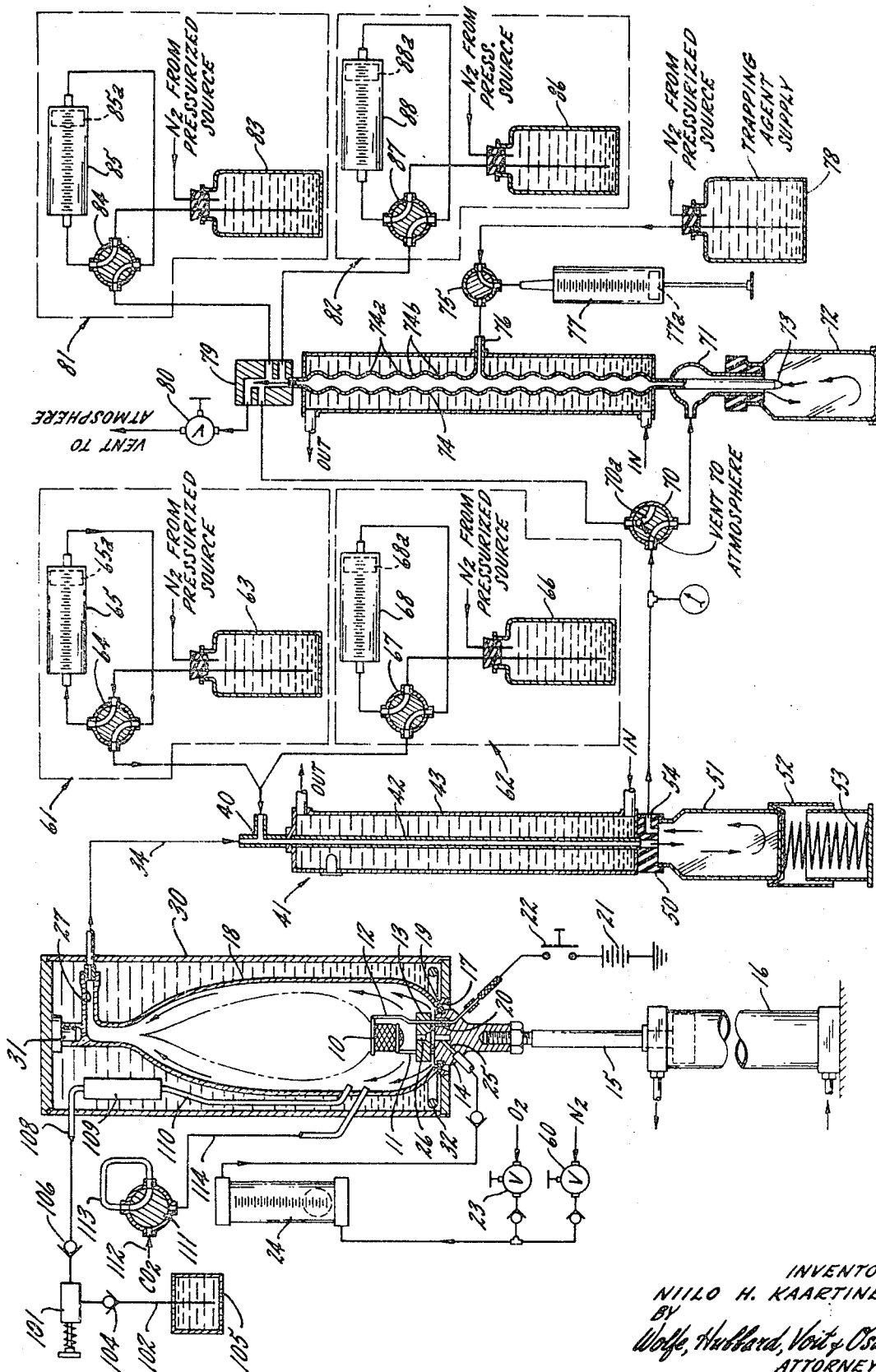


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APPARATUS FOR THE PREPARATION OF LIQUID FROM SAMPLES FOR  
RADIOACTIVE ISOTOPE TRACER STUDIES  
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## APPARATUS FOR THE PREPARATION OF LIQUID FORM SAMPLES FOR RADIOACTIVE ISOTOPE TRACER STUDIES

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### ABSTRACT OF THE DISCLOSURE

Refinements are provided in a system for preparing liquid samples for radioactive nuclide assays. In the basic system, a primary sample containing at least one radioactive nuclide oxidizable to a recoverable gas-form oxide is oxidized, and the resulting combustion products are treated for the recovery of the radioactive nuclide oxide as a final liquid sample. Advantageously, near the beginning of the oxidation, a gas-form oxide of a non-radioactive isotope of the radioactive nuclide is introduced. This introduction simultaneously increases recovery of the radioactive nuclide and decreases "memory" of the system. Where the introduced oxide is water, corresponding to tritium in the primary sample, the resulting apparatus is additionally useful for monitoring both memory and background count, for making quenched standard samples uncontaminated by atmospheric oxygen, and for matching water quenching in samples obtained from primary samples of different size.

### CROSS-REFERENCE TO RELATED APPLICATIONS

Reference is made to the following United States applications previously filed by the present inventor: Ser. No. 728,553, filed May 13, 1968, now U.S. Pat. No. 3,485,565; Ser. No. 728,939, filed May 14, 1968.

Ser. No. 729,047, filed May 14, 1968, now U.S. Pat. No. 3,542,121; and Ser. No. 729,212, filed May 15, 1968, now abandoned. Reference is also made to the following Finland patent applications filed by the same inventor: Ser. No. 1390/67, filed May 16, 1967; Ser. No. 828/68, filed Mar. 25, 1968; and Ser. No. 829/68, filed Mar. 25, 1968.

