To the Graduate Council:

I am submitting herewith a thesis written by Francis Marion Welch, Jr. entitled "Recovery of O-18 target water after its use for F-18 fluorodeoxyglucose production." I have examined the final copy of this thesis for form and content and recommend that it be accepted in partial fulfillment of the requirements for the degree of Master of Science, with a major in Chemistry.

George K. Schweitzer

George K. Schweitzer, Major Professor

We have read this thesis
and recommend its acceptance:

M Depa

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Accepted for the Council:

Associate Vice Chancellor and
Dean of The Graduate School

RECOVERY OF O-18 TARGET WATER AFTER ITS USE FOR F-18 FLUORODEOXYGLUCOSE PRODUCTION

A Thesis

Presented for the

Master of Science

Degree

The University of Tennessee, Knoxville

Francis Marion Welch, Jr.

December, 1999

ACKNOWLEDGMENT

The author wishes to express his appreciation and respect to Dr. George K. Schweitzer for his guidance, patience, and friendship during graduate study.

Appreciation is also extended to Mr. Wes Fellers for assisting in experimental development, Dr. Al Tuinman for assistance with mass spec measurements, and Dr. Richard Pagni for assistance with photochemical techniques.

The author also expresses appreciation to CTI, Inc. for financial assistance for graduate research, and to The University of Tennessee, Knoxville for a Teaching Assistantship during graduate study.

Finally, the author expresses appreciation to his parents, Susan and Francis Welch, and to his wife Karen for their patience, understanding, and encouragement during his graduate study.

ABSTRACT

Oxygen-18 (O-18) water is routinely used for production of fluorine-18 (F-18) containing radiolabeled tracers used for diagnosis of various diseases and disorders by positron emission tomography (PET). After the use of O-18 water in a cyclotron to produce F-18 containing compounds, many contaminants are left behind in the O-18 water. O-18 water is quite expensive and rare; therefore, the O-18 water should be recovered for reuse. However, most PET facilities are privately run and there are no widely used procedures for the use of O-18 water, so the types of impurities in used O-18 water vary widely from one facility to another. Therefore, there needs to be developed a widely applicable procedure for the recovery of O-18 water for reuse.

The two basic types of contaminants in used O-18 water are organic and ionic contaminants. Many experiments involving ion-exchange, organic adsorption, distillation, UV irradiation, and permanganate oxidation were attempted with the goal of recovering O-18 water for reuse. In order for a technique to be successful, it needs to remove most of the organic and ionic contamination from the used O-18 water regardless of what the specific contaminants are. The technique also should not result in the dilution the O-18 water samples with O-16 water. After much experimentation, the most successful technique was found to be a reflux of the used O-18 water samples with potassium permanganate followed by two distillations.

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CHAPTER I

BACKGROUND

A. Positron Emission Tomography

Positron emission tomography (PET) is an imaging technique which monitors the distribution of positron annihilations resulting from positron emitting radiolabeled tracers deposited in the human body. Some common positron emitting isotopes used in PET are C-11, N-13, O-15, F-18, and Rb-82 with half-lives of 20.3 min, 10.0 min, 124 sec, 110 min, and 75.5, sec respectively.[1] PET is most commonly used to measure glucose metabolism in the body by monitoring the uptake of 2-deoxy-2-[F-18]- fluoro-D-glucopyranose (FDG).[1-5] The increase or decrease in FDG uptake in the brain has been used for the diagnosis and classification of brain tumors, epilepsy, dementia, movement disorders, Parkinson's disease, and schizophrenia.[1-5] The monitoring of FDG uptake by the heart muscle has also been studied to assess myocardial viability.[2]

When a positron is emitted from a radioactive nuclide, it first loses its kinetic energy by absorption. The positron then encounters an electron and the two are annihilated resulting in the simultaneous emission of two 511 keV gamma rays 180° apart. The gamma rays can then be detected by scintillation crystals. When a gamma ray encounters a scintillation crystal, a multiphoton pulse of light is emitted by the crystal. This light is then detected by a photomultiplier tube. Based on the detection of multiple gamma rays by a surrounding cylindrical array of scintillation crystals in the PET instrument, a tomograph of a region of the body is produced. This tomograph shows differences in regions of high and low numbers of positron annihilations in the body.[1,3]

B. Fluorine-18 Production

Fluorine-18 (F-18) for PET is produced by bombarding oxygen-18 (O-18) water with protons in a cyclotron. A cyclotron consists of a proton source, a magnet, and electrodes which accelerate the charged particles. The protons spiral outward in a vacuum in the magnetic field. While traveling in the spiral pattern, the protons pass between two electrodes of alternating polarity. Each time the proton passes between the two electrodes it is accelerated.[6] Cyclotrons used for PET typically accelerate protons to energies in the range of 8-20 million electron volts (MeV).[1] After the protons are accelerated, they are deflected from their spiraling path by a negative electrode. The protons then contact the target.

There are many different target materials which are used for the production of F-18 including silver, titanium, tantalum, nickel, copper, stainless steel, and havar.[7] The principal target design used in cyclotrons produced by CTI, Inc. in Knoxville, Tennessee, is presented in Figure 1.[8] The target is made of pure silver. The O-18 water is housed in the target. O-18 water volumes range from 0.2 - 1.0 mL. The small target volume is necessary in order to minimize the amounts of expensive O-18 water used. A layer of helium gas for cooling flows between the target and the cyclotron. The helium is separated from the cyclotron by a thin layer of aluminum foil and is separated from the O-18 water by a thin layer of havar foil. Both foils are almost transparent to the proton beam. Havar is an alloy consisting of the following elements:

Cobalt	42 %	Nickel	13%	Molybdenum	2%
Chromium	20 %	Tungsten	3%	Carbon	<1%
Iron	18 %	Manganese	2%	Beryllium	<1%

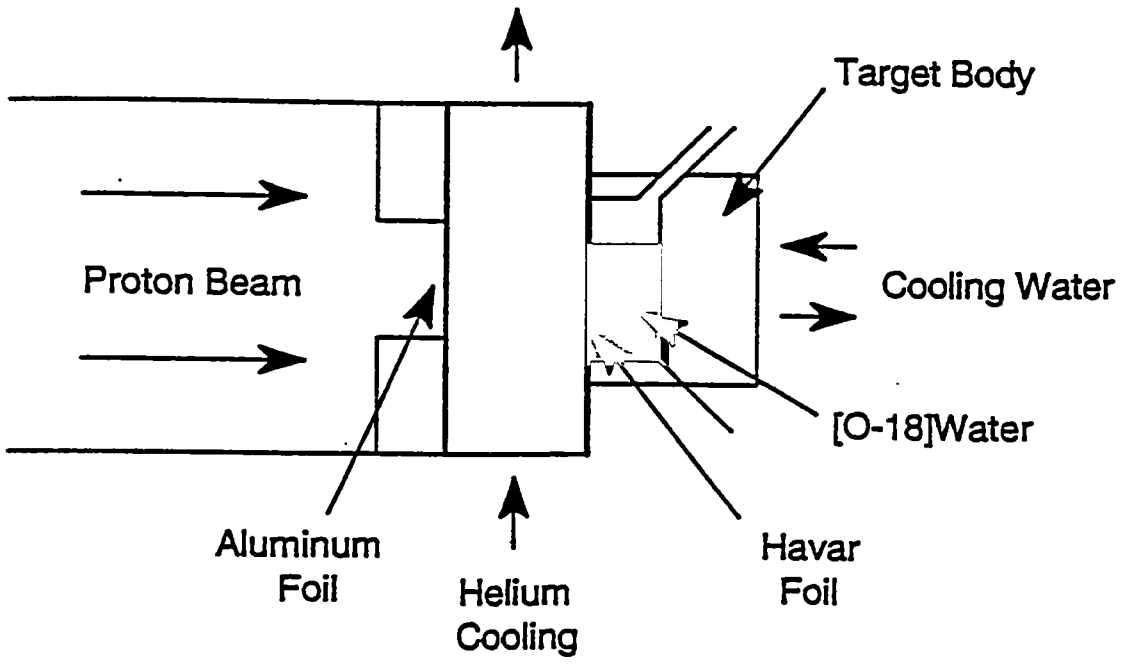

FIGURE 1

Target design used by CTI, Inc., Knoxville, Tennessee

In the target, the O-18 nucleus undergoes a transformation to an F-18 nucleus by the following reaction:

$$^{18}_{8}O + ^{1}_{1}p^{+} \rightarrow ^{18}_{9}F^{+} + ^{1}_{0}n \quad (1)$$

In the presence of O-18 water, the fluorine is transformed to the fluoride ion (F-18$^-$). The O-18 water is bombarded up to 1 hour with an up to 100 μA beam current.[1] The targets are pressurized with argon up to 600 psig (approximately 42 atm).[8] During bombardment, up to 1 Ci of F-18 is produced[8,9] resulting in an F-18$^-$ concentration of $10^{-6.3}$M for 1 mL volumes. After bombardment, the O-18 water containing the F-18$^-$ is removed from the target so that the F-18$^-$ can be separated from the O-18 water.

C. Fluorine-18 Separation

There are a number of methods for recovering F-18$^-$ from O-18 water. One method is an electrochemical separation. With this method, the F-18$^-$ is deposited onto a positively biased graphite crucible in an electrochemical cell. The O-18 water is then removed from the cell. Natural (O-16) water is then placed in the cell and the polarity is reversed in order to release the F-18$^-$ from the now negatively biased graphite crucible. The O-16 water containing the F-18$^-$ is then removed from the cell and the FDG synthesis is performed.[10]

Another method for the recovering the F-18$^-$ from O-18 water involves the evaporation of O-18 water. The O-18 water containing the F-18$^-$ is delivered by teflon tubing directly from the target to a vial containing potassium carbonate and a magnetic stirrer. The vial is then heated to boiling under a flow of argon. The heated vial is connected to another vial that is cooled in an ice bath. The O-18 water is transferred to

the cooled vial while the F-18$^-$ remains behind as potassium fluoride in the heated vial. The F-18$^-$ can then be used for FDG synthesis.[9]

The most common method used for F-18$^-$ removal from O-18 water, which is the method used by CTI, Inc., involves the use of an anion exchange resin.[7,11-16] The target water containing the F-18$^-$ is transferred by polyethylene or teflon tubing to a small column containing a strong anion exchange resin. The column needs to be as small as possible to avoid loss of O-18 water. CTI, Inc. uses disposable Sep-Pak® cartridges containing 130 mg of Accell™ Plus QMA anion exchange resin from Waters Chromatography Columns and Supplies. The ion exchange resin is an acrylamide copolymer on diol silica with a quaternary ammonium salt surface functionality: $-C(O)NH(CH_2)_3N(CH_3)_3^+ Cl^-$.

