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(54) Method of preparing a radioactive isotope-containing liquid, as well as device for generating said liquid.

(57) The invention relates to a method of preparing a radioactive isotope-containing liquid by allowing a solution of a radioactive parent isotope to pass through an adsorption agent in a column, the parent isotope being adsorbed on the adsorption agent and producing there a radioactive daughter isotope by decay, and by then eluting the daughter isotope from the adsorption agent with an eluent. The elution is carried out at elevated temperature.

The invention also relates to a method of preparing a gold-195m-containing liquid by elution of an adsorption agent on which mercury-195m is adsorbed, which agent comprises at least two layers having different adsorption capacities for the parent isotope. The invention further relates to a device for generating a radioactive isotope-containing liquid, which device comprises a column with an adsorption agent, which column is provided with external heating means, to a generator column for said device, and to a method of preparing said generator column.

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METHOD OF PREPARING A RADIOACTIVE ISOTOPE-CONTAINING LIQUID, AS WELL AS DEVICE FOR GENERATING SAID LIQUID.

The invention relates to a method of preparing a liquid comprising a radioactive isotope, by allowing a solution of a radioactive parent isotope to pass through an adsorption agent in a column, the parent isotope being adsorbed on the adsorption agent and producing there a radioactive daughter isotope by decay, and by subsequently eluting the daughter isotope from the adsorption agent by means of an eluent. The invention also relates to a device for generating said liquid, to a generator column for said device, as well as to a method of preparing said generator column.

Radioactive isotopes having a half life up to a few days, are frequently used in medicine for diagnostic purposes. One radioactive isotope which is frequently used for diagnostic purposes is technetium-99m. For certain applications, for example for cardiological investigations, however, the comparatively long half life of technetium-99m, namely 6 hours, is a disadvantage. As a result of this the radioactive material remains circulating in the body for a long period of time, so that immediate repetition of a certain diagnostic examination is not possible.

However, another radioactive isotope, namely gold-195m, has proved to be very suitable for such above-mentioned examinations. Gold-195m is an isotope having a half life of 30.6 sec., and only emits gamma rays, and that of a suitable energy, namely 261 keV, and in a sufficient quantity to enable a good observation by means of apparatus suitable for this purpose, for example a gamma camera.

From Netherlands Patent Application 8002235 in the name of Applicants it is known to generate gold-195m in a satisfactory manner from the radioactive parent isotope mercury-195m. This process is preferably carried out in a so-called radioisotope generator, in this case a Hg/Au generator, from which the user can withdraw a quantity of radioactive isotope-containing liquid at any desired moment. Such an instantaneous production is of great practical importance due to the fast decay of the comparatively short-living isotope.

A radioisotope generator as mentioned above comprises a column having an adsorption agent suitable for the parent isotope. The generator is loaded with the parent isotope by allowing a solution of the parent isotope to pass through the adsorption agent in the column. The adsorbed parent isotope produces the radioactive daughter isotope suitable for diagnostic purposes by decay during a given period of time which depends on the half life of the isotope. The user can withdraw a quantity of liquid comprising the daughter isotope from the generator at any desired instant during this period of time. In this elution process a suitable eluent is allowed to pass through the column, in which the formed daughter isotope dissolves in the eluent and can be collected, but the parent isotope remains in the column entirely or substantially entirely. A large number of adsorption agents and eluents have proved suitable for preparing a gold-195m-containing liquid from the parent isotope mercury-195m.
As is also stated in the above-mentioned Netherlands Patent Application, the adsorption agent in the column may be loaded at will with an activity of mercury-195m varying between, for example, approximately 3 and 80 mCi. As appears from Example X of the same Patent Application, the degree of loading is of influence on the elution efficiency. In the case of a lower loading, an elution efficiency of approximately 70% could be reached, while with a loading with 83 mCi of parent isotope the elution efficiency was at most only 53%.

In practice, i.e. in performing an experiment in a larger animal or for diagnostic applications in a human being, a loading with 83 mCi of mercury-195m as a parent isotope is, however, often insufficient. For one single experiment, an injection, in practice, with 20-40 mCi of gold-195m would be desired. According to the known decay parameters, one millicurie of mercury-195m, adsorbed on an adsorption agent in the generator column, yields 0.458 mCi of gold-195m in the equilibrium condition. This would mean that when the generator is used it would have to contain at least 45-90 mCi of mercury-195m in the adsorbed condition in order to be able to supply a sufficient activity of gold-195m upon elution.