### BACKGROUND AND OBJECTS

The present invention relates generally to the processing of fluid materials. In its principal application, the invention relates to methods and apparatus for the preparation of samples for radioactive isotope tracer study or, in other words, to the preparation of samples for radioactive nuclide assays. More particularly, the invention concerns an improved system for preparing such samples by oxidation of a primary sample containing one or more radioactive nuclides.

In medical and biological research it is often necessary to determine the carbon-14 or the tritium radioactivity of organic samples, herein called "primary samples." Frequently these primary samples are insoluble in liquid scintillation solvents or, even if soluble, the counting efficiency is poor and erratic due to light absorption (quench) caused by the presence of organic molecules (chemical quench) or other colored materials (color quench). Moreover, since both carbon-14 and, especially, tritium are low energy level radioactive nuclides, if any of the primary sample is insoluble in the scintillation solvents only a very small fraction of the emitted beta particles can reach the scintillator.

Accordingly, much attention has been devoted to providing combustion techniques to convert primary samples to water and tritium oxide and to carbon dioxide and carbon-14 dioxide. In theory, combustion solves the fore-

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going problems in that the combustion products are readily soluble in efficient scintillation solvents and there is little if any difficulty due to color or chemical quench effects.

Early devices for practicing combustion of primary samples containing radioactive nuclides and for recovery of the combustion products have not been widely accepted. Thus, one publication by Peets et al., Anal. Chem., 32; 1465-1468 (1960), describes an oxygen train combustion system, but this system was criticized in a later publication by Knoche et al., Anal. Biochem., 12; 49-59 (1965) as having "limitations in regard to the combustion of a series of samples varying in weight, dryness, and activity." In turn, the combustion tube-furnace of Knoche et al. was recently characterized in a paper by Davidson et al., presented at the Massachusetts Institute of Technology in April 1969, as "generally quite complicated and time-consuming."

Many difficulties associated with these earlier systems have been minimized or eliminated in a system described by the present inventor in applications Ser. No. 728,553, filed May 13, 1968, now U.S. Pat. No. 3,485,565, Ser. No. 728,939, filed May 14, 1968, Ser. No. 729,047, filed May 14, 1968, now U.S. Pat. No. 3,542,121, and Ser. No. 729,212, filed May 15, 1968, now abandoned. An object of the present invention is to provide certain refinements to this system, which refinements are broadly applicable for the improvement of heretofore existing apparatus and methods.

The limitation of many existing systems is in their ability to treat small primary samples, of the order of 100 milligrams or even down to nanogram quantities. Upon oxidation of samples containing carbon-14, tritium, or sulfur-35, the small amount of radioactive oxide gas is difficult to recover. Accordingly, a principal object of the present invention is to provide a method and apparatus for increasing the quantitative recovery of radioactive nuclides produced as oxides by the combustion of relatively small samples. An associated object is to improve the separation of individual radioactive nuclides when the primary sample is double-labeled, or in other words, contains a plurality of radioactive isotopes.

Additionally, and particularly when the primary sample is small, the phenomenon of "memory" occurs, whereby the system appears to remember a previous high-activity sample. In reality, memory is caused by adsorption and slow desorption of radioactive nuclides on vessel walls, with the result that a subsequent low-activity sample is contaminated by desorbed radionuclides from a previous high-activity sample. This memory effect has been recognized, as for example by Peets et al. and Knoche et al., both of whom suggested methods for mitigating against it. An important object of the invention is to reduce this memory without concurrently increasing the time necessary for sample preparation.

A general object of the invention is to provide a rapid, simple, and precise system for monitoring the extent of memory and the memory-free background count of an analytical apparatus.

A further object is to provide a method for making quenched standard samples uncontaminated from atmospheric oxygen; previously, quenched standards have been quite difficult to prepare unless extensive provisions were made for excluding atmospheric oxygen.

Another advantage and object of the invention is to provide a system for producing liquid form samples having constant quench characteristics from primary samples of widely different sizes.

### BRIEF DESCRIPTION OF DRAWING

Other objects and advantages of the invention will become apparent from the following detailed description

and upon reference to the accompanying drawing, in which the figure is a schematic diagram of a sample preparation system embodying the present invention, for use in the preparation of liquid form samples for radioactive nuclide assays.

### DETAILED DESCRIPTION

While the invention will be described in connection with certain preferred embodiments, it will be understood that it is not intended to limit the invention to these particular embodiments. On the contrary, it is intended to cover all alternatives, modifications and equivalent arrangements may be included within the spirit and scope of the invention as defined by the appended claims.

Turning now to the figure, there is illustrated a sample preparation system for use in the preparation of samples for radioactive isotope tracer studies, such as studies involving tissue distribution and residue levels of drugs in plants and animals. In the preparation of such samples, a sample of the starting material containing the radioactive isotope tracer, such as a sample of the plant or animal tissue, is burned to convert the carbon in the starting material to carbon dioxide and the hydrogen to water, and the radioactive isotope tracer is then recovered from the resulting combustion products. For example, if the particular radioactive isotope tracer employed is  $^{14}\text{C}$ , it appears in the combustion products as  $^{14}\text{CO}_2$  gas; if the tracer is tritium ( $^3\text{H}$ ), it appears in the combustion products as  $^3\text{H}_2\text{O}$  in the form of a condensable vapor. Although  $^{14}\text{C}$  and  $^3\text{H}$  are the most commonly employed tracers, it will be understood that a number of other radioactive isotopes may be employed, such as  $^{35}\text{S}$  which is converted to sulfate during combustion.

In order to provide samples which can be analyzed for radioactivity, the compounds containing the isotope tracers are recovered from the combustion products, and separated from any materials therein which might interfere with the radioactivity determination. For example, the  $^3\text{H}_2\text{O}$  is recovered by cooling the combustion products to condense the vapors therein, including the  $^3\text{H}_2\text{O}$ , after which the condensed vapors are separated from the remaining gases. The  $^{14}\text{CO}_2$  may also be recovered by condensation or freezing at extremely low temperatures, such as by the use of liquid nitrogen for example, but it is more conventional to react the  $^{14}\text{CO}_2$  with a liquid trapping agent such as ethanolamine; the resulting reaction product is then recovered and mixed with a liquid scintillator to provide a sample suitable for use in making a radioactivity determination.