Columns are sometimes pretreated with a sodium bicarbonate solution in order to avoid bacterial growth during storage. If a column is prewashed with bicarbonate, it should be washed with deionized O-16 water just before use. In order to reduce isotopic dilution of O-18 water, the column should be as dry as possible before the target contents are added. The column should be purged with air in order to remove as much O-16 water as possible. The columns are sometimes washed with acetonitrile in order to aid in evaporation of the O-16 water while purging with air. Acetonitrile does not serve as a contaminant to the FDG synthesis since acetonitrile is used in the first step of the synthesis. The column is then ready to be used to remove F-18$^-$ from the target water.[11]

Institutions other than CTI, Inc. use different resins such as Toray TIN-200 from C.I. Specialty Chemicals in New York, NY[12], and Dowex 1X-10[13] available from

Bio-Rad. Other institutions also use different pretreatments such as washing with an NaOH solution in order to convert the resin to the hydroxide form.[13] Some also wash the resin with a very small amount of O-18 water in order to help minimize isotopic dilution of O-18 water.[12]

After the resin column has been prepared, the target water is delivered to the column with polyethylene or teflon tubing, and the O-18 water is collected. The $F\text{-}18^-$ must then be eluted from the column. An appropriate eluent which does not interfere with the FDG synthesis and contains an anion which will displace the $F\text{-}18^-$ from the column is used. Most institutions, including CTI, Inc., use potassium carbonate solution as the eluent.[11-14]

D. FDG Production

CTI, Inc., uses a computer controlled chemistry process control unit (CPCU) for automated production of FDG. The CPCU uses several vials, vessels, valves, and tubing to deliver and react various chemicals during the FDG synthesis process.[17] A plumbing schematic is given in Figure 2. The vials are connected to the reaction vessel by polyethylene or teflon tubing. Each vial and reaction vessel is connected to a manifold which utilizes either nitrogen or argon pressure to deliver the contents of one vial or vessel to another. The CPCU can be programed by the user to synthesize biologically active chemicals other than FDG. The CPCU is also shielded in order to protect the user from radiation.

In the first step of the FDG synthesis, as mentioned in the previous section, the target contents are delivered to the anion exchange column. The $F\text{-}18^-$ is then eluted from

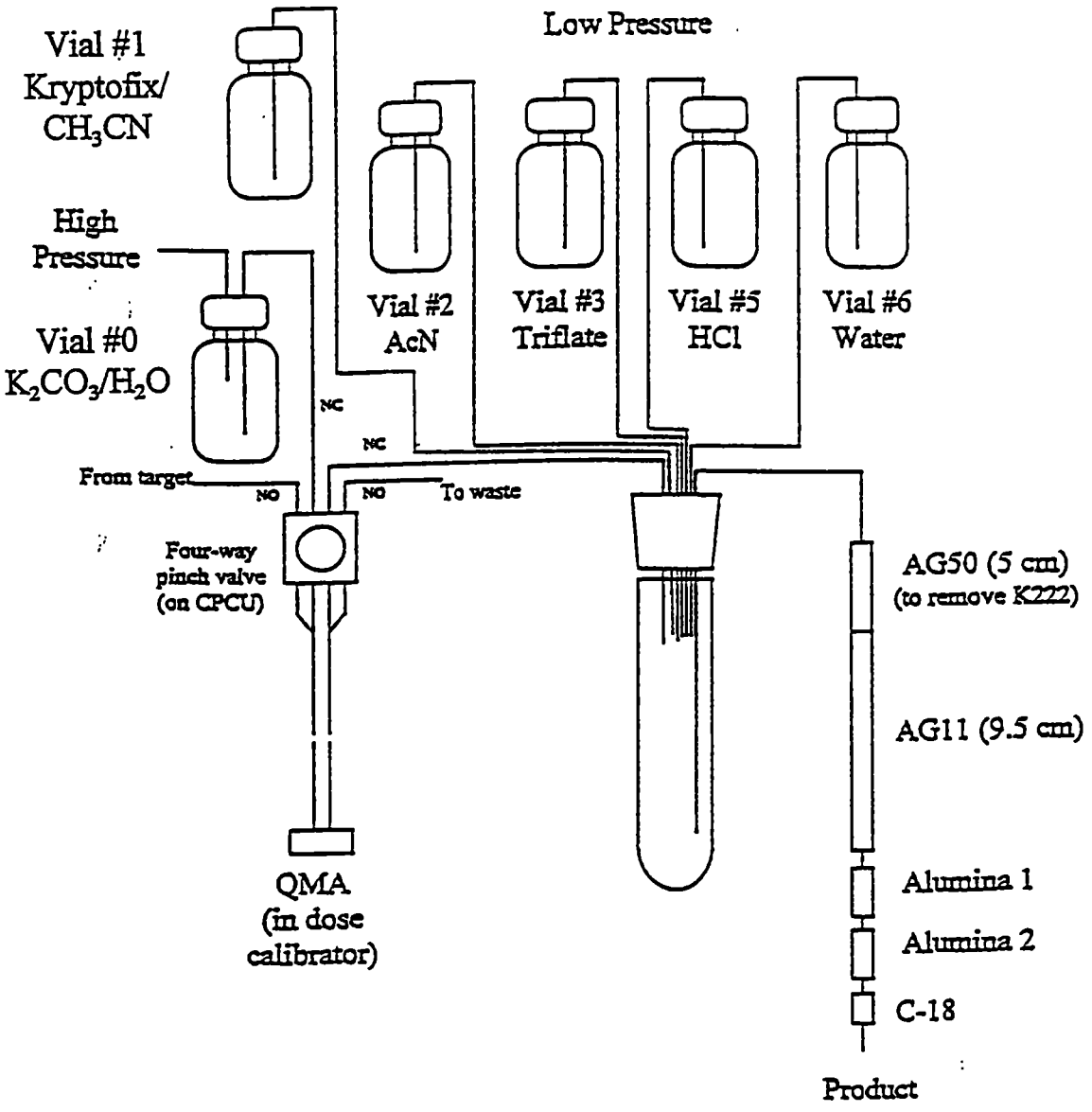

FIGURE 2

Plumbing schematic for FDG synthesis by CTI, Inc., Knoxville, Tennessee

the column, and delivered to the reaction vessel with a potassium carbonate solution. A solution of the aminopolyether, 4,7,13,16,21,24-hexaoxa-1,10-diazabicyclo[8.8.8]-hexacosane (Kryptofix 2.2.2) in acetonitrile/water is added to the reaction vessel. The contents of the vessel are then evaporated. The purpose of Kryptofix is to serve as a phase transfer catalyst by complexing with the $F\text{-}18^-$ to give a kryptofix fluoride salt when dried. This salt is then soluble in the anhydrous acetonitrile synthesis medium.[15] Other phase transfer catalysts have been employed including the tetrabutylammonium ion.[15,16]

After the evaporation of the water in the presence of a phase transfer catalyst, anhydrous acetonitrile is added to the reaction vessel. The reaction mixture is then evaporated again in order to azeotropically remove any residual water from the mixture. After this evaporation, the reaction vessel is cooled, and a solution of 1,3,4,6-tetra-*O*-acetyl-2-*O*-trifluoromethanesulfonyl-β-D-mannopyranose (mannose triflate) in anhydrous acetonitrile is added to the reaction vessel. The fluoride substitution for the *O*-trifluoromethanesulfonyl (triflate) group then occurs while heating and bubbling nitrogen or argon through the reaction mixture. This reaction produces the intermediate, 2-deoxy-2-[F-18]-fluoro-1,3,4,6-tetra-*O*-acetyl-β-D-glucopyranose. The reaction mixture is then evaporated, and cooled again. 1M HCl is added to the reaction mixture in order to replace the acetyl groups with hydroxy groups giving FDG. The mixture is heated for the hydrolysis to occur, and cooled again.

The mixture is transferred from the reaction vessel to a series of columns used for purification.[11,12,14-19] The reaction vessel is then rinsed with water twice. Each washing is transferred to the columns. The first column is a cation exchange column used to remove

Kryptofix from the mixture in the form of the ammonium polyether ion.[18] The mixture then travels through an ion retardation (desalting) resin in order to neutralize the solution and to remove decomposed sugar byproducts.[16] The next column is an alumina cartridge used to remove $F\text{-}18^-$ and decomposed sugar byproducts from the solution.[16,19] Finally, the mixture goes through a reversed-phase column in order to remove any of the hydrophobic unhydrolyzed reaction intermediate.[19] The purified FDG solution is then transferred to a sterile vial through a sterile filter and is ready to be administered to a patient.

E. O-18 Water Condition

In the last ten to fifteen years, the increase in use of PET coupled with the scarcity and expense of O-18 water has resulted in the desire to reuse O-18 water after FDG production.[20,21] The O-18 water after irradiation can contain a number of contaminants including ionic and organic materials. Significant amounts of O-18 water could also be lost due to radiolysis of the O-18 water to give oxygen and hydrogen gases. Radiolysis occurs when water is bombarded with high energy (8-20 MeV) protons. Many institutions have reported the successful re-irradiation and FDG synthesis with previously used and distilled O-18 target water.[7-9,10,13,21] Most of these successful re-irradiations were accomplished with changing procedures or materials during O-18 water irradiation or during $F\text{-}18^-$ separation.

Many PET facilities are privately run, meaning that some procedures are performed differently by different facilities. Therefore, in order to improve the marketability of PET, manufacturers such as CTI, Inc. need to ensure PET users that

O-18 water supplies will be readily available at reasonable prices. To ensure these things, a widely applicable procedure for O-18 water recovery needs to be developed.

CHAPTER II

O-18 WATER RECOVERY

A. Suspected Contaminants

1. Ionic Substances

There are numerous ionic substances that could contaminate O-18 water during $F\text{-}18^-$ production and $F\text{-}18^-$ separation. O-18 water is collected after $F\text{-}18^-$ separation, so nothing used during FDG synthesis comes in contact with the O-18 water. Therefore, those substances used during FDG synthesis are not contaminants.

The target is made of pure silver, and during proton bombardment, some of the silver may be ionized yielding soluble silver ions in solution. The target uses a window made of havar. Havar is an alloy consisting of a number of metals mentioned in Chapter I, Section B. Any of these metals could be ionized during bombardment of the O-18 water resulting in soluble metal ion contaminants in the solution. Silver or metals contained in the havar could also be put into the O-18 water in metallic form during the proton bombardment. These metals could then be ionized yielding metal ions in solution.

Since fluoride ion complexes strongly with many metal ions, metal ion contaminants could complex with the $F\text{-}18^-$ reducing the amount of free $F\text{-}18^-$ available to attach to the anion exchange resin. This complexation could also reduce the amount of the $F\text{-}18^-$ available to substitute into the mannose triflate. Metal ion contaminants could complex with the aromatic mannose triflate producing an unreactive complex.[22] Also, due

to the proton bombardment, radioactive metal ion isotopes may be produced. These radioactive contaminants may be long lived posing problems in the used O-18 water.

Many of the anion exchange resins used for the $F\text{-}18^-$ separation come in the chloride form. During the ion-exchange process, the chloride exchanges with the $F\text{-}18^-$ in the O-18 water resulting in chloride contamination in the O-18 water. With each use, the O-18 water would experience an increase in chloride ion contamination. After numerous uses of the O-18 water, the chloride ion concentration may be sufficiently large to take up too many sites on the resin, not allowing all of the $F\text{-}18^-$ to attach to the resin. This reduction in the amount of $F\text{-}18^-$ attaching to the resin would reduce the amount of $F\text{-}18^-$ available for FDG production.

