P405 A HPLC METHOD FOR DETERMINATION OF ^{201}Tl(III) IN ^{201}Tl(I)Cl RADIOPHARMACEUTICAL

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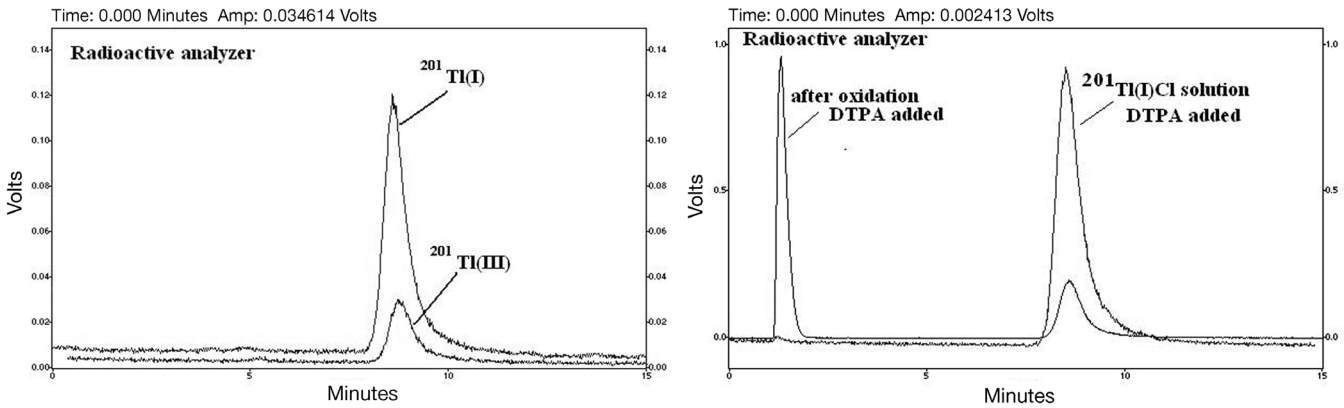
Introduction: Thallous chloride (Tl-201) radiopharmaceutical is routinely used for heart imaging in nuclear medicine departments. The goal of this research was to study the radioanalytical quality control of Tl-201 chloride using high performance liquid chromatography) HPLC). The HPLC method data were compared with data obtained from electrophoreses method recommended in usp.

Experimental: Thallous chloride (^{201}Tl(I)Cl) was obtained from NRCAM and oxidized slightly to ^{201}Tl(III)Cl_3 by O_3. A cation exchange column (Hamilton PRP-X800,150×4.1mm), acetate buffer (100mM, pH=4.5 and flow rate=1 ml/min) as eluent and radioactive flow scintillation analyzer were applied for measurement. Free ^{201}Tl(I) and ^{201}Tl(III) have same properties over cation exchange resins and they can't be separated. DTPA solution was added to ^{201}Tl(I) and ^{201}Tl(III) for masking of ^{201}Tl(III) and separation of it from ^{201}Tl(I). Effect of DTPA solution concentration and pH was evaluated.

Results and Discussion: The retention time values of both free ^{201}Tl(I) and ^{201}Tl(III) were 8.6 min. The retention time value of ^{201}Tl(III)-DTPA complex was 1.3 min. The DTPA concentrations (0.02, 0.05, 0.1 molar) and pH(4-7) didn't affect the measured data. Data obtained from this method had good compatibility with data obtained from electrophoresis method recommended in USP.



Conclusion: This method is short and accurate and can be used for routinely radioanalytical quality control of thallous chloride radiopharmaceutical.

Keywords: Thallous Chloride (201Tl(I)Cl), Radioanalytical Quality Control, HPLC, DTPA

P406 RADIONUCLIDIC PURITY AND ACCURATE HALF-LIFE MEASUREMENTS FOR Lu-177g AND Lu-177m

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Introduction: ^{177g}Lu ($t_{1/2}$=6.734 d, β^- emission 100%, $E_{\beta max}$=489.3 keV, $<E_\beta>$=163.1 keV and main γ lines at 112.9 and 208.4 keV) is a low energy negatron emitter, that is going to find several applications in nuclear medicine, especially in metabolic radiotherapy. This radionuclide is produced in thermal nuclear reactor either by neutron capture on natural or enriched targets of ^{176}Lu, with unavoidable co-production of the long-lived ^{177m}Lu, or by indirect neutron capture on enriched ^{176}Yb targets, followed by negatron decay, *i.e.* ^{176}Yb(n,γ)^{177}Yb$\rightarrow$^{177g}Lu. The latter method produce high specific activity ^{177g}Lu in *no-carrier-added* form (NCA), but a selective radiochemical separation is mandatory. Quantifying radionuclidic impurities allows a correct evaluation of the dose to patient and radioprotection measures to be taken into account and also the identification of the production method adopted.

Experimental: Some radiopharmaceutical samples labelled with ^{177g}Lu and some sample of radioactive solutions (i.e. $^{177}LuCl_3$) used to label radiopharmaceuticals, have been investigated with two radioanalytical techniques: γ spectrometry with HPGe detectors and β spectrometry with liquid scintillation counting (LSCS). All samples were obtained from the nuclear medicine division of IEO.

Results and Discussion: The major radioisotopic contaminant identified is the long-lived ^{177m}Lu even if it's only a very small fraction respect to the ground state. In samples of $^{177}LuCl_3$ other non-radioisotopic impurities were sometimes found, but in a very small percentage (*e.g.* ^{46}Sc and ^{60}Co). The experimental half-lives (Tab.1) obtained with this work are in a very pretty agreement with the reference values taken from the literature (*i.e.* 6.734 d for ^{177g}Lu and 160.4 d for ^{177m}Lu, from Table-of-Isotopes, 8–th Ed., 1998 Update on CD-ROM).

Half-lives obtained for the 2 radioisotopes with the 2 different radioanalytical techniques

^{177g}Lu	**6.709±0.001 d**	With γ spectrometry
^{177g}Lu	**6.680±0.006 d**	With β spectrometry
^{177m}Lu	**160.066±0.117 d**	With γ spectrometry
^{177m}Lu	150.33±0.010 d	With β spectrometry

Conclusion: RNP was typically found to be 99.98% at time of measurement and at time of labelling and injection onto patients (a week before) it was better than this value. Experimental half-lives obtained by γ spectrometry are very close to reference data, while measurements with LSCS led to a small but significant underestimation of half-life of the long-lived impurity, due probably to the poor stability of scintillation cocktail. These measurements allow the unambiguous identification of the production method, and consequently the CA or NCA form.

Keywords: Lutetium-177g,m, Radionuclidic Purity, Half-Life, Specific Activity, CA vs. NCA

P407 QUALITY CONTROL OF FDOPA

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Introduction: L-3,4-Dihydroxy-6-[^{18}F]-fluorophenylalanine (FDOPA) is an established radiotracer for PET examination of the dopaminergic system in the brain and a useful tool for the diagnosis of Parkinson's disease. The clinical demand for FDOPA is increased due to its successful utilization for PET visualization of different grade tumors. These facts accentuate the importance of validated and reliable quality control (QC) of FDOPA. We developed a new, short, and efficient set of methods to assess the quality of FDOPA.