Referring now more specifically to the figure, the sample to be burned is placed in a sample basket 10 which forms a part of the electrical ignition system, and also functions as a catalyst for efficient combustion for the sample contained therein. The basket 10 is suitably made of platinum or a platinum-rhodium alloy, so that the basket can be used both as an electrical resistor in the ignition system and as a catalyst for the combustion of the sample. A pair of electrical conductors 11 and 12 extend upwardly from a mounting plate 13, to support the basket 10 at the upper and lower ends thereof, while also making electrical contact with the basket to connect it into the electrical ignition system. The conductors 11 and 12 extend vertically down through the plate 13 and terminate in depending connector pins beneath the plate 13.

In order to facilitate the loading of successive samples, the mounting plate 13 is supported on the top of a small platform 14 threaded on to the end of a pneumatic piston rod 15. To load a sample in the basket 10, the pneumatic cylinder and piston assembly 16 associated with the rod 15 is actuated to retract the piston rod 15, thereby lowering the basket 10 through an opening 17 in the bottom of a combustion chamber 18. The sample is then loaded in the basket, and the cylinder and piston assembly 16 is actuated to advance the rod 15 and thereby

raise the basket 10 through the opening 17 into the combustion chamber 18. As the platform 14 enters the opening 17, a sealing ring 19 mounted in a groove in the outer periphery of the platform 14 engages the tapered walls of the opening 17 to form a gas-tight seal therewith, as shown in the figure.

For the purpose of igniting a sample contained in the basket 10 after it has been raised into the combustion chamber 18, the connector pins depending from the plate 13 fit into complementary electrical receptacles 20 in the top of the platform 14. The receptacles 20, in turn, are connected to an electrical igniter circuit including a power source such as battery 21 and an ignition switch 22 for applying an electrical voltage across the basket 10, which serves as a resistive type heating element in the igniter system. Thus, the sample is ignited by simply closing the switch 22, which is opened again as soon as combustion has been initiated.

In order to supply the oxygen required for combustion of the sample contained in the basket 10, pure oxygen is supplied to the combustion chamber 18 through a valve 23, a flow meter 24, and a pair of cooperating passageways 25 and 26 formed in the platform 14 and the plate 13. The gas discharge passageway 26 in the plate 13 is positioned directly beneath the center of the basket 10, so that the oxygen is fed directly into the combustion zone. The oxygen flow rate is adjusted, via the valve 23 and flow meter 24, to a level slightly above that required to support combustion of the sample in the basket 10, so that there is a slight excess of oxygen within the combustion chamber. Consequently, there is generally a relatively thin layer of an oxygen-rich atmosphere between the combustion flame and the inside walls of the combustion chamber 18, as indicated by the arrows in the figure. This excess oxygen rises through the combustion chamber and is exhausted from the combustion chamber 18 along with the combustion products through a lateral exit 27 at the top of the chamber.

The combustion chamber is open at the upper end thereof with the sidewalls extending upwardly and inwardly above the sample basket so as to approximate the shape of the flame of a burning sample, thereby minimizing the volume of oxygen-rich atmosphere around the flame, and the walls of the combustion chamber are preheated so as to maintain the wall temperature above the condensation temperature of the vapors contained in the combustion products. With this design, the combustion products tend to be swept directly into the exit 27, with the rising layer of oxygen-rich atmosphere along the chamber sidewalls tending to isolate the combustion products from the sidewalls. Moreover, any combustion products that do contact the chamber walls remain in the gas state, even during initiation of the combustion, because the walls are pre-heated and maintained at a temperature above the condensation temperature. Thus, in the illustrative embodiment of the combustion chamber illustrated in the figure, the walls of the combustion chamber 18 extend vertically upwardly past the sample basket 10, and then slope inwardly above the basket so as to approximate the shape of the flame represented in broken lines. Surrounding the combustion chamber 18 is a cylindrical vessel 30 which defines an annular cavity around the outer surface of the chamber 18 for receiving a preheating fluid. To center the combustion chamber 18 within the vessel 30, the upper end thereof meshes with a complementary mounting element 31, while the lower end fits into a complementary hole in the bottom wall of the vessel 30.

Prior to ignition of the sample contained in the basket 10, the fluid contained in the annular cavity between the combustion chamber 18 and the vessel 30 is heated by means of a heating coil 32 at the lower end of the cavity. The fluid distributes this heat along the walls of the combustion chamber 18 so that the walls are uniformly heated to a temperature above the condensation

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temperature of the vapors contained in the combustion products to be produced. It has been found that the preheating of the combustion chamber walls to maintain the combustion products in gaseous form even during ignition, combined with the flame-shaped configuration of the chamber, permits the combustion products to be exhausted from the combustion chamber, on a continuous basis, so efficiently that there is virtually no residue of combustion products deposited on the chamber walls. The illustrative system also prevents condensation within the exit 27 of the combustion chamber 18, since the exit is also surrounded by the preheated fluid in the annular cavity between the combustion chamber 18 and the surrounding vessel 31.

In accordance with the invention, provisions are made for introducing into the system one or more gasiform oxides of a non-radioactive nuclide which is an isotope of a radioactive nuclide present in the primary sample. By way of example, if the primary sample contains carbon-14 and tritium, either carbon dioxide or water, or both, are introduced into the system of the invention. As the term is used herein, "water" refers to either liquid or gas-form water, although it will be appreciated that at the temperature prevailing within the vessel 30, typically 200° C., the water exists as water vapor, or steam.

