



Contribution ID: 361

Type: Poster

## Chemical and biological studies on $^{105}\text{Rh}$ -labelled tetrathioethers conjugated to TATE

Thursday, May 15, 2014 5:30 PM (1h 15m)

**Objectives:** In clinical practice, there is a demand for no-carrier-added radionuclides emitting particles of short range that demonstrate a therapeutic effect on small neoplastic lesions diffuse over a large area of tissue or tumour metastases. Rhodium-105 meets all requirements for application in radionuclide therapy [1] and might be an alternative to  $^{177}\text{Lu}$ . Tetrathioether crown complexes with  $^{105}\text{Rh}$  have been generally considered as candidates for radiopharmaceutical precursors to be combined with carrier biomolecules. The aims of our work were: (i) synthesis of  $^{105}\text{Rh}$  labelled bioconjugates with bifunctional acyclic (333S4diAcOH) and cyclic (16S4COOH) tetrathioether ligands conjugated to [Tyr3]octreotate, (ii) studies of their properties and (iii) conduction of in vitro experiments on cell line AR42J.

**Methods:** Rhodium-105 was obtained by neutron activation of ruthenium salt,  $(\text{NH}_4)_2[\text{Ru}(\text{H}_2\text{O})\text{Cl}_5]$ , for 8 h with flux of  $7 \cdot 10^{13} \text{ n}\cdot\text{cm}^{-2}\cdot\text{s}^{-1}$  in the Maria reactor in Świerk, Poland.  $^{105}\text{Rh}$  was separated from the ruthenium target material by method described previously [2].

Acyclic ligand was synthesised through 1,5,9,13-tetrathiatridecane intermediate and 16S4COOH by method previously described [3]. The ligands were combined with N-hydroxysuccinimide to obtain active esters, which were subsequently conjugated with N-terminus of TATE. The respective products were isolated and analyzed by MS, NMR and elemental analysis.

**Results:** The bifunctional ligands were synthesized with total reaction yield of 21% and 1% for 333S4diAcOH and 16S4COOH, respectively. The active esters and bioconjugates were obtained in high yield. The last step of synthesis was cleavage of Dde protecting group from Lys.

The complex  $[\text{RhCl}_2(16\text{S4COTATE})]^+$  was obtained as reference material for HPLC. The bioconjugates were labelled with  $^{105}\text{Rh}$ , their distribution coefficients were measured. For bioconjugate  $[\text{}^{105}\text{Rh}(16\text{S4COTATE})]^+$ , the stability in PBS, Cys, GSH and human serum was examined, and the kinetics of internalization into AR42J cells was set.

**Conclusions:** The use of  $^{105}\text{Rh}$ -labelled tetrathioether precursors conjugated to peptides in radionuclide therapy seems possible, but requires further biological studies. Good stability of  $^{105}\text{Rh}$ -labelled bioconjugate 16S4COTATE in human serum with a high degree of its internalization meet the requirements for potential receptor radiopharmaceuticals.

**Research Support:** The work has been carried out within the system project "The scientific potential as support to the economy of Mazovia - scholarships for doctoral students" under Sub-measure 8.2.2 Human Capital Operational Programme 2007-2013.

**References:** [1] Grażman B., Troutner D. E., (1988) Appl Radiat Isot, 39, 257, [2] Krajewski S., Bilewicz A., (2010) J Radioanal Nucl Chem, 285, 293, [3] N. Goswami, C. Higginbotham, et al., (1999) Nucl Med Biol, 26, 951.

**Primary author:** Dr KRAJEWSKI, Seweryn (Institute of Nuclear Chemistry and Technology, Warsaw, Poland)

**Co-authors:** Prof. BILEWICZ, Aleksander (Institute of Nuclear Chemistry and Technology, Warsaw, Poland); Mrs LASZUK, Ewa (National Centre for Nuclear Research, Świerk, Poland); Dr PRUSZYŃSKI, Marek (Institute of Nu-

clear Chemistry and Technology, Warsaw, Poland); Dr GARNUSZEK, Piotr (National Centre for Nuclear Research, Świerk, Poland); Prof. MIKOŁAJCZAK, Renata (National Centre for Nuclear Research, Świerk, Poland); Dr KARCZYK, Urszula (National Centre for Nuclear Research, Świerk, Poland); Dr WOJDOWSKA, Wioletta (National Centre for Nuclear Research, Świerk, Poland)

**Presenter:** Dr KRAJEWSKI, Seweryn (Institute of Nuclear Chemistry and Technology, Warsaw, Poland)

**Session Classification:** Poster Session - Radiopharmaceutical Chemistry, Labelled Compounds

**Track Classification:** Radiopharmaceutical Chemistry, Labelled Compounds