Results and Discussion: Important parameters to verify the quality of radiopharmaceuticals are the *chemical*, *radiochemical* and *radionuclide purity*. The estimation of the *radiochemical purity* and particularly the quantification of residual [^{18}F]fluoride (F^-) appeared as a big challenge in the QC of FDOPA since F^- is strongly, covalently retained on all silica based HPLC columns. According to the USP, the radiochemical purity of FDOPA is performed by HPLC on a Nucleosil column, which proved to retain also F^- and therefore the quantification of the FDOPA radiochemical purity according to this method is not accurate. The total recovery of F^- was unsuccessful on many other different columns and mobile phase compositions. The retention of F^- was impossible to be prevented even by using HPLC columns, filled with deactivated silica stationary phases. To avoid these problems the radio-TLC appeared to be a method of choice. An optimal separation of FDOPA and F^- with reasonable speed was achieved by using TLC with cation-exchange stationary phase and a 0.5M HCl solution containing 0.5% sodium fluoride as the mobile phase. Under these conditions F^- migrates along the plate whereas FDOPA stays at the origin. This prevents any radio-artifacts from FDOPA degradation during the TLC analysis and avoids the use of a stabilizer. The addition of NaF to the eluent suppresses the binding of F^- to the stationary phase and improves its accurate quantification in the sample. The *chemical purity* of FDOPA was done by HPLC following the Ph. Eur. The evaluation of residual solvents (acetonitrile and chloroform) in FDOPA was done by a GC method developed in our laboratory. Finally, the enantiomeric purity of FDOPA was established by HPLC on a chiral column, according to the USP. Thus, the complete FDOPA QC can be accomplished within 30min.

Conclusion: To optimize the rate and the efficiency of FDOPA QC we gathered the most suitable methods from the Ph. Eur. and the USP. In addition we have set up a precise, rapid and easy TLC technique for the determination of FDOPA radiochemical purity.

Acknowledgement: The Forschungszentrum Rossendorf and EuroPET are kindly acknowledged for having shared with us their own experience on the FDOPA QC.

Keywords: L-3,4-Dihydroxy-6-[^{18}F]-Fluorophenylalanine, Chemical, Radiochemical and Radionuclide Purity, [^{18}F]Fluoride, Radio-TLC

P408 DESIGN AND FABRICATION OF ^{57}Co STANDARD VIALS

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Introduction: Cobalt-57 ($t_{1/2}$=271.79 d) is accepted as one of the best radionuclides for routine QC of dose calibrators, due to its medium half life and main gamma energies. Standard vials are used as check sources for checking the accuracy, stability, precision and linearity of dose calibrator response at certain intervals and daily control of dose calibrator before use.

Due to the importance of administration of the correct dose to patients, availability of standard sources is quite essential to nuclear medicine centers. Therefore after the production of ^{57}Co in our center, we decided to fabricate standard vials using this radionuclide, traceable to NIST standard for country use.

Experimental: *Production of ^{57}Co:* ^{57}Co was produced at our 30 MeV cyclotron by 22 MeV proton bombardment of a ^{58}Ni target [1]. QC tests showed a desirable radionuclide and chemical purity product.

Chemical preparation: Polyester resin ($C_{12}H_{12}O_4$) was selected as the best matrix for homogenous distribution of the radioactive material. The desired activity was added to the resin base and mixed vigorously. A few drops of MEKP (hardener), ethanol and cobalt naphtanate were added while mixing. CHNS analysis determined the exact percentage of constituent elements as required for dosimetry calculations.

Geometric preparation: The container should be as similar as possible to the reference container. Therefore 25ml LDPE vials (1mm thickness, 25mm int. dia.) were used as the container. Considering the sensitive part of the SSDL activity meter, the active resin was poured in the container up to 2cm height and was covered with the same amount of inactive resin. The lid was sealed using a γ ray resistant epoxy based adhesive.

Effect of the material and shape of the source container and the matrix were investigated by Monte Carlo simulation using MCNP-4C code.

Shield Design: Suitable shields were designed for safe transport of the sources. The shield thickness was determined using MCNP-4C code and also by direct measurement; 16 mm lead for 5 mCi vials.

Quality Control: Quality control equipments were designed and manufactured according to ISO 2919(1999).Radiation leakage and stability at high and low temperature, high and low pressure conditions, structural resistance against impact and puncture were all tested according to ISO 2919(1999) and ISO 9978(1992).

Labeling: Labels were prepared for each source containing the required information according to international standards and the IAEA regulations for the safe transport of radioactive material. Documents were also prepared for each source.

Results and Discussion: Results of quality control tests confirmed a successful design. The activity is traceable to NIST primary standard by less than 5% uncertainty with a confidence interval of 99%. SPECT imaging showed a uniform distribution of activity over the source.

Conclusion: Due to the necessity of using standard sources in nuclear medicine centers, this product is easily available and can be used at every center all over the country.

Reference: [1] S. Spellerberg, P. Reimer, G. Blessing, H.H. Coenen and S.M. Qaim, Appl. Radiat. Isot., 9(12), (1998) 1519-1522.

Keywords: Co-57, Standard Vials, Quality Control, Dose Calibrator

P409 DETERMINATION OF CHEMICAL PURITY OF $^{177g,m}LuCl_3$ FOR RADIOIMMUNOTHERAPY, BY ET-AAS AND INAA

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Introduction: Radioactive solutions of $^{177g,m}LuCl_3$ [$t_{1/2}$ = 6.734 d, β^- 100%, $E_{\beta max}$= 489.3 keV, $<E_\beta>$=163 keV, main γ lines 113 and 208 keV] are used for labelling of organic compounds for metabolic radiotherapy and radioimmunotherapy. The determination of radioactive solutions' *chemical purity* is fundamental to improve radiochemical labelling yield. In these processes the chemical properties of Lu^{III} are obviously involved, so the presence of other stable impurities in the same oxidation state could result in an isomorphous dilution of radioactive ^{177g}Lu, leading to a lower labelling yield as well. Moreover, the long-lived radioisotopic impurity ^{177m}Lu was always present, even if in negligible amounts (*i.e.* 0.01%).

Experimental: Samples of $^{177g}LuCl_3$, obtained from IEO-Milano, were analysed with instrumental neutron activation analysis (INAA) and flameless atomic absorption spectroscopy (ET-AAS) in order to quantify chemical impurities with a special regard for trivalent elements. Neutron irradiations were carried out with the research nuclear reactor TRIGA MARK II (GA, USA) of the Università degli Studi di Pavia. For γ-ray spectrometry of irradiated samples HPGe detectors were used (15% and 40% relative efficiency). Contemporary, samples were analysed with an electrothermal atomic absorption spectrometer (Varian, USA), in order to quantify elements with poor detection limit for the first technique and also to perform intercomparison of analytical results.

