RESEARCH AND DEVELOPMENT OF METHODS FOR PREPARATION OF LYOPHILIZED KITS FOR LABELLING WITH ^{99M}TC

Centro de Radiofarmácia - IPEN/CNEN-SP

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Technetium-99m is the most useful radionuclide in diagnostic procedures in Nuclear Medicine due to its appopriated physical characteristics like short half life (6.02 h), gamma monoemission of low energy (140 keV) and absence of particulated emissions. The ^{99m}Tc can be easily obtained by ^{99}Mo-^{99m}Tc (IPEN-TEC) generator system, that permits the use of this short-lived radiopharmaceutical in different locals, distants from the production center. The synthesis of compounds not commercially available and the development of new lyophilized kits are necessary to introduce new technetium-based radiopharmaceuticals. Lyophilized kits allows the instant preparation of the labelled molecules with 99mTc without purification steps prior to administration.

Synthesis of MIBI- the development of synthetic approach to produce 2-methoxiisobutil isonitrile (MIBI) was concluded. The product was obtained in a five steps synthesis approach, with high yield and purity degree, compatible with the preparation of liopylized kits. The kits were prepared and presented high stability stored over six months under refrigeration. Labeling of lyophilized kits with technetium-99m resulted in a complex with high radiochemical purity and stability. Three different approaches were evaluated to determine radiochemical purity of the labeled compound. Biological distribution studies in animals showed high uptake in heart and the ratio heart:liver and heart:lung compatible with the clinical application of the compound. This work is related with a MSc thesis concluded in 2004.

^{99m}Tc-Ciprofloxacin- Labeling and biodistribution studies with the antibiotic ciprofloxacin were done using as radiomarker Tc-99m. A freeze-dried formulation was developed. The study demonstrated the potential of 99mTc-ciprofloxacin as a diagnostic agent for infections process. Production of this kit is in process by the Radiopharmaceutical Center.

^{99m}Tc-Anti-CEA-1and Ior-egf-r3- Monoclonal antibodies have been used for immunoscintigraphy application in clinical diagnosis since it was introduced in nuclear medicine practice. There are two different methods available for radiolabelling MAb with ^{99m}Tc: a direct method reacting the reduced antibody witch reduced ^{99m}Tc and an indirect method in which a bifunctioal chelating agents is first conjugated with an antibody. The direct method for radiollabeling reduced MAbs with 99mTc in presence of methylene diphosphonate (MDP) as a weak competing ligand has been proven as a good procedure to obtain high-labelling efficiency and a stable labeled MAb. The aim of this work is to label monoclonal antibodies (Anti-CEA1 and Ior-egf-r3) with ^{99m}Tc using a direct method and prepare a lyophilized kit. Different parameters were studied: the 2-mercaptoethanol reducing agent; the purification and identification of reduced antibody fraction by spectrophotometer method; mass of Anti-CEA and MDP; time and temperature of lyophilized method. The best conditions for lyophilized kits were selected and the labelling efficiency was determined using ascending paper chromatography on Whatman 3MM paper and TLC-SG in 0.9 % saline and methyl ethyl ketone as a solvent. This work belongs to Project RLA - ARCAL LII "Preparación, control de calidad y validación de radiofármacos de Tc-99m basados en anticuerpos monoclonales".

Development of ^{99m}Tc based small bio-molecules using novel ^{99m}Tc cores - International Atomic Energy Agency (IAEA) Co-ordinated Research Programme - The advent of the new, low-valent, ^{99m}Tc-carbonyl metal core and of the ^{99m}Tc-nitrido metal fragment as well as the Tc(III) "4 + 1" system have introduced new avenues for Tc-99m labeling of biologically active compounds and is considered to provide good opportumities for multi-institutional efforts for investigating new Tc-99m molecules with potential new applications New ligands as peptide with sequence RGD, annexine, glucose analogue, and quinazoline analogue will be labeled with the Tc cores cited above and evaluated for tumor uptake *in vivo* (2003-2006).