However, because it often occurs that the clinic where the diagnostic examination is carried out, is far remote from the place where the generator is produced, during the production the generator must be loaded with a considerably higher activity of mercury-195m than is necessary for use. This is because the parent isotope mercury-195m has a half life only of approximately 40 hours. When approximately 40 hours are necessary to transport the generator from the site of production to the clinic (including packaging, making ready for shipment, receipt, etc.), the loading with mercury-195m must be approximately twice as high in order that sufficient activity remains when the generator is used. In addition, the elution efficiency or elution yield of radioisotope generators never is 100%. As already stated hereinbefore, an elution of approximately 50% could be reached in a Hg/Au generator with a rather high loading, namely 83 mCi of mercury--195m. This means that the loading would have to be another two times as high in order to be able to withdraw sufficient activity of gold-195m from the generator during use.

Then there is a third factor which contributes to a necessary increase of the degree of loading the generator. In practice, the parent isotope mercury-195m is always contaminated with another mercury isotope, namely mercury-195 having a half life of 9.9 hours. Upon decay, said mercury isotope does not produce the desired gold-195m isotope and consequently does not contribute to the necessary activity of gold-195m. This undesired mercury isotope is formed as a by-product in the preparation of the parent isotope mercury -195m by radiation of a gold "target" in a cyclotron.

All these factors lead to the fact that in the production of a Hg/Au generator it is of great importance to load the generator with at least 200 mCi, preferably with 400-1,000 mCi, of "contaminated" mercury-195m, so that the user can withdraw from it an activity of gold-195m which is sufficient for practical applications.

It has been found, however, that the efficiency of the generator, i.e. the elution efficiency, only decreases when the loading increases. It is hence of great importance to improve

the efficiency of the generator so that also in the case of higher loading of the generator column an elution yield which is sufficiently high for practical applications is reached. Although the above applies in particular to a Hg/Au generator, an improvement of the elution yield is also of utmost importance in other generators where the same or similar problems may occur.

It has surprisingly been found that the elution efficiency can be considerably improved by carrying out the elution at elevated temperature. As will become apparent from the Examples, by doing this the elution yield could be increased by approximately 70%.

A suitable temperature at which the elution can be carried out according to the invention is 30 to 100°C; the best results are achieved at temperatures between 60 and 80°C. In a Hg/Au generator with a loading of mercury-195m of 200 mCi the elution efficiency was found to improve from approximately 38% to approximately 50% when the elution was carried out at temperatures between 60 and 80°C instead of at room temperature.

In this elution at elevated temperatures no disadvantages have been found. With a suitable choice of adsorption agent and eluent, the gold-195m-containing eluate was substantially free from parent isotope, both after the usual elution at room temperature and after elution at elevated temperature. Hence the quality of the eluate was not adversely influenced by carrying out the elution at elevated temperature. On the contrary, the yield of gold-195m was considerably improved, whereas the "contamination" of parent isotope mercury-195m in the eluate did not increase noticeably.

The elution at elevated temperature can be carried out by heating the column, in which the adsorbed parent isotope is present, during the elution. During the elution, both the eluent and the column with adsorbed parent isotope may be kept at elevated temperature. The method according to the invention may in principle be used to improve the elution efficiency during the preparation of various radioactive isotopes-containing liquids, but it is suitable in particular

to improve the elution efficiency during the preparation of a gold-195m-containing liquid by elution of an adsorption agent on which mercury-195m is adsorbed. Moreover, the gold-195m isotope presents excellent perspectives for radio-diagnostic application, in particular due to the favourable radiation characteristics and the simple method of preparation which has become known from the above-mentioned Netherlands Patent Application 8002235.