Results and Discussion: From preliminary measurements, presence of several metallic non-isotopic stable impurities was assessed. In particular, trivalent elements were found in amounts of the same order of magnitude of Lu carrier, *i.e.* lanthanoids, La^{III}, Yb^{III} other than Al^{III}, Cr^{III}, Sc^{III} and Fe (as Fe^{III}). Based on preliminary data, further measurements were carried out in order to have an accurate and precise determination of these elements. Finally, the determination of the amount of isotopic carrier of Lu was performed effectively by INAA, while results obtained by ET-AAS are still unreliable. Other non-trivalent elements were determined in the ppb to ppm concentration range (Ni, Pb, Zn).

Conclusion: Quantifying the amount of trivalent stable elements in radioactive solution of $^{177g,m}LuCl_3$, used to label radiopharmaceuticals, is relevant from the point of view of labelling yield. The labelling procedure for this nuclide is based on the oxidation state (III). Several trivalent stable elements, that can compromise the labelling, were determined with two sensitive analytical and radioanalytical techniques.

Keywords: Lutetium-177, Chemical Purity, Instrumental Neutron Activation Analysis, Electrothermal Atomic Absorption Spectrometry

P410 HPLC DETERMINATION OF THE SPECIFIC RADIOACTIVITY OF (^{18}F)FLUORIDE ION AS ITS La^{3+}-ALIZARIN COMPLEXONE TERNARY COMPLEX

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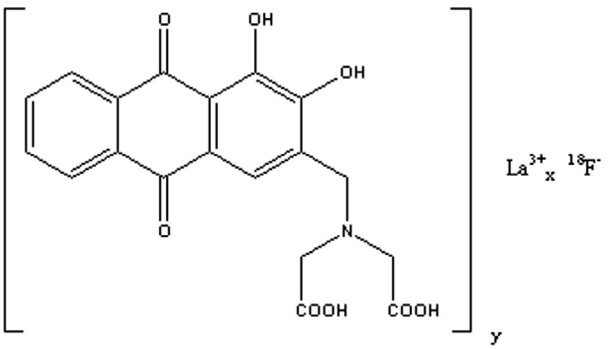
Introduction: For measuring the specific radioactivity (s.a.) of cyclotron-produced [^{18}F]F^- an HPLC method that uses an alternative to the less accessable electrochemical detection [1], would be useful. This work investigates the possibility of measuring [^{18}F]F^- as its La^{3+}- alizarin complexone ternary complex with HPLC and absorbance detection in the visible region [2].



Experimental: HPLC: Ultrasphere C18, 250 x 4.6 mm, MeOH/0.001M acetate buffer pH 4.3 = 27/73, 1 mL/min, detection: GM and VIS (568 nm).

F^- reagent: aq.0.002M alizarin complexone/aq. 0.002M $La(NO_3)_3$/aq. 0.1M acetate buffer pH 4.3/acetone 2:2:1:4.

Weigh a sample of [^{18}F]F^- solution ($\geq$ 150 μL in case of target water and after complete decay if wished) into a weighed vial. Dilute to ~2 mL with deionized H_2O. Add reagent (4 mL) and wait 30 min. Add H_2O (3 mL) and NEt_3 (1 mL) and weigh. The density is 0.9528 g/L. Inject 20 μL immediately. Estimate the amount of F^- by comparison the mass peak with a calibration curve correlating absorbance with sample fluoride concentration, normalizing for the amount of sample and relative amount injected. Radioactivity concentration in the [^{18}F]F^- solution is measured independently of HPLC.

Results and Discussion: Peak surface is indirectly linked to the initial F^- concentration through an unknown complexation yield and stoichiometry, so radioactivity under the collected peak cannot be used. We found, in contrast to ref.2, that [^{18}F]F^--La^{3+}- alizarin complexone is not stable after NEt_3 addition. In 30 min 40% of the activity has become [^{18}F]F^- and in 3 h little complex is left. Nevertheless, NEt_3 is needed to avoid on column decomposition and should be added immediately before HPLC analysis. With the original[2] mobile phase (MeOH/H_2O 19/81) we found strong variations in k values and separation depending on the number of injections and their spacing in time, possibly caused by NEt_3, so we modified it using a buffer. The complex is not formed in the presence of kryptofix.

Analysis of samples of known F^- concentration gave concordant results. A first measurement of the F^- concentration in $H_2{}^{18}O$ after ^{18}F decay gave 250 nmol/mL which is in line with our habitual s.a. range.

Conclusion: The presented method is suitable for the s.a. measurement of [^{18}F]F^-. Comparison with the s.a. of [^{18}F]F^--derived radiopharmaceuticals and determination of the accuracy of the method are underway.

References: [1] Shiue, C.Y. et al, J. Nucl. Med. 26, 181-186 (1985). [2] Xu, X.R. et al, Chromatographia 59, 745-747 (2004).

Keywords: [^{18}F]Fluoride, Specific Radioactivity

P411 INSTANT THIN LAYER CHROMATOGRAPHY (ITLC) – A SAFE, TRUE AND ECONOMICAL METHOD FOR THE DETERMINATION OF RADIOCHEMICAL PURITY OF ^{99m}Tc-LABELED RADIOPHARMACEUTICALS

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Introduction: Determination of Radiochemical purity(RCP) usually involves paper chromatography method or some sort of column chromatography such as ion exchange or gel filtration technique.In this study a modified chromatography method with thin-layer support called instant thin Layer chromatography (ITLC) was used for the measurement of radiochemical purity. The aim of the study was to present ITLC-Silica-Gel technique as a fairly rapid,convenient and inexpensive system for the screening of radiochemical impurities of ^{99m}Tc-labeled radiopharmaceuticals.

Experimental: The experiment was carried out at INMU,Dhaka.Radiochemical purity of seven types of ^{99m}Tc-labeled radiopharmaceuticals,namely ^{99m}Tc-DTPA,^{99m}Tc-MIBI,^{99m}Tc-HDP,^{99m}Tc-DMSA,^{99m}Tc-Tetofosmin,^{99m}Tc-Fyton and ^{99m}Tc-ECD were measured by the use of two solvent dual-ITLC system.Commercially available ITLC plate (20cm $\times$20cm) impregnated with sillica gel (ITLC-SG:Merck,Germany) was used as a stationary phase for the measurement of radiochemical impurities. Acetone, ethyl methyl ketone,chloroform and methanol were used to measure the amount of free pertechnetate and 0.9% saline was used in all cases as solevnt (mobile phase) to measure the the amount of the hydrolyzed-reduced technetium colloid in the labeled radiopharmaceuticals.

Results and Discussion: The results showed that the measured RCP of ^{99m}Tc-DTPA,^{99m}Tc-MIBI,^{99m}Tc-HDP,^{99m}Tc-DMSA,^{99m}Tc-Tetofosmin,^{99m}Tc-Fyton and ^{99m}Tc-ECD were acceptable for all the studied samples except two samples of ^{99m}Tc-MIBI, one sample of ^{99m}Tc-Fyton and two samples of ^{99m}Tc-ECD, where the measured RCP were not within the acceptable RCP limits of commonly used radiophamaceuticals (RCP should be 90% to 100% for ^{99m}Tc compounds-USP XXI).