A similar anionic contaminant is carrier (non-radioactive) fluoride ion. Any $F\text{-}18^-$ not separated out by the anion exchange resin, would be eliminated in a day due to the short 110 min half-life. However, it has been shown that non-radioactive fluoride ion concentrations increase in O-18 water after repeated passes of the water through a target.[22] This carrier fluoride ion contamination is probably due to the use of fluorine containing compounds employed in the production of plastics used in valves and other components. Also, if Teflon®, which contains fluorine, is used in any lines or valves, it may serve as a source of carrier fluoride ion contamination. An increase in carrier fluoride ion concentration, if sufficiently large, would be expected to take up too many sites on the resin, not allowing all of the $F\text{-}18^-$ to attach to the resin. This reduction in the amount of $F\text{-}18^-$ attaching to the resin would decrease the amount of $F\text{-}18^-$ available for FDG production.

2. Organic Contaminants

There are numerous organic substances that can contaminate O-18 water during $F\text{-}18^-$ production and $F\text{-}18^-$ separation. In route from the target to the $F\text{-}18^-$ separation resin, the O-18 water flows through polyethylene lines and valves containing plastic materials. The O-18 water could leach organic contamination from these lines and valves. The O-18 water also comes in contact with the anion exchange resin during $F\text{-}18^-$ separation. Organic materials from the resin could be leached by the O-18 water while the water is in contact with the resin. The anion exchange resin is treated with sodium bicarbonate, acetonitrile, and sometimes Kryptofix before the resin contacts the O-18 water, making these three substances suspected contaminants also. The amounts of organic contamination could be enhanced by the fact that the O-18 water contains radioactive $F\text{-}18^-$. The radioactivity could cause a breakdown of the polymers in the lines, valves, or resin, increasing organic contamination in the O-18 water. Any organic contaminants could react with the $F\text{-}18^-$, reducing the amount of $F\text{-}18^-$ available for FDG production.[22]

Any organic contamination might be present in the O-18 water during re-irradiation. Such an organic contaminant could possibly polymerize in the target during the proton bombardment. The polymerization would probably be due to radical formation resulting from the high energy proton bombardment. This polymerization would introduce different types of organic contamination which could react with the $F\text{-}18^-$ reducing the amount of $F\text{-}18^-$ available for FDG production. The $F\text{-}18^-$ could also be incorporated in

the polymers which would again reduce the amount of $F\text{-}18^-$ available for FDG production.

B. Radiolysis of O-18 Water to Give Oxygen and Hydrogen Gases

It is possible for significant amounts of O-18 water to be lost due to the radiolysis of the water to give oxygen and hydrogen gases. When water is bombarded with 8-20 MeV protons, the energy is sufficient to decompose the water. This decomposition is probably due to the high numbers of radicals formed during the proton bombardment.[23] Target water losses of 1-4% have been reported.[7,23] A significant loss of O-18 water is undesirable because of the expense of O-18 water. It may be possible to minimize the radiolysis of O-18 water by increasing the target pressure in order to deter the decomposition reaction according to Le Chatelier's principle.[8]

C. Removal of Contaminants

1. Ion-exchange Chromatography

Ion-exchange chromatography employs ion-exchangers to separate substances based on their charges. An ion-exchanger contains positively or negatively charged functional groups covalently bound to a polymeric support resin yielding an anion or cation exchange resin. When charged species are treated with an ion-exchange resin containing functional groups of opposite charge, the charged species are adsorbed. Ion-exchange resins are commonly used to purify water by removing ionic contaminants by this adsorption of charged species. If a sample of O-18 water is applied to a mixed bed resin containing a mixture of strong cation and strong anion exchange resins, effective deionization of the water may be observed. This deionization is only observed if the

counter ions of the two resins are hydrogen and hydroxide ions or if the resin is self-absorbed (contains paired cation and anion exchange sites).

Most ion-exchange resins are supplied wet. It is recommended that the resins be washed with a large amounts of pure water before their use to avoid contamination due to organic materials being leached from the resin. If wet ion-exchange resins are used to purify O-18 water, the O-18 content of the water will be isotopically diluted with O-16 water. A small amount of O-18 water will also be lost due to hold up on the resin. Drying the resins before they are used may not be an option because many resins will partially decompose or collapse upon heating and/or drying making them less effective ion-exchangers. The decomposition or collapse of a resin may also introduce new organic substances at the surface of the resin which could be leached by the O-18 water resulting in contamination. However, if a resin is washed and then partially purged with air before use, isotopic dilution of the O-18 water or decomposition of the resin can be minimized.

2. Organic Adsorption

Organic adsorption separates substances based on their differing affinities for a solid organic phase. A mixed bed ion-exchange resin will remove any charged organic molecules from water but will not usually remove neutral organic substances. An organic adsorbent which has a higher affinity than water does for neutral organic molecules can effectively remove organic substances from water. Activated carbon is one such adsorbent. Activated carbon is a solid containing surface carbon atoms with unfilled bonding sites. These activated carbons will bond with organic molecules, adsorbing them

onto the solid carbon. The organic contaminants can then be removed by filtration of the O-18 water to remove the activated carbon which will contain the organic contaminants.

Reversed-phase resins are another type of organic adsorbent. One type of reversed-phase resin separates neutral compounds from water based on polarity.[24] Organic molecules are generally less polar than the water molecule, and will prefer to leave water and attach to a resin with a functional group less polar than water. Another type of reversed-phase resin separates neutral organic molecules from water based on hydrophobicity. Many organic molecules are hydrophobic and when introduced to a resin with a hydrophobic surface functionality, will separate out of the water onto the resin.

Many of the same concerns with using ion-exchange resins apply to the use of organic adsorbents. All organic adsorbents should be washed with purified natural water to reduce the amounts of organic materials leached from the adsorbents. The organic adsorbent resins can also collapse upon drying. Since the resins cannot be dried, they will contain small amounts of O-16 water which will isotopically dilute O-18 water. Similar to the ion-exchange resins, the organic adsorbents can be partially purged with air to minimize isotopic dilution of O-18 water with O-16 water. O-18 water hold up concerns also apply with all organic adsorbents.

3. Distillation

Distillation separates substances based on differences in boiling points. When water containing small amounts of impurities is distilled, the water is heated to boiling, and the water vapor is then condensed and collected. Materials with lower boiling points than water will be distilled over before the water. Substances with higher boiling points than

water will be left behind in the distillation pot. When distilling a solution containing ionic substances, the ionic salts will be left behind after distillation. Organic substances with boiling points higher than 100°C will also be left behind. Volatile organic substances with boiling points lower than 100°C will distill over before the water distills. However, the amounts of volatile organic substances are so small that they cannot be collected separately from the water. Volatile organic substances such as acetonitrile and ethanol azeotrope with water and cannot be separated from water by distillation.

When distilling, small amounts of O-18 water will be lost due to hold up in the distillation apparatus. Even if the O-18 water is distilled to dryness, there will be a small amount of O-18 water remaining in the condenser as well as a small amount of water vapor in the distillation pot. The amounts of O-18 water lost to hold up can be minimized by distilling in large batches. The total hold up volume is the same regardless of the size of the distilled batch. Therefore, the percentage of O-18 water loss is less when more O-18 water is distilled in each batch. There is also a possibility that the O-18 water in the distillation apparatus can exchange with O-16 water in the air due to the times required for distillation. The distillation apparatus should be set up so that the outlet to the atmosphere is as small as possible to minimize the exchange of O-18 water with O-16 water in the air.

4. Ultraviolet Irradiation

Ultraviolet (UV) irradiation can be used to remove organic contaminants from water by oxidizing the organic substances to carbon dioxide (CO_2), water, and other inorganic species.[25,26] In order to use non-vacuum UV irradiation, a catalyst is usually used to aid in the oxidation reaction. Powdered TiO_2 anatase is one of the most widely

used photocatalysts. Illumination of TiO_2 produces photoelectrons and positive holes. A positive hole reacts with adsorbed hydroxide to produce the OH radical, or it reacts with adsorbed oxygen gas to produce the superoxide (O_2^-) radical. Both OH and O_2^- radicals are powerful oxidants and can oxidize the organic molecules. If illuminated for sufficient time, the organic species should be oxidized completely to CO_2, water, and other inorganic species. When performing UV irradiations, the vessel must be vented in order to release the CO_2 produced. This venting leads to the possibility of O-18 dilution with atmospheric O-16 water. This dilution can be minimized by making the vent as small as possible. It may be possible for adsorbed O-18 hydroxide to exchange with O-16 in the TiO_2 or adsorbed O-16 oxygen gas from the atmosphere, isotopically diluting the O-18 water.[27] It may also be possible for O-16 from the organic contaminants to be added to the O-18 water isotopically diluting the water. If the UV irradiation is sufficiently strong, O-18 water could be lost to radiolysis or evaporation. This loss could be minimized by carefully monitoring the UV irradiated water to ensure that little or no O-18 water is being lost.

5. Permanganate Oxidation

The permanganate ion (MnO_4^-) is a powerful oxidizing agent. MnO_4^- may be used to remove organic contaminants from water by oxidizing the organic substances to CO_2, water, and other inorganic species. The oxidation may be performed by adding a small amount of potassium permanganate ($KMnO_4$) to O-18 water and refluxing to aid in the oxidation process.[8] If refluxed for sufficient time, the organic species should be oxidized

completely to CO_2, water, and other inorganic species. After refluxing the O-18 water can be distilled to remove the $KMnO_4$.

While refluxing the vessel must be vented to avoid pressure buildup during heating. This venting leads to the possibility of O-18 dilution with O-16 water. This dilution can be minimized by making the vent as small as possible. It may be possible for O-16 from the MnO_4^- to be added to the O-18 water, isotopically diluting the water. It may also be possible for any O-16 in the organic species to be added to the O-18 water, isotopically diluting the water.

