Radiochemical separation of $^{64}$Cu and $^{55}$Co from proton-bombarded nat-nickel via non-aqueous ion-exchange chromatography

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SCIENTIFIC OBJECTIVES

The project aim is to produce a solution of pure $^{64}$Cu and test the radiolabelling efficiency. Specific aims may be defined as follow:

i) develop a process for separating $^{64}$Cu from irradiated nickel on low energy cyclotron; which enables simultaneous separation of $^{55}$Co and recycling of the starting material nickel (an adaptation of process develop by Prof Suzanne Smith at ANSTO).

ii) develop a quality control process for determining the specific activity of $^{64}$Cu using the ANSTO patent technology, SarAr.

PROGRESS REPORT and RESEARCH OUTCOMES

A process is now in place at SCGH for separating the isotopes produced from irradiating 64Ni. This process is also suitable for separating irradiated nat-Ni (refer to scientific objective i).

An effective separation of isotopes of Ni, Co and Cu is achieved using a small anion exchange column (0.5 g) and small volumes of eluents (<25mL). The separation is complete within 30 minutes and evaporation of fractions was considerably faster than reported for strong acid mixture.

The process has been successfully performed four times as part of the AINSE grant, on three $^{64}$Ni targets and one nat-Ni target. The solutions have been analysed at ANSTO by gamma spectrometry (appendix 1). The results for three $^{64}$Ni samples are very promising, with a radiochemical purity of the $^{64}$Cu at > 99.6%.

Development of a quality control process for measuring the specific activity of $^{64}$Cu using SarAr (scientific objective ii) has begun. This is not a trivial undertaking, and it has required that several techniques be learnt in order to develop the method for measuring the specific activity. The specific activity will be measured by adding varying quantities of SarAr to standard solutions of $^{64}$Cu, to produce a calibration graph that plots the percent of $^{64}$Cu complexed at known molar quantities of SarAr. SarAr complex $^{64}$Cu quantitatively (1:1 ratio) and essentially irreversibly under the condition investigated. Therefore it is possible to interpolate the concentration of $^{64}$natCu from the concentration of SarAr when all the $^{64}$natCu is complexed. This will give the molar amount of $^{64}$Cu present in solution, from which the specific activity can be derived. The conditions of the $^{64}$Cu solution (ie. pH, presence or absence of carrier Cu, etc.) and reaction time must be chosen so that only Cu binds with the SarAr, even if other isotopes such as Co are present. In order to set up this process, it is essential know how to complete a kinetics study using radioisotopes.

Kinetics studies were performed using $^{57}$Co and $^{64}$Cu with DiamSar in a pH 5 buffer (0.1M NaCl:0.1M EDTA). Carrier-added radioisotope was added to one solution of DiamSar, and the addition was timed. Aliquots (2uL) of the reaction mixture were removed at known times and spotted onto a filter paper over a range of time interval (up to...
120 mins). The filter paper was developed in a suitable solvent. Free metal ion moves with solvent front, while metal complexes of the diamsar remain at the origin. The filter paper was counted using a gamma counter (refer appendices 2 and 4) to determine the percent of activity that remains at the origin (refer appendices 3, 5 and 6), and thus study the amount of radioisotope reacted with DiamSar in a given time in a given solution. This is essential for choosing the correct conditions for the specific activity measurement – by choosing the correct amount of reaction time and pH, $^{64}$Cu will be preferentially bound, even if other elements are present in the solution.

In addition to performing the above kinetic studies, a third kinetic study was undertaken. This kinetic study extended the technique to measuring the kinetics of radiolabelling a SarAr-protein conjugate with $^{57}$Co (refer appendices 7 and 8). The protein studied was bovine serum antiglobulin. Conjugating SarAr to a protein molecule is essential to further research that aims to develop suitable radiopharmaceuticals for use with PET/CT imaging (that will be carried out separately to this work).

The $^{57}$Co-SarAr-BSA molecule was purified (refer to appendix 9), then analysed using size exclusion chromatography (appendices 10 and 11). The retention time is proportional to the molecular weight of the molecule – the major peak corresponds to $^{57}$Co-SarAr-BSA. There are small peaks that indicate the dimer product has formed, as well as a small amount of ‘conglomerate’ protein. The radioactive peak (appendix 11) shows that there are two major labeled compounds (desired product and the dimer) and a small amount of labeled conglomerate.

The capabilities developed through this research project will assist in developing the next generation of $^{64}$Cu radiopharmaceutical at the Sir Charles Gardiner Hospital (SCGH). A joint program SCGH and ANSTO for infrastructure is underway and it will be used to provide novel $^{64}$Cu agents for the local region. The initial benefits of the research will be to support the local research community by supplying $^{64}$Cu. Currently, there is no commercial manufacturer for $^{64}$Cu in Australia. Long term goal are to develop $^{64}$Cu agents for clinical studies.

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Signature of Investigator preparing the report: Charmaine Jeffery
After signing this report please fax this page with your signature for our files

Proj: 10P037
Date: 15 February 2011

PUBLICATIONS / REPORTS arising as a result of your work.

No publications.

PhD STUDENTS

Not applicable.