Conclusion: The findings of the study indicate that routine RCP test of ^{99m}Tc-labeled radiopharmaceuticals through ITLC-SG method is a reliable one.Routine RCP measurement by this method not only prevents repeated patient study that results increased radiation exposure to technologists and patients but also prevents the delay in reporting the study and the additional time and expense involved.

Acknowledgement: Special thanks to Md.Jaharul Islam (Scientific Officer) and Md. Joynal Abedin(Scientific Officer) of INMU, Dhaka.

Keywords: Radiochemical purity, Instant Thin Layer chromatography (ITLC), 99mTc-Labeled Radiopharmaceuticals.

P412 MicroBeta TriLux PLATE COUNTER FOR *IN VITRO* EVALUATIONS OF I-123 AND F-18 LABELLED COMPOUNDS

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Introduction: Receptor binding assays are a critical component in lead identification and characterization in drug development. MicroBeta TriLux, a microplate liquid scintillation counter (LSC), has been widely applied to drug receptor studies with vast savings in time, consumables and wastes. Besides the applications for commonly used isotopes such as ^{3}H, ^{14}C, or ^{125}I, the use with ^{64}Cu, ^{177}Lu and ^{149}Pm has been reported and provided greater sensitivity compared to gamma counter counting. In the present study, we explored the feasibility of using a MicroBeta TriLux for *in vitro* assays for ^{123}I and ^{18}F labeled compounds.

Experimental: Crosstalk for both ^{123}I and ^{18}F was determined by applying a sample of radioactivity (25μl, 2.5μCi for ^{123}I, 0.1 μCi for ^{18}F) to a central well of the desired plate (96-well filter or 24-well tissue culture plate) followed by scintillation fluid (100 μl, Wallac Optiphase SuperMix) to all wells in the plate. The plate was counted with both a broad and optimal enrgy window with a microbeta plate counter. Counting efficiency with a microbeta plate counter for both ^{123}I and ^{18}F was measured and compared with the gamma counter measurement. The use of a microbeta plate counter for ^{123}I was validated by saturation binding studies with a ^{123}I-protein on MCF-7 cell membranes. The potential of using a microbeta plate counter to measure ^{18}F was tested by adherent cell uptake studies with ^{18}F-SPA-RQ, an NK1 receptor tracer.

Results and Discussion: Using a broad energy window, crosstalk was measured to be 0.06- 1.8% for ^{123}I, and 7.5% for ^{18}F in the closest adjacent well and 0.6% or lower for all other wells. By redefining the energy windows, crosstalk for ^{123}I was reduced to 0.1% -0.3%. However, ^{18}F crosstalk remained 7% for the closest adjacent well. Cell uptake studies for ^{18}F-SPA-RQ were performed in the wells which were not adjacent, ensuring minimal crosstalk interference, and measured with a default energy window. The counting efficiency for ^{123}I was improved from 27.6% with a gamma counter to 33.5% with a microbeta plate counter with optimal window. Microbeta plate counter increased ^{18}F counting efficiency by approximately 40% compared to a gamma counter. Saturation studies with ^{123}I-protein on MCF-7 cell membranes measured by both gamma counter and microbeta plate counter provided comparable Kd (nM) values of 5.19± 1.0 from gamma counter counting vs. 3.8 ± 0.8 from microbeta plate counter counting. Cell uptake studies of ^{18}F-SPA-RQ with transiently expressed CHO cells measured with both gamma counter and plate counter showed similar time-dependent uptake curves and retention patterns.

Conclusion: It is feasible to use a microbeta plate liquid scintillation counter for binding studies (^{123}I) and cell uptake studies (^{18}F), providing greater counting efficiency and vast savings.

P413 AUTOMATED MANUFACTURE AND STABILITY STUDIES OF 16α-(^{18}F)FLUORO-17β-ESTRADIOL USING TRACERLAB FX_{FDG}

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Introduction: 16α-[^{18}F]-fluoro-17β-estradiol ([^{18}F]-FES) is a steroid based radiopharmaceutical that has emerged as a valuable positron emission tomography (PET) tracer to predict the response to hormone therapy in recurrent or metastatic breast cancer patients. Following its development in the early eighties the synthesis procedure for [^{18}F]-FES has been automated to increase the reaction efficiency, to reduce the production time, to maintain consistent quality that may be more acceptable to regulatory agencies and to minimize the radiation exposure to laboratory personnel.

Experimental: Automated synthesis of [^{18}F]-FES is being carried out at our centre under GMP conditions using a GE TRACERlab FX_{FDG} synthesis unit incorporating modifications to the literature methods. Briefly, 2 ± 0.5 mg of 3-methoxymethyl 16β, 17β cyclic sulfate epiestriol is dissolved in acetonitrile and substituted with dried [^{18}F]-fluoride at 110°C for 10 min under critical pressurized conditions. After evaporation, the intermediate product is hydrolyzed two times with 0.1 N HCl in 90% acetonitrile/water at 100°C for 3 min followed by the evaporation of the solvent. This hydrolyzed crude [^{18}F]-FES is dissolved in 50% aqueous ethanol loaded on to a preparative reversed phase high performance liquid chromatography column and eluted with ethanol/water (52:48) at a flow rate of 1.8 mL/min. The pure [^{18}F]-FES fraction is collected in a sterile multi dose product vial, containing 10 mL sterile saline, after passing through a sterile 0.22 mm filter.

Results and Discussion: This controlled manufacturing process affords pure [^{18}F]-FES in >26% ± 6 yield (n=5, decay uncorrected) and is completed in 78 min including the purification time. The radiochemical purity and activity concentration were >98% and >200 MBq/mL respectively. Purified [^{18}F]-FES was studied for its stability over a period of 12 h under normal storage conditions to prove its chemical and radiochemical integrity. The stability studies demonstrated that [^{18}F]-FES was stable during this time period in saline containing 15-20% ethanol in both upright and inverted vial positions. When the preparation did not contain saline, the radiochemical purity of the product declined rapidly after 2 h.

Conclusion: The current procedure provides [^{18}F]-FES as a routine product with high yield and radiochemical purity. [^{18}F]-FES is being used at the Edmonton PET Center in conjunction with [^{18}F]-FDG studying estrogen receptor status and tumor glycolysis in breast cancer patients.

Acknowledgement: Canadian Breast Cancer Foundation, Alberta Cancer Board, David Clendening, Jayden Sader, and Courtney C Doerksen at Edmonton PET Center, Cross Cancer Institute, Edmonton, Canada.

Keywords: 18-F-FES, Automated Synthesis, Stability Studies, Estrogen Receptors, PET

P414 FINDING A NICHE FOR XRFS IN THE PET RADIOCHEMISTRY LAB

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Introduction: X-ray fluorescence spectroscopy (XRFS) is a broad band technique for *elemental* analysis, though now largely supplanted by more sensitive ICP-MS and ICP-AES. Modern solid state detectors provide baseline separation between elements and the non-destructive sample preparation favors XRFS, but the expense of GBq excitation sources can be considerable. This is particularly true for the PET radiochemistry lab that needs to assay contaminants in the final product (Sn, Hg or Br in F-DOPA) only infrequently during the inital validation, with the system otherwise mothballed.

