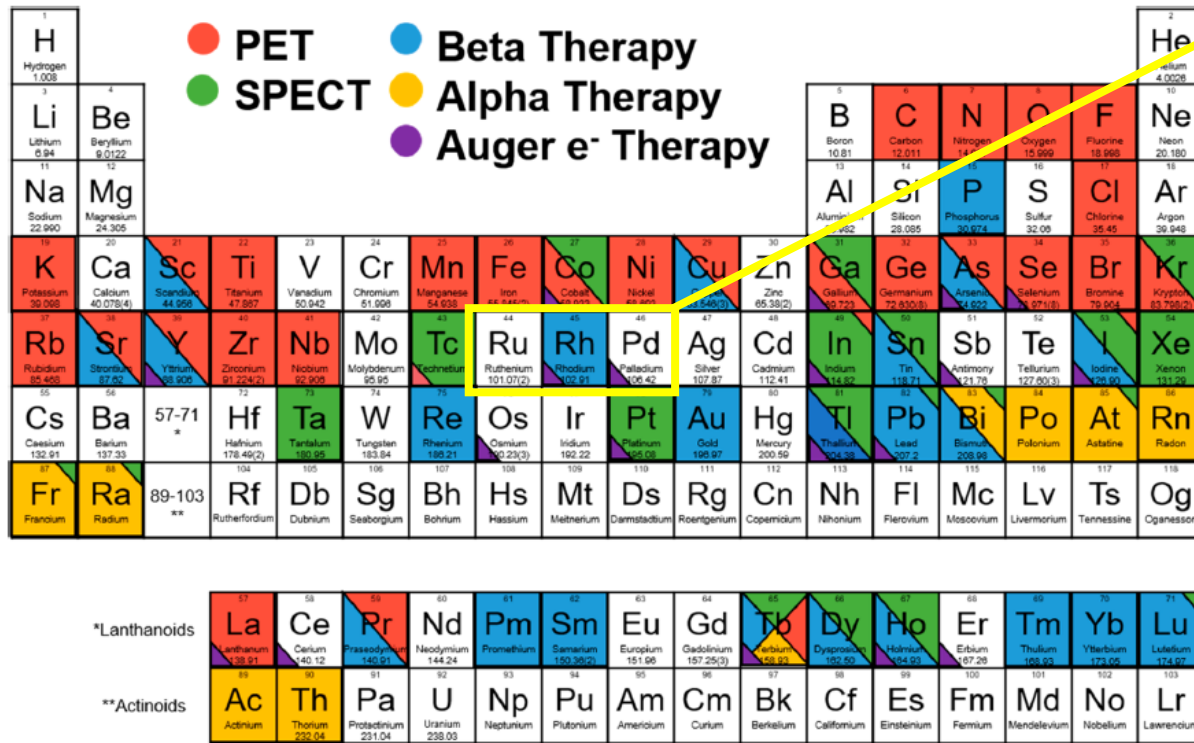
→ <sup>119</sup>Sb, <sup>71</sup>Ge, <sup>58m</sup>Co, <sup>189m</sup>Os, <sup>103m</sup>Rh, <sup>103</sup>Pd, <sup>191g</sup>Os, <sup>161</sup>Ho, <sup>197</sup>Hg, <sup>239</sup>Am, <sup>177</sup>Ta, <sup>189</sup>Ir, <sup>155</sup>Tb, <sup>201</sup>Tl, <sup>125</sup>I and few other. [1]

# I – Context

## $^{103m}\text{Rh}$ : potential candidate for Auger therapy

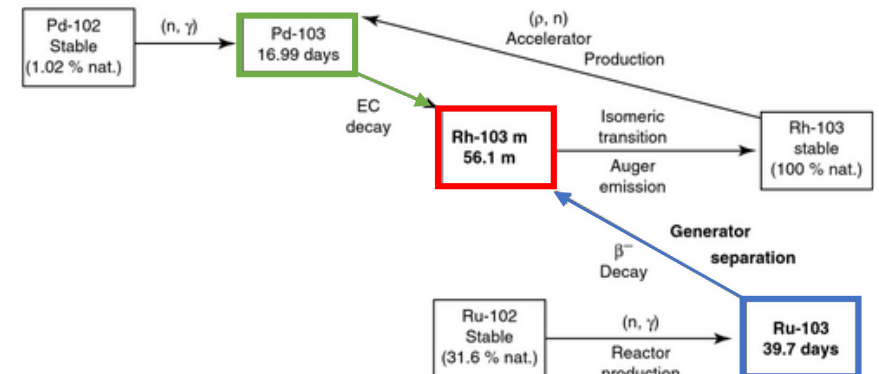
$^{103m}\text{Rh}$  (56,1 min) : identified as a very promising therapeutic Auger electron emitter

