[a] *Departamento de Ciências Fisiológicas, Faculdade de Ciências Médicas da Santa Casa de São Paulo, São Paulo, SP, Brazil*
[b] *Departamento de Imagem, Hospital Israelita Albert Einstein, São Paulo, SP, Brazil*
[c] *Positronpharma S.A, Chile*

Introduction/Justification: Early evidence appointed fibroblast activation protein (FAP), a type II transmembrane serine protease, as highly expressed in the stroma of various tumor entities, designating FAP as the next target for cancer studies in nuclear medicine. Several radiolabeled fibroblast activation protein inhibitors (FAPI) are currently in development and investigation as potential PET imaging agents for different neoplasms, with the potential for future theranostic applications. **Objectives:** The aim of this study was to implement the efficient and convenient automated synthesis of [68Ga]Ga-FAPI-46 from ABX, using Modular Lab Pharm Tracer and the generator Gallia Pharm® from Eckert & Ziegler, for clinical applications in nuclear medicine services, as well as to evaluate routine quality control parameters such as radiochemical yield and purity, radiochemical stability, and sterility tests in accordance with the GMP rules. **Materials and Methods:** The synthesis was conducted in automated module, employing disposable cassettes in an adapted synthesis template with high purity raw materials and reagents. [68Ga]GaCl3 was percolated through resin and eluted with 0.5 mL of 5.5 M HCl in saline into a reaction vial containing 50 μg of FAPI-46 in 1.5 mL of 0.1 M acetate buffer (pH = 4.5) and 100 μL of ethanol. The solution was heated at 95°C for 10 min. The resulting product was purified through a Sep-Pak C18 cartridge, which was preconditioned with ethanol and 0.9% saline, and eluted with 0.4 mL of 70% ethanol. The final product was diluted with 0.9% saline and filtered through a Millipore 0.22 μm filter. Radiochemical yield (RCY) was assessed by determining the activity retained in the module in relation to the final product. Radiochemical purity (RCP) of [68Ga]Ga-FAPI-46 was analyzed by ascending chromatography using either ITLC-SG strip and 0.1 M ammonium acetate and methanol (1:1) solution or TLC and 1 M sodium citrate (pH = 5.5), and Sep-Pak C18 cartridge. Radiochemical stability was assessed through UHPLC analysis. Microbiological, pyrogenic, and filter tests were conducted on all batches. Additionally, in-vitro studies were carried out to assess Log P and serum protein binding for [68Ga]Ga-FAPI-46. **Results:** The automated synthesis produced [68Ga]Ga-FAPI-46 with an activity of 684 ± 67 MBq, a RCY of 88.4 ± 2.6%, and pH = 4.5 (n = 8). The RCP was determined as 97.32 ± 1.92% by ascending chromatography and 97.74 ± 2.12% by Sep-Pak C18 cartridge. The RCP remained above 97% for more than 120 min as analyzed by UHPLC, showing high radiochemical stability. Microbiological assays demonstrated that the final product was obtained as a sterile and pyrogen free solution. The filter test passed for all batches. The Log P was determined as -3.57 ± 0.15 (n = 10), showing the hydrophilic characteristics of [68Ga]Ga-FAPI-46 with a serum protein binding of 52.11 ± 1.49% (n = 6). **Conclusion:** The [68Ga]Ga-FAPI-46 was synthesized with consistently high RCY and RCP, exhibiting reproducibility, yielding a sterile and pyrogen free final solution, that means an efficient way for routine syntheses in nuclear medicine services confirmed by clinical application in six patients.