Experimental: An XRFS resource has been configured at the UW Medical Physics cyclotron facility, consolidating detectors (Amptek XR-100T Si(Li), 7 mm ^{2} x 300 μm: Canberra 1 cm ^{2} x 1 cm HPGe) and a battery of excitation point sources listed in Table 1. The facile production of hundred mCi levels of ^{107}Cd presents the opportunity of making XRFS excitation sources *on demand*. A water-cooled silver disc is capable of handling 40 μA of 11 MeV protons without sublimation of the volatile cadmium. The target blank is then transferred to the XRFS photon howitzer, shadowing the primary source from the detector as shown in Fig 1.

Table 1

Source	$t_{1/2}$	E_γ (keV)	Preparation	Activity	to excite
^{107}Cd	6.5 hr	22	^{nat}Ag(p,n)	29 mCi/μA	transition metals
^{241}Am	452 yr	59	commercial	10 mCi	rare earths
^{99m}Tc	6 hr	140	electroplated from MEK	10 mCi	heavy elements
X-ray generator	10-50 kV brem	1-100 μA	Oxford		

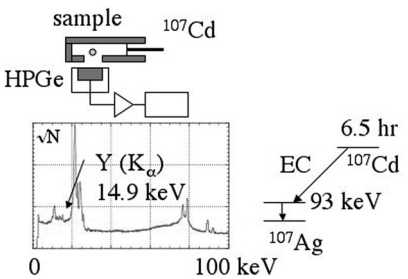

Fig. 1

Results and Discussion: The ppm sensitivity of XRFS hinges on choosing an excitation photon slightly above the K-shell binding. The EC decay of ^{107,109}Cd, with the concomitant silver K X-rays at 22 and 24 keV, are well-suited to the fluorescence near $Z \asymp 40$, ideal for the assay of breakthrough Sr in ^{86}Y or Y in ^{89}Zr. A 16 μM YCl_3 solution is assayed to 3% in 10 minutes, shown compressed by the square root display. Lead X-rays and Rayleigh scattering of the Ag K_α primaries dominate the spectrum.

Conclusion: XRFS comes in a poor second in sensitivity against modern inductively coupled plasma techniques. Yet there arise situations where the lack of *a priori* knowledge of possible contaminating elements makes X-ray fluorescence an attractive assay. In those infrequent occasions, the ability to quickly fashion an effective excitation source of ^{107}Cd or ^{99m}Tc takes some of the financial sting out of the technique.

Acknowledgement: The support of DE-FG01-01NE23052 is gratefully acknowledged.

Keywords: X-Ray Fluorescence Spectroscopy, Elemental Analysis, Chemical Purity of PET Tracers, Cd-107, Excitation Sources on Demand

P415 PREPARATION AND QUALITY CONTROL OF ^{177}Lu-BASED THERAPEUTIC RADIOPHARMACEUTICALS

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Introduction: Reactor produced ^{177}Lu is emerging as an important radionuclide for cancer therapy since it decays with a half-life of 6.71d by the emission of b^- particles with E_b of 498 keV (78.6%), 384 keV (9.1%) and 176 keV (12.2%) to stable ^{177}Hf. A chelating agent, EDTMP has proven to be an effective radiotherapeutic agent in the treatment of metastatic bone cancer pain.DOTA-Tyr3-Octreotate has proven very successful in tumour reduction in patients with metastatic neuroendocrine tumours.

Experimental: Solid and liquid $Lu(NO_3)_3$ targets (natural and enriched) were used for the production of ^{177}Lu in PARR-I Reactor. Preparation of ^{177}Lu-EDTMP and ^{177}Lu-DOTA-Tyr3-Octreotate complexes was studied for different pH, temperature and incubation period. The labelling yield of ^{177}Lu-EDTMP was measured by silica gel paper developed in acetone. Radiochemical purity of ^{177}Lu-DOTA-Tyr3-Octreotate was determined by radio TLC with C18 plates developed in 70:30 MeOH: 10%NH_4Oac. Stabilities of these complexes were studied in the acetate/ascorbate buffer and in the saline for different time intervals. Animal studies of these complexes using rats were also done. Internalization of ^{177}Lu-DOTA-Tyr3-Octreotate was carried out with AR42J pancreatic cells.

Results and Discussion: The results showed that a specific activity of 6.5 Ci/mg of ^{177}Lu for solid $Lu(NO_3)_3$ and of 8 Ci/mg for liquid $Lu(NO_3)_3$ could be obtained in the reactor at a neutron flux of $1.5x10^{14}$ $n/cm^2.s$ for a period of 96 hours. The data on the preparation of ^{177}Lu-EDTMP complex showed high labelling (>99%) at pH 5-7 with incubation period of 25 minutes at 30°C. The results on the labelling yields of ^{177}Lu-DOTA-Tyr3-Octreotate complex indicated optimum labelling yield (>98%) at pH 4 to pH 5 with incubation period of more than 25 minutes at 90°C. The complexes were found to be stable in both acetate/ascorbate buffer and in saline for the period of 36 hours. Animal studies of ^{177}Lu-EDTMP indicated its uptake in bone and excretion root was through kidney. Similarly the critical organ of ^{177}Lu-DOTA-Tyr3-Octreotate was the pancreas. Internalization studies showed more than 5% of internalization into AR42J cells after 80 minutes.

Conclusion: High specific activity ^{177}Lu radionuclide has been produced in PARR-1 reactor, which has been used for the preparation of high purity ^{177}Lu-EDTMP and ^{177}Lu-DOTA-Tyr3-Octreotate complexes as agents for therapeutic radiopharmaceuticals.

Acknowledgement: Financial support by the International Atomic Energy Agency under IAEA Research Contract No. 12130 is acknowledged.

Keywords: Lu-177, Therapeutic Radiopharmaceuticals, Bone Metastases, Cancer Treatment

P416 A RAPID, ROBUST AND FULLY AUTOMATED METHOD FOR ANALYSIS OF RADIOACTIVE METABOLITES IN PLASMA SAMPLES FROM PET STUDIES

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Introduction: The analysis of radioactive plasma components from blood samples taken during PET studies of receptor ligands is vital for the correct quantification of the data. For ^{11}C-labelled ligands rapid analysis is a pre-requisite due to the time constraints imposed by the short half-life of carbon-11 (20.4 min). On-line HPLC column switching methods have been reported which enable direct injection of unadulterated plasma samples, thus allowing a more rapid analysis (Hilton et al. 2000). These methods use a small capture column to extract the lipophilic components from the plasma whilst measuing the non-extracted radioactivity with a on-line radiodetector. The trapped radioactivity is eluted by reversing the flow and directing the flow through an analytical HPLC column with on line detection. Reported here is an optimised method which utilises the latest HPLC column technology.

