DEVELOPMENTAL WORK ON ECONOMIC PRODUCTION OF HIGH AND LOW SPECIFIC ACTIVITY ^{64}CU – SUITABLE FOR PRECLINICAL STUDIES USING ACCELERATOR NEUTRONS

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Introduction: ^{64}Cu is unique as it decays by three different routes, namely, electron capture and β− and β+ decays. Hence, this radioisotope holds promise toward development of PET imaging probes for noninvasive visualization of diseases and can also be used in targeted radiotherapy. Its half-life of 12.8 h makes it versatile – short enough to be useful for tracers with rapid pharmacokinetics such as small molecules and peptides, yet long enough to be useful for tracers with slow pharmacokinetics. However the utilization of ^{64}Cu is mostly limited to studies, sourcing no carrier added ^{64}Cu, produced via irradiation of expensive ^{64}Ni ^{64}Ni(p, n)^{64}Cu reaction in a medical cyclotron. This study investigates the potential of producing low specific activity ^{64}Cu via ^{65}Cu(n,2n) + ^{63}Cu(n,g) ^{64}Cu and high specific activity ^{64}Cu via ^{64}Zn(n,p) ^{64}Cu, in an economic way utilizing accelerator neutrons.

Irradiation parameters: Natural foils of Cu and Zn were irradiated in the neutron field (slow + fast neutrons) produced during the irradiation of ^{18}O, in the routine production of ^{18}F via ^{18}O(p,n)^{18}F. 2.4 mL of 98% ^{18}O water was loaded onto a standard silver cavity target and irradiated at 55 μA in the 16.5 MeV PETtrace cyclotron at Radiation Medicine Centre, Mumbai India.

Table 1: Irradiation parameters and activity of ^{64}Cu at end of bombardment

Irradiation time (h)	Target and weight (g)	^{64}Cu (Bq/g)	^{64}Cu(Bq/g*μA*h)
1.1	Cu (0.02)	29218	483
1.2	Cu (0.022)	28475	431
1.1	Zn (0.026)	53179	879
1.2	Zn (2.1)	56246	851

Off-line gamma-ray spectrometry: Radioactivity levels of ^{64}Cu and other radioisotopes co- produced were determined by the quantification of photo-peaks by off-line gamma -ray spectrometry. The γ-ray counting of radionuclides was performed using a pre-calibrated HPGe detector coupled to a PC based 4K channel analyzer. The energy resolution of the detector system was 1.8 keV FWHM at the 1332.5 keV γ-ray peak of ^{60}Co. The energy and efficiency calibration of the detector system was done by using a standard ^{152}Eu source. Spectroscopy software, Interwinner 7 was used for the analysis. Radioactivity levels were determined by the quantification of the following photo-peak counts of the γ-lines: ^{65}Zn (1115.5keV), ^{69m}Zn (438.6 keV), ^{67}Cu (184.6keV) and ^{64}Cu (1345.8 keV).

Separation of ^{64}Cu from irradiated zinc: No carrier added 64Cu was separated from the irradiated zinc by solvent extraction [1]. The solvent extraction method is based on (a) selective extraction of Cu dithizonate into organic solvent from a dilute acidic solution of the bulk Zn target and (b) back extraction of Cu into aqueous phase.

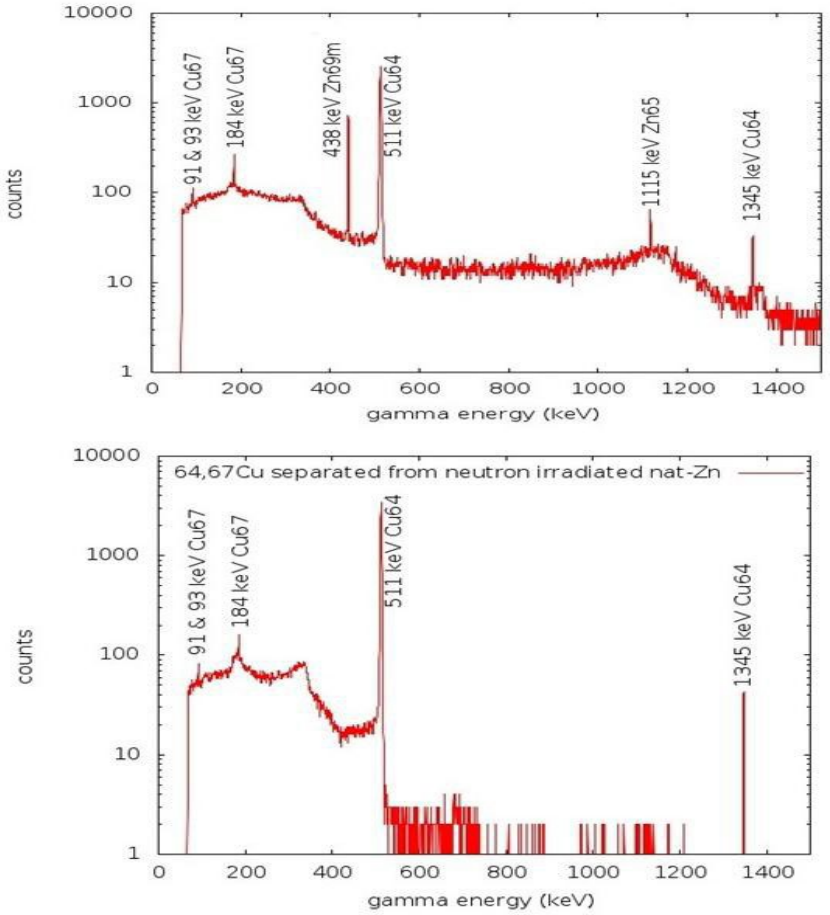

Fig 1: *Gamma ray spectra of irradiated ^{nat}Zn before and after the radiochemical separation*

Results and conclusion: High separation yields of > 90%, with high radionuclidic purity and good reproducibility was achieved. Radionuclide impurities ^{65}Zn and ^{69m}Zn are not detected in the final product, indicating achievement of high radionuclidic purity. This method demonstrates an economical method of obtaining ^{64}Cu with activity levels suitable for radiochemical experiments, aiding in development of new radiopharmaceuticals / preclinical studies.

REFERENCES

1. Gopalakrishna, A., Suryanarayana, S.V., Naik, H., Dixit, T.S., Nayak, B.K., Kumar, A., Maletha, P., Thakur, K., Deshpande, A., Krishnan, R. and Banerjee, S., 2018. Production, separation and supply prospects of ^{67}Cu with the development of fast neutron sources and photonuclear technology. *Radiochimica Acta*, *106*(7), pp.549-557.