As another aspect of the invention it has been found that the elution efficiency in preparing a gold-195m-containing liquid can even be further improved by using an adsorption agent for the parent isotope mercury-195m which comprises at least two layers of different adsorption capacities for the parent isotope and, upon loading, leading the solution of the parent isotope through the adsorption agent in such manner that the liquid passes through the layers in a sequence of increasing adsorption capacity. In this manner the elution efficiency can again be improved further by approximately 10% as will become apparent from the Examples.
Fro practical considerations, such a gradient-packed column will preferably comprise not more than approximately 4 layers of different adsorption capacities for the parent isotope, but a column filling having a continuously varying adsorption capacity, so actually comprising a very large number of very thin layers, can also be readily realized.
The use of a gradient-packed column in preparing a gold-195m-containing liquid can give a considerable improvement of the elution efficiency also without elution at elevated temperature as will become apparent from the Examples. A combination of gradient-packed column and elution at elevated temperature, however, gives the best results.

According to the above-mentioned Netherlands Patent Application 8002235, the elution efficiency of a gold-195m-containing generator can be improved by adding a small quantity of sodium nitrate. Such an addition is no doubt an advantage in generators having a smaller loading, for example, up to approximately 160 mCi. In generators having a loading of at least 200 mCi, an addition of sodium nitrate is surely

insufficient and provides only a small improvement of the elution efficiency.

A suitable adsorption agent for the parent isotope mercury-195m is a zinc sulphide-containing adsorption agent on the basis of silica gel, aluminium oxide, natural or synthetic aluminium silicate, active carbon or glass. As a matching eluent for the daughter isotope gold-195m may successfully be used an aqueous solution of thiosulphate. In this case, a gradient-packed column according to the invention may be used with an adsorption agent comprising at least two layers of different contents of zinc sulphide. Particularly favourable results can be achieved with an adsorption agent comprising at least two layers having contents of zinc sulphide increasing from approximately 0.5 to approximately 20 mg of zinc sulphide per g of adsorption agent, preferably, as will become apparent from the Examples, 3 or 4 layers having contents of zinc sulphide of approximately 2, 3 or 6 mg, respectively, or approximately 1, 2, 3 and 6 mg, respectively, of zinc sulphide per g of adsorption agent.

A radiodiagnostic examination in a living being, in particular in a human being, can be carried out by means of the liquid which contains a radioactive isotope and which has been obtained as described above. This examination may be carried out as described, for example, in the above-mentioned Netherlands Patent Application 8002235, by administering the liquid to the living being, preferably directly in the blood circulation of the being, and then recording the radioactivity emitted by the being.

As described in the preamble, the invention also relates to a device for generating a liquid comprising a radioactive isotope, which device comprises a column having an inlet aperture and an outlet aperture, which column comprises an adsorption agent having a radioactive parent isotope adsorbed hereon, and a reservoir for the eluent connected to the inlet aperture. The device according to the invention is suitable for performing in it an elution at elevated temperature. For that purpose, either the column with the adsorption agent, or both the reservoir for the eluent and

the column with the adsorption agent is/are provided externally with heating means, or is/are placed in a room having heating means. For the former method of heating are considered the following heating means: jackets in which a heatable liquid may be present or through which a heatable liquid can be passed, electric heating jackets or heating coils, and/or one or more layers of a semiconducting material to be connected to a voltage source; heating coils, immersion heaters and/or heating plates are preferred for the latter method of heating. The above provision in which the column or the column and the eluent reservoir is or are heated by means of a layer of a suitable semiconductor is to be preferred because this provision can be provided simply and hence cheaply, occupies little space and enable a good temperature regulation and temperature control.

An insulation jacket or insulation jackets around the layer or layers of semiconducting material is, of course, very much desired. An efficacious heating can already be achieved by simply providing the column with adsorption agent externally with a layer of a semiconducting material to be connected to a voltage source. In another favourable embodiment the column comprises between the inlet aperture and the adsorption agent an "empty" space, i.e. a space which is not filled with the adsorption agent, sufficient to comprise a quantity of eluent for at least one elution. When said column, inclusive of the said "empty" space, is provided with external heating means, preferably a layer of a semiconducting material, not only the contents of the column but also the quantity of eluent necessary for one elution is heated during the elution to the desired temperature. In another also favourable embodiment, the column with the adsorption agent is surrounded entirely or partly by a jacket having inlet and outlet apertures through which the eluent can flow, the outlet aperture of the jacket being connected with the inlet aperture of the column. In this latter embodiment the jacket has external heating means, preferably a layer of a semiconducting material, by which the eluent flowing through the jacket during the elution is heated to the desired temperature.