Experimental: The HPLC system used comprises a BioTrap 500 MS extraction column (20 x 4 mm, ChromTech Ltd. UK) and an Onyx Monolithic C18 analytical column (50 x 4.6 mm, Phenomenex, USA) Using two six-position valves, the flow is directed through on-line UV and radioactivity detectors. Up to 4 mL filtered plasma is loaded into the injection loop and the flow through both columns is 4.5 mL/min. Extraction of the lipophilic components takes upto 3.5 minutes, depending on the injection volume. Elution of the lipophilic components from the extraction column and subsequent analysis on the analytical column takes a further 1-2 minutes. Regeneration of the extraction column takes a further 1 minute.

Results and Discussion: 4 mL filtered plasma was analysed by this method within 7-8 minutes and 0.5 mL plasma in only 5 minutes. In this HPLC set-up the backpressure was only 90 bar using a flow rate of 4.5 mL/min for both columns. Figure 1 shows a typical chromatogram of a ^{11}C-labelled ligand in 4 ml plasma. Experience to date suggests that the BioTrap extraction column can be used for analysis of at least 500 mL unadulterated plasma without loss of extraction efficiency. Due to the nature of monolithic HPLC columns, the analytical column should also be extremely robust.

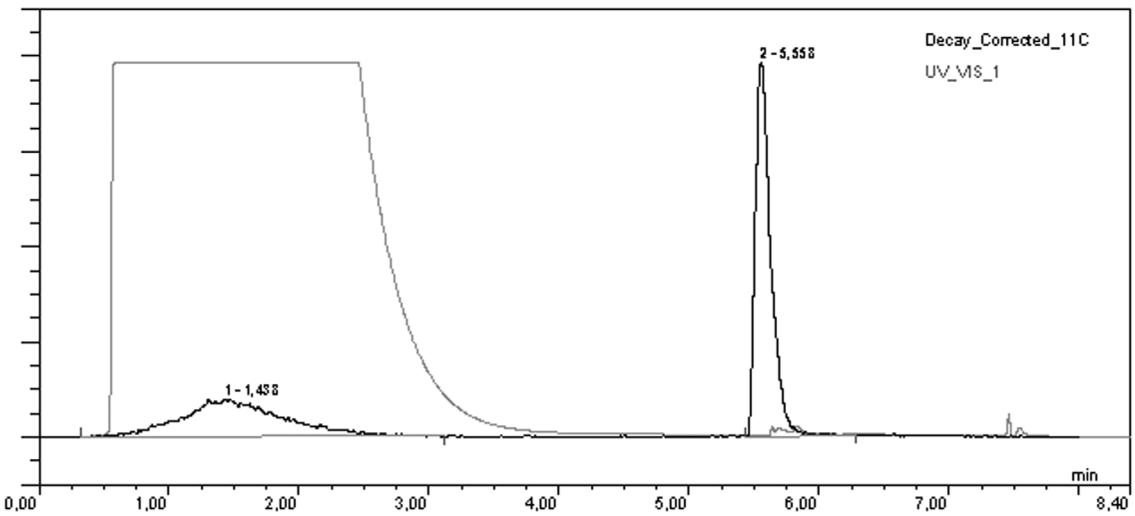

Fig. 1

Conclusion: The described HPLC set-up is very rapid and robust and will allow for analysis of upto 10 plasma samples from a PET study using a ^{11}C-labelled receptor ligand.

Keywords: Plasma Metabolites, Carbon-11, HPLC

P417 BACTERIOSTATIS AND FUNGISTATIS TEST AS VALIDATION OF STERILITY TEST METHOD FOR RADIOPHARMACEUTICALS

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Introduction: Many diagnostic and therapeutic products need to be certified as sterile. Products free of contaminating microorganisms that receive a strict and controlled conditions of sterility testing can meet these high requirements. The same criteria as for non-radioactive medicines products apply to radiopharmaceuticals. False negative results can be caused by anti-microbial properties of the radiopharmaceutical product. Bacteriostatis and fungistatis test are performed to validate the sterility tests by assuring that there are no inhibiting factors that exist in the product.

The aim of this work was validation test for sterility of chosen radiopharmaceuticals: MIBG-^{131}I, sodium iodohippurate-^{131}I, $^{89}SrCl_2$, $Na^{131}I$, and ^{99m}Tc-generator eluate, in accordance with the pharmacopoeial method.

Experimental: The test was repeated three times for each sample of product with each type of organism (aerobes *B. subtilis*,*S. aureus*, *P. aeruginosa*; anaerobes: *C. sporogenes*; fungi: *A. niger*, *C. albicans*).

In direct inoculation method not more than 100 cfu of the challenge organism was applied directly to the both thioglicollate broth (*P. aeruginosa, C. sporogenes, S. aureus*) and trypcase-soy broth (*A. niger*, *C. albicans, B. subtilis*) media containing product. Growth promotion test of media as positive control and sterility test of preparations as negative control. The every challenge inoculum was verified by concurrent viable plate counts. All test containers of media containing microorganisms were incubated for not more than 5 days. Containers with thioglicollate broth were incubated at 35°C whereas containers with TSB at 25°C. The test was invalid if challenge organisms didn't show clearly visible growth within 5 days in the test media containing product. The visual recovery was compared to the growth promotion test. Apparent organisms growth in media was verified by subculture to solid media (except *A. niger)*.

Results and Discussion: The validation tests pass if minimum of 70% of viable bacteria are found with reference to the control plates.

Results

	A. niger % TSB	*B. subtilis* % TSB/Thio	*C. albicans* % TSB/Thio	*P. aeruginosa* % TSB/Thio	*C. sporegenes* % TSB/Thio	*S. aureus* % TSB/Thio
MIBG^{131}I	+	59/79	101/–	83/79	–/*93	117/*88
$^{89}SrCl_2$	+	91/–	81/–	–/*72	–/*68	179/87
Hippurate–^{131}I	+	165/–	95/–	165/96	–/*117	*84/–
$Na^{131}I$	+	131/–	89/–	–/*68	–/*73	90/–
^{99m}Tc	+	84/–	83/–	–/*71	–/*71	96/70

*the test was performed 2 times for each sample of product, +growth in liquid medium, Thio-thioglicollate broth

Conclusion: Validation tests for sterility of MIBG-^{131}I, sodium iodohippurate-^{131}I, $^{89}SrCl_2$, $Na^{131}I$, and ^{99m}Tc-generator eluate show that any inhibiting factors seems to exist in the these preparations.

Keywords: Growth Promotion Test, Bacteriostatis, Fungistatis

P418 THE IUPAC PROJECT: TERMINOLOGY, QUANTITIES AND UNITS CONCERNING PRODUCTION AND APPLICATIONS OF RADIONUCLIDES IN RADIOPHARMACEUTICAL AND RADIOANALYTICAL CHEMISTRY

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Introduction: Several people of the Nuclear and Radiochemistry community found unclear definitions and even misleading in present literature in the field of nuclear chemical sciences and technologies. A new IUPAC Project has been presented, discussed, approved and financed during the 42th IUPAC GA in Ottawa, Aug 2003. Updated at 43rd IUPAC GA in Beijing, Aug 2006.

Examples of unclear definitions are: isotopic and non-isotopic carrier, carrier free, no carrier added, isomorphous carrier, specific activity, isotope dilution factor, activity concentration, coprecipitation, carrier form speciation.

