Radiolabeling optimization and characterization of three ^{67}Ga DOTA conjugated peptides.

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INTRODUCTION

- In this work we report a preliminary study of radioactive labeling of different peptides with ^{67}Ga for possible use in oncology. For this purpose the following peptides were used: KCCYSL, a probe of aberrant expression of ErbB-2, member of the epidermal growth factor family of receptors, and it has been implicated in the formation of various malignancies including ovarian cancer [1]; TATE, a synthetic somatostatin analog, which binds specifically to somatostatin receptors present on the cell surface of neuroendocrine tumors [2]; Substance P, peptide which has an important role in modulating pain transmission trough neurokinin type 1 (NK1r) and 2 receptors (NK2r), may play a role in the pathogenesis of pancreatic tumors and malignant glial brain tumors as well [3]. These three peptides are conjugated to DOTA (1,4,7,10-tetraazacyclododecane-1,4,7,10-tetraacetic acid) used as chelator of lanthanide ions [4].

MATERIALS AND METHODS

- Different radiolabeling methods were assayed to establish the optimum conditions for obtaining the highest yield of labeled KCCYSL, TATE and substance P. Briefly, a stock solution of each DOTA-peptide derivative was prepared dissolving it in Milli Q water (1 mmol/L each solution). After that, 20 µg of each DOTA-peptide was added to three different eppendorf tubes containing 0.2 mL ammonium acetate buffer (pH 4.8, 0.5 mol/L) and 10 MBq of $^{67}GaCl_3$ (0.02 mL/0.1 mol/L HCl) was added to a reaction solution. The reaction mixtures were kept for 30 min at 80 °C. After cooling down, the preparations were studied by HPLC (C18 reversed phase column with gradient system was used with 0.1 % trifluoroacetic acid/water (Solvent A) and acetonitrile (Solvent B) as mobile phase).

RESULTS

- The three peptides were successfully labeled with high yield (> 99 %) at optimized conditions (Figure 1) and kept stable for more than 48 hours at room temperature.

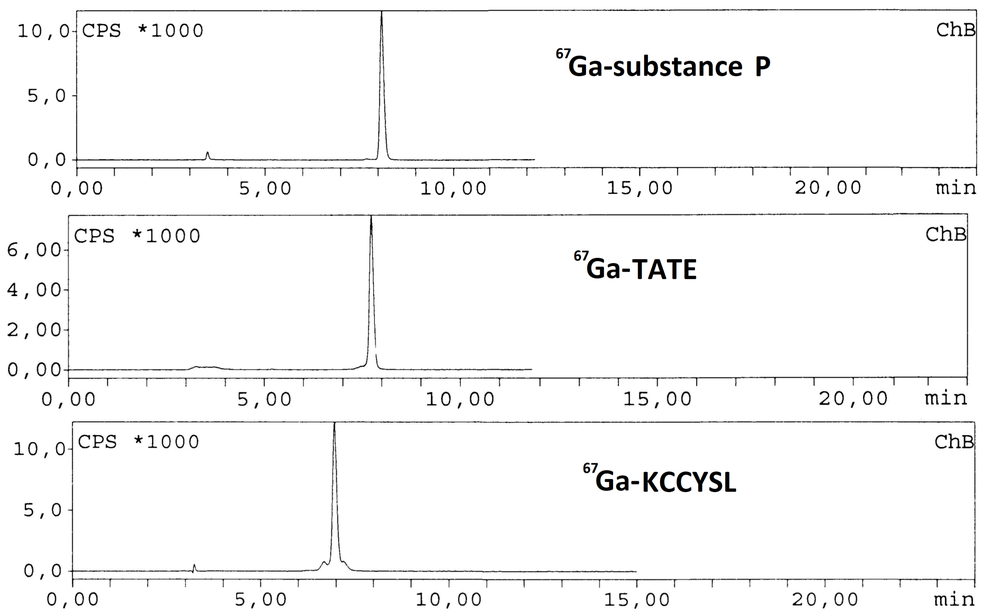

Figure 1. HPLC profile (1 h post labelling) of the different peptides bound to DOTA and radiolabeled with ^{67}Ga is shown.

DISCUSSION

- It is concluded that the radiolabeling technique with ^{67}Ga mentioned in this work is very well adapted to different peptides previously conjugated to DOTA chelator, and it stays stable over time. In future works, cellular and biological studies of the three radiolabeled peptides will be carried out.

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