DEVELOPMENT OF A RHODIUM TETRATHIOETHER BOMBESIN ANALOGUE AND INVESTIGATION OF CYCLIC AND ACYCLIC LIGAND SYSTEMS FOR $^{105}$RHODIUM (III)

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ABSTRACT

Rhodium-105 is an attractive nuclide for radiotherapeutic applications due to its nuclear properties (566 keV $\beta^-$, 319 keV [19%], 306 keV [5%]) and the kinetic stability of Rhodium (III) complexes with soft sulfur donor atoms. Extension of previous research involving tetrathioether chelate systems to include a targeting molecule may have implications for prostate cancer therapy. This work reports on the synthesis and evaluation of a new bombesin peptide targeted Rh (III) tetrathioether analogue, $\text{[Rh-S4-8Aoc-BBN(7-14)NH}_2\text{]+}$, which shows high affinity for the BB2r receptor on PC-3 cancer cells ($\text{IC}_{50} = 2.2 \pm 0.3 \text{ nM}$). However, multiple $^{105}$Rh labeled species were obtained under the radiolabeling conditions investigated.

To better understand the results observed for $^{105}\text{Rh-8Aoc-BBN(7-14)NH}_2\text{]+}$, the chemistries of previously investigated $\text{[Rh-S4-Diol]+}$ and $\text{[Rh-S4-(COOH)$_2$]+}$ were re-evaluated using more recently available techniques. A quantitative evaluation of the $\text{[Rh-S4-Diol]+}$ and $\text{[Rh-S4-(COOH)$_2$]+}$ systems using NMR, ESI-MS and HPLC reveals formation of multiple species resulting from both exchange of the coordinated chlorides at the metal center and esterification of pendant carboxylate groups. While a predominate trans-chloro Rh(III)-S4 species may be favored by addition of excess NaCl, both ethanol and acid are required for radiolabeling. Thus, ligand systems utilizing pendant carboxylate groups are not compatible with traditional $^{105}$Rh radiolabeling techniques. Future studies involving a $^{105}$Rh tetrathioether bombesin analogue without pendant carboxylate groups are recommended.