STRUCTURE-ACTIVITY RELATIONSHIP OF OCTREOTIDE ANALOGUES LABELED WITH RHENIUM AND TECHNETIUM-99m

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ABSTRACT

The goal of this research is to cyclize octreotide analogues with ^{99m}Tc and $^{186/188}$Re radiometals to be used as diagnostic and therapeutic agents for neuroendocrine tumors, respectively. Several series of octreotide analogues that differ in their sequences, and/or coordination systems (S_2N_2 and S_3N) were developed. Their *in vitro* receptor binding affinity toward somatostatin receptors was measured *via* IC_{50} studies.

In vitro stability studies were carried out under physiological conditions on ^{99m}Tc-cyclized analogues in phosphate buffered saline, mouse serum, and under high cysteine concentration. The only analogue that expressed high receptor binding affinity was not stable at the tracer level; however, the other analogues were stable at the tracer level but at the expense of their receptor affinity.

The effect of metal-cyclization on Tyr^3-octreotate's receptor binding site was determined *via* three-dimensional molecular structure calculation, using two-dimensional NMR experiments as experimental constraints. From the obtained structures, it was concluded that the metal-cyclized Tyr^3-octreotate's receptor binding site configuration was, to some extent, similar to that of the usually disulfide-cyclized counterpart.