- High electron-to-photon yield
- Associated gamma emissions are negligible (avoids non-specific irradiation)
- Decay on a stable nucleus ( $^{103}\text{Rh}$ )
- Short half-life = higher dose rate



[2] T. I. Kostelnik and C. Orvig, *Chem. Rev.*, 2019, **119**, 902–956.

Can be obtained from  $^{103}\text{Ru}$  or  $^{103}\text{Pd}$

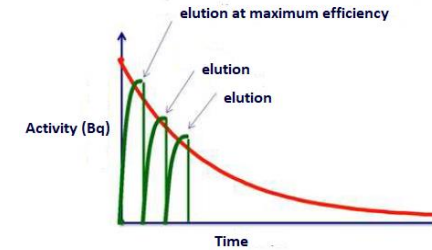
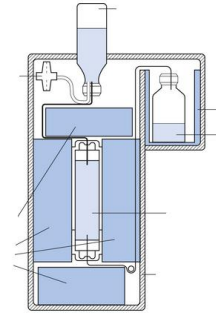


[4] Vértés, A. and al. ; *Handbook of Nuclear Chemistry* : Vol. 1.

# I – Context

$^{103m}\text{Rh}$  : production via generator

$^{103m}\text{Rh}$  : a short half-life (56,1 min)



Radionuclide Generator

## $^{103}\text{Pd}/^{103m}\text{Rh}$ Generator

*More famous*

- **Abundance of  $^{102}\text{Pd}$  in  $^{\text{nat}}\text{Pd}$  is very low (1,02%) : reactor production is difficult**
- **More suitable separation characteristics ( and more studies)**
- $t_{1/2} = 17,0$  days for  $^{103}\text{Pd}$
- **No gamma ray emission for  $^{103}\text{Pd}$  = no indication of its presence**
- ***in vivo* generator possible**



## $^{103}\text{Ru}/^{103m}\text{Rh}$ Generator

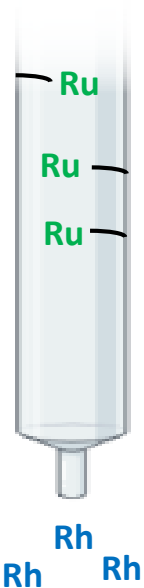
*Our work*

- **Several ways to produce  $^{103}\text{Ru}$**  (neutron irradiation of  $^{\text{nat}}\text{Ru}$  or  $^{\text{nat}}\text{U}$ , from  $^{99}\text{Mo}$  production,...)
- **$^{103}\text{Ru}$  easily produced in large quantities (neutron activation of Ru)**
- **Complex chemical behavior**
- **$t_{1/2} = 39,7$  days for  $^{103}\text{Ru}$**
- **Gamma ray  $^{103}\text{Ru}$  : 610 keV**

## II – Evaluation of Ru/Rh separation with chelating resin

**Main goal :** Find an effective way of separating Ru and Rh (using a chromatographic system, in chlorinated media)

**Not an easy task**



Very similar chemistries  
*neighbour in the periodic table*

44 101.1 <b>Ru</b> Ruthenium Transition Metal	45 102.9055 <b>Rh</b> Rhodium Transition Metal	46 106.42 <b>Pd</b> Palladium Transition Metal
76 190.2 <b>Os</b> Osmium Transition Metal	77 192.22 <b>Ir</b> Iridium Transition Metal	78 195.08 <b>Pt</b> Platinum Transition Metal

Complex chemistries

*Mixture of species with different charges, polynuclear species, colloids...*

**Lack of data on Ruthenium chemistry in HCl and aqueous medium**



Ruthenium speciation (my first thesis work ;  
Poster S.Huclier)

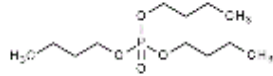


## II – Evaluation of Ru/Rh separation with chelating resin

### A- Litterature review

#### Liquid-liquid separation

- $\text{CCl}_4$  as organic phase + oxidising agent (*Epperson and al / Chiv and al*)
- Tri-n-butyl phosphate (*Haasbroek and al*)



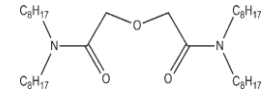
#### Combinaison of solvent extraction and evaporation via $\text{RuO}_4$

$^{103}\text{Ru}/^{103\text{m}}\text{Rh}$  generator proposed by Bartos and al.