The heated eluent in turn heats the contents of the column to the elevated temperature desired for the elution.
A large number of different known semiconducting materials is suitable to serve as a heating layer. The semiconductor preferably chosen is a material which consists entirely or substantially entirely of stannic oxide or indium trioxide to which a small quantity of antimony trioxide has been added.

Also often a different heating facility is preferred, namely a heating plate, which can be fitted very simply. Such a heating plate is especially suited for heating the air in a room wherein the column is place, for example a lead shielding vessel closed by a lead cover. If an improved temperature control is desired, it is recommended to replace the air surrounding the column by a suitable liquid, having better heat conduction and transfer than air.

According to another aspect of the invention, the device for generating a gold-195m-containing liquid comprises a gradient-packed column, i.e. that an adsorption agent with parent isotope mercury-195m adsorbed hereon is present in the column and comprises at least two layers of different adsorption capacities for the parent isotope, the layers being arranged between the apertures of the column in a sequence of increasing adsorption capacities. This device comprising a gradient-packed column may be constructed, if desired, with a facility for heating column or eluent reservoir and column, as described hereinbefore.
In a very suitable embodiment the column comprises a zinc sulphide-containing adsorption agent on the basis of silica gel, aluminium oxide, natural or synthetic aluminium silicate, active carbon or glass, which adsorption agent comprises at least two layers having different contents of zinc sulphide, preferably increasing from approximately 0.5 to approximately 20 mg of zinc sulphide per gram of adsorption agent.

The invention furthermore relates to a generator column for a device as described above. Said generator column consists of an entirely or substantially cylindrical body which is open at each end and whose apertures are closed by means of rubber stoppers which comprise or may be provided

with connection means from the interior of the body to a reservoir for the eluent and to a receptacle for the radioactive daughter isotope-containing liquid, respectively, said stoppers being connected in or on the open ends of the body so as to seal circumferentially, in which body an adsorption agent for the parent isotope is or can be enclosed between filters which are present inside the body on the upper side and the lower side, respectively, of the adsorption agent. Such a column, as described, for example, in Example X of the above-mentioned Netherlands Patent Application 8002235, consists preferably of a glass tube which at each end is widened and provided with flanged parts, in which tube the adsorption agent is enclosed between filters of sintered glass and porous plastic. The column according to the invention is characterized in that the entirely or substantially cylindrical body has external heating means as desdribed hereinbefore. According to another aspect of the invention the generator column for a device for generating a gold-195m--containing liquid is characterized in that an adsorption agent which comprises at least two layers of different adsorption capacities for the parent isotope mercury-195m is present in the entirely or substantially cylindrical body, the layers being arranged between the filters in a sequence of increasing adsorption capacity. As indicated hereinbefore, said gradient-packed column may also be constructed with a facility to heat the column, as described hereinbefore.

Finally the invention relates to a method of preparing a gradient-packed generator column for a device for generating a gold-195m-containing liquid. As stated in the above-mentioned Example X of Netherlands Patent Application 8002235, a generator column is packed or filled by providing an adsorption agent for the parent isotope mercury-195m on a first filter, which is present in the entirely or substantially cylindrical column body which is open at each end and of which filter the circumference adjoins the inner wall of the body, then providing on the upper side of the adsorption agent in the body a second filter whose circumference also adjoins the inner wall of the body, and finally closing the

