7. ABSTRACT

Somatostatin analogues labelled with radionuclides are used for diagnosis and therapy of some tumours, mainly neuroendocrine ones, in which receptors specifically binding these radiolabelled analogues of somatostatin are occurred. However, the therapeutic usage of these radiolabelled analogues of somatostatin is limited due to nefrotoxic undesirable effects originated because of their accumulation in the renal proximal tubules after reabsorption from the glomerular filtrate.

The aim of the study was to contribute to knowledge in the renal transport systems responsible for reabsorption of radiolabelled somatostatin analogues in the renal tubular cells and then on the base of such data to find some substances which could reduce the renal accumulation and prevent the damage of the renal tissue.

In experiments, the isolated renal cells obtained from rat kidney by collagenase method were used. After the verification of presence and function of transport mechanism by known indicators of active and passive transport, the accumulation of two somatatostatin analogues labelled with radionuclides - ^{111}In-DOTA-NOC and ^{125}IDOTA-Tyr$_3$-octreotate were studied on these renal cells. The active transport of these radiopeptides was verified by reduce of incubation temperature. Then changes of accumulation of these peptides were investigated after adding substances affecting different membrane transport mechanisms.

From results of the work some influence of accumulation is unmistakable. The accumulation of ^{111}In-DOTA-NOC was reduced by albumin on 68 % and the accumulation of ^{125}I-DOTA-Tyr$_3$-octreotate was reduced by gentamicin on 84 %. Both of these substances are substrates of megalin/cubilin transport system. The accumulation of ^{111}In-DOTA-NOC was also reduced by lysine on 52 % and by maleat on 50 %, the accumulation of ^{125}I-DOTA-Tyr$_3$-octreotate was reduced by maleat on 74 %, it probably happened because of the interaction with cationic binding sites on renal tubular cells and the inhibition of binding studied peptide on these sites. The accumulation of ^{111}In-DOTA-NOC was six-times higher than the accumulation ^{125}IDOTA-Tyr$_3$-octreotate.

It means if our results were right, the studied peptides were transported to the cells by all of these transport systems. The different rate of accumulation in kidney was demonstrated in different radiopeptides.