Referring to the figure, where water is to be introduced, a manually operated spring-loaded plunger pump 101 draws liquid water via conduit 102 and a check valve 104 from an enclosed water flask 105. The pump 101 discharge is through a similar check valve 106 and conduit 108 through the ambient temperature heater 109 located within the vessel 30. In the exchanger 109 the water is vaporized, and the resulting superheated steam is conveyed via the conduit 110 to the interior of the combustion chamber 18 via a suitable inlet as shown.

It has been found that a stroke volume of about 70 microliters is a convenient capacity for the plunger pump 101. For certain of the objects recited earlier and as will be explained hereinafter, one or more depressions of the pump 101 is associated with each combustion of a primary sample in the combustion chamber 18.

For certain purposes, particularly when the primary sample is small in size and it is desired to assay for carbon-14, non-radioactive carbon dioxide may be introduced into the combustion chamber 18 through a counterpart of the water introduction system described earlier. To this end, a four-way valve 11 is connected to a carbon dioxide source via conduit 112, and two ports in the valve 111 are connected to form a sample loop 113. The third port connects via conduit 114 to the combustion chamber 18 at a location near that of the end of conduit 110. Carbon dioxide gas under a pressure higher than that within the combustion chamber 18 is collected in the sample loop 113 when the plug of the valve 111 is in position corresponding to nine and twelve o'clock. When this plug is rotated 270° clockwise, the entrapped carbon dioxide is discharged into the combustion chamber 18.

Whichever of water or carbon dioxide is introduced it is advantageously added in the beginning of the combustion, most preferably simultaneously with the onset of the application of current to the basket 10. While it is unnecessary that the timing is precise, introduction of water or carbon dioxide should be sufficiently near to the beginning of combustion such that the non-radioactive gases mix well with the products of combustion when the primary sample is ignited.

The amount of water and/or carbon dioxide added to the system via either the plunger pump 101 or the valve 111 depends upon sample size and on the purpose for which the water and/or carbon dioxide is needed. In the case of water, significant increase in the recovery of tritium oxide and in the reduction of memory are achieved with a single 70 milligram injection of liquid water in a system having a gas flow rate of about 0.1 to about 4

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liters per minute. Stated on another basis, the total volume of water vapor used to improve the recovery of radioactive nuclides and to reduce memory is in the range of about 1%, advantageously 10%, to about 50% of the volume of gas flow leaving the combustion chamber 18. Where a single injection is inadequate to provide sufficient separation or memory reduction, a second simultaneous injection, or continuous addition while combustion is occurring, will generally suffice.

For tritium recovery carbon dioxide introduction may be omitted and only water injection employed. Tritium, heretofore a difficult material to collect and assay, is almost quantitatively recovered when water is injected into the combustion system.

The use of water or a like gasiform oxide provides several additional advantages. Although memory is significantly reduced with water, it occasionally happens that an unusually active sample will establish a high background count for a considerable period subsequent to its combustion. When this occurs it becomes desirable to determine when the background count has been reduced, corresponding to sufficient desorption of the adsorbed radionuclide. To check or monitor the memory or background count, a simulated combustion is carried out, with no primary sample present in the combustion chamber 18. Water introduced from the pump 101, together with desorbed contaminants, are thus the only materials recovered in the liquid sample. Counting of the sample thus provides a measure of the background or memory, and should the count be too high it is easily reduced in one or more additional simulated combustions with a few injections of water in each.

In addition, the provision of water injection from a pump delivering a fixed predetermined amount of water provides a convenient method for preparing a series of quench standards. It is well known that water quenches most scintillator liquids, and to correct for this quench the analyst requires a series of standards, each containing the same quantity of a standard activity radionuclide but each with a different amount of water. In the past such a series of standards quenched only with water has been difficult to prepare and the sample vials almost unavoidably become contaminated with atmospheric oxygen, which itself is an effective quench medium. With the injector system described herein, a series of standard quench samples is readily prepared by carrying out a combustion cycle, but in the absence of a primary sample, and introducing a progressive number of 70-milligram amounts of water. Thus, liquid samples containing a scintillator, a standard radionuclide, and differing amounts of quench may be prepared in a few minutes.

In keeping with another aspect of the invention, water injection is advantageous for matching quench effects in scintillation samples obtained from hydrogen-containing primary samples of different sizes. Where, for example, one primary sample is large and another is smaller, counting efficiencies are different by reason of the additional quench attributed to the higher water content produced from the larger sample. If, however, the amount of water is introduced the pump 101 when the smaller of the two samples is being combusted which corresponds approximately to the additional water provided by the larger primary sample, the total amount of water in each respective scintillation sample will be approximately the same, and the quench and hence the counting efficiencies will likewise be equalized.

In the remaining discussion herein it will be appreciated that the injected water and/or carbon dioxide mixes with the combustion products and is carried through the recovery system. Accordingly, no distinction is hereafter made between the oxides of radioactive and of non-radioactive nuclides.

A particularly useful advantage of the invention is to improve separations of different radionuclides when preparing liquid samples from a multiple labeled primary

sample, for example one containing both carbon-14 and tritium. As will be explained hereafter, the recovery system is designed to collect water in the vial 51 and carbon dioxide (as carbamate) in the vial 72. Inevitably, however, some carbon dioxide is absorbed in the water-collecting vial 51 and, conversely, some water collects in the CO<sub>2</sub>-collecting vial 72. Where the amounts of labeled water and CO<sub>2</sub> from the primary sample are small, losses of water and CO<sub>2</sub> by collection in the incorrect vial can be quite significant. However, when water is injected in accordance with the invention, the absolute amount of water and tritium oxide lost to the incorrect vial is constant, but as there is now more water, the relative amount of all water, and particularly tagged water, collected in the water-collecting vial is increased. Otherwise stated, a higher proportion of the tagged water is collected in the proper water-collecting vial 51. The net effect therefore is to improve the resolution of the tagged gases so that, for practical purposes, counting the sample in the water-collecting vial 51 counts essentially all the tritium in the primary sample.