two ends of the body with rubber stoppers which comprise or may be provided with connection means from the interior of the body to a reservoir for the eluent and to a receptacle for the radioactive daughter isotope-containing liquid, respectively, by connecting said stoppers in or on the open ends of the body so as to be sealing circumferentially. For filling a gradient-packed generator column according to the invention at least two compositions of different adsorption capacities for the parent isotope are used, while the compositions, arranged in layers in a sequence of increasing or decreasing adsorption capacity are provided on the first filter. Particularly suitable for this purpose are compositions of a zinc sulphide-containing adsorption agent on the basis of silica gel, aluminium oxide, natural or synthetic aluminium silicate, active carbon or glass, having different contents of zinc sulphide, said compositions being provided on the first filter in layers arranged in a sequence of increasing or decreasing zinc sulphide content. After closing the column, the adsorption agent in the column according to the invention may be loaded with parent isotope mercury-195m by allowing a solution of the parent isotope to pass through the adsorption agent through the connection means in the rubber sealing stoppers, for example, tubes or injection needles which are pierced through the stoppers, in such manner that the layers of the adsorption agent are passed through the liquid in a sequence of increasing adsorption capacity. In case a zinc sulphide-containing adsorption agent is used, upon loading a solution of the parent isotope is passed through the adsorption agent in such manner that the liquid passes through the layer in a sequence of increasing zinc sulphide content.

The invention will now be described in greater detail with reference to the following specific Examples.

EXAMPLE I

Figures 1a, 1b and 1c are cross-sectional views of favourable embodiments of heatable generator columns according to the invention. In Figures 1a and 1b, the glass tube (column body) 3 is widened at the two open ends and provided with flanges.

The rubber stoppers 2 are connected to the open ends of the tube by means of caps or folded capsules 1 having a central aperture. The adsorption agent 7 is present between two filters, one filter 4 of sintered glass (G2) on the side of the upper end, i.e. the side where the eluent is admitted to the column, and one filter 8 of porous plastic, for example, of vyon plastic, on the side of the other end, namely where the eluate is drained from the column. The plastic filter is supported by a polypropylene supporting ring 9. The column in Figure 1a can be heated by means of a heating coil, in this case a coiled resistance wire 5 which can be connected to a voltage source. The column in Figure 1c can be heated by means of a layer 12 of semiconducting material which can be connected to a voltage source and which surrounds the central part of the glass tube. The semiconducting material consists of a mixture of stannic oxide and antimoney trioxide. The heating means are enveloped by insultation jackets 6. In the generator column in Figure 1b, the glass tube (column body) 10 is surrounded by a jacket 11 having an inlet aperture and an outlet aperture, so that a heated liquid of a constant temperature can be circulated by pumping (see arrows).

Figure 2 is a cross-sectional view of a suitable embodiment of a gradient-packed generator column according to the invention. Column components corresponding to those of Figure 1 are referred to by the same reference numerals. The column is packed with three layers of different adsorption capacities for the parent isotope mercury-195m, namely layers 15, 14 and 13 with a decreasing content of zinc sulphide per gram of silica gel. The layers 15, 14 and 13 comprise approximately 6, 3 and 2 mg of zinc sulphide per gram of silica gel, the less concentrated layers being obtained from the concentrated layer (approximately 6 mg per gram of silica gel) by dilution with silica gel.

Figure 3 shows the same gradient-packed column as Figure 2 but now also provided with a heating in the form of a layer of a semiconducting material (SnO_2/Sb_2O_3), which layer can be connected to a voltage source. The reference

numerals are the same as used in Figures 1 and 2.

Figure 4 shows a few other embodiments of heatable gradient-packed columns. The glass tube (column body) 16 shown in Figure 4a is so long that besides the packing or filling (13, 14, 15 in decreasing zinc-sulphide concentrations) which is enclosed between the filters 4 and 8, a space 17 remains which can comprise a quantity of eluent which is approximately sufficient for one single elution. The flow of the eluent through the column is indicated by arrows. Simultaneously with the column filling, the quantity of eluent admitted to the space 17 of the column body destined for this purpose, can be heated to the desired temperature by means of a heating in the form of a layer 12 of a semiconducting material, which layer can be connected to a voltage source. The glass tube (column body) 22 shown inFigure 4b is filled with adsorption agent (13, 14 15 in decreasing zinc-sulphide concentrations) in the same manner as the column body of Figure 4a. The column body 22 sealed by double perforated rubber stoppers 19 which are kept in their locations by folded capsules 18 provided with central apertures, is enveloped by a jacket 20 through which the eluent can flow (see arrow). A U-shaped tube 21 comprising sharp ends is pierced through the lower stopper and communicates the interior of the jacket with that of the column. Through this tube the eluent can reach the column filling. After having passed the column filling, the eluate may be drained from the column on the upper side (see arrow). The eluent in the jacket can be heated by means of a layer 12 of a semiconducting material which can be connected to a voltage source, while the column filling can be brought at the desired temperature by the heated eluent in the jacket.