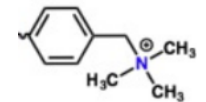
#### Resins tested: poor retention of Ru/ no real separation

- DGA resin Triskem<sup>®</sup> in  $\text{HCl}$  or  $\text{HNO}_3$  : retention  $\text{Ru} < 50\%$



- Amberlite IRA400  $\text{Cl}^-$  ,  $\text{HCl}$  2M + oxidising condition (*Berman al al.*)

$\alpha_{\text{Ru/Rh}} \approx 10$

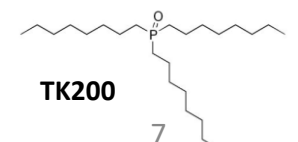
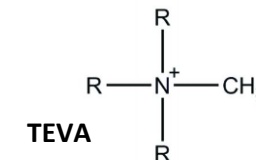


#### Optimal conditions :

Use of chelating resin (more specific)  
Separation based on the difference in the degree of oxidation ; via  $\text{Ru(IV)}$  and  $\text{Rh(III)}$



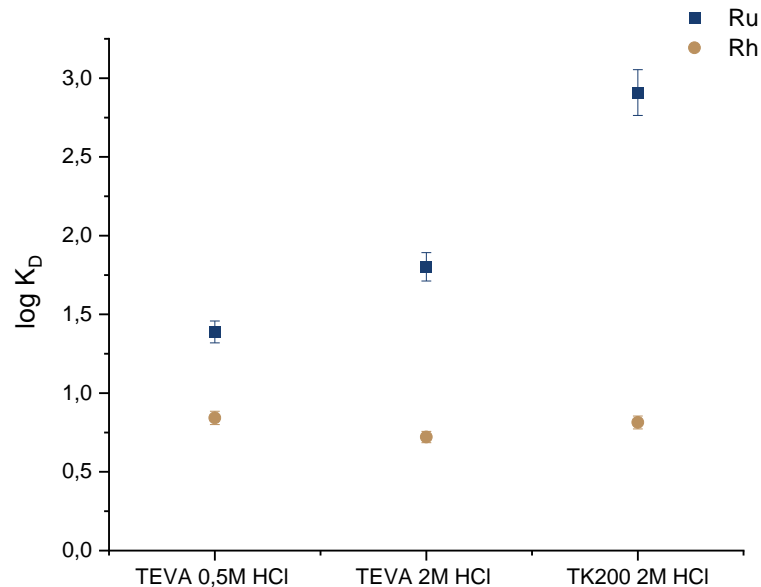
#### Triskem<sup>®</sup> TEVA and TK200





## II – Evaluation of Ru/Rh separation with Triskem<sup>®</sup> chelating resin

### B- Retention Evaluation : Batch experiments



$$\alpha_{Ru/Rh} = \frac{K_{D Ru}}{K_{D Rh}}$$

	%Ru on resin	%Rh on resin	$\alpha(Ru/Rh)$
TEVA 0,5M HCl	32±1%	17±1%	~3
TEVA 2M HCl	49±2%	12±1%	~7
TK200 2M HCl	97±7%	0,5 ±0,3%	~1600

Comparison of Ru and Rh retention on different Triskem resins ;  $m_{résine} = 250mg$  ; contact time =24h ; element concentration determined by ICP-MS measurment.

