

ABSTRACT

Study of renal bioelimination of xenobiotics at cellular level I.

Synthetic somatostatin analogues labeled with convenient metal radionuclides are used in nuclear medicine for scintigraphy and, recently, they are also used for targeting radiotherapy in some types of malignant tumors with high expression of somatostatin receptors. Their therapeutical use is limited due to a potential radiotoxic effect on the kidney. This effect is a consequence of accumulation of the radiopeptides in the renal tubular cells. The reason of the cumulation is an intensive reabsorption of radiopeptides in the renal tubules. The mechanism of accumulation has not been explained fully so far. The aim of this work was to study the accumulation of an experimental receptor specific derivate of somatostatin, DOTA-TATE (DOTA-Tyr³-octreotate) labeled with indium-111 (¹¹¹In-DOTA-TATE). The experiments were mainly aimed at a study of the mechanism of renal uptake and at possibilities how to modify the unfavourable accumulation of the studied radiopeptide in the renal cells. Freshly isolated renal rat cells obtained by the collagenase method were used as an experimental model. Verification of the vitality of renal cells was made by trypan blue exclusion test. The preparates of the cells showed viability approximately 90% and therefore they could have been used for the given type of experiments. Paradoxically, albumin, a substrate and an inhibitor of megalin endocytic system, increased moderately the accumulation of the radiopeptide instead of the expected inhibition of the uptake. Surprisingly, probenecid, an inhibitor of organic anion transporters, decreased the accumulation of the radiopeptide markedly. The found results could mean that the renal uptake of ¹¹¹In-DOTA-TATE can be mediated by the transporters for organic anions. However, it is necessary to exclude a possibility that the concentrations used for the inhibitors are potentially cytotoxic. A lower number of viable cells in the samples due to any toxic action of the tested inhibitor can also result in a lower rate of radiopeptide accumulation. The expected participation of megalin endocytic system on the renal accumulation of the studied radiopeptide was not proved in our experiments.