Separations in the case of double labeled primary samples are even further improved by augmenting the combination products with both water and carbon dioxide. This has the effect of providing more of the water and tritium oxide, and more of the CO<sub>2</sub> and carbon-14 oxide to the recovery system, so that the collection of either tagged nuclide in its appropriate collection vial represents an even greater proportion of the original amount of that tagged nuclide.

As the exhausted gases leave the exit 27, they enter a transfer tube 34 which is insulated to maintain the fluids passing therethrough in a gaseous state. In the particular embodiment illustrated, the transfer tube 34 is double walled with a metallic inner shell and an insulating outer shell to minimize the heat loss therethrough. From the transfer tube 34, the gaseous combustion products are passed through a T connection 40 into a heat exchanger 41 for cooling the exhausted combustion products to condense the vapors therein. The heat exchanger 41 includes an inner member 42 forming a fluid passageway for receiving the combustion products from the tube 34, and an outer shell 43 defining an annular cavity around the inner member 42 for receiving a cooling liquid to maintain the walls of the inner passageway at a temperature of the vapors passing therethrough. When the radioactive isotope tracer is in the form of a condensable vapor, such as <sup>3</sup>H<sub>2</sub>O for example, the heat exchanger 41 functions to convert the tracer from a vapor to liquid form. In cases where the radioactive isotope tracer is in the form of a gas to be reacted with a trapping agent, for example, the heat exchanger 41 functions to remove the condensable vapors from the tracer gas before it is reacted with the trapping agent.

The fluid passageway of the heat exchanger is formed of thermally conductive material designed to provide laminar flow of gases and vapors passing therethrough in the absence of condensation, and the cross section of the fluid passageway is sufficiently small in at least one direction transverse to the fluid flow to provide capillary attraction on the type of liquid condensed within the passageway. Thus, the inner member 42 comprises a straight thin walled metal tube having an inside diameter of about 0.05 inch, with a wall thickness of about 0.004 inch, and a length of about 5 inches. Although both the volume and the heat transfer surface area of such a tube are obviously very small, it has been found that such a heat exchanger is capable of reducing the temperature of the combustion gases to the condensation temperature with such a high degree of efficiency that virtually 100% of the condensable vapors can be recovered in liquid form at the outlet end of the heat exchanger. Moreover, this heat transfer is effected without producing a high back-pressure or otherwise inhibiting the exhaustion of the

combustion products from the combustion chamber directly upstream of the heat exchanger inlet.

Although it is not intended to limit this aspect of the system to any particular theory, it is believed that the fluid passageway causes droplets of liquid condensate to form along the walls of the passageway, thereby providing extremely efficient heat transfer conditions. This drop-wise condensation may be caused or promoted by the capillary nature of the fluid passageway. When the fluid passageway in the heat exchanger is in tubular form as in the illustrative embodiment, a pulsating pressure is detected at the inlet of the passageway, and it is believed that drop-wise condensation may account for this pulsating pressure. It will be appreciated, however, that the fluid passageway may have forms other than tubular, such as a narrow slot, since capillary attraction is present whenever the surface of a liquid where it is in contact with a solid is elevated by the relative attraction of the molecules of the liquid for each other and for those of the solid.

A separating means is connected to the outlet end of the heat exchanger for receiving the combustion products, including the condensed vapors, from the heat exchanger and separating the condensed vapors from the remaining gas products, and control means are associated with the combustion chamber for terminating the oxygen supply and supplying an inert gas to the combustion chamber upon completion of the burning of each sample so as to sweep any residual combustion products out of the chamber and on through the heat exchanger into the separating means. Thus, in the illustrative system, a resilient connector 50 is provided at the lower end of the heat exchanger 41 for connecting the outlet of the fluid passageway member 42 to a conventional sample or counting vial 51. The vial 51 is supported on a platform 52 which is biased upwardly against the connector 50 by means of a biasing spring 53 to provide a gas-tight seal around the upper periphery of the vial. As the combustion products are discharged from the lower end of the heat exchanger 41, they flow downwardly into the sample vial 51 so that the liquids are retained in the vial by gravity, while the gases continue on through a discharge passageway 54 formed in the resilient connector 50.

When the combustion of a given sample has been completed, the valve 23 is closed to terminate the oxygen supply to the combustion chamber, and a valve 60 is opened to supply an inert gas such as nitrogen to the combustion chamber via the same flow meter 24 and passageways 25, 26 previously used to supply the oxygen. This inert gas, which is supplied under a slight pressure, sweeps upwardly through the combustion chamber 18 so as to purge the chamber of any remaining combustion products, and continues on through the chamber exit 27, the transfer tube 34, and the heat exchanger 41. Consequently, it can be seen that the entire system from the combustion chamber 18 to the sample vial 51 is immediately purged of all gaseous combustion products following each sample combustion, and the purging gas also tends to sweep any remaining liquid condensate out of the heat exchanger. Moreover, since the inert purging gas is discharged from the heat exchanger 41 into the headspace of the sample vial 51 which is used as a part of the liquid-gas separating means, it may also be used to purge oxygen from the vial headspace to avoid the quenching effect of such oxygen during analysis of the resultant sample for radioactivity. Thus, when the sample vial 51 is disconnected from the resilient connector 50 to place a sealing cap on the vial, the throat of the vial may be maintained directly under the nitrogen discharge from the connector 50 by simply tilting the vial laterally, so that the nitrogen purges the headspace of the vial by displacing any oxygen remaining therein to the atmosphere. As will be apparent to those familiar with this art, this is an important feature because oxygen is a severe quenching agent, i.e., it dis-

torts the radioactivity measurements made by liquid scintillation counting techniques unless certain steps are taken to compensate for the effect of the quenching agent. Although several means of compensating for such quenching effects are known, they complicate the radioactivity measuring procedure.