Keywords: Automated syntheses, PET-CT, Quality control., [68Ga]Ga-FAPI-46.

https://doi.org/10.1016/j.htct.2024.04.059

CONTINUING EDUCATION IN RADIOPHARMACY IN LATIN AMERICA

Maria Emilia Tejeria Perez, Mariella Adriana Terán, Ana María Rey

Área Radioquímica, Facultad de Química, Uruguay

Introduction/Justification: Radiopharmacy is an area with increasing development and technological complexity. According to WHOs official documents (WHO Annex 2,3) the production of radiopharmaceuticals requires the supervision of qualified personnel with postgraduate training and appropriate experience in their function. Although most countries in Latin America have adopted these documents in their legislation the real situation is highly heterogeneous and specific qualification in Radiopharmacy is not clearly specified in the national regulations. Furthermore, the adequate educational offer is very restricted and heterogeneous in all Latin American countries. **Objectives:** With the objective to prepare the future generations of Radiopharmacists according to international and national regulations we have developed a series of options for postgraduate and continuing education in the field. **Materials and Methods:** N/A. **Results:** The Diploma of Specialization in Radiopharmacy offers a postgraduate program for specialization in Radiopharmacy. This diploma integrates comprehensive theoretical knowledge with the necessary practical experience to prepare professionals for specialized roles in this field. Admission to the program requires candidates to hold a university degree, with a minimum duration of four years, in Pharmacy, Chemistry, or Biochemistry, obtained from institutions in Uruguay or other countries. Applications from candidates with alternative qualifications are reviewed by a dedicated admission committee, and additional courses may be prescribed to supplement their foundational knowledge. The curriculum comprises both theoretical and practical components, totaling approximately 300 hours of instruction. The courses can be partially performed virtually, thus facilitating the participation of foreign students. However, practical laboratory sessions and supervised practice are required to be completed in Uruguay, typically spanning a duration of 3-4 months. Additionally, partial validation of prior studies may be considered, allowing eligible students to receive credit for relevant coursework completed elsewhere. Besides the postgraduate program we also offer the possibility of taking continuous education courses both with basic (physics of radiation, chemistry of radiopharmaceuticals, etc) and applied topics (legislation, clinical applications, et). We also offer customized courses for institutions or private radiopharmaceutical firms. Up to the moment we have more than 10 graduates, 40% coming from Colombia, Costa Rica or Bolivia and 7 students, 6 of which are from different countries in Latinamerica. Our continuing education courses have been taken by around 100 professionals from Chile, Costa Rica, México, Bolivia, Ecuador, Perú, Costa

Rica, Panamá, República Dominicana, etc. Conclusão: Radiopharmacy is a flourishing specialty of increasing complexity that requires solid theoretical knowledge and specialized practical skills. The Radiochemistry Area in the public University of Uruguay is fostering the development and generational replacement in our continent with the objective to improve the quality of the Radiopharmaceuticals received by our population. **Acknowledgments:** Centro Uruguayo de Imagenología molecular, CUDIM and Centro de Medicina Nuclear e Imagenología Molecular del Hospital de Clínicas.

Keywords: Education, Online courses, Posgraduate, Radiopharmacy.

https://doi.org/10.1016/j.htct.2024.04.060

EVALUATION OF POTENTIAL PEPTIDE INHIBITORS THAT INTERACT WITH THE EGF RECEPTOR. RELEVANCE TO GLIOBLASTOMA

Lorena Marinelli Mendes,
Danielle Vieira Sobral,
Érica Victória dos Santos,
Leonardo Lima Fuscaldi, Luciana Malavolta

