INTERNATIONAL COOPERATION TO STRENGTHEN SUPPLIES OF MOLYBDENUM-99 AND THE IAEA ROLE

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Objectives: There are serious disruptions in supplies of ^{99}Mo since fall 2007 due to vulnerability of irradiation services from five aged research reactors (RR) used for isotope production. Ageing RR facilities are challenging to safely operate and ^{99}Mo supply chain remains fragile. Only additional capacity expected in 2009 is from OPAL/ANSTO. AECL announcement of termination of MAPLE reactors in May 2008, NRU re-licensing need in 2011, expected shutdown of OSIRIS in 2015, with no new reactors expected until 2015 at the earliest, increase concerns on long term supplies. Another issue is dependence on highly enriched uranium (HEU) targets for >95% ^{99}Mo production. In view of security and proliferation concerns, production needs to convert to using low enriched uranium (LEU). NAS study findings/recommendations are significant for sustainability and a call for global efforts.

Methods: The IAEA is implementing activities to foster use of LEU targets as well as help identify and expand the number of reactors engaged in ^{99}Mo production for better reliability/sustainability. These include coordinating research (CRP) on Developing techniques for small scale indigenous ^{99}Mo production using LEU fission or neutron activation, encouraging potential facilities to become actual producers (e.g. Egypt) and establishment of RR coalitions to expand/strengthen network of reactors capable of providing irradiation services (e.g. Poland, Romania). The IAEA launched a new CRP in 2008 on feasibility evaluation of Aqueous Homogeneous Reactors of LEU salt solution fuel for production of ^{99}Mo and other fission isotopes. Use of enriched ^{98}Mo for n,γ route and photo-fission of ^{238}U are other likely options in future.

Results: The CRP team includes countries with potential, as evident by either physical progress, e.g. Chile, Egypt, Pakistan, or plans underway, e.g. Libya, Romania, to become part of ^{99}Mo supply network, especially if supported by major producers. The 3rd Meeting of CRP held in MURR/USA in Oct 2008 was joined by over 20 observers from industries and governments interested in ^{99}Mo production and ^{99m}Tc generators, SNM and US-NAS. OECD-NEA, in cooperation with the IAEA, organised a Workshop on Security of supply of medical radioisotopes in Jan 2009 and most stakeholders participated.

Conclusions: Building additional/buffer production capacity and conversion to using LEU targets would impact cost of ^{99}Mo. It is necessary to engage all stakeholders to achieve international cooperation among industries, reactor centres, end users and governments. The IAEA as global facilitator can bring them together for objective analysis and taking necessary actions.

IAEA ACTIVITIES ON RADIOPHARMACEUTICAL SCIENCES FOR MEMBER STATES: PROGRESS DURING 2007-2009

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Objectives: Different types of activities are undertaken by the IAEA to assist Member States in radiopharmaceuticals development as well as in building capacity for manufacturing. These include Coordinated Research Projects (CRP), Technical Cooperation (TC) projects, technical meetings and publication of documents.

Methods: The CRP is a group activity in which ~ 15 participants come together to work towards an identified objective. The five ongoing CRPs cover radiopharmaceuticals for SPECT, PET and therapy, as well as cyclotron targetry. The activities on Tc-99m focus on the use of the Tc cores that yield high specific activity tracers usable for cancer diagnosis. The CRP on F-18 radiopharmaceuticals is aimed towards developing products beyond FDG and bringing them to the clinical arena. Therapeutic radiopharmaceutical program is focused on isotopes that can be produced in large quantities in several MS. IAEA convenes technical meetings with specific objectives to identify the needs of the MS, formulation of CRPs or preparing IAEA documents.