D. Recovery of O-18 Water from Oxygen and Hydrogen Gases

One method of recovering water from oxygen and hydrogen gases involves the use of a catalyst. Palladium catalyst on 1/8 inch alumina pellets has been used to recombine the two gases.[23] Oxygen and hydrogen molecules are adsorbed onto the alumina surface, and activated by the palladium. The pellets can be suspended above the target water in the target chamber on a perforated plate. The recombined O-18 water will be in the vapor state because of the heat given off by the exothermic recombination reaction. The water will then condense on the walls of the target and run back down to the target water. A sample target design utilizing a catalyst is given in Figure 3.[23]

E. Proposed Research

There are many different methods of water purification including ion-exchange, organic adsorption, distillation, UV irradiation, and permanganate oxidation. Distillation, UV irradiation, and permanganate oxidation have been used to purify O-18 water in the past.[7-9,13,21,28] According to the literature, ion-exchange and organic adsorption have not

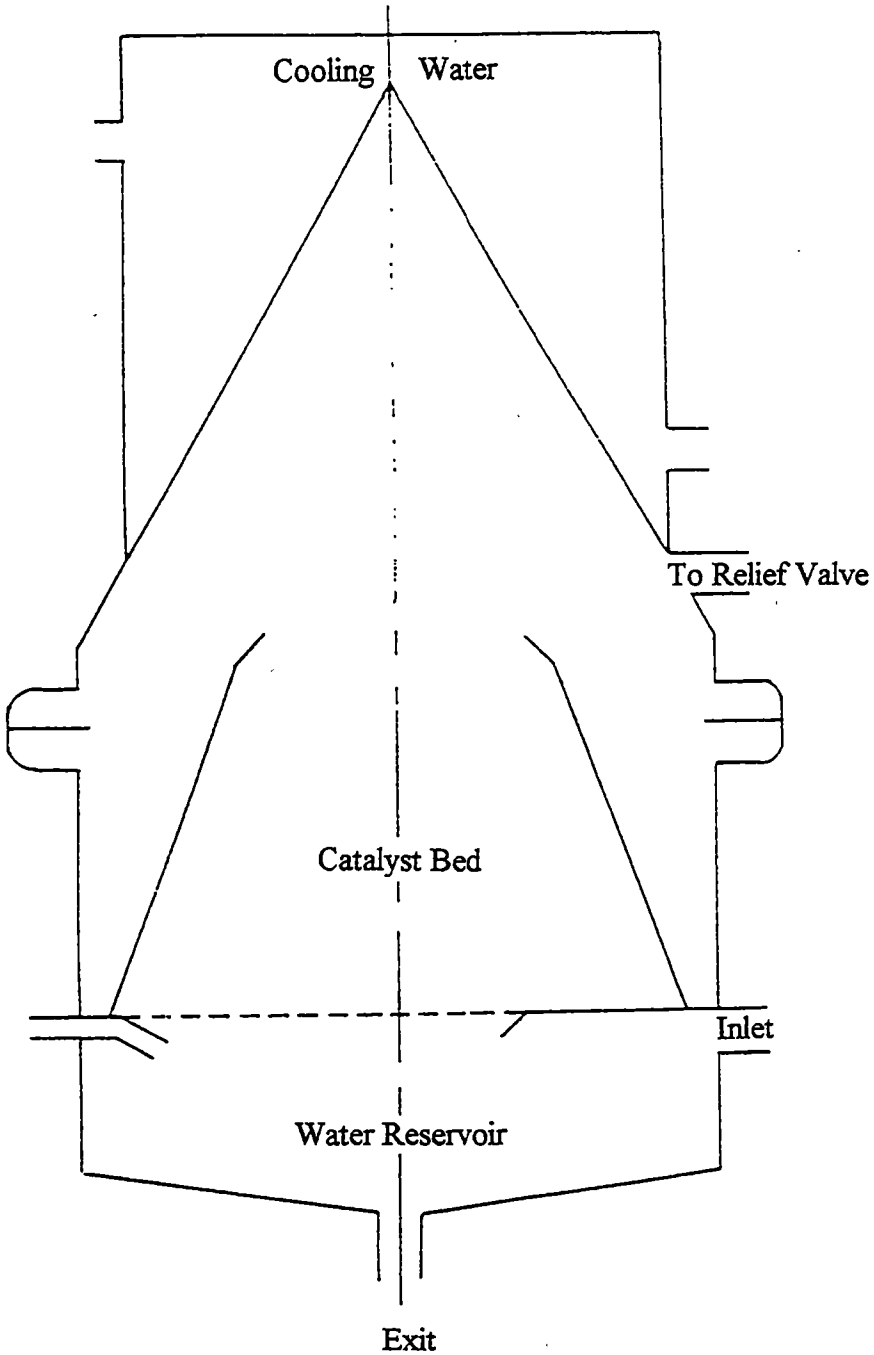

FIGURE 3

Target design incorporating a catalyst for recombination

of O-18 water decomposition products

been used in the past to purify O-18 water. Successful recovery of O-18 water has been performed by researchers who have produced the used O-18 water themselves. No method of recovery of O-18 water has been developed to recover O-18 water not previously used by the researcher recovering the water. Therefore, recovery of O-18 water by ion-exchange, organic adsorption, distillation, UV irradiation, and permanganate oxidation needs to be investigated. The development of a method involving one of, or a combination of, the aforementioned techniques will be investigated.

Recovery of oxygen and hydrogen gases from decomposed O-18 water has been previously investigated.[23] The ability of a palladium on alumina catalyst to convert the gases back to water needs to be investigated. In a target, it is assumed that the hydrogen and oxygen gases are formed in a stoichiometric ratio. Since a target and cyclotron are not readily available in the laboratory, another method of producing the stoichiometric ratio of hydrogen and oxygen gases needs to be developed. A stoichiometric ratio of the gases can be readily produced by electrolytic decomposition of water. Therefore an apparatus for electrolytic production of hydrogen and oxygen gases by decomposition of water needs to be developed. This apparatus should be constructed so that the ability of the palladium on alumina pellets to convert the gases back to water can be readily tested.

CHAPTER III

APPARATUS AND TECHNIQUES

A. Ion-exchange Chromatography

1. Choice of Resin

As mentioned in Chapter II, polymeric ion-exchange resins were a possible choice for removal of ionic materials from O-18 water. A mixed bed of cation and anion exchange resins was used with hopes of removing both positively and negatively charged ionic species. The mixed bed resin of choice was AG 501-X8 deionization resin from Bio-Rad. This resin consisted of equivalent amounts of Bio-Rad's AG50W-X8 strong cation exchange resin in the H^+ form and AG 1-X8 strong anion exchange resin in the OH^- form. This resin was chosen because it is supplied as an equivalent mixture of strong cation and strong anion exchange resins. Therefore, mixing of cation and anion exchange resins in the laboratory was avoided. AG501-X8 was also chosen because it is supplied in the H^+ and OH^- forms. If the resin were not supplied in the H^+ and OH^- forms, the resin would have to be converted to these forms in order to avoid the introduction of ionic contamination to a sample from the resin.

2. Batch Method

There were two possible methods of introducing the ion-exchange resin to the O-18 water. One of these methods was a batch method. When using the batch method, the resin could be added directly to the water sample followed by shaking or stirring the

resin/water mixture. The water sample could then be removed from the resin by filtering the mixture or decanting the liquid.

Prior to adding the resin to the sample, the resin needed to be washed with deionized O-16 water in order to remove contaminants that could be leached from the resin by the water. Removal of possible contaminants was attempted by placing approximately 0.5 g of the resin in a beaker, and washing the resin with 20 mL of deionized water several times. The resin was equilibrated with each 20 mL wash by stirring the resin/water mixture for approximately one hour. After each equilibration, the wash water was decanted from the resin, and two or three drops of the wash water was evaporated from a watch glass in order to determine if any visible residue remained after all of the water had evaporated. It was determined that after two washings, almost no residue was detectable after evaporation of three drops of the wash water. This amount of residue left after two washings was comparable to the amount of visible residue left behind after evaporation of an equivalent amount of deionized water.

After washing the resin with O-16 water, as much of the O-16 water as possible was removed from the resin by allowing the resin to air dry on filter paper. This excess O-16 water was removed from the resin in order to minimize isotopic dilution of an O-18 water sample with O-16 water. The resin was not completely dried in order to avoid decomposition or collapse of the resin. The resin was then ready to be added to the sample of interest.

3. Column Method

The second method of introducing the ion-exchange resin to the O-18 water was in a column. When using the column method, the water sample could be added to a column containing the ion-exchange resin. The sample should be permitted to flow very slowly through the column to allow as much contact time as possible between the water sample and the resin so that efficient ion-exchange could occur. Since small volumes of water were being used, a small column was needed. A 10 mL buret was determined to be sufficiently small. The use of the buret also allowed for sample flow to be controlled by the stopcock at the bottom of the buret.

To prepare the column, a small plug of glass wool was placed in the buret and pushed to the bottom near the stopcock. The stopcock of the buret was closed and the buret was filled with deionized water. Fresh AG501-X8 mixed bed deionization resin was then added directly to the water in the buret and allowed to settle. The resin was added until approximately 2.0 cm of resin had settled at the bottom of the buret. Deionized water was then allowed to flow through the resin in order to remove any contamination that might be leached from the resin by water. Periodically, two or three drops of effluent from the column was evaporated from a watch glass to determine if any visible residue remained after evaporation of the effluent.

After no significant visible residue was found to remain on the watch glass after evaporation of the effluent, the column was gravity drained. After gravity draining, a pipet bulb was placed onto the top of the column and air was pushed through the column to drain any excess water from the column. While pushing air through the column, a

Kimwipe® was placed at the tip of the buret to absorb water from the tip so that no water was pulled back into the tip by capillary action. This water was removed so that when O-18 water was added to the column, the dilution of the O-18 water with O-16 water would be minimized. The column was then ready for treatment of a water sample.

The column method was chosen over the batch method because the washing and drying of the resin, as well as treatment of a sample with the resin, was less laborious when using the column method. During the batch method, the wash water had to be removed from the resin by decanting, and the resin had to be partially dried on filter paper. The resin then had to be transferred to a vessel containing the sample to be treated with the resin. After treatment of a sample, the resin had to be removed from the sample by decanting the liquid or filtering the sample.

During the column method, once the resin was in the column, it stayed in the column at all times. The wash water flowed through the column and did not need to be decanted from the resin. The resin was partially dried by blowing air through the column, so the resin did not need to be taken out of the column to be dried on filter paper. After the resin was washed and partially dried, the sample of interest could simply be added to the column so the resin did not need to be transferred to a container containing the sample. Also, after treatment of the sample of interest, the resin was left behind in the column so the sample did not need to be decanted or filtered to remove the resin.

In order to avoid unnecessary expense, when testing ion-exchange or any other O-18 recovery technique, natural water containing primarily O-16 was used instead of O-18 water. When analyzing for contaminants, mock solutions containing suspect

contaminants were made using O-16 water. The desirable O-18 recovery technique was used to recover the O-16 water. A representative sample of the recovered O-16 water was then analyzed to see if the suspect contamination had been removed. If the technique was deemed successful at removing contamination of O-16 water, then the technique was tested using O-18 water.

B. Organic Adsorption

1. Activated Carbon

Activated carbon was one type of organic adsorbent that was considered for removal of organic contamination from O-18 water. FISHERbrand 50-200 mesh activated carbon from Fisher Scientific was used. Like the ion-exchange resins, treatment of a sample with activated carbon could have been performed by batch or column method. However the column method was the method of choice since it involved less handling of the activated carbon as was witnessed with the ion-exchange resin.

However, before the column method was attempted, experiments were done in batches to determine if any contaminants that would be leached from the activated carbon by water could be removed. Attempted removal of contaminants from the activated carbon was performed by placing approximately 0.5 g of activated carbon in a beaker, and washing the carbon with 20 mL of deionized water several times. The activated carbon was equilibrated with each 20 mL washing for approximately one hour. After each washing, the water was filtered from the activated carbon with an 0.1 μm nylon filter. The water was filtered because it could not be decanted from the carbon since the carbon did not rapidly settle. After each equilibration and filtration, two or three drops of each

filtrate was placed onto a watch glass and allowed to evaporate in order to determine if any visible residue remained on the watch glass after all of the water had evaporated. After five washings, it was determined that as much visible residue remained after evaporation of the fifth washing as remained after evaporation of the first washing. This amount of residue was much greater than the residue left behind after evaporation of deionized water.

Since the amount of contamination leached from activated carbon by water was not reduced with repeated washings, activated carbon was determined not to be an appropriate method for removal of organic contamination from O-18 water. Another method for removal of organic materials from O-18 water would need to be investigated.

