IAEA-SR-209/14

Preparation, quality control and animal test of ^{153}Sm DTPA-Octreotide

Fan Hongqiang Jin Xiaohai Bai Hongsheng Wang Fan Chen Daming
Isotope Department China Institute of Atomic Energy, P.O. Box 275(58), 102413, Beijing, CHINA

Somatostatin is a 14 amino acid containing peptide. The native hormone is susceptible to rapid enzymatic degradation, therefore, it is not suitable for long-term therapeutic use. For that reason, synthetic derivatives with a similar bioactive structure as somatostatin have been developed, which are not only less susceptible to biologic degradation but also have a strange inhibitory effect on hormone release by the relevant tumors. This peptide has a large biologic half-life than somatostatin itself and, hence, prolonged inhibitory effects on normal growth hormone production. Large number of high-affinity binding sites for native somatostatin and synthetic octreotide have been defected on most endocrine active tumors. But octreotide cannot be radiolabeled easily with a gamma-emitting radionuclide, a synthetic analogue (tyr^3-octreotide) has been developed in which phenylalanine has been replaced by tyrosine allowing radioiodination of the molecule. This compound has been used successfully as an iodine-123 radioligand for in vitro and in vivo somatostatin receptor studies. The procedure is now performed using ^{111}In-DTPA-octreotide, a DTPA-coupled somatostatin analog, characterized by easy and efficient labeling, fast clearance and predominantly renal excretion, with only minimal hepatobiliary clearance. Furthermore, number of publications reporting on the use of other radioactive peptide for scintigraphic demonstration of various tumors and infectious processes. This work studied very litter of in this topic in China. But it is studied in labeling Tyr^3-octreotide with ^{131}I (^{125}I), and labelling DTPA-octreotide with ^{111}In, ^{99}Tc^m etc. Our research is to find the clinical agents for therapy of somatostatin receptor positive tumors. This report has done the research work of labelling DTPA-octreotide carrier-containing radionucides ^{153}Sm.

Materials and methods

DTPA-octreotide were obtained from Peptide Int. Japan. DTPA-octreotide was labelled in different molar ratios of Samarium-153. The radiochemical purity of labelled peptide was checked by HPLC with a Waters 600E multisolvent delivery system connected to a μ-Bondapak-C18 reversed-phase column (300 mm x 4.0 mm, particle size 10 μm). Elution was carried out at a flow of 1 ml/min, with a linear gradient of 40% to 80% methanol in 0.05 mol/L acetate buffer solution in 20 min and latter composition was maintained for another 5 min. Eluted was monitored on-line (pH=5.5, sample volume: 10 μl. flow pool volume: 150 μl) using a radioisotope monitor (EG&G Berthold).

Animal test: A rat (weight 15-18 g) was injected 0.1 ml ^{153}Sm-DTPA-octreotide (concentration: 0.1 mCi/ml) by tail vein. The rat was killed at different postinjection. Tissue distribution data showed that, I) Different molar ratios of ^{153}Sm-DTPA-octreotide was similar rate of metabolism in rats. II) The labeling compounds was dissociated in vivo. III) The dissociation in vivo changed with the molar ratio of ^{153}Sm-DTPA-octreotide IV) Low specific activity Samarium-153 labeled octreotide not a good idea for somatostatin receptor therapy.

Percent injected dose of ^{153}Sm-DTPA-octreotide per gram of tissue sample (%ID ± -SE, n=3)

Tissue	blood	liver	kidneys	lung	heart	spleen	adrenals	intestines	muscle
0.5 h	0.83	0.98	6.67	0.18	0.54	0.39	1.67	0.32	0.25
	0.79	1.34	5.86	0.19	0.46	0.67	1.14	0.57	0.32
	1.02	2.05	4.52	0.12	0.62	0.74	0.95	0.41	0.39
3 h	0.34	1.45	8.05	0.44	0.21	0.13	2.13	0.65	0.17
	0.28	4.41	6.32	0.35	0.34	0.22	1.85	0.24	0.24
	0.33	18.9	3.47	0.37	0.18	0.18	1.52	0.43	0.26
24 h	0.02	2.05	0.74	0.04	0.02	0.02	1.70	0.01	0.02
	0.02	3.47	0.45	0.05	0.02	0.04	1.02	0.02	0.01
	0.01	9.82	0.23	0.02	0.02	0.05	0.52	0.01	0.01

References

1. Bakker WH, et al. Receptor Scintigraphy with a Radioiodinated Somatostatin Analogue: Radiolabeling, Purification, Biological activity, and In Vivo Application in Animals. *J Nucl Med* 1990;1501-1509.
2. Bakker WH, et al. ^{111}In-DTPA-D-Phe-1-octreotide, a potential radiopharmaceutical for imaging of somatostatin receptor-positive tumors: synthesis, radiolabeling and in vitro validation. *Life Sci* 1991;1589-1591.
3. Bakker WH, et al. In vivo application of [^{111}In-DTPA-D-Phe-1]-octreotide for detection of somatostatin receptor-positive tumors on rats. *Life Sci* 1991;1593-1601.
4. Stolz B, et al. Radiotherapy with yttrium-90 labeled DOTA-tyr^3-octreotide in tumor bearing rodents. *J Nucl Med* 1997;38:18P.