Poster Presentations - Physicians/Scientists/Pharmacists
Radiopharmaceutical Chemistry Track

^{99m}Tc-Asymmetrical nitrido complex of annexin analog and RGD analog

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Objectives: Peptides containing the RGD sequence have been evaluated in cancer due to their affinity to $\alpha_v ß_3$ integrin expressed during tumor angiogenesis, and integrin may be used for the same purpose . The aim was to study labeling procedures for cyclic RGD analog (c(Arg-Gly-Asp-D-Tyr-Lys) and Annexin analog (Ala-Glu-Val-Leu-Arg-Gly-Thr-Val-Thr-Asp-Phe-Pro-Gly-OH) derivatized with cysteine residue in the molecule using the ^{99m}Tc-nitrido core by an asymmetrical method.

Methods: Radiolabeling was conducted by adding Na^{99m}TcO$_4$ to a vial containing commercial freeze-dried formulation for preparation of ^{99m}Tc-nitrido intermediates (CIS Bio International,Schering). The vial was left standing 30 min at room temperature. Then diphosphine dissolved in ethanol was simultaneously added with the ligand to the precursor vial.The reaction mixture was incubated for one hour at 100^{o}C. Radiochemical evaluation of ^{99m}TcN precursor and ^{99m}TcN(PNP6)-Cys-peptides was performed using ITLC-SG with a solvent system Ethanol/Chloroform/Toluene/Ammonium Acetate 0.5 M (E/C/T/AA, 5; 3; 3; 0.5) and ethyl acetate. Radiochemical stability of the compounds till 6h and transchelation to cysteine (0.1 to 100 mM) during 4 hours, as well partition coefficient was also evaluated.

Results: By comparing TLC analysis with HPLC profiles and filtration by SepPak cartridge, radiochemical species were determined. Radiochemical purity of ^{99m}TcN(PNP)Cys-RGD and ^{99m}TcN(PNP)Cys-Annexin conjugate were very similar,around 92%. Total labeling procedure took 1.45 hour. ^{99m}TcN-RGD complex as well ^{99m}TcN-Annexin complex showed good stability for 6 hours, with a loss of purity of just 6%. They were also quite inert regarding transchelation by free cysteine. Only ^{99m}TcN-RGD was relatively more suscetible to cysteine challenge , with a reduction of 4.7%. The partition coefficient for the complexes determined in octanol and phosphate buffer showed the same value of 0.36, within the hydrophilic range.

Conclusions: Asymmetrical labeling with a nitrido core was successfully performed in the presence of phosphine coligand. Both annexin analog and RGD analog displayed favorable stability properties, with a small advantage for the former molecule. Biological studies in animal models may now be considered.

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