After the purging of the combustion chamber and the heat exchanger, the inert purging gas is preferably turned off by closing the valve 60, and the inlet of the heat exchanger 41 may be sequentially connected to a pair of liquid supply systems generally indicated at 61 and 62. The first supply system 61 includes a supply vessel 63 containing a liquid solvent of the type conventionally used in the preparation of samples to be subjected to sub-freezing temperatures, so as to maintain the sample in a liquid state. It will be understood that this first liquid supply system 61 is not normally used in the preparation of samples to be handled at above-freezing temperature. Referring now more specifically to the liquid supply system 61, an inert gas such as nitrogen is supplied to the head-space of the supply vessel 63 under a slight pressure, so as to force the liquid solvent through a valve 64 into a metering dispenser 65 including a movable piston 65a. As long as the valve 64 remains in the position illustrated in the figure, the piston 65a in the metering dispenser 65 remains in the position illustrated in the figure and no liquid flows out of the dispenser because the output thereof is effectively closed. However, when the valve 64 is turned 90° to its second position, the pressure of the fluid from the supply vessel 63 urges the piston 65a to the left as viewed in the figure until it reaches a preselected stop position, thereby metering a preselected quantity of liquid through the valve 64 and the T connection 40 into the heat exchanger 41. As the piston 65a moves to the left, the supply of liquid within the dispenser 65 is continuously replenished through the right hand end thereof. Thus, when the metered quantity of liquid solvent has been dispensed, the system is ready to dispense the same preselected quantity of liquid the next time the valve 64 is turned 90°. It will be understood that the piston 65a moves alternately to the left and to the right during successive dispensing operations.

The second liquid supply system 62 is used to feed a preselected quantity of liquid scintillator into the heat exchanger 41 in the same manner described above for the solvent supply system 61. Thus, the liquid scintillator is fed from a supply vessel 66 through a four-way valve 67 into a metering dispenser 68, and is dispensed alternately from opposite ends of the dispenser in response to successive 90° turns of the valve 67. From the valve 67, the liquid flows into the T connection 40 and then downwardly through the heat exchanger 41 into the vial 51.

In order to insure that all the liquid supplied to the T connection 40 from the liquid supply systems 61, 62 flows downwardly through the heat exchanger 41, a restriction (not shown) may be formed in the transfer line 34 to prevent liquid from backing up into the line 34 from the T connection 40. As the liquids from the systems 61, 62 flow downwardly through the heat exchanger 41, they are discharged through the connector 50 into the sample vial 51, where they are retained along with the condensed vapors collected previously.

It will be appreciated that the connection of the two liquid supply systems to the heat exchanger inlet not only provides a convenient means of supplying these liquids to the sample vial connected to the outlet of the heat exchanger, but also insures that substantially all the condensed vapors are recovered from the walls of the heat exchanger tube 42. In this connection, one of the important advantages of the illustrative system is that the radioactive tracer never passes through any valves or other devices having movable parts, thereby facilitating recovery of the tracer and elimination of equipment memory. Moreover, due to the small volume of the heat exchanger, any fluid contained therein changes at a relatively high rate when fluid

is flowing therethrough. To insure that all the liquids fed into the heat exchanger 41 are discharged therefrom, it is preferred to resume the nitrogen flow through the heat exchanger, via the combustion chamber, for a short interval of about five seconds, for example, after the liquid flow from the two systems 61, 62 has been terminated. (This nitrogen flow can also be used to purge the head-space of the vial 51 as it is removed from the connector 50, prior to placement of the cap thereon, in the manner described previously.) With this system, it has been found that essentially 100% of the radioactive isotope tracer present in the starting material can be recovered in the sample vial 51, when the isotope is in the form of a condensable vapor.

For recovering tracers by reaction with a trapping agent, the gases which are separated from the condensed vapors are passed into a reaction column including means for receiving a liquid trapping agent and reacting the gases with the trapping agent as the gases flow through the column. The reaction column is also provided with means for reversing the direction of the gas flow through the column for discharging the trapping agent and the reaction product from the column, and a sample vial is connected to the reaction column for receiving the trapping agent and reaction product from the column in response to the reversal of the gas flow. Thus, in the illustrative system, the gases discharged from the first sample vial 51 through the discharge passageway 54 in the resilient connector 50 are passed through a valve 70 which, when in the position shown in the figure, conducts the gases through a connector 71 into a second sample vial 72. From the sample vial 72, the gases enter the lower end of a depending stem 73 of a reaction column 74 comprising a series of smoothly contoured reaction chambers 74a interconnected by smoothly contoured necked down portions 74b with the interconnecting walls of the chambers 74a and the necked down portions 74b forming a smooth curvilinear configuration. When the reaction column 74 is used, i.e., when a radioactive isotope tracer is to be recovered by reaction with a trapping agent, a valve 75 is turned 90° from the position shown in the figure so as to feed a preselected amount of liquid trapping agent into an inlet stem in the middle of the reaction column 74 just after the oxygen supply to the combustion chamber 18 is turned on. Thus, gas is already flowing upwardly through the reaction column 74 when the liquid trapping agent first enters the column. With the particular configuration of reaction column provided by this invention, it has been found that the liquid trapping agent becomes uniformly distributed throughout the various reaction chambers 74a, and such distribution is maintained, as long as gas flows continuously up through the column 74. That is, the upward gas flow through the reaction column causes the liquid trapping agent to become distributed along the walls of the bulbous or enlarged reaction chambers 74a while preventing the trapping agent from flowing down through the elongated depending stem 73 at the bottom of the reaction column, so that no liquid trapping agent enters the vial 72.