**TK200 Triskem resin in 2M HCl = best candidate**  
But slight retention of Rh on resin possible

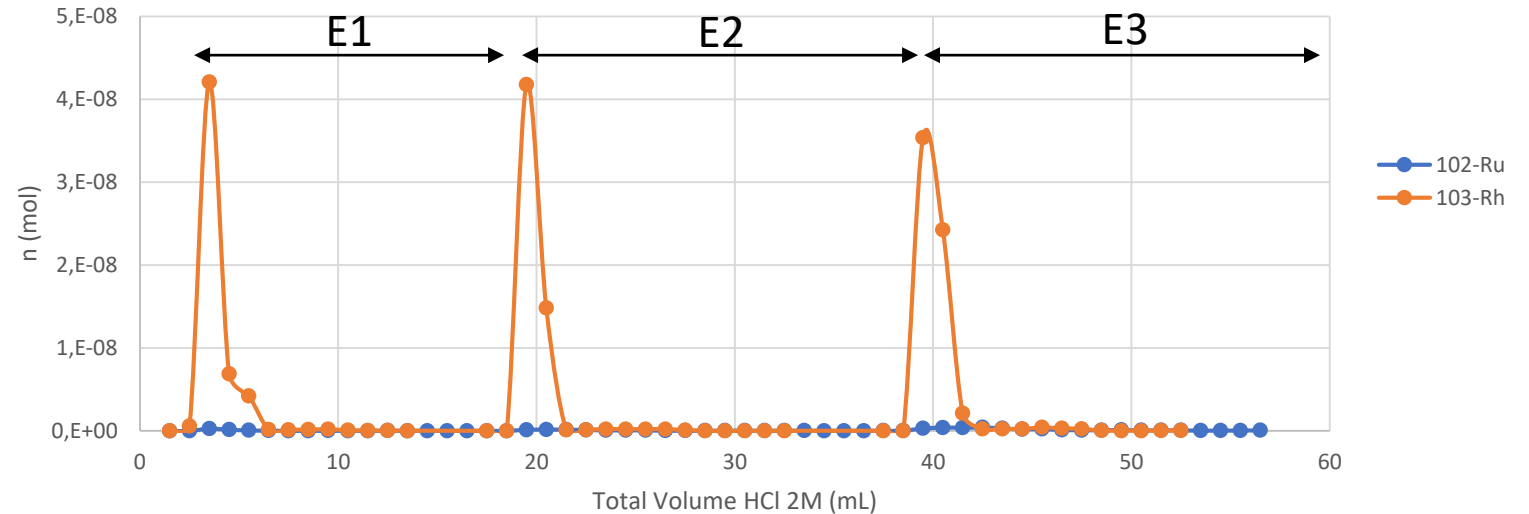


**First tests in column  
Ru/Rh generator simulation**

## II – Evaluation of Ru/Rh separation with Triskem<sup>®</sup> chelating resin

### C- Column tests : generator simulation

**Conditions**  
 $n_{Ru} = n_{Rh} \sim 5.10^{-8}$  mol (generator simulation with  
 A= 100-200 MBq)  
 1 load of Ru / 3 load of Rh  
 V=1mL  
 2M HCl  
 $m_{resin} = 1,51g$   
 81,5 $\mu$ L/min  
 Quantification by ICP-MS



	E1	E2	E3
<b>Age (day)</b>	0	1	7
<b>Ru breakthrough (%)</b>	1,74±0,07%	2,6±0,2%	7,4±0,3%
<b>Rh eluted (%)</b>	80,5±0,6%	86±3%	94±3%