2. Polymeric Reversed-phase Resins

Polymeric reversed-phase resins were one type of organic adsorbent that was considered for removal of organic contamination from O-18 water. After consulting with a representative from Supelco Chromatography Products, Amberlite XAD-2 adsorbent from Supelco was chosen as the polymeric reversed-phase resin to be used. This resin was chosen because it contains a polyaromatic functional group which is capable of adsorbing a wide range of organic molecules with molecular weights up to 20,000 amu from aqueous solutions.[24]

Like the treatment of a sample with an ion-exchange resin or activated carbon, treatment of a sample with XAD-2 could have been performed by batch or column method. The column method was chosen since the column method involved less handling of the resin as was witnessed when using the ion-exchange resin.

Before the column method was attempted, experiments were performed in batches in an attempt to determine if any contaminants that could be leached from the XAD-2 by water could be removed by washing the resin. Due to the hydrophobicity of the XAD-2 resin, approximately 0.5 g of the resin was stirred with approximately 20 mL methanol for 15 min in order to wet the resin as was recommended by the manufacturer. The methanol was decanted, and the resin was then washed with 20 mL of water several times. After each addition of water, the resin/water mixture was equilibrated by stirring the mixture for approximately 1 hour. After each equilibration the wash water was decanted, and 20 mL more water was equilibrated with the resin. After each wash, two or three drops of the wash water was evaporated on a watch glass to determine if any visible residue remained after evaporation of the water. After four washings, the amount of residue remaining after evaporation of the wash water was determined to be comparable to the residue left behind after evaporation of two or three drops of deionized water.

After the determination that any visible contamination that may be leached by water could be removed from the XAD-2 resin, a column of the XAD-2 was prepared. Once again a 10 mL buret was used as the column. The XAD-2 resin was placed in the column along with the AG501-X8 deionization resin. The two resins were placed in the column together because the XAD-2 resin would not remove ionic impurities. The deionization resin would be needed to remove ionic materials. The XAD-2 was placed in the column first so that it would be below the ion-exchange resin as seen in Figure 4. This arrangement was chosen so that any organic materials possibly leached from the AG501-X8 would be removed by the XAD-2.

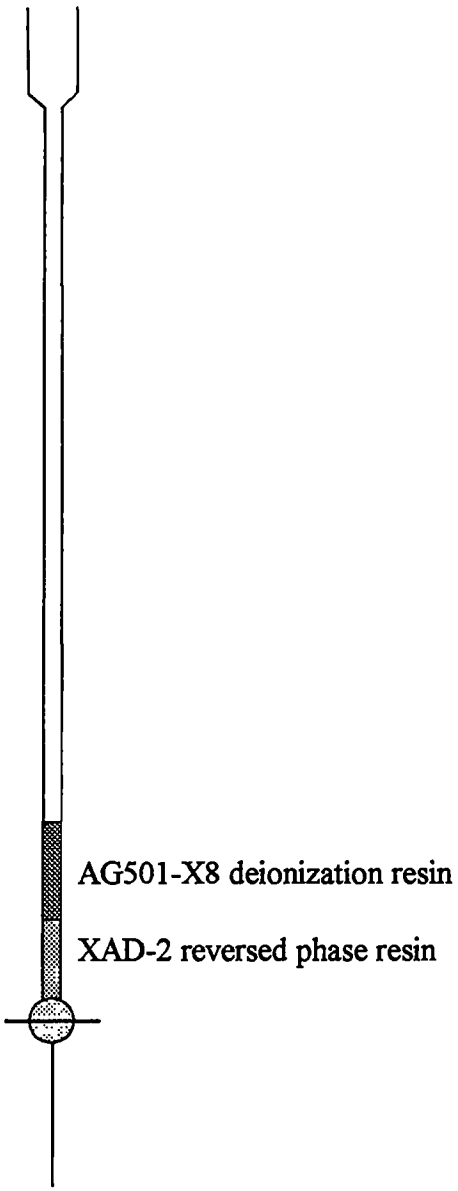

FIGURE 4

Column design utilizing AG501-X8 deionization resin and XAD-2 reversed-phase resin

To begin preparation of the column, a small amount of XAD-2 (more than would be needed to give 2.0 cm in the buret) was placed in a beaker and covered with methanol, stirred for two minutes, and allowed to stand for 15 min. The methanol was decanted, and the resin was covered with water, stirred for one minute, and allowed to stand for ten minutes. A small plug of glass wool was placed in the buret and pushed to the bottom of the buret. The stopcock of the buret was closed and the XAD-2 resin/water mixture was added to the buret until approximately 2.0 cm of the resin had settled in the bottom of the buret. Since the XAD-2 did not settle very well, the water was periodically drained to just above the top of the resin bed in order to bring suspended resin particles down to the resin bed in order to aid in the settling of the XAD-2. The buret was filled with water very slowly as not to disturb the XAD-2 resin in the bottom of the buret. Fresh AG501-X8 deionization resin was added to the buret using the technique described in Chapter III, Section A. Deionized water was then allowed to flow through the resins. Periodically, two or three drops of the effluent from the column were collected on a watch glass and evaporated to determine if any visible contamination was still being leached from the resins.

After it was determined that no significant amounts of visible contaminants were being leached from the resins, the column was gravity drained. A pipet bulb was then placed onto the top of the buret, and the excess water was pushed from the resin with air. While pushing air through the column, a Kimwipe® was placed at the tip of the buret to absorb water from the buret tip so that no water was pulled back into the tip by capillary

action. This water was removed so that when O-18 water was added to the column, the isotopic dilution with O-16 water would be minimized.

After water was gravity drained from the column and the column was partially purged with air, air pockets were noticed in the XAD-2 resin bed. These air pockets were probably formed when the water was drained from the resin bed. Due to the hydrophobic nature of the XAD-2 resin, the resin did not remain wet when the water was drained from the column. When the resin dried, it likely collapsed. This collapse of the resin could have caused new organic contaminants to be leached from the resin. The collapse would have also likely caused channeling of the resin bed which would reduce the amount of contact between the sample of interest and the XAD-2 resin. Therefore, it was determined that an organic adsorption resin should probably not be used since most organic adsorption resins are hydrophobic in nature and would collapse when partially purged with air.

C. Distillation

Distillation was one method that was considered for removal of ionic and some organic contaminants from O-18 water. An Ace Glass catalog number 9313-12 minimum holdup still as shown in Figure 5 was used. Appropriate sized distillation and receiver flasks were used depending on sample size. Most samples varied from 7-15 mL; therefore, a 25 mL flask was usually used. All joints were 14/20 with the exception of the thermometer joint which was a 7/12 joint.

Before any samples were distilled, experiments were performed to determine how much water would be lost during distillation. Several 10 mL water samples were distilled.

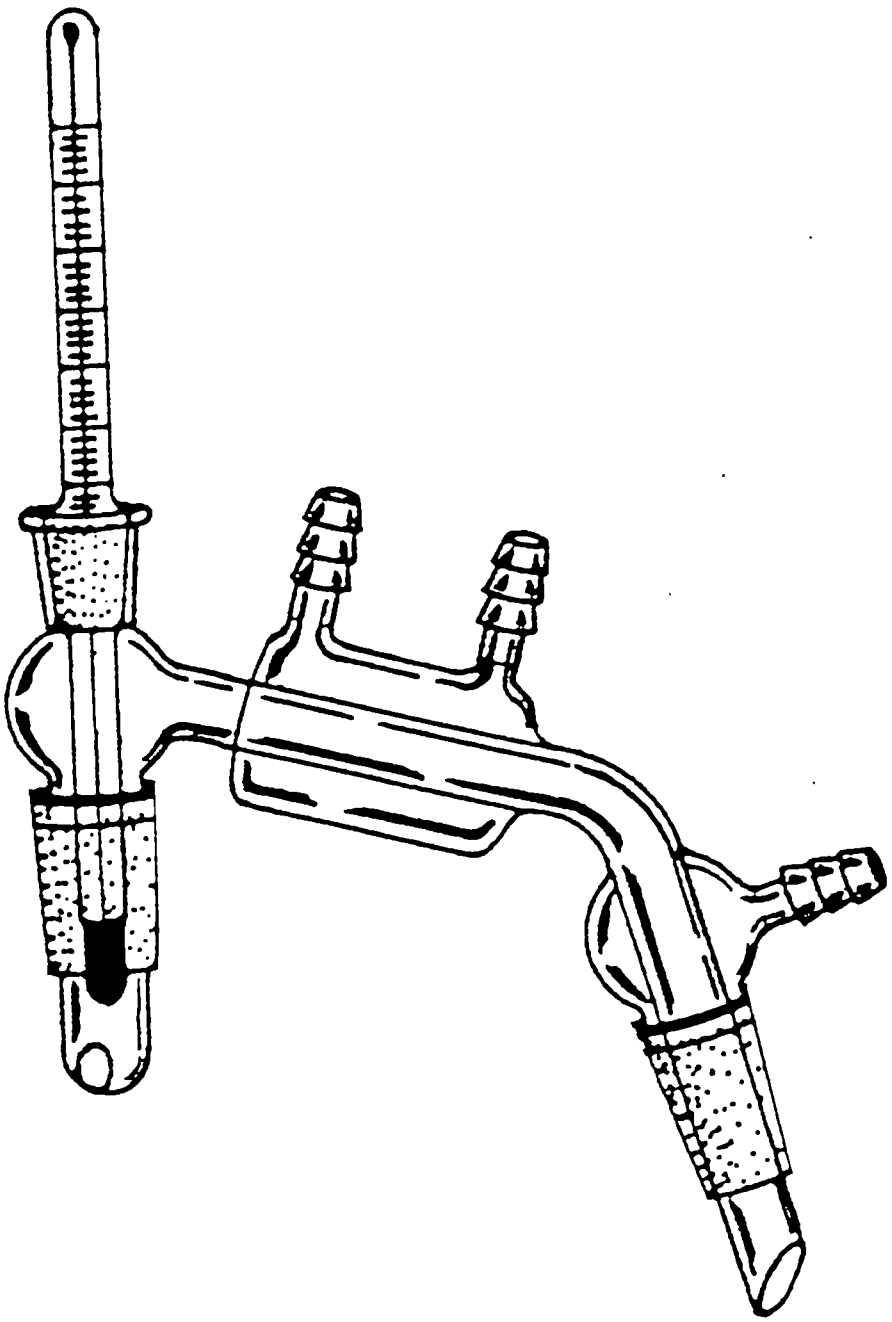

FIGURE 5

Ace Glass catalog number 9313-12 minimum holdup still

Water losses were found to be between 0.5 and 1.0 mL when all of the water was collected during a distillation to dryness. However, in order to aid in the removal of contaminants with boiling points lower than the boiling point of water, sometimes approximately 1 mL of the distillate was collected before the collection of the sample of interest was begun. This loss of water was a concern due to the expense of O-18 water. However, if larger samples were distilled then the total percent of water lost was minimized.

Distillation is much more easily performed on small samples than ion-exchange. Therefore, if distillation and ion-exchange are found to be equally effective at removing ionic contaminants, distillation will be the method of choice. However, if distillation is used, another method of organic removal will likely need to be employed. Distillation cannot effectively remove a substance such as acetonitrile which azeotropes with water. Also, if there are very small quantities of organic materials with lower boiling points than water, it is likely that these compounds will not be completely separated from water by distillation.

