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SYNTHESIS AND EVALUATION OF DIFFERENT CHELATORS FOR MOLECULAR TARGETED PEPTIDES USING 68GA AS RADIONUCLIDE

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BACKGROUND-AIM

The purpose of this article is to show the possibility to use a automatic synthesis module, as versatile platform, for the synthesis of new target molecules for analysis in positron emission tomography (PET).
The tumor target molecules as □v□3 integrin have an important ligand such as tri-peptide RGD (L-Arginyl-Glycyl-L-Aspartic acid or Arg-Gly-Asp). This target are located in several cells like endothelial, epithelial and glioblastoma cells. RGD receptors coniugates with □v□3 have a meaning of angiogenesis control, cell prolification and migration. Many studies shows an interest future on RGD conjugates (especially with radioisotopes).

METHODS

68Ga generator was purchased from Eckert & Ziegler (Berlin, Germany), with nominal activity of 1100 MBq and was eluted with 0,1 N HCl (Fluka, Milan, Italy). Pre-cleaning method is used.
Substances used for chemical synthesis are synthesized in chemical laboratory of University of Padua or purchased by ABX (Radeberg, Germany).
All organic reagents were purchased by Sigma-Aldrich Chemie Gmbh Munich, Germany. Solid phase extractor cartridges were purchased by Waters S.A.S. Saint-Quentin, En Yvelines Cedex, France.
Reversed phase high performance liquid chromatography analysis was carried out using a Agilent 1260 HPLC system (Agilent, Santa Clara, CA, USA) with four pumps and a vis/UV detector an C18 Polar 120A small molecule 53mm x 7mm particle size 3µm (Grace Discovery Sciences, Columbia, Maryland, USA) column were employed, and a radiometric detector (Raytest, Straubenhardt, Germany). The HPLC method was acetonitrile (ACN) / 0,1% trifluoroacetic acid (TFA) called B solution and water/ 0.1% TFA as A solution. Gradients employed: for 0 – 2 min 10% B solution, 7 min to 36% B solution, 7 – 9 min. 36% B solution, 9 – 10.5 min 36% solution B, 10.5 – 14 min 10% solution B, 14 – 15 at 10% solution B.

RESULTS

It has been shown the binding of target molecules to 68Ga especially the study focuses on the use of DOTA-RGD, NODAGA-RGD, DOTA-BOMBESIN and NOTA-BOMBESIN.
The synthesis was carried out methodically with acetone-free method with a new SPE cartridge by obtaining levels of radiochemical purity higher than 99%, no other co product in addition to the peptide was detective in UV/radiometric HPLC analysis.

CONCLUSION

The 68Ga labeling protocol was optimized concerning temperature, peptide concentration and reaction time, by obtaining improvements in timing compared to previous studies.