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Short Research Article

Radiolabelling of somatostatin analogues lanreotide and octreotate with therapeutic radionuclides†

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Introduction

Our goal in this work was to study, select and optimize the radiolabelling parameters of the somatostatin analogues with ^{177}Lu, ^{188}Re and ^{131}I as well as the *in vitro* experiments for quantification of the biological properties. The radiolabelling was performed using biologically and radioactively therapeutic doses.

Results and discussion

Methods for radiolabelling of somatostatin analogues Lanreotide, Octreotide and Octreotate with therapeutic radionuclides were selected and optimized.[1–3] The chemical structures of the peptides as well as physical properties of radionuclides were considered aiming to obtain a good stability of radiolabelled peptides, high radiochemical purity and an optimal *in vivo* behaviour.

DOTA-Lan DOTA-d-β-NaI-Cys-Tyr-d-Trp-Lys-Val-Cys-Thr-NH2
DOTA-TOC DOTA-d-Phe-Cys-1-NaI-d-Trp-Lys-Thr-Cys-Thr(ol)
DOTA-TATEDOTA-d-Phe-Cys-Tyr-d-Trp-Lys-Thr-Cys-Thr

The direct and indirect methods were developed in the case of radiolabelling of 8-mer Lanreotide with Re-188, using DOTA (1,4,7,10-tetraazacyclotetradecane-N,N',N'',N'''-tetraacetic acid) as bifunctional agent for the indirect approach and stannous ions as reducing agent. The radiochemical purity obtained was higher than 95% in both cases, but the biological activity of labelled peptides may be altered by the presence of radionuclide bounded to SH groups resulting from disulphide bridges. It is hoped that the radionuclide attached to DOTA might have only a small influence on *in vivo* behaviour of radiolabelled peptide. The *in vitro* stability of the labelling at room temperature was tested. The radiochemical purity of ^{188}Re-DOTA-Lan and ^{188}Re-Lan was higher than 95% at 4 h after labelling.

The radiolabelling of Octreotide and Octreotate with Lu-177 was performed by the indirect approach. The DOTA-Octreotate and DOTA-Octreotide were labelled with high-specific activity Lu-177 (45 Ci/mg); the reaction parameters, as temperature and incubation time, were established for the best radiolabelling yield.

The radioiodination (I-131) of somatostatin analogues to tyrosine leads to stable and high radiochemical purity peptides. The electrophilic substitution depends on ^{131}I to Chloramine-T and DOTA-TATE to Chloramine-T molar ratios. Radioiodination of peptides was done for comparative evaluation of *in vitro* and *in vivo* properties of the radiopeptides labelled with radiometals.

The radiopeptides were obtained with radiochemical purity higher than 95% and did not demand further purification. The labelling processes are controlled by the specific activity of the radioisotope, temperature, pH and incubation time. Lanreotide, Octreotide and Octreotate can be labelled with 177Lu, 188Re and 131I, using the indirect approach. The labelling methods are easy and show reproducible results.

The somatostatine receptor (sstr) binding studies confirm that the radiopeptides are able to bind the brain cortex membrane receptors as the IC_{50} and K_d values show a high binding affinity of the radioligand for somatostatin receptors (Figures 1 and 2). The binding affinity was not compromised by the labelling

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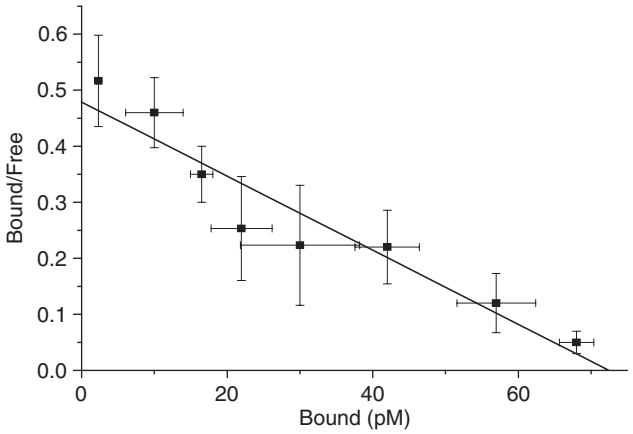

Figure 1 SSTR binding of ^{177}Lu-DOTA-TATE.

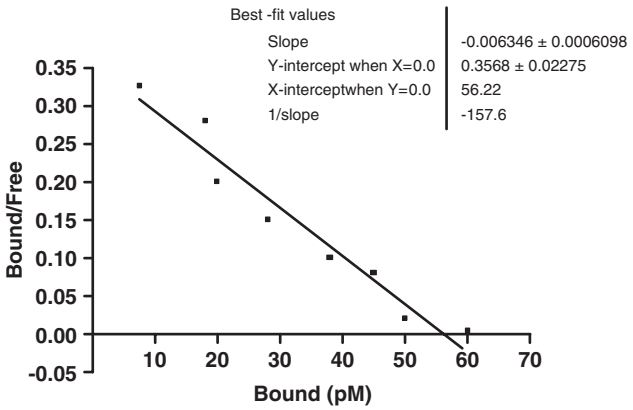

Figure 2 SSTR binding of ^{131}I-DOTA-TATE.

processes and changing of C-terminal alcohol from Tyr-octreotide with C-terminal acid (TATE) from the somatostatin analogue.

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