Abstract

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Title of Doctoral Thesis: Analysis of the biological behavior of receptor-specific radiopharmaceuticals in vitro

In the present work were studied receptor-specific radiopharmaceuticals and their biological behavior. Studies were performed with radiolabelled somatostatin and gastrin analogues. All of these substances are potentially useful in the diagnosis and therapy of neuroendocrine tumors.

Somatostatin analogues under study: DOTA-TATE and DOTA-NOC labelled with 111 indium, 177 lutetium, 90 yttrium and 125 iodine. The studies were performed on AR42J cell line (rat pancreatic tumour cells). Internalization rate of these analogues and their specific binding to the cells with high density of appropriate receptors were determined. The data were compared with values obtained after intravenous administration of the same peptides to rats. The uptake of radioactive peptides in tissues with high density of somatostatin receptors in vivo were correlated with the results obtained in vitro conditions.

We have compared four ^{111}In labelled gastrin analogues (so called minigastrins /MG/, namely MG11, MG45, MG47 and MG48) linked to the metal chelating DOTA with results obtained in preclinical experiments. Radiolabelled peptides were particularly tested for the peptide binding on CCK-2 receptor bearing cell line AR42J and for their pharmacokinetics in normal rats.

The experiments suggest that all somatostatin and gastrin analogues exhibited similar and relatively rapid internalization into AR42J cells.

Obtained data suggest that ^{111}In-DOTA-minigastrin analogues and somatostatin analogs under study are promising candidates for scintigraphy and/or therapy of CCK-2 and

somatostatin receptor-expressing tumours. ^{111}In-DOTA-MG47 seems to be.the most promising for potential clinical use.