Results: Thanks to the IAEA efforts, radiopharmaceuticals development with Lu-177 is pursued by several countries as this isotope can be produced in large quantities in more than 25 reactors spread across the world. Key results of a CRP on radionuclide generator are the development of an electrochemical generator capable of giving radionuclidically pure Y-90 and an extraction paper chromatography for estimation of Sr-90 in Y-90. CRP on cyclotron targets is leading to the development of new targets for enhancing the production yields. Seventy five research groups from countries across the world are participating in the above CRPs and the outcomes of the CRPs are expected to improve the availability, quality, safety and efficacy of radiopharmaceuticals. Based on relatively modest funding from the IAEA, the CRP mechanism works effectively to develop and transfer useful technologies and techniques by pooling expertise and resources from both developed and developing countries. IAEA supports about 50 technical cooperation projects in MS dealing with implementation of GMP in radiopharmaceuticals production, setting up of facilities for the manufacture of radiopharmaceuticals including generators, cyclotrons and PET radiopharmaceuticals production laboratories. IAEA TC projects facilitate capacity building through expert services and training opportunities as well as limited equipment support. The new series of publication on Cyclotron produced radionuclides i. Principles and practice; ii. Physical characteristics and production methods and iii. Guidelines for setting up a facility - is expected to help the MS planning new cyclotron facilities for radiopharmaceuticals production as well as to enhance the capabilities of the existing centres to make other radionuclides.

Conclusions: IAEA activities have helped in capacity building in MS and developing international networks of radiopharmaceutical scientists. The publications on radiopharmaceuticals are widely cited, appreciated and can be freely downloaded from the IAEA or the SRS website.

RING-OPENING OF AZIRIDINES WITH 18F-FLUORIDE: A DIRECT METHOD FOR LABELING BIOMOLECULES FOR PET STUDIES

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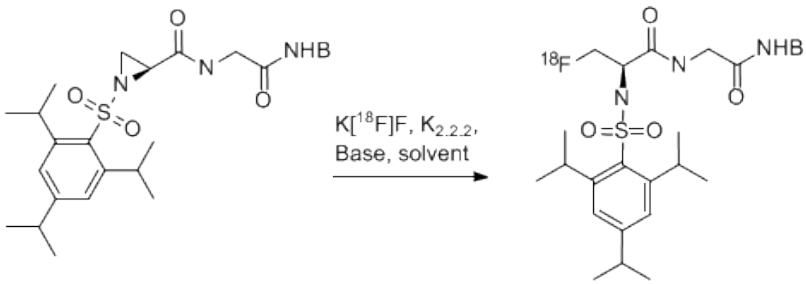
Objectives: The direct labeling of peptides and other large biomolecules with fluorine-18 is difficult due to the harsh reaction conditions employed during nucleophilic substitution reactions and indirect methods using ^{18}F-labeled prosthetic groups have been the method of choice1. This approach, however, is tedious because it requires a multi-step procedure. A direct labeling method is therefore highly desirable. Besides the silicon/boron-based direct labeling method 2, a direct method via ring-opening of an activated aziridine moiety in a biomolecule using ^{18}F-fluoride is an option. We have investigated this approach and report now on our results.

Methods: A series of activated aziridine-based model compounds were synthesized and the most promising building block was coupled to different biomolecules. These aziridine-based model compounds and biomolecules were labeled with fluorine-18 via a ring opening reaction using a one-step reaction sequence (Scheme I) and the influence of different activating groups, reaction temperature, solvent and base were investigated.The crude reaction mixtures were analyzed by HPLC.



Scheme I. ^{18}F - Radiolabeling of aziridine-based biomolecules (B = biomolecule)

Results: In most cases, 66-97% of ^{18}F-incorporation was achieved under mild labeling conditions (50-70°C, 15min) for the aziridine-based model compounds. The application of the most promising building block for the labeling of biomolecules was successfully demonstrated. The [^{19}F]fluoride ring-opening of the derivatives investigated was highly regioselective since only 3-fluoro-2-amino-amides were obtained (NMR studies). The investigated compounds showed good hydrolytic stability within the time period required for a PET study.

Conclusions: Ring-opening of aziridines with fluorine-18 was successfully demonstrated. This method may be useful for the direct labeling of biomolecules such as peptides.

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