In house production of ^{99m}Tc-EDDA-HYNIC-[Tyr$_3$]-octreotide

for somatostatin receptor scintigraphy

M. Almangano (1); S. Filippone(1); K. Marzo (1); G. Vale Gomes (2); M. Marycel Figols (3); A. Chiti (1)

(1) Nuclear Medicina Department, Istituto Clinico Humanitas, Milano, Italy

(2) Nucleos, Brasilia, Brazil

(3) Radiopharmacy Center – IPEN/CNEN, São Paulo, Brazil

Aim: Scintigraphy using ^{111}In-diethylene-triamine-penta-acetic-acid-D-Phe1-octreotide (DTPA-octreotide) gained widespread acceptance. Radio-labeling of peptides with indium-111 as has some drawbacks, including suboptimal gamma energy. Recently, a new technetium labeled peptide was developed. The somatostatin analogue is an octreotide derivative with high specific tumor uptake, and showed promising results in the detection of neuroendocrine tumors.

Methods: Reagents were purchased from Sigma-Aldrich.

HYNIC-[Tyr3]-octreotide (HYNIC–TOC) was purchased from PiChem.

$^{99m}TcO_4^-$ was obtained from commercial ^{99}Mo/^{99m}Tc generator produced by G.E. Healthcare

Radio-labeling experiments were performed using the protocol issued by the University Hospital of Innsbruck.

Overall the following formulation and labeling conditions with reproducible labeling yields of >90% were established: 20 mg HYNIC–TOC, 10mg EDDA, 20 mg tricine, 10 mg $SnCl_2$. $2H_2O$, pH 6.5–7.5, labeled with 1200 MBq $^{99m}TcO4^-$ in a total volume of 2 ml, reaction time: 10 min in boiling water.

Quality control was performed as follows:

HPLC: Reaction solutions were tested for radiochemical purity by HPLC.

Column: Dionex Acclaim 300 ODS 5 μm, 4.6 mm x 250 mm.

Mobile phase: linear gradient of increasing concentrations of ACN in 0.01 *N* phosphate buffer pH 6,2: 0–3 min 0% ACN, 3–5 min 0% 25% ACN, 5-18 min 25% ACN, 18–22 min 25%–70% ACN, 22–24 min 70%, 24-25 70%–0% ACN 25-30 min 0% ACN. Flow rate: 1 ml/min.

Detection: a sodium-iodide detector interfaced to a multichannel analyzer (Raytest).

Thin-layer chromatography: instant thin-layer chromatography on silica gel (ITLC-SG, Gelman Sciences) was performed using different mobile phases.

Sep-Pak Purification: A C-18-SepPak-Mini cartridge (Waters) was activated using 5 ml ethanol, followed by 5 ml of water and 5 ml of air. The radiolabeling mixture was passed through the cartridge which was then washed with 5 ml of water. The radiolabelled peptide was eluted with 1 ml ethanol and 1 ml of water.

Results: This method of preparation has been safely used in more than 30 patients in our Department with always a purity yield of more than 95% with a preparation time of approximately 30 minute.

Conclusion: The high specific tumor uptake, rapid blood clearance, and predominantly renal excretion make ^{99m}Tc-EDDA-HYNIC-TOC a promising candidate for an alternative to 111In-DTPA-octreotide for tumor imaging.