D. Ultraviolet Irradiation

Ultraviolet irradiation in the presence of TiO_2 catalyst was one method considered for the removal of organic contaminants from O-18 water. When in the presence of finely powdered TiO_2, organic species should be photo-oxidized to CO_2, water, and other inorganic species. TiO_2, anatase, 99.9%, 32 nm average particle size, from Alfa Aesar Research Chemicals was used as a photo-catalyst. Two different light sources were used. One source was a Rayonet model RPR-208 350 nm peak wavelength, 100 Watt

incandescent light source. The other source was a 350-380 nm wavelength, 6.8 Watt/cm^2 laser light source provided by CTI, Inc. In most experiments 0.5 in diameter quartz test tubes with lengths of 6 in were used to contain the samples.

In all experiments, approximately 5 mg of TiO_2 catalyst per 10 mL of sample was used. The samples were placed in test tubes, and the TiO_2 was added directly to the samples. Each sample was then stoppered and agitated to suspend the TiO_2. The samples did not need to be agitated during irradiation since the TiO_2 was so finely powdered that settling of the catalyst during the reaction did not occur. To remove the TiO_2 after irradiation, all samples were distilled using the Ace 9313-12 minimum holdup still and 25 mL distilling flask. Distillation was used for removal of TiO_2 since a distillation step may be needed to remove ionic contamination anyway. Also filtering of the 32 nm TiO_2 particles from water was attempted and found to be a very difficult process. It was also found that the amount of sample lost during UV irradiation followed by distillation was comparable to the amount of sample lost after distillation alone. This water loss was usually about 1 mL when 10 mL samples and 25 mL distillation flasks were used.

In the incandescent reactor, eight U-shaped bulbs were used. Each bulb was directly opposite another bulb with the bottom of the U facing upwards to give a vertical cylindrical light box. The reactor had a circular hole in the top which was used for sample introduction. Sample tubes were placed in the reactor by hanging the tubes from wires. The sample tubes were stoppered to keep contamination from entering into the sample tubes. In order to allow for any CO_2 produced during the photo-oxidation to be released, the samples were vented by pushing syringe needles through the stoppers.

Because the second UV light source was a laser, the UV light was very tightly focused. Therefore, the light source and sample needed to be oriented so that there would be maximum contact between the light and the sample being irradiated. When irradiating a sample, the sample test tube was oriented vertically in a rack. The UV source was then placed directly above the test tube and aimed downward so that the light emitted would travel straight down the test tube, passing through as much of the sample as possible. There was no need to vent the samples, because in order to allow light into the test tubes, there was no stopper placed on the test tubes during irradiation.

Due to the fact that organic adsorption was considered to be an inappropriate method of O-18 water recovery, and that distillation cannot remove from water organic materials which form azeotropes with the water, UV oxidation was the first method that gave promise as a suitable method for removal of organic materials from O-18 water. UV oxidation was relatively simple to perform, and if it proved to effectively remove organic contamination from water without significant isotopic dilution of O-18 water, it would be a suitable technique.

E. Permanganate Oxidation

Permanganate oxidation was one method that was considered for removal of organic contamination from O-18 water. When refluxed in the presence of MnO_4^- under basic conditions, organic species should be oxidized to CO_2, water, and other inorganic species. $KMnO_4$ and KOH pellets, both Certified A.C.S. grade from Fisher Scientific, were used. Flasks that were the appropriate sized (25 or 250 mL) were used depending on sample size. Each flask had a 14/20 joint and was attached to a condenser with the

same sized joint. The top of the condenser was left open to allow for expansion in the system when refluxing. If significant amounts of water were being lost, or if O-16 water in the air was exchanging significantly with O-18 water in the refluxing system, then the size of the hole in the top of the condenser could be made smaller in order to minimize the loss of O-18 water due to evaporation or isotopic exchange.

In all experiments, approximately 50 mg of $KMnO_4$ and 50 mg of KOH per 10 mL of sample were used. A sample was placed in a boiling flask, then the $KMnO_4$ and the KOH were added directly to the sample and allowed to dissolve. The samples were then refluxed for four to six hours. The samples were stirred with a small Teflon® magnetic stir bar during the reflux to enhance mixing of the solution.

After being refluxed, the samples were distilled twice with the Ace 9313-12 minimum holdup still shown in Figure 5. Since the joints on the boiling flasks were the same size as the joints on the still, the boiling flask used for reflux was used as the distilling flask in the first distillation so the sample was not transferred unnecessarily. Then the collection flask from the first distillation was used as the distilling flask in the second distillation again so the sample would not be transferred unnecessarily. Minimizing the number of times the sample was transferred during the reflux and distillations minimized sample loss. The amounts of sample lost were comparable to the amounts lost during two distillations.

It was found that the amounts of sample lost and the difficulty of performing permanganate oxidations were quite comparable to the sample lost and difficulty of performing UV irradiations. Therefore if one of the two techniques is found to remove

organic contaminants from O-18 water better than the other without significant O-18 dilution then that technique will be the method of choice.

F. Recovery of O-18 Water from Oxygen and Hydrogen Gases

As mentioned in Chapter II, the catalyzed recombination of the assumed stoichiometric ratio of oxygen and hydrogen gases to water was a possible method of recovering O-18 oxygen gas produced during the radiolysis of O-18 water. In order to determine if the gases could be effectively recombined, a stoichiometric ratio of the gases was produced electrolytically in the custom-made apparatus diagramed in Figure 6.

A 125 mm x 65 mm crystallizing dish was used as the bottom water reservoir. A custom-made bottle containing electrodes and a hole in the bottom was used as a chamber for the production of the gases. A straight-tube adapter and 13 mm inside diameter thin walled Tygon® tubing was used to connect the gas production bottle to the gas reservoir. A Hoffman-style tubing clamp was used to control the flow of gas and/or water between the gas production bottle and the gas reservoir. A 250 mL round-bottomed flask with a 13 mm outside diameter glass tube connected at a hole in the bottom of the flask connected the gas reservoir to the top of the tygon tubing. A 90° threaded stopcock was attached to the top of the gas reservoir to control flow of the gases to the catalyst chamber. A 29/12 weighing bottle was used as the catalyst reservoir and was permanently fused to the side of the threaded stopcock. A copper screen platform was placed inside the weighing bottle to support the catalyst so that it would not be touching the bottom or sides of the weighing bottle. All ground glass joints with the exception of the 29/12

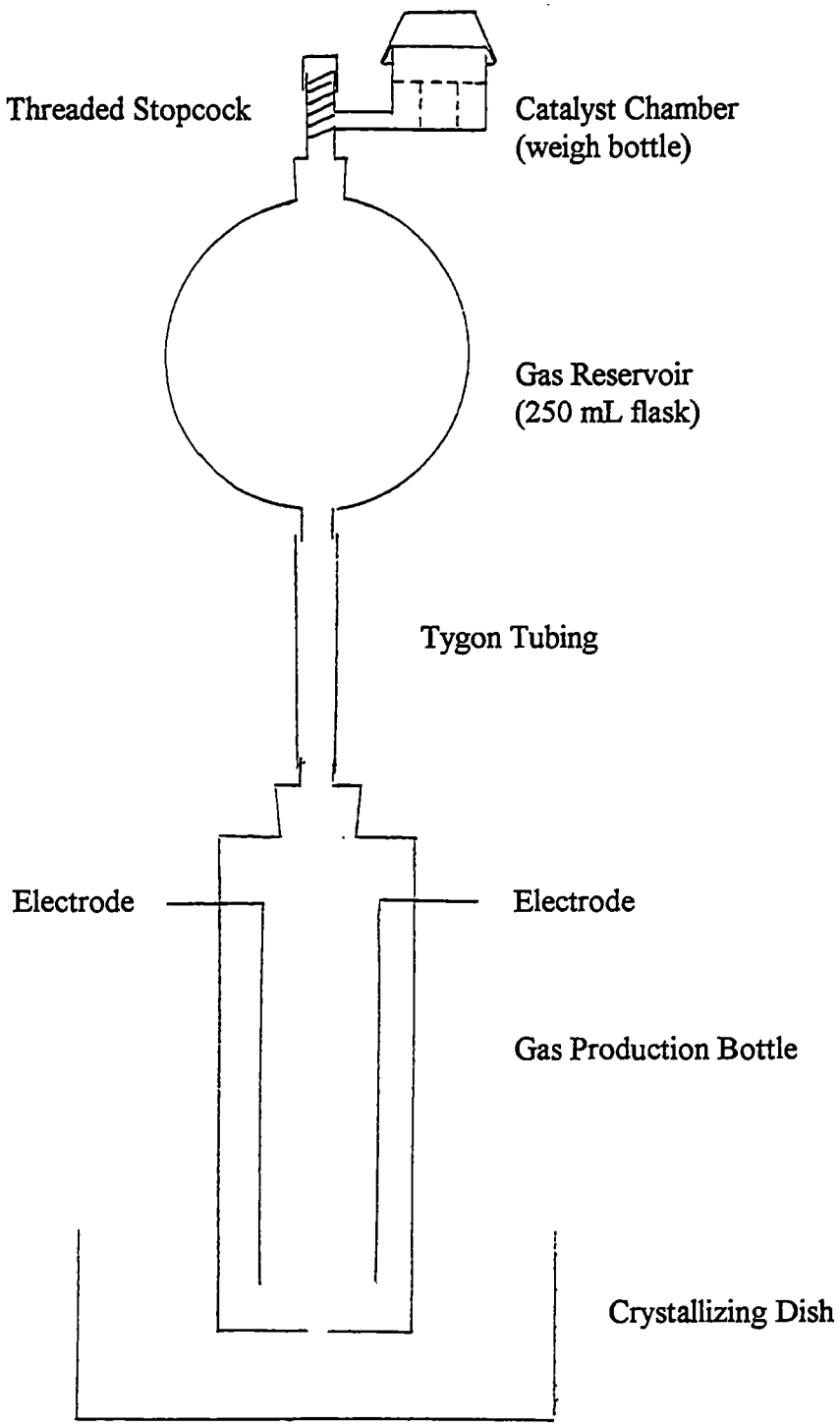

FIGURE 6

Apparatus for production and catalytic recombination of oxygen and hydrogen gases

connection between the weighing bottle and its lid were 19/22 joints. A standard DC power supply was used to supply voltage across the electrodes.

Before the apparatus was used to recombine oxygen and hydrogen gases, the apparatus needed to be tested to ensure that the gases could be produced from water effectively. All water used in the apparatus had a very small amount of sulfuric acid added so that the solution would conduct electricity. The crystallizing dish was partially filled with the sulfuric acid solution. The hole in the bottom of the gas production bottle was sealed with parafilm so that the solution would not drain from the system. The bottle was then filled with solution. The bottle was suspended a few centimeters above the bottom of the crystallizing dish with the hole completely immersed in the solution in the dish. The tubing on the bottom of the gas reservoir was then pinched closed with the tubing clamp. The gas reservoir was filled with solution and connected to the top of the gas production bottle with the tubing. With the stopcock in the closed position the threaded stopcock/weigh bottle was connected to the top of the gas reservoir and the lid was placed on the top of the weigh bottle to seal the system. The parafilm was then removed from the hole in the bottom of the gas production bottle while allowing the hole to remain immersed. The tubing clamp was also removed from the tubing connecting the gas production bottle to the gas reservoir. The system did not drain which indicated that it was effectively sealed.

