Public Abstract
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Title: Investigation of the replacement of cysteine residues in DOTA-[Tyr^3]-octreotate: synthesis, characterization and evaluation of biological activities

This dissertation deals with introducing structural changes in the cyclic peptide: DOTA-[Tyr^3]-octreotate and evaluating the chemical and biological changes brought about by these changes. DOTA-[Tyr^3]-octreotate is known to bind specifically to receptors found on the surface of cancer cells. In literature, peptides in which similar changes (in the structure of the peptide) were made showed higher affinity or selectivity towards receptors in comparison to the original peptide. The changes made in the structure involve replacement of the cysteine residues in the peptide with other amino acids, such as *D*-cysteine, *D*-penicillamine or Penicillamine.

Synthesis of the peptides was performed by using Fmoc synthetic methods, followed by characterization by using techniques such as HPLC and LCMS. After the synthesis, the peptides were cyclized by using DMSO or $[Pt(en)_2Cl_2]Cl_2$. After successful cyclization of the peptides, purification was carried out using methods such as preparative HPLC or Sep-Pak®. After isolation of the purified peptides, they were radiolabelled with ^{111}In, a radionuclide which emits gamma rays. Gamma rays can be detected easily using suitable detectors and this allows the localization of the molecule which has the radionuclide present. The radiolabelled peptides were isolated using HPLC techniques. These were then subjected to a number of in vitro tests, which allowed the evaluation of the biological properties of the peptides. The modified peptides were found to be stable in serum, and had lower affinities towards the receptor in comparison to DOTA-[Tyr^3]-octreotate.