In order to feed a preselected amount of trapping agent to the reaction column, the liquid is supplied by means of a metering device 77 having a movable piston therein with a predetermined stop position. Thus, the piston 77a is stopped at the same position during each feeding operation, so that the same amount of liquid trapping agent will be supplied for each sample. As long as the valve 75 is in the position illustrated in the figure, the piston 77a in the metering device 77 remains in the position shown in the figure and no liquid flows into the inlet stem 76. When the valve is turned 90° clockwise, the output of the device 77 is connected to the inlet stem 76, and subsequent advancement of the plunger 77a dispenses a preselected quantity of trapping agent into the reaction column 74; although a manually actuated plunger 77a is shown in the drawings, it will be under-



stood that the dispensing of the liquid trapping agent could be made automatically responsive to the turning of the valve 75. After the metered amount of trapping agent has been fed into the reaction column, the valve 75 is returned to its normal position as illustrated in the figure, and the metering device 77 is automatically refilled with liquid trapping agent from a supply bottle 78, the liquid being fed from the bottle 78 into the metering device 77 by means of pressurized nitrogen in the headspace of the supply bottle 78.

As the gases containing the radioactive isotope tracer, such as  $^{14}\text{CO}_2$  for example, are passed upwardly through the reaction column, the radioactive compound is reacted with the trapping agent, such as ethanolamine for example, to form a reaction product which is held within the reaction chambers 74a along with the liquid trapping agent. The amount of reaction product contained in the series of reaction chambers 74a varies along the length of the reaction column, but it has been found that the reaction effected by the particular reaction column configuration provided by this invention traps over 99% of the isotope tracer. The unreacted gases are exhausted from the upper end of the reaction column through a connector member 79 and vented to the atmosphere through a valve 80.

To control the reaction temperature within the column 74, a heat transfer fluid is passed through an annular jacket surrounding the column 74. In this connection, it has been found that the reaction column provided by this invention provides effective heat transfer with a high degree of efficiency when used to carry out gas-liquid reactions. It is believed that the interaction of the upwardly flowing gas with the liquid that is held within the enlarged reaction chambers 74a brings all portions of the liquid into intimate contact with the column walls, thereby effecting efficient heat transfer between the liquid and the column walls.

After the sample combustion has been completed, the flow of nitrogen gas is continued for a suitable purging period, e.g. 30 seconds, and the valve 70 is then turned 90° so as to conduct the purging nitrogen gas into the upper end of the reaction column 74, thereby effecting a reversal of the direction of gas flow through the column. As the gas flows downwardly through the reaction column 74, it sweeps the liquids contained therein, including the reaction product formed by reaction of the liquid trapping agent with the gas compound containing the isotope tracer, into the sample vial 72. The gases are discharged from the vial 72 upwardly through the connector 71 and vented to the atmosphere through the valve 70 via passageway 70a therein.

The valve 70 is then returned to its original position to resume the gas flow upwardly through the reaction column, and the connector 79 at the upper end of the reaction column 74 may be sequentially connected to a pair of liquid supply systems generally indicated at 81 and 82. The first supply system 81 includes a supply vessel 83 containing a liquid solvent to be used to dissolve the reaction product formed by reaction of the isotope compound with the trapping agent; the solvent may also serve to maintain the resultant sample in a liquid condition where it is to be handled at sub-freezing temperatures, as described previously in connection with the liquid supply system 61. An inert gas such as nitrogen is applied to the headspace of the supply vessel 83 under a slight pressure so as to force the liquid solvent through a valve 84 into a metering dispenser 85 including a movable piston 85a. As described previously in connection with the liquid dispensers 65 and 68, the piston 85a moves back and forth within the dispenser 85 in response to successive 90° turns of the valve 84, so as to feed a preselected quantity of liquid solvent through the valve 84 into the connector 79 each time the valve 84 is turned 90°. This liquid flows downwardly into the reaction column 74 and is distributed therethrough in the same manner described previously for the liquid trapping agent

supplied through the inlet stem 76. It has been found that the combination of the upward gas flow and the liquid input at the top of the column, provides a scrubbing action on the inside walls of the reaction column so that substantially all the reaction produce contained therein is recovered in the sample vial 72. In fact, it has been found that the recovery effected by this reaction column is so efficient that it has substantially no memory whatever, and over 99% of the isotope tracer is recovered in the vial 72.

After the first liquid has been dispensed into the top of the reaction column, the nitrogen flow is continued upwardly through the column for a period of about 15 to 45 seconds, depending upon the concentration of  $\text{CO}_2$  relative to the trapping agent. The valve 70 is then again turned 90° to reverse the gas flow through the reaction column, thereby sweeping the liquid solvent downwardly through the reaction column into the sample vial 72. The valve 70 is then again returned to its original position so that the inert purging gas once again flows upwardly through the reaction column, and the liquid scintillator is metered into the upper end of the reaction column from the second liquid supply system 82. More particularly, liquid scintillator is fed from a supply bottle 86 through a four-way valve 87 into a metering dispenser 88. When the valve 87 is turned 90° from the position illustrated in the figure, with the dispenser piston 88a in the position shown, a preselected quantity of liquid scintillator is forced out of the dispenser by the pressure of the nitrogen in the headspace of the bottle 86, thereby advancing the piston 88a to the left to force liquid through the valve 87 into the connector 79 at the top of the reaction column 74. Due to the upward gas flow through the reaction column, this liquid again provides a scrubbing action on the walls of the reaction column 74. After the liquid has been dispersed into the column, the upward nitrogen flow is continued for about 5 to 10 seconds, at which time the gas flow is again reversed in the column 74, by turning the valve 70, to discharge the liquid scintillator into the vial 72. In addition to providing a convenient means of admitting the liquid scintillator into the vial 72, the liquid supply systems associated with the reaction column 74 provide a rapid and efficient means of achieving recoveries in excess of 99% with attendant low memories of  $\frac{1}{1000}$  or less. Moreover, it will be appreciated that the isotope tracer is passed through only a single valve 70, and then only while it is in the gas form, thereby further facilitating complete recovery of the radioactive tracer.

