ABSTRACT

The finding of increased expression of certain types of regulatory peptide receptors in some tumors led to research on regulatory peptide analogs as potential receptor-specific radiopharmaceuticals for imaging and tumor-targeted therapy. Analogues of gastrin and cholecystokinin belong to one of the perspective groups. However, accumulation of radiopeptides in the renal tissue may cause radiotoxic renal damage and may limit their clinical use. Study of renal mechanisms is therefore an essential premise for further developments in this group.

The aim of this work was to study in vitro the rate of renal accumulation of gastrin derivatives, DOTA-minigastrins (DOTA-MG), labeled with indium-111, and to examine general mechanisms responsible for their uptake in kidney cells. Accumulation of three compounds, ^{111}In-DOTA-MG11, ^{111}In-DOTA-MG45 and ^{111}In-DOTA-MG46 was evaluated using a renal cellular model.

Experiments were carried out using isolated rat cells obtained from native rat renal kidney tissue. The renal cells were used to determine the rate of accumulation of ^{111}In-minigastrins. To evaluate the participation of active and passive transport mechanisms in the renal uptake, accumulation under physiological and decreased temperature was determined. To assess the quantitaty of ^{111}In-DOTA-minigastrin accumulation, a comparative agent, ^{99m}Tc-dimercaptosuccinic acid (^{99m}Tc-DMSA), actively accumulated in the kidney was used. Possible participation of the endocytic megalin system in the renal uptake of ^{111}In-DOTA-minigastrins was tested by using an inhibitor of the system, albumin.

The results indicated that ^{111}In-minigastrins showed relatively low rate of accumulation in the rat kidney cells. The uptake was different and decreasing in the order ^{111}In-DOTA-MG45 > ^{111}In-DOTA-MG11 > ^{111}In-DOTA-MG46. However, the accumulation of all ^{111}In-minigastrins was much lower in comparison with ^{99m}Tc-DMSA. A partial reduction (20-40%) of the uptake in the cells incubated at low temperature when energy-dependent processes were inhibited was found but a significant decrease was observed only in ^{111}In-DOTA-MG11 and ^{111}In-DOTA-MG46. Albumin failed to reduce uptake in ^{111}In-DOTA-MG11. The found data show that the studied radiolabelled minigastrins are characterized by a relatively low accumulation in the rat renal cells in vitro and their transport across the cellular membranes is mediated mainly by passive transport with a partial contribution of active transport mechanisms.