The power supply was connected to the leads from the electrodes in the gas production bottle. The power was turned on and gases evolved from the two electrodes. An in-line ammeter gave a reading of 300 mA. A voltmeter built into the power supply

showed a reading of 18-20 V The gases produced proceeded upwards through the tubing and into the gas reservoir. The water in the reservoir was then pushed downwards by the pressure of the gases and the level of water in the crystallizing dish increased. After approximately one hour, the level of water in the apparatus had dropped to just below the tubing connecting the gas production bottle to the gas reservoir. The power was turned off and the tubing was pinched.

When a catalyst was ready to be tested, it could be placed in the weigh bottle, and with the weigh bottle sealed the threaded stopcock could be opened to allow the gases to come in contact with the catalyst. If the gases were converted back to water, then a vacuum should build up inside the gas reservoir. The tubing clamp could then be opened to allow the water to fill the evacuated space in the reservoir. If the gases were completely converted back to water, the water level in the reservoir should return to the level of the water before gas production was begun.

CHAPTER IV

EXPERIMENTAL RESULTS

A. Distillation

An experiment was performed to determine how effectively distillation would remove ionic contaminants from water. To make this determination, a sample of tap water was distilled. Samples of the tap water before distillation (sample TAP) and after distillation (sample TAPA) were sent to Huffman Laboratories, Inc., Golden, CO, for conductivity analyses to quantify the ionic character of the tap water before and after distillation. A sample of deionized water (sample DI402) was also sent for conductivity analysis so that the purity of the distilled tap water could be compared to the purity of deionized water. A sample of tap water treated with AG 501-X8 deionization resin (sample TAPB) was also analyzed for conductivity to determine how distillation compared to ion-exchange. The results from Huffman Labs are given below and summarized in Table 1.

It was found that the conductivity of tap water was reduced from 1.90×10^3 μmho/cm to 8.63 μmho/cm by distillation. The conductivity of the tap water was only reduced to 28.5 μmho/cm by ion-exchange. Deionized water was found to have a conductivity of 3.74 μmho/cm. Therefore it was determined that distillation effectively removed the ionic material from tap water so that the ionic character of the tap water was comparable to the ionic character of deionized water. Ion-exchange was not as effective as distillation for the removal of ionic materials from tap water.

TABLE 1

Conductivity of tap water before and after distillation and ion-exchange

Sample	Treatment	Conductivity
TAP	none	1.90×10^3 μmho/cm
TAPA	distillation	8.63 μmho/cm
TAPB	ion-exchange	28.5 μmho/cm
DI402	none	3.74 μmho/cm

Experiments were then performed to determine how much if any dilution of O-18 water with O-16 water would occur during distillation. Six used O-18 water samples were distilled. After distillation, two of the samples were sent to P.E.T.Net Pharmaceutical Services, LLC, Los Angeles, CA, to determine if the distilled, used O-18 water could be reused for FDG production. These two samples were also sent to Huffman for determination of total carbon content by combustion. Before and after distillation, the O-18 water samples were analyzed for O-18 content by mass spectrometry (MS) by Dr. Al Tuinman, Department of Chemistry, University of Tennessee, Knoxville, TN. The O-18 analyses were performed at an accuracy of ±3% O-18. The O-18 analyses were not performed at a higher resolution in order to reduce expenses. It was determined that knowing the O-18 content of a sample to ±3% would be sufficient to determine if an O-18 water sample had been significantly diluted with O-16 water. The MS, total carbon, and FDG production results are given below and summarized in Table 2.

It was found that distillation of O-18 water samples did not significantly reduce the O-18 content of the six samples distilled. Also, the radiochemical yield of the FDG produced using the previously used and distilled O-18 water was found to be high in one sample (sample LA1: 78%) and low in the other (sample TP1: 21%). A satisfactory radiochemical yield when using new O-18 water (95% O-18) is 80%.[8] When bombarded, TP1 also became murky brown. The brown discoloration was probably due to the polymerization of organic materials remaining in the distilled O-18 water. However, LA1 contained 120 ppm total carbon while, TP1 contained only 57 ppm total carbon.

TABLE 2

O-18 content of previously used and distilled O-18 water, and radiochemical yield and total carbon content of samples reused for FDG production

Sample	$F-18^-$ removal resin	O-18 original*	Treatment	O-18 treated*	Total Carbon treated†	Radiochemical yield
LA1	MP-1	89%	distillation	87%	120 ppm	78%
LA2	MP-1	82%	distillation	79%		
OM1	MP-1	84%	distillation	80%		
TP1	QMA	89%	distillation	89%	57 ppm	21%
TP2	QMA	88%	distillation	88%		
TP7	QMA	38%	distillation	44%		

* O-18 content was measured by MS and measurements are accurate to ±3%

† Total carbon analyses were performed by combustion and are accurate to ±5 ppm

Therefore, the polymerization was likely due to the nature of the organic materials in the samples and not the quantity of organic materials in the samples.

It was noted that these two samples of O-18 water had been previously treated with different $F\text{-}18^-$ removal resins during their first use. LA1 had been treated with a resin referred to as MP-1. Many institutions are now beginning to use MP-1. TP1 had been treated with Accell™ Plus QMA referred to in Chapter 1, Section C. Many PET facilities still use QMA. A widely applicable O-18 recovery technique was being sought. Therefore, it was determined that distillation alone would not be an appropriate universal technique for O-18 water recovery since water previously treated with QMA was not reusable after distillation alone. It was determined that an organic removal technique needed to be attempted in order to remove organic materials from the used O-18 water. It was of little concern what the nature of the organic materials in used samples was if essentially all of the organic contamination could be removed.

B. Organic Adsorption Coupled with Ion-exchange and Distillation

In an attempt to remove organic material from water, organic adsorption was performed. The organic adsorption was coupled with ion-exchange and distillation in order to remove ionic contaminants as well as organic contaminants. The organic adsorption and ion-exchange were performed in a 10 mL buret by the technique described in Chapter III, section B, part 2.

Two samples (TP3 and TP4) were treated, each with fresh resins. TP3 was distilled after it was treated with XAD-2 and AG 501-X8. TP4 was distilled before it was treated with XAD-2 and AG 501-X8. The treated O-18 water samples were then

analyzed for O-18 content to determine if treatment of the O-18 water with the resins diluted the samples with O-16. TP3 was also sent to P.E.T.Net to determine if it was reusable after treatment. The results are given below and summarized in Table 3.

When reused for FDG production, TP3 gave a poor radiochemical yield of 48%. When bombarded, TP3 also yielded brown discoloration similar to TP1. This discoloration again likely meant that the organic contamination had not been removed from the sample.

The O-18 content of TP3 was found to decrease from 94% to 83%. The O-18 content of TP4 decreased from 95% to 87%. This decrease was significant and was likely due to the fact that the resins were not completely dried. However, with the drying technique described in Chapter III, section B, part 2, the XAD-2 had already begun to collapse and any further drying would only enhance this phenomenon. The AG 501-X8 also shrunk slightly, this leading to channeling, and further drying would enhance this channeling. Therefore, any technique involving the organic removal resin coupled with ion-exchange was not recommended since the resins, if wet, would dilute the O-18 water with O-16. If the resins were to be dried, they would collapse and be less effective at removing contamination. However, removal of organic contaminants was still necessary, so other techniques were attempted.

C. Ultraviolet Irradiation

Several experiments were performed to determine if organic contamination could be removed from water samples by irradiating the samples with UV light in the presence of a powdered TiO_2 photo-catalyst. Initially, mock O-16 solutions were made with

TABLE 3

O-18 content of samples used and treated with XAD-2 and AG 501-X8,

and radiochemical yield of samples reused for FDG production

Sample	**$F-18^-$ removal resin**	**O-18 original***	**Treatment**	**O-18 treated***	**Radiochemical yield**
TP3	QMA	94%	ion-exchange/ organic adsorption then distillation	83%	48%
TP4	QMA	95%	distillation then ion-exchange/ organic adsorption	87%	

* O-18 content was measured by MS and measurements are accurate to ±3%

ethanol to give varying concentrations of carbon in solutions. The solutions were then irradiated using the techniques described in Chapter III, section D. After irradiation, all solutions were sent to Huffman for analyses of total carbon content by combustion. A sample of deionized water (sample DI402) was also sent to Huffman so that the total carbon content of treated water could be compared to the total carbon content of deionized water.

The first experiment was to simply add approximately 5 mg of TiO_2 to approximately 8 mL each of the mock O-16 water samples with varying carbon concentrations. The samples were placed in Pyrex test tubes and irradiated for 1 hour using the incandescent source. The solutions were then distilled to remove the TiO_2, and total carbon determinations were performed for each sample. The results indicated that the total carbon concentration of the samples did not decrease reproducibly with this treatment. The results of individual samples are given in Table 4.

In the next experiment, the irradiations were performed identically to the first experiment. The only difference was that quartz test tubes were used, and the irradiation time was increased to 12 hours. Again after analysis of the treated samples, it was shown that the total carbon concentration of the samples did not decrease reproducibly with the longer irradiation time. The results for individual samples are given in Table 4.

A third experiment was performed using the UV laser from CTI rather than the incandescent UV source. Again quartz test tubes were used, but the irradiation times were cut to 10 min because of the high power of the laser. Again, after analysis of the

TABLE 4

Total carbon content before and after UV irradiation

Sample	Total carbon original†	UV source	Irradiation time	Total carbon treated†
DI402	3 ppm			
25UV	25 ppm	incandescent	1 hour	30 ppm
50UV	50 ppm	incandescent	1 hour	48 ppm
75UV	75 ppm	incandescent	1 hour	71 ppm
100UV	100 ppm	incandescent	1 hour	55 ppm
33UV	33 ppm	incandescent	12 hours	29 ppm
65UV	65 ppm	incandescent	12 hours	55 ppm
25UVL	25 ppm	laser	10 min	32 ppm
50UVL	50 ppm	laser	10 min	57 ppm
75UVL	75 ppm	laser	10 min	76 ppm
100UVL	100 ppm	laser	10 min	103 ppm

† Total carbon analyses were performed by combustion and are accurate to ±5 ppm

treated samples, it was shown that the total carbon concentration of the samples did not decrease with this technique. The results of individual samples are given in Table 4.

After numerous attempts under differing conditions, it was shown that UV irradiation did not reproducibily decrease the total carbon content of O-16 solutions spiked with ethanol. Therefore, it was determined that UV irradiation was not a suitable technique for removal of organic contamination. Another technique would need to be investigated.

D. Permanganate Oxidation

Several experiments were performed to determine if organic contamination could be removed from O-18 water by refluxing the samples with $KMnO_4$ and KOH. Before any O-18 water samples were treated, O-16 ethanol solutions were used to determine if permanganate oxidation was effective. All refluxes were performed using the technique outlined in Chapter III, section E. All samples were distilled twice to remove the $KMnO_4$ and KOH after refluxing.

Two O-16 samples containing 75 ppm carbon from ethanol were refluxed for 5.5 hours. After refluxing both samples were distilled twice. With one sample (75PMAA), all of the distillate was collected during both distillations. With the other (75PMAA-3), during the first distillation, the first milliliter of distillate was not collected in an attempt to aid in the removal of volatile organic materials from the samples. As a comparison, two samples containing 75 ppm carbon from ethanol were distilled twice without refluxing. When distilling one sample (75AA), all of the distillate was collected during both distillations. When distilling the other (75AA-3), during the first distillation, the first

milliliter of distillate was not collected. The results of these experiments are given below and summarized in Table 5.