Experimental: Example of historical definition of "carrier" by Glenn Seaborg: "carrier is any chemical or physical species able to carry on a radioactive element present in trace amounts in a radioactive mixture" After Wolf et al, JNM., 22 (1981) 392: "carrier consists of any stable isotopes of the same element present in a radioactive preparation of either a labeled compound or radiopharmaceutical."

Results and Discussion: Examples of improved definitions:

Carrier: "A chemical species – already present in the preparation or intentionally added – which will carry a given radionuclide in its associated species through the radiochemical procedure and/or prevents the radionuclide in its associated species from undergoing non-specific processes due to its low concentration".

Isotopic carrier: "A carrier, which is isotopic with the given radionuclide and is present in the same chemical form".

Specific activity, A_S: "For a given radionuclide the activity at time t divided by the mass of the sum of all radioactive and stable isotopes isotopic of the element involved. Units: Bq/mol or Bq/kg ".

Activity concentration (or radioactive concentration), C_A: "For a given radionuclide, the activity of a material at time t divided by the mass or volume of that material. Units Bq/kg and Bq/m3 ".

No-carrier-added: A preparation of a given radionuclide where special attention has been paid to procedures, equipment and materials in order to minimize the introduction of isotopes (both stable and radioactive) of the element in question in the same chemical form or as a species enabling isotopic exchange reactions.

Isotope dilution factor, IDF: the ratio at time t after end of radiochemical processing, including labeling, if applicable, of a radionuclide, between the number of all atoms (both stable and radioactive) isotopic with radionuclide of interest and the number of atoms of radionuclide itself.

Conclusion: The updated terminology will be presented with the aim to improve the IUPAC Orange Book: "Compendium of Analytical Nomenclature". After approval, the Provisional Recommendations will be put on IUPAC website for public discussion.

Acknowledgement: The author presents the paper as chairman of IUPAC Task Group.

Keywords: IUPAC Project, Terminology, Radioanalytical Chemistry, Radiopharmaceutiocal Chemistry, Orange Book

P419 COMPUTERIZED SYSTEMS AND GMP IN PET RADIOPHARMACEUTICAL PRODUCTION

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Introduction: In validation of apparatuses and methods for the production of PET-tracers some special characteristics, like the short half-life of the radioisotopes, the potentially very high radioactivity amounts used and also the possible combination of pharmaceutical production and R&D with the same devices, must be taken into account. Validation and the existence of a quality system is a prerequisite for collaboration between Pharma industry and the PET-world. Initially collaboration with Pharma is focused on R&D when new radiotracers are developed. At this stage validated systems that are used in production can be used.

Experimental: Validation is carried out according to combined recommendations, guidelines and rules of various regulatory bodies [1-4] and also pharma companies. Validation is a team effort that requires a vast amount of information from various sources. The quality has to be built into the system already at the initial stages of the process.

Risk assessment is a central part in the beginning of the life cycle of the system. It helps in focusing validation work where it is most needed and helps in finding a proper approach and scope in validation that is in line with the intended use of the system. On the other hand, the chain of validation starts with the user requirements.

Results and Discussion: The documents produced in the validation process form then an efficient forum of information and a ground for discussion. Validation as such does not improve the process, but it ensures that the process works as it is supposed. The documents associated with the validation of computerized systems help in conforming to the demands of regulatory bodies. An important part is then also the management of the life cycle of the system, which is a GMP requirement.

Conclusion: The system owner is responsible for the validation of systems and apparatuses. Validation after the qualification process and system implementation must also be taken into account, in order to keep the validation status updated. This involves change control, operator training, deviation management etc.

At the Turku PET Centre we have developed our quality system with increasing focus on computerized systems for PET-radiotracer production.

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Keywords: Computerized Systems, GMP, PET, Validation

P420 FULLY AUTOMATED PRODUCTION OF Ga-68-LABELED PEPTIDES

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Introduction: The aim of this work was to construct and evaluate a fully automated module for the production of Ga-68-labeled peptides, e.g. [Ga-68]DOTATOC. To minimize the radiation exposure for the personal, all relevant parts, i.e. elution of the generator, radiolabeling, purification and formulation were included.

Experimental: For elution of the Ge-68/Ga-68 generator (Obninsk Cyclotron Co. Ltd.), 0.1M HCl was used. The fraction containing Ga-68 was separated and transferred into a reactor containing 7-10μg (5-10 nmol) peptide and 150 μL 2.5M HEPES. Labeling was carried out at pH 3.5 at 90°C for 5 min. After the mixture was transferred onto a Sep-Pak C18 Plus-cartidge, the reactor was purged with 2 mL water. To eliminate contaminations and free Ga-68, the cartridge was washed with another 2 mL water. Subsequently, the product was eluted with 500 μL ethanol, followed by 11 mL 0.1 M phosphate buffered saline through a sterile filter into a sterile vial (CIS). For quality control purposes, HPLC, TLC and γ-spectrometry was performed and pH, sterility and apyrogenicity were checked. Automation, incl. all required components and a suitable control software, was realized using a variable construction system (Variosystem, Scintomics, Germany).

Results and Discussion: Peak fractionation provided 80-85% of the maximum Ga-68-activity in 1.2-1.5 mL 0.1N HCl. The automated production was completed in less than 20 min and yielded the desired peptide in 11.5 mL 0.1 M PBS (4% EtOH, pH 7.0) and 48±5% uncorrected yield (n=35). The radiochemical purity of the products were in the range of 97-99% (TLC: 98-99%, HPLC: 97%). To quantify breakthrough of Ge-68, γ-spectrometry was performed two days after production. In all samples investigated no significant Ge-68 activity was detected (contaminations: 0-20Bq Ge-86 per product vial; 11.5mL). All production runs yielded sterile and apyrogenic formulations. Technical malfunctions did not occur so far. A leakage of the Ge-68/Ga-68 generator (corrosion of the upper Al-crimp-cap) resulted in an exchange of the generator. The system can easily be extended by a Ga-68 prefixation step, which either includes an anionic prefixation (GaCl4-: fixation with 5M HCl onto SCX material, elution with water) or cationic fixation (AG50W-X4 or –X8, 0.1M HCl, elution of contaminations with 80% acetone/diluted HCl; elution of Ga-68 with 95-98% acetone/diluted HCl)[1,2,3].

Conclusion: A fast, simple, reliable, cost-effective and fully automated module has been established which is now in use for production of Ga-68-peptides in a clinical setting.

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Keywords: Automation, Ga-68, Peptide Labeling

P421 DEVELOPMENT AND VALIDATION OF AN ULTRA-FAST LC METHOD FOR THE QUALITY CONTROL OF PET RADIOPHARMACEUTICALS

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Introduction: Rapid and sensitive analysis is the key demand in quality control (Q.C.) of short-lived radiopharmaceuticals, since the Q.C. tests must be performed before human administration and the synthetic products are often extremely low levels (ng-μg/mL) due to high specific radioactivity. LC is most commonly used for this purpose; however, it does not always provide sufficient speed and sensitivity under the traditional conditions (*e.g.* described in the USP and EP). The recent introduction of fast-LC and ultra performance LC technology made possible higher throughput analysis than traditional LC. These LC utilize a short column packed with small-particles (< 3 μm) at high pressure allow the fast analysis with excellent resolution and sensitivity. In the present study, we established the ultra-fast and sensitive LC method for the determination of specific radioactivity, radiochemical and chemical purity for wide variety of PET pharmaceuticals.