In one illustrative embodiment of the invention, a one-gram sample of tritium-labelled organic material is combusted. The combustion is initiated by the electrical igniter, heated to a temperature of about 1500° C., and the oxygen flow rate is set at about two liters per minute. One 70-milligram shot of water is injected as oxidation begins. The pressure inside the combustion chamber during combustion is less than 0.1 atmosphere above atmospheric pressure. The walls of the combustion chamber are pre-heated and thermostatically maintained at approximately 170° C. which is sufficient to prevent any noticeable condensation of the combustion products on the inside walls of the combustion chamber. During combustion, the combustion products are continuously exhausted through the upper end of the combustion chamber into a heat exchanger, comprising a straight tube of stainless steel having an inside diameter of 0.080 inch, a wall thickness of 0.020 inch, and a length of 10.00 inches. The walls of the tube are maintained at a temperature of about 0° C. From the heat exchanger, condensed vapors including condensed  $^3\text{H}_2\text{O}$  drip into the counting vial connected to the lower end of the heat exchanger, while the remaining gases pass on through the vial and are vented to the atmosphere.

The combustion of the sample is completed in about 45 seconds, after which the oxygen is turned off and

the nitrogen supply to the combustion chamber turned on so that nitrogen is fed into the combustion chamber at a rate of seven liters per minute for about five to ten seconds. The nitrogen is then shut off and a selected quantity of dioxane (liquid scintillator) is fed from the metering dispenser into the inlet of the heat exchanger. The metering dispenser is preset to feed ten milliliters of the liquid scintillator into the heat exchanger over a period of about five seconds, after which the liquid supply line to the inlet of the heat exchanger is closed, and the nitrogen feed to the combustion vessel resumed for an additional five seconds at a rate of about four liters per minute. During this final nitrogen feed, the counting vial is removed from the resilient connector at the outlet of the heat exchanger and tilted with the open mouth of the vial positioned below the passageway from the heat exchanger outlet so that the nitrogen supplied to the counting vial during this interval purges the vial of oxygen. The vial cap is then quickly threaded onto the vial to seal the sample contained therein in a nitrogen atmosphere, and the sample is analyzed for radioactivity.

It will be understood from the foregoing description that the illustrative sample preparation system may be used to prepare samples from starting materials labelled with only a single tracer to be recovered either as a condensed vapor or by reaction with a trapping agent, or from double-labelled samples containing tracers to be recovered by both means. In the event that the material is labelled with only a single tracer to be recovered as a condensed vapor, the gases discharged from the first sample vial 51 are, of course, simply passed on through the balance of the system and vented to the atmosphere. In the case of a sample labelled with only a single tracer to be recovered by reaction with a trapping agent, it is not necessary to supply a liquid scintillator to the heat exchanger 41, although it may be desired to feed some other liquid through the heat exchanger in order to remove the condensed vapors therefrom between successive combustions. Similarly, there is no need to feed any liquids whatever into the reaction column 74 when the sample is labelled with only a single tracer to be recovered as a condensed vapor, since the gas is discharged from the vial 51 and will normally be vented to the atmosphere via valve 70 during the preparation of such samples. If it is desired to prepare only tritium-labelled samples, for example, that portion of the system downstream of the vial 51 may even be eliminated.

It will also be appreciated that any of the manual operations required in the illustrative system may be readily converted to automatic operation. For example, the opening and closing of the oxygen and nitrogen valves 23 and 60, respectively, may be controlled by timing mechanisms according to a predetermined time schedule for particular types of samples. Similarly, the valves 64, 67, 75, 84, and 87 associated with the various liquid supply systems, as well as the valve 70, could be controlled by timing mechanisms according to predetermined time schedules.

I claim as my invention:

1. An apparatus for preparing liquid form samples for radioactive nuclide assays, which comprises:

means including an enclosed combustion chamber for burning material to produce gaseous combustion products,

exiting means at the top of said combustion chamber for exhausting said combustion products,

a receptacle within the lower portion of said chamber for holding the material sample to be burned, the side wall of said chamber extending upwardly and inwardly so as to approximate the shape of the flame of the burning material,

means for supplying oxygen to said combustion chamber,

means for combusting in said chamber, with the oxygen containing gas, a primary sample containing at least one radioactive nuclide oxidizable to recoverable gasiform oxide,

supply means containing an oxide of a non-radioactive isotope of said nuclide having conduit means connected to the combustion chamber,

an injection device interposed in said supply means conduit for introducing to said combustion chamber a predetermined fixed amount of gasiform oxide of said non-radioactive isotope of said nuclide from the supply means determined according to the volume of gas flow leaving the combustion chamber, and means for recovering the resulting mixed gasiform oxides of said radioactive nuclide and said non-radioactive nuclide as a liquid form sample.

2. Apparatus of claim 1 wherein said gasiform oxide introducing means introduces said oxide near the beginning of said combustion.

3. Apparatus of claim 1 wherein said primary sample contains tritium and said gasiform oxide of a non-radioactive isotope is water, and wherein said injection means includes a plunger operated pump and vaporization means disposed in said conduit to convert the water to a gasiform oxide prior to introduction into the combustion chamber.

4. Apparatus of claim 1 wherein said recovering means includes heat exchanger means for receiving combustion products and for condensing the condensable vapors therein, and separating means for receiving said combustion products including the condensed vapors from said heat exchanger and separating said condensed vapors from the balance of the combustion products.

5. Apparatus of claim 1 wherein said primary sample contains carbon-14 and said gasiform of an oxide of a non-radioactive isotope is carbon dioxide, including means defining a closed loop adapted to confine the predetermined fixed amount of the carbon dioxide gas and said injection device include a valve connecting the closed loop with said conduit so that a first position of said valve connects the loop to said supply means for trapping the predetermined amount of said gasiform oxide in the loop, a second position of said valve confines the predetermined amount of gas in the loop and a third position introduces said gasiform oxide to the combustion chamber through said conduit means.

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