Slight retention of Rh on resin

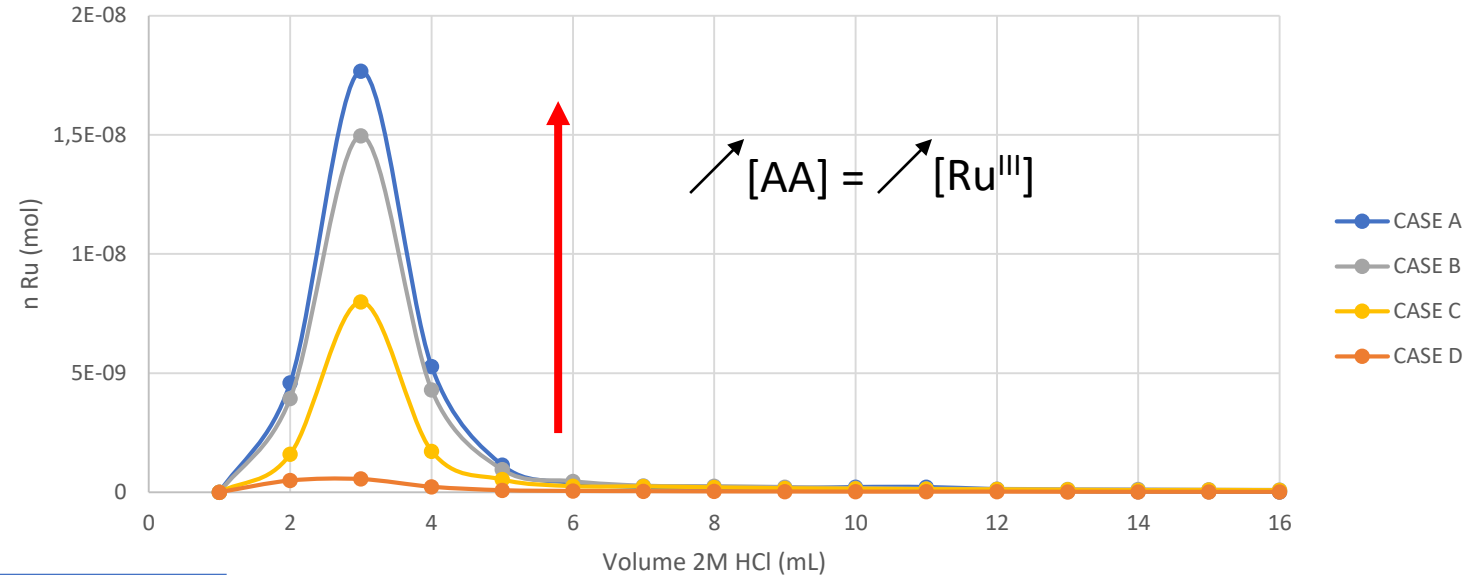
Ruthenium breakthrough increase with time

Hypothesis : partial reduction of Ru(IV) to Ru(III), not retained ??

## II – Evaluation of Ru/Rh separation with Triskem<sup>®</sup> chelating resin

### D- Column tests : Ru<sup>III</sup> retention evaluation

**Conditions**  
 $n_{Ru} \sim 5.10^{-8}$  mol (generator simulation with  
 A= 100-200 MBq)  
 V= 500 $\mu$ L  
 2M HCl  
 $m_{resin} = 1,01$  g  
 1mL/min  
 Variable ascorbic acid concentration :  
 Quantification by ICP-MS

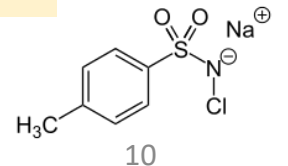


CASE	[AA] (mol/L)	Supposed %Ru(III)	% Eluted Ru
A	$1,2.10^{-2}$	100%	80 $\pm$ 5
B	$3,75.10^{-5}$	50%	55 $\pm$ 5
C	$1,87.10^{-5}$	25%	28 $\pm$ 5
D	0	?	5 $\pm$ 5

Ru<sup>III</sup> not retained on TK200  
 Partial reduction of Ru<sup>IV</sup> in 2M HCl

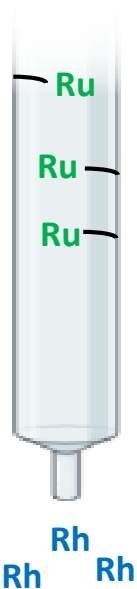
**Use an oxydant** to ensure that all Ru is in Ru<sup>IV</sup> form ( $1,0 \text{ V} < E^\circ < 1,3 \text{ V}$ )

Experiments are in progress with Chloramine-T as oxydant



### III – Conclusion and outlooks

**Main goal :** Find an effective way of separating Ru and Rh (using a chromatographic system, in chlorinated media)



- TK200 seems to be the best candidate  $\longrightarrow \alpha_{\text{Ru/Rh}} \sim 1600$
- **Tests in column (Ru/Rh generator simulation)** : Slight retention of Rh + Ru breakthrough (increase with time)
- **Test retention Ru(III) on TK200** : Ru(III) not retained + partial reduction of Ru(IV) in HCl 2M

#### Outlooks

- Tests with an oxydant (e.g Chloramine-T) to ensure Ru<sup>IV</sup> form
- First tests with <sup>103</sup>Ru

**Thank you for your attention !**