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Labeling and purification studies on cancer targeting DOTA-TATE labeled with radiolanthanides

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Molecular imaging and targeted radiotherapy are emerging fields for cancer treatment. DOTA-Tyr (3)-Thr(9)-octreotate (DOTA-TATE) is used for peptide receptor-mediated radionuclide therapy (PRMRT) in neuroendocrine tumours. These biomolecules can be radiolabeled with an appropriated radioisotope to produce radiopharmaceuticals for diagnostic and therapeutic applications. The DOTA-TATE molecule is comprised of a bifunctional chelate (DOTA) that is capable of stably binding a radiolanthanide as well as being covalently attached to a targeting biomolecule (e.g.,octreotate). Among the radiolanthanides, Ho-166, Tb-161 and Lu-177, that were used to label the peptide, Lu-177 was used to obtain optimum conditions. Direct neutron capture on Lu-176 produces Lu-177. The indirect production of Lu-177 proceeds by neutron capture on Yb-176 producing Yb-177, which beta decays to Lu-177. Chromatographic separation yields high specific activity Lu-177 that minimizes the presence of cold Lu-176. Lanthanides have similar chemical properties that allow further studies to apply similar conditions as those developed for Lu-177. In addition, longevity of half-life of Lu-177 enables longer periods of dose delivery to targeted tumors. This research focused on identifying appropriate buffer solutions and volumes that could neutralize the acidic radioisotope to appropriate pH levels to label the peptide in high yield. The sample was purified from the unlabeled peptide by using HPLC separations methods and adding stabilizing agents (ascorbic and gentisic acid) to prevent radiolysis of the radiolabeled peptide. The results for the labeled peptide with various radioisotopes shows that 0.4 M NH4OAc, 0.4 M NaOAc, and 0.01 M HEPES buffer solution in 500 µL yields 99% labeling at pH ranging from 6.0 to 7.5. The labeled ligand at equimolar ratio with the metal yields 3 mCi/µg of the ligand, whereas as high specific activity sample can label up to 6.68 mCi/µg of the ligand. Carrier free Lu-177-DOTA-TATE was labeled using 0.01 M HEPES buffer at pH 6.0 and remains stable after using ascorbic acid; gentisic acid shows interference on HPLC which may cause some purification problems. (Ho-holmium, Tb- terbium Lu- lutetium)