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11. Radiopharmacy.

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Tatiana Lavinás, Constância P. G. da Silva, Elaine B. de Araujo.

Instituto de Pesquisas Energéticas e Nucleares - IPEN/CNEN-SP

Correspondencia:

Tatiana Lavinás. Instituto de Pesquisas Energéticas e Nucleares - IPEN/CNEN-SP E-mail: tlavinás@net.ipen.br

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11.03 Direct labeling of chemotactic peptide fornlfnleyk with radioiodine.

Objective: Various conventional radiopharmaceuticals are currently available for scintigraphic imaging of infection and inflammation. Although a wide variety of infectious and inflammatory foci can be detected with these agents, several disadvantages limit their application. These limitations have stimulated the search for new radiopharmaceuticals. In the past decade a new class of radiopharmaceuticals has emerged: radiolabelled receptor-specific small proteins and peptides. These proteins and peptides are naturally occurring inflammatory mediators which specifically bind to receptors abundantly present in the area of inflammation. In addition, owing to their small size, they rapidly clear from all non-target tissues.

For-MLF is a bacterial product that initiates leukocyte chemotaxis by binding to high affinity receptors on the white blood cell membranes. These receptors are present on both polymorphonuclear leukocytes (PMNs) and mononuclear phagocytes. There are many synthetic analogs with equal or greater affinity compared to the native peptide. ForNleLFNleYK is one of these synthetic analogs. This hexapeptide contains one tyrosine residue susceptible to iodination using an oxidative electrophilic substitution agent. In this work, we described the production of radioiodinated ForNleLFNleYK with high radiochemical yield.

Methods: The labeling procedures employed synthetic ForNleLFNleYK (25 ug, Sigma) dissolved in 5 uL of DMF; 5 uL of Chloramine T (1.0 mg Chloramine T/ mL DMF) as oxidant agent; [131I]NaI solution (3.7 - 7.4 MBq/10 uL) and after 10 minutes of reaction at room temperature and gentle stirring, the reaction was terminated by the addition of 5 uL of sodium methabisulfite solution (2.0 mg Na₂S₂O₅/mL distilled water). Aliquots of the reaction mixture were injected into a HPLC system (column RP C18, 5 um, 150 x 4.6 mm, Dyonex) eluted isocratically with two different solutions: 73% aqueous TFA (trifluoroacetic acid 0.1% solution) and 27% acetonitrile with a flow rate of 0.5 mL/minute and 1.0 mL/minute; 60% aqueous TFA (trifluoroacetic acid 0.1% solution) and 40% acetonitrile with a flow rate of 0.5 mL/minute and 1.0 mL/minute. Free radioiodine was determined by

horizontal zone electrophoresis (Amersham) on Whatman 1MM paper, 0.05M barbital buffer, pH 8.6, using a field of 295V for 40 minutes.

Results and Conclusions: We concluded that radioiodinated ForNleLFNleYK can be obtained with high radiochemical purity, in a short reaction time using Chloramine T as oxidant agent. The HPLC system possibilited the separation of labelled ForNleLFNleYK with high specific activity, necessary for receptor-mediated diagnostic procedures with radiopharmaceuticals.

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