Experimental: For all ^{11}C, ^{18}F- labelled compounds examined (33 pharmaceuticals) the common column and mobile phase modifier was used. The LC was performed on a short Waters XBridge RP_{18} column (50 mm x 3.0 mm id) packed with 2.5 μm particles and a mixture of three modifiers (A. 90% CH_3CN, B. 100 mM ammonium-phosphate buffer (pH 2.1), C. 50 mM ammonium-phosphate buffer (pH 9.3)) as the mobile phase using conventional LC apparatus (max. pressure: 30 MPa). Detection was achieved by simultaneous monitoring of low-wavelength UV absorption and radioactivity.

Results and Discussion: The use of a fast-LC system allowed excellent separation of target analytes within a very short run time of 60 sec; only a 3% decline of the radioactivity was observed during the analysis of ^{11}C-compounds. The combination of ammonium-phosphate buffer and low wavelength UV detection results in an improvement in the applicability and sensitivity. All of the compounds examined could be detected including MP4A (*N*-methyl-4-piperidyl acetate), which only was detected at *ca.* 210 nm with weak alkaline medium. The limits of detection were about 10 times better compared with traditional LC. Satisfactory reproducibility, linearity and recovery were obtained during the validation study, and the proposed method could be successfully applied to the Q.C. tests of pharmaceutical samples. We could perform the analysis of different pharmaceuticals in a short period since this method utilized common column and mobile phase.

Conclusion: This method fulfils the requirements for the routine Q.C. tests in terms of rapidity, sensitivity and applicability. Furthermore, ultra sensitive analysis was achieved by the incorporation of fluorescence, electrochemical, chemiluminescence detection to this LC system.

Keywords: Ultra-Fast LC, Quality Control, PET Radiopharmaceuticals

P422 COLORIMETRIC METHOD FOR QUANTITATIVE DETERMNIATION OF SMALL PEPTIDES IN PHARMACEUTICAL KITS

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Introduction: GMP preparation of pharmaceutical kits demands a number of tests including the assay of active substance in the vial with lyophilisate. Usually peptides, such as somatostatin analogues, are at microgram quantities in a vial, rendering certain difficulties in application of HPLC for their quantitative assessment, due to several artifacts related to this method. The aim of this study was to overcome limitations of HPLC and to establish quantitative method based on the BCA Protein Assay colorimetric detection, and its sensitivity to detect peptidic bonds after quantitative separation of peptide from excipients in the kits for ^{99m}Tc labeling of HYNIC-Tyr^3-octreotide (HYNIC-TOC).

Experimental: Test is based on Cu^{2+} reduction to Cu^{1+} in presence of 2 neighbouring peptidic bonds in an alkaline medium and selective colorimetric detection of the cuprous cation (Cu^{1+}) using a bicinchonic acid, BCA (max. absorbance at 562 nm). Standards for calibration (0.010, 0.015, 0.020, 0.025 and 0.030 mg/ml) were prepared from 1 mg/ml solution of HYNIC-TOC (PiChem) in 0.9% NaCl. BCA (BCA™ Protein Assay Kit, Pierce) components A and B were mixed 33:1 (v:v). To the eppendorf vials 0.25 ml of each standard dilution and 0.75 ml of BCA mix were added and incubated at 60°C for 1 h with shaking. Absorbance was measured at 562 nm in microplate reader in triplicates after dispensing 0.25 ml of each solution to the 96-well plates. Tested sample was prepared by dissolving kit content (HYNIC-TOC, $SnCl_2$, tricine, mannitol) in 1 ml of 0.9% NaCl and incubation at 50°C for 30 min. Peptide fraction was separated by passing this solution through the Sep-Pak Light C-18 cartridge, washing the column with 15 ml of 0.9% NaCl and eluting with 1 ml MeOH. Test samples for BCA assay were prepared as above.

Results and Discussion: Calibration curve parameters showed detection limit of 2.13 mcg/ml and determination limit of 7.12 mcg/ml at the expected working range of about 20 mcg/ml. Precison expressed as RSD is 2.71%. In 6 independent series the determined values of HYNIC-TOC assay per vial were found to be in the range 17,839–19,487 mcg. SepPak separation recovery was 97.52% ± 1.21%.

Conclusion: BCA method has been proved useful for the quantitative determination of small peptides in pharmaceutical kits. Modification of method by prior separation of peptide from excipients eliminates factors influencing the sensitivity of this colorimetric method.

Acknowledgement: This work has been partly supported by the research grant No. 2 P05A 02428 of the Polish Ministry of Science and Higher Education.

Keywords: Peptide Assay, BCA Method, 99mTc-HYNIC-TOC, Pharmaceutical Kits

P423 LIPOSOME TECHNOLOGY AND ROLE OF RADIOLABELLING

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Introduction: Liposomes are vehicles in which an aqueous volume is entirely enclosed by a membrane composed of lipid molecules (i.e. phospholipids). They are formed spontaneously when the lipids are dispersed in aqeous media, giving rise to a population of vesicles which may range in size from tens of nanometres to tens of micrometres in diameter. They can be constructed so that they entrap materials both within their aqueous compartment and within the membrane. Liposomes may be composed of entirely natural or artificial components and used as drug delivery systems for medical applications and targeting.

Experimental: Film method was used for the preparation of gel or liquid state liposomes as a radiopharmacutical diagnosis tool. Primaquine diphosphate (PQ), dexamethasone sodium phosphate (DSP), urea, iopromide, diethylene triamine penta acetic acid (DTPA), dimercapto succinic acid (DMSA), streptokinase, urokinase and diclofenac sodium phosphate (DSP) were used as the active substances. Several quality control and biological tests were applied for radiolabelling and imaging studies.

Results and Discussion: When the characterization, radiolabelling, biodistribution studies were evaluated, it was found that the (10:1:4) and (7:1:4) molar compositions of (phospholipid: charge inducer:cholesterol) were the effective formulations and 2-10 mCi Tc-99m was found as a good radionuclide for the diagnostic and therapeutic targeting purposes.

Conclusion: Liposomes have been found successful and effective as the functional drug delivery systems and radiopharmaceuticals for the diagnostic and therapeutic treatment of several diseases. Furthermore, imaging can successfully be achieved with different types of liposomes.

Acknowledgement: This presentation was made possible with the valuable support through: Hacettepe Univ. Foundation projects (89-02-013-001), (94-02-013-012), (94-02-013-020), (95-02-013-006), (99-02-301-001), and TUBITAK projects (SBAG-1767) and (100S 055, SBAG 2303).

Keywords: Liposomes, Diagnostic Imaging, Radiolabelling, Quality Control, Radiopharmaceuticals