DIRECT SYNTHESIS OF OXYGEN-15 LABELLED WATER AT HIGH SPECIFIC ACTIVITIES

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SUMMARY

Oxygen-15 labelled water has been prepared at high specific activities (> 100 mCi/ml) by nuclear recoil techniques available for use after 1 min from EOB. Radiogenic oxygen-15 atoms generated in a cyclotron by the $^{14}N(d,n)^{15}O$ reaction, are allowed to react directly with molecular hydrogen in the gas phase to produce labelled "carrier-free" $H_2{}^{15}O$ which can be used for biomedical purposes.

Key Words: Oxygen-15, recoil labelling, ^{15}O-water, cyclotron, carrier-free.

INTRODUCTION

The oxygen isotope of mass fifteen (^{15}O) is a cyclotron produced radionuclide and decays with a half-life of 2.03 min by the emission of positrons. The combination of a pure positron emitter and its relatively short physical half-life has rendered this radioisotope an important radiotracer in biomedical studies (1,2,3). This is becoming even more evident with the advent of Positron Emission Transaxial Tomographs, which allow quantitation of activity in a small volume element of tissue. The short half-life of oxygen-15 is advantageous because of minimization of the adsorbed radiation dose, particularly in situations where sequential experiments are performed.

Water labelled with oxygen-15 has been used for determination of regional cerebral (4) and myocardial (5) blood flow. Oxygen utilization rates by neo-

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plastic tissue (6) have also been studied. The preparation of oxygen-15 labelled water ($H_2{}^{15}O$) was reported for the first time by West and Dollery who prepared small amounts of $H_2{}^{15}O$ by passing labelled molecular oxygen ($O^{15}O$) together with hydrogen gas over a heated palladium catalyst. Recent improvements of this method (8) have increased the yield of the recovered water to about 50 mCi/ml.

More recently, Welch and co-workers (9) have prepared $H_2{}^{15}O$ by an exchange method. This technique utilized the fast exchange reaction between labelled carbon dioxide ($CO^{15}O$) and water, $CO^{15}O$ is prepared by reacting $O^{15}O$ with activated charcoal heated to 400°C. Using this method they were able to prepare water with a specific activity of 80 mCi/ml. They have also labelled water <u>in situ</u> when labelled $CO^{15}O$ was passed through blood, though this procedure was less efficient.

The present paper describes a method for the preparation of oxygen-15 labelled water at high specific activities by nuclear recoil techniques.

EXPERIMENTAL METHOD

The oxygen-15 atoms were generated by bombarding a nitrogen target with 3.5 MeV deuterons via the $^{14}N(d,n)^{15}O$ nuclear reaction at the 60" Isochronous Cyclotron at Brookhaven National Laboratory. The recoiling oxygen-15 atoms are allowed to react with the 5% of molecular hydrogen contained in the irradiation target to produce labelled "carrier-free" $H_2{}^{15}O$. Since it is virtually impossible to eliminate all H_2O especially that adsorbed on glass walls, etc., the $H_2{}^{15}O$ can never be truly carrier free. Nevertheless it will be of extremely high specific activity even when carrier is added.

The irradiations were carried out in a 25 ml cylindrical quartz irradiation cell fitted with a grease-free stopcock. This cell was filled in a conventional vacuum line with dry hydrogen (99.99%) and then, pure and dry nitrogen (Matheson Zero grade) was introduced until the appropriate pressure and composition was achieved.

The initial beam energy of 21.7 MeV is degraded to about 3.5 MeV by the combination of the collimator aluminum foil and the quartz front window. The use of higher on-target deuteron energies is unadvisable since at 2.8 MeV the corresponding excitation function has reached its maximum (10). Increasing

amounts of ^{13}N and also ^{11}C from the $^{14}N(d,dn)^{13}N$ and $^{14}N(d,\alpha n)^{11}C$ reaction are produced at energies over 5 or 6 MeV. Higher energies are not used in production runs because of contamination with ^{13}N. In work on the excitation function for oxygen-15 formation we found about 0.5% ^{13}N and 1% ^{13}N at 6.4 and 10.7 MeV on target respectively. (10)

After irradiation, 0.1-1.0 ml of carrier water is introduced into the irradiation cell and the radioactivity ($H_2{}^{15}O$) is removed with a syringe. The radiochemical purity is greater than 99.7% as confirmed by radiogas chromatography (small amounts, < 0.3% of dissolved oxygen ($O^{15}O$) are detected as an impurity). The radionuclidic purity is greater than 99.9%, as determined by decay analysis, the impurity being nitrogen-13.

RESULTS AND DISCUSSION

The novel feature of this technique is that water is produced directly by the reaction $^{15}O + H_2 \longrightarrow H_2{}^{15}O$ with the advantage that further chemical reactions and manipulations are thus avoided.

The radiochemical yields were optimized by varying the target composition and beam intensities. In a series of experiments, the effects upon changing the ratio H_2/N_2 in the target gas was studied by keeping the total pressure of N_2 and the irradiation time constant and varying the hydrogen pressure. These results are shown in Table I; the yields of $H_2{}^{15}O$ are practically constant for compositions between 4 and 10% of H_2.

In another series of experiments the beam intensities were varied while the composition (H_2 = 5%) and the pressure of nitrogen (1 atm) were kept constant. Fig. I shows that the yields of $H_2{}^{15}O$ depend linearly on the beam intensity, at least up to the range covered in the present studies.

Using this recoil labelling method, 30 mCi of $H_2{}^{15}O$ have been prepared using a microampere deuteron beam for 6 min on target (87% saturation). The removal of this activity can be accomplished using as little as 0.1 or 0.2 ml of carrier water. Specific activities in the range of 100-180 mCi/ml are available for use after 1 min from EOB.

For the routine production of $H_2{}^{15}O$ at levels of 10-20 mCi, typical experimental conditions are: a 25 ml quartz irradiation cell filled with about

2 atm of N_2 containing 5% of H_2 is irradiated for 2-3 min with 3.5 MeV deuterons with a deuteron beam intensity of 0.5-0.8 microamperes. Under these conditions no extra precautions such as additional target cooling are necessary. By proper handling of the glassware and of the carrier water $H_2{}^{15}O$ pyrogen-free and sterile can be prepared for studies in humans.

Table I. Target Composition

% Hydrogen	$H_2{}^{15}O$ $(\frac{mCi/atm\ N_2}{\mu A \times min.})$
26	2.50
15	2.45
9	2.70
6	2.75
4	2.95

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