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Original Article

Synthesis and Evaluation of a New Radiolabeled Bombesin Analogue for Diagnosis of GRP Receptor Expressing Tumors

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Abstract:

Introduction: Bombesin (BN), a 14-amino acid neuropeptide, shows high affinity for the human GRP (gastrin releasing peptide) receptors, which are overexpressed by a variety of cancers, including prostate, breast, pancreas, gastrointestinal, and small cell lung cancer. Aim was to prepare [6-hydrazinopyridine-3-carboxylic acid ($HYNIC^0$), D-Tyr^6, D-Trp^8] - BN [6-14] NH_2 that could be easily labeled with ^{99m}Tc and evaluation of its potential as an imaging agent.

Methods: Synthesis of the peptide amide was carried out onto Rink Amide MBHA (4-Methylbenzhydrylamine) resin. A bifunctional chelating agent (BFCA) was attached to the N terminal peptide in solid-phase. ^{99m}Tc labeling was performed by addition of sodium pertechnetate to solution that include [$HYNIC^0$, D-Tyr^6, D-Trp^8] Bombesin [6-14] NH_2, tricine, ethylenediamine-N,N′-diacetic acid (EDDA) and $SnCl_2$. Radiochemical evaluation was carried out by reverse phase high-performance liquid chromatography (HPLC) and instant thin layer chromatography (ITLC). In-vitro internalization was tested using human prostate cancer cells (PC-3) with blocked and non-blocked receptors. Biodistribution was determined in rats.

Results: [^{99m}Tc/tricine/EDDA-$HYNIC^0$, D-Tyr^6, D-Trp^8] bombesin [6-14] NH_2 was obtained with radiochemical purities >98%. Results of in-vitro studies demonstrated a high stability in serum and suitable internalization. Biodistribution data showed a rapid blood clearance, with renal excretion and specific binding towards GRP receptor-positive tissues such as pancreas.

Conclusion: In this study, labeling of this novel conjugate with ^{99m}Tc easily was performed using coligand. The prepared ^{99m}Tc-HYNIC-BN conjugate has promising characteristics for the diagnosis of malignant tumors.

Keywords:

Bombesin , 99mTc , Tumor , HYNIC

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