Poster Presentations - Physicians/Scientists/Pharmacists
Radiopharmaceutical Chemistry Track

Optimization and stability studies of thymidine analog complex with organometallic core

Rodrigo Santos[1], Bluma Faintuch[1], Rodrigo Teodoro[1], Ivane Nunes[1] and Roger Schibli[2]

[1] Radiopharmacy Center, Institute of Energy and Nuclear Research, Sao Paulo, SP, Brazil [2] Center of Radiopharmacy, Paul Scherrer Institute, Villigen, ZU, Switzerland

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Objectives: Radiolabeled thymidine analogs can be used to track rapidly proliferating tumor cells . For the current study thymidine was functionalized at the C5'position of the sugar moiety with the tridentate iminodiacetic acid chelator for complexation and radiolabeling with ^{99m}Tc(I)-tricarbonyl core. The aims were optimization of the labeling procedure and analysis of stability of the radiolabeled compound.

Methods: The precursor $^{99m}Tc(H_2O)_3(CO)_3$ was prepared by flushing the mixture of sodium carbonate, sodium borohydride and sodium-potassium tartrate tetrahydrate with CO gas during 30 min. Pertechnetate was added and the vial was heated for 35 min at 75 ^{o}C. The reaction was stopped in ice bath, and pH was adjusted to 7. Then 50 uL of the precursor was added to 10^{-4} M of the ligand and heated again for 60 min at 75 ^{o}C. Radiochemical purity of the precursor and the product was checked by HPLC, TLC and paper chromatography. Optimization was achieved by varying reaction time (30 to 60 min),ligand concentration ($0.5.10^{-4}$ to $2.5.10^{-4}$ Mol/L), final reaction volume (300 to 500 µL) and total activity(170 to 1330 MBq). Radiochemical stability (24 hours), in- vitro stability in human plasma, and response to cysteine challenge at different molar ratios was also evaluated.

Results: Radiochemical purity (RP) with reaction time of 30 minutes was 90.7 +/- 1.6%, and by one hour it reached 93.2+/-1.4 %, using a concentration of thymidine analog of $0.5.10^{-4}$ Mol/L.By increasing the ligand concentration to $2.5.10^{-4}$ Mol/L, 94.1+/-1.7% of RP was achieved. Reduction of final reaction volume or elevation of activity resulted in no improvement. The complex was stable for 24 hours with loss of 4% of RP only. Stability test in human plasma during 4 hours showed a decrease of 26%, and stability regarding cysteine from 0.1 mM to 100 mM diminished from 97.3+/- 0.5% to 88.7+/- 0.8%, respectively.

Conclusions: Favorable labeling conditions could be established, with relatively few changes when reaction parameters were modified. Radiochemical stability was excellent, but tests with plasma and cysteine yielded somewhat weaker results. Nevertheless, the final product is suitable for biological studies *in vivo*.

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