Faculdade de Ciências Médicas da Santa Casa de São Paulo, São Paulo, SP, Brazil

Introduction/Justification: Peptides are implicated to various physiological responses and exhibit considerable potential for disease treatment, encompassing diverse types of tumors. The significant therapeutic promise of peptides is related from their characteristics, including the ability to inhibit angiogenesis, induce tumor apoptosis and block of epidermal growth factor receptor (EGFr) signaling. Their relevance is underscored by overexpression in a range of human cancers, notably glioblastoma, which represents the most prevalent and aggressive form of malignant brain tumors. **Objectives:** This study aims to assess the growth inhibition of rat (C6 cells) and human (U-87 MG cells) glioblastoma tumor cells using peptides that interact with the EGFr. **Materials and Methods:** The anti-EGFr peptides were synthesized through the solid-phase peptide synthesis using the Fmoc/tBut strategy. Peptide cleavage from the resin was performed using a mixture containing a high concentration of trifluoroacetic acid (reagent K). Subsequently, the peptides underwent a characterization and purification process employing high performance liquid chromatography (HPLC) and mass spectrometry. C6 and U-87 MG cell lines were cultured in supplemented DMEM F-12 medium at 37°C and 5% CO2 until reaching 90% confluence. To assess the effect of peptides on cell proliferation, cells were seeded at a concentration of 5×103 in 6-well plates, with the presence of 80 μM of each proposed peptide. Growth curves were performed in sextuplicate over a 7-day period, with cell counts conducted on days 1, 3, 5, and 7. Cell viability in the presence of peptides was determined using the MTT test. For this analysis, cells were plated at a concentration of 5×103 in 96-well plates, with peptide concentrations of 80, 120, and 160 μM. Spectrophotometric analyses were performed after 24 h and 7 days of incubation at 595 nm. **Results:** Anti-EGFr-LP and anti-EGFr-LG peptides were synthesized efficiently with yields of approximately 45 and 98%, respectively. Chromatographic analyzes obtained by HPLC confirmed that the entire synthesis, cleavage, and characterization process of peptides were performed efficiently, as evidenced by the presence of only a single peak corresponding to the synthesized peptides. Following the determination of growth curve profiles of C6 and U-87 MG cell lines, without the presence of peptides, the interaction of the peptides with both tumor cell types was assessed. The results demonstrated that both anti-EGFr-LP and anti-EGFr-LG peptides significantly interacted with and inhibited the growth of C6 and U-87 MG strains ($p < 0.0001$). Studies conducted with C6 cells showed inhibition percentages of approximately 55.3% and 99.1% for the Anti-EGFr-LP and anti-EGFr-LG peptides, respectively. On the other hand, an inhibition percentage of growth of U-87 MG cells was 44.4% for the Anti-EGFr-LP and 46.4% for the anti-EGFr-LG. Finally, based on the MTT test, the peptides exhibited no toxicity at any of the three concentrations tested. **Conclusion:** The findings indicate that both proposed peptides, at a minimum concentration (80 μM) effectively reduced the proliferation of tumor cells without inducing toxicity. While further experiments are warranted, the peptides have demonstrated the capability to inhibit tumor cell growth associated with glioblastoma, suggesting a potential therapeutic alternative.

Keywords: C6 cells, EGFr-targeting peptides, glioblastoma, U-87 MG cells.

https://doi.org/10.1016/j.htct.2024.04.061

INVESTIGATION OF THE IN VITRO ASSESSMENT OF 99MTC-LABELED LAMININ-111 PEPTIDES AS PROSPECTIVE BIOMARKERS FOR BREAST CANCER

Fernanda Ferreira Mendonça [a],
Maria Emilia Tejeria Perez [b], Paula Decuadra [b],
Maia Zeni [b], Ana Rey [b],
Leonardo Lima Fuscaldi [a], Luciana Malavolta [a]

[a] *Faculdade de Ciências Médicas da Santa Casa de São Paulo, São Paulo, SP, Brazil*
[b] *Faculty of Chemistry at the University of the Republic, Montevideo, Uruguay*

Introduction/Justification: Breast cancer constitutes a significant public health issue as the second most prevalent type of tumor among women. In the past decade, radiolabeled peptides have been employed in both therapeutic interventions and tumor imaging, representing a substantial promise in the specific targeting of tumorigenic cells. Several studies demonstrate that biologically active peptides derived from laminin-111 regulate gene expression in breast cancer-derived cells, including the YIGSR and IKVAV peptides. **Objectives:** To synthesize the HYIGSR and HIKVAV fragments, derived from laminin-111, standardize and optimize their radiolabeling process with technetium-99m (99mTc), as well as, to assess the in vitro biological characteristics of these radiolabeled peptides as potential biomarkers for breast cancer. **Materials and Methods:** The HYIGSR and HIKVAV peptides were