Sample 75AA showed no reduction in total carbon after two distillations. Sample 75AA-3 had a reduction in total carbon from 75 ppm to 13 ppm probably due to the fact that the first milliliter of the first distillate was not collected. Both sample 75PMAA and 75PMAA-3 had a reduction in total carbon from 75 ppm to 3 ppm regardless of whether the first milliliter of the first distillate was collected or not. Therefore it was determined that essentially all of the organic materials in the ethanol solutions were destroyed during the reflux with permanganate.

In the next experiment an 18.4 g sample of O-18 water that had been previously treated with QMA was refluxed with $KMnO_4$ and KOH for 5 hours. After refluxing, the sample was distilled twice. During the first distillation, the first milliliter of distillate was not collected. Both the reflux and distillations were performed using 25 mL flasks, with a total sample loss loss of only 2 mL. A sample of the O-18 water before and after treatment was sent to Huffman for total carbon and conductivity analysis. A sample was also sent for O-18 analysis before and after treatment. Additionally, after treatment, the sample was sent to P.E.T.Net to determine if it would give a good radiochemical yield when reused for FDG production.

After refluxing with permanganate and two distillations, the total carbon content of the sample decreased from 13 ppm to 6 ppm. The conductivity of the sample decreased from 19.5 to 7.4 μmho/cm. The O-18 content did not change significantly changing from 95% O-18 before treatment to 92% O-18 after treatment. The radiochemical yield of

TABLE 5

Total carbon concentration of samples before and after

permanganate oxidation followed by two distillations

Sample	Treatment	Total carbon original†	Total carbon treated†
75AA	distillation collecting entire sample	75 ppm	84 ppm
75AA-3	distillation - 1st mL of soln	75 ppm	13 ppm
75PMAA	permanganate oxidation / distillation of entire sample	75 ppm	3 ppm
75PMAA-3	permanganate oxidation / distillation - 1st mL of soln	75 ppm	3 ppm

† Total carbon analyses were performed by combustion and are accurate to ±5 ppm

FDG produced from the treated O-18 water during reuse was satisfactory. Therefore, it was determined that permanganate oxidation with distillation technique was a suitable technique for O-18 recovery.

E. Recovery of O-18 Water from Oxygen and Hydrogen Gases

An experiment was performed to determine if a Pd on alumina catalyst as used by Chu, Engstrom, and Sundberg[23] in 1977 would effectively convert the oxygen and hydrogen gases back to water. The gases were produced at atmospheric pressure by the apparatus described in Chapter III, section F and shown in Figure 7. Palladium, 0.5%, in the reduced form on 1/8 inch alumina pellets from Alfa Aesar Research Chemicals was used as the catalyst.

The apparatus was filled with a dilute sulfuric acid solution. The tubing clamp was opened between the gas production chamber and the gas reservoir. The threaded stopcock was in the closed position. Fifteen catalyst pellets were placed onto the copper screen platform in the catalyst chamber. The power supply was then turned on and the gases were produced. The gases rose upwards into the gas reservoir, pushing the level of the water down in the reservoir.

When the level of the water was below the tubing connecting the gas production bottle to the gas reservoir, the tubing was clamped. The threaded stopcock was opened to allow for the gases to come in contact with the catalyst. Approximately ten minutes later, water vapor was forming on the cap to the catalyst chamber and heat could be felt due to the exothermic recombination of the gases. After one hour of exposure of the gases to the catalyst, the stopcock was closed and the tubing was opened. The water level rose to half

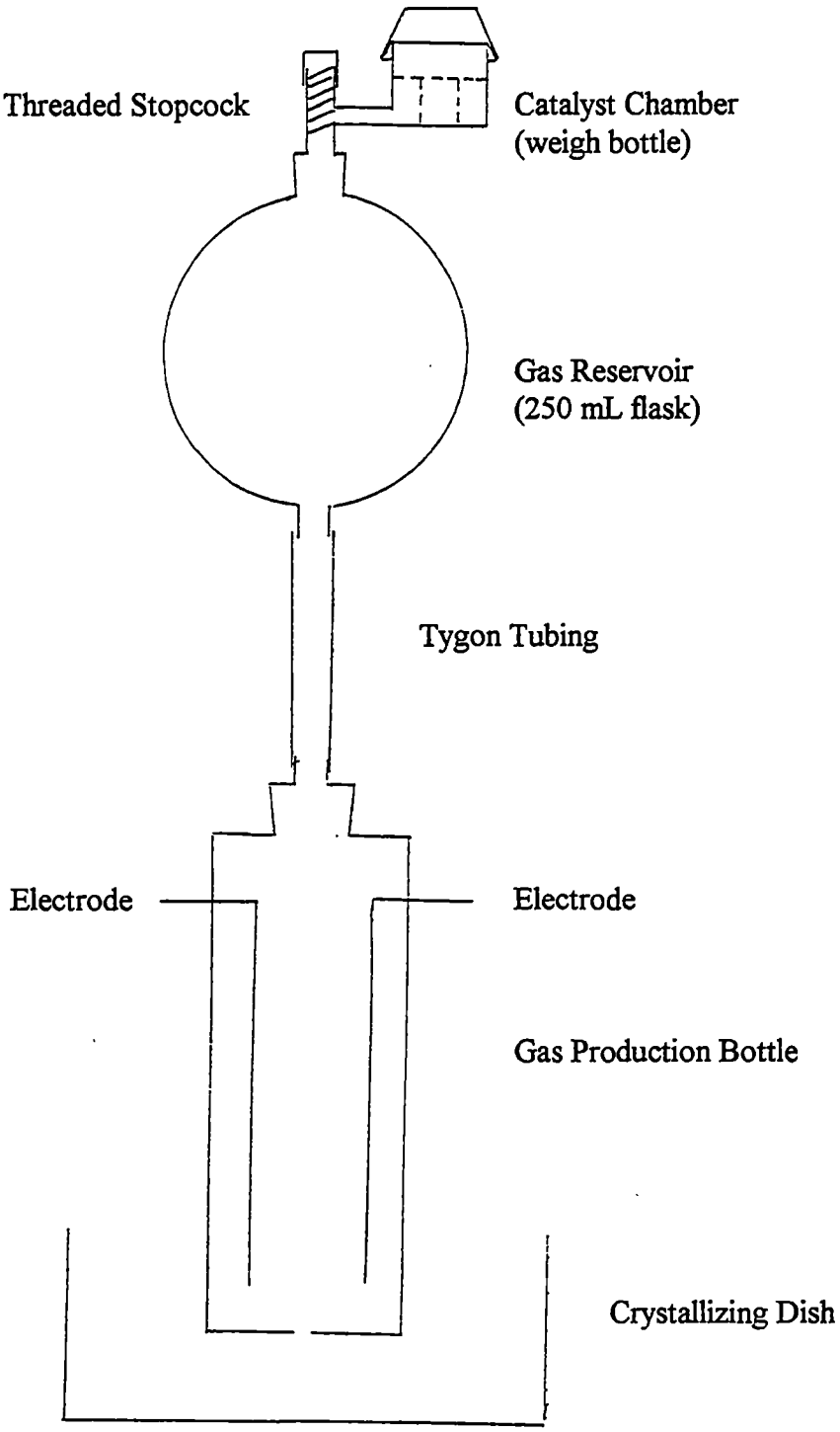

FIGURE 7

Apparatus for production and catalytic recombination of oxygen and hydrogen gases

fill the gas reservoir. After fifteen more minutes, the water level had risen to the original level of the water before gas production indicating that the gases had been largely converted back to water.

An experiment was then performed to determine if the catalytic recombination of the gases could be accomplished at a rate that would keep up with the electrolytic formation of the gases, and to determine how many pellets would be required to keep up the pace. The solution remaining in the apparatus from the previous experiment was used. The stopcock was closed and one pellet was placed in the catalyst chamber. The chamber was capped, the stopcock was opened, and tubing clamp was removed. The power supply was turned on and gas production began. After running for 1 hour, the level of water in the gas reservoir had dropped only slightly. After repeating this experiment with two and three pellets, it was determined that three pellets would recombine the gases as quickly as the gases were produced electrolytically. Therefore, the catalytic recombination of the gases was a successful technique for the recovery of O-18 water from the oxygen and hydrogen gases produced by the radiolysis of the O-18 water.

CHAPTER V

CONCLUSIONS

A. Removal of Impurities

With the recent increase in use of Positron Emission Tomography, the use of O-18 water for production of F-18 containing radioisotopes has experienced a dramatic increase. Because of the small world supply of expensive O-18 and the great cost of building new O-18 production facilities, the recovery of used O-18 water is not only cost effective, but necessary. Also, since the use of O-18 for radioisotope production is performed in large part by privately run institutions, the types and quantities of contaminants in used O-18 water vary widely from one user to the next. Therefore, the development of a widely applicable O-18 recovery technique is desirable.

In order to develop a widely applicable O-18 recovery technique, a treatment needed to be developed that would remove most organic and ionic contamination from a sample regardless of what the contamination might be. The O-18 water needed to be recovered without appreciable dilution of the O-18 with naturally more abundand O-16. The O-18 water also needed to be recovered without significant loss of the O-18 water.

Numerous experiments were performed utilizing distillation, organic adsorption, ion-exchange, UV irradiation, and permanganate oxidation in order to find a suitable method for the recovery of O-18 water. It was determined that the best recovery technique was a reflux of the O-18 water with $KMnO_4$ and KOH followed by two distillations of the sample. This method yielded an O-18 water sample with very low

levels of organic and ionic contaminants. The treatment did not significantly reduce the O-18 concentration of the sample treated while resulting in a sample loss of only a few milliliters when treating sample sizes up to 200 mL. This treatment also gave good FDG radiochemical yields when the treated sample was reused for FDG production.

Since only one permanganate reflux experiment was performed using O-18 water, the technique needs to be tested on multiple samples to ensure that it gives consistently reusable O-18 water. However, when a technique yields samples with total carbon contamination of less than 10 ppm and conductivities of less than 10 μmho/cm, it appears that there is not enough contamination present to pose a problem with reuse of the sample.

B. Recovery of O-18 Water from Oxygen and Hydrogen Gases.

The radiolysis of O-18 water to give oxygen and hydrogen gases can be a mechanism of water loss during $F\text{-}18^-$ production. The recovery of these gases was performed in the lab by electrolytically producing the gases with O-16 water and catalytically converting the gases back to water using a Pd on alumina catalyst. At atmospheric pressure, three 1/8 inch pellets in the apparatus used converted the gases back to water as quickly as the gases were produced electrolytically. With the requirement of such a relatively small amount of catalyst for recombination of the gases, a target could be developed that incorporated the catalyst into the design of the target. However, with some new higher pressure targets, the radiolysis of O-18 water is not a problem because the production of oxygen and hydrogen gases is deterred according to Le Chatelier's principle. Therefore, a study needs to be performed to determine which is more cost

effective: the production of higher pressure targets, or the production of targets that incorporate a recombination catalyst into the design of the target.

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