Of course, various heating means are also possible without departing from the scope of the present invention, for example the heating plate mentioned before. A heating plate as such is so well known, that such a device does not need further illustration.

EXAMPLE II

A generator column as shown in Figure 1b and described in

Example I was loaded with mercury-195m by contacting the adsorption agent with a solution of radioactive mercury nitrate having a pH of 5-6, which solution had been obtained by dissolving 200 mCi ^{195m}Hg obtained from a cyclotron target in 2-4 ml of concentrated nitric acid, then diluting the resulting concentrate with water up to approximately 10 ml, and finally bringing at a pH of 5-6. Upon loading the column with radioactive ^{195m}Hg isotope, the column was placed upside down so that the sintered glass filter was present at the top of the column, after which the adsorption agent in the column was contacted with the isotope-containing loading solution by causing the solution to flow through the sintered glass filter into the column. By loading the column in this manner, accidental adsorption of ^{195m}Hg on the plastic structural components of the column is avoided. The adsorption of ^{195m}Hg on the adsorption agent is substantially quantitative in which not more than approximately 0.1% of the activity used was found again in the liquid flowing out of the column after the loading has been completed.

An eluent for the column was prepared by dissolving approximately 29.8 g of sodium thiosulphate ($5H_2O$) and approximately 10 g of sodium nitrate in approximately 1,000 ml of water. The column of the isotope generator was eluted in the reverse position with the eluent by injecting 2 ml under pressure in the generator. In a very short time, namely 2 to 3 seconds, the ^{195m}Au-containing eluate could be collected from the column. The elution was carried out at various temperatures by pumping water of a constant temperature both through a jacket provided around the eluent reservoir and through the column jacket.

The number of millicuries in the eluate was derived from the count rate of the eluate measured on a rapid gamma analyzer with a single channel, the gamma energy channel of 261 keV being used. The resulting count rate was corrected (besides the usual correction factors of geometry, efficiency and dead time) for the loss of counts by the decay of ^{195m}Au during the measuring time and also for the loss of activity during the time lapsed between elution and beginning of the measure-

ment of the counts for each eluate.

The formed number of millicuries of ^{195m}Au in each eluate was normalised to an elution time of 14.00 hours on the day at which the elutions took place so that all results would be directly comparable.

The elution yield which is defined as the percentage of eluted ^{195m}Au with respect to theoretically available ^{195m}Au, was derived from the known number of millicuries at ^{195m}Hg with which the generator column was loaded and the decay parameters (1 mCi of ^{195m}Hg yields 0.458 mCi of ^{195m}Au), while the above normalization was used.

The radionuclidic purity of the eluates was determined by counting—after complete decay of the eluted ^{195m}Au—560 keV gamma rays emitted by ^{195m}Hg remained in the eluates. The found values were expressed either as a percentage of the overall quantity of ^{195m}Hg with which the generator column was loaded, or as the number of microcuries of ^{195m}Hg per millicuries of eluted ^{195m}Au, while all results were again normalized as described above.

In Figure 5 the elution yields Y found, in per cent, are plotted against the elution temperature T: curve N. The improvement of the elution yield at elevated temperature is significant.

EXAMPLE III

A gradient-packed generator column as shown in Figure 3 and described in Example I was loaded with 200 mCi of mercury--195m, as described in Example II, by leading the solution of radioactive mercury nitrate through the column in such manner that the layers were passed by the solution in the sequence of increasing zinc sulphide concentrations, so layer 13 ⟶ layer 14 ⟶ layer 15. The elution was carried out at various temperatures as described in Example II. The elution yields Y shown in Figure 5 were found and plotted against the elution temperature: curve G.

EXAMPLE IV

A gradient-packed generator column as shown in Figure 2 and described in Example I was loaded with quantities of mercury--195m (including mercury 195) varying between approximately

400 and 800 mCi.

For comparison, a column, packed homogeneously with silica gel which had been modified with 6.3 mg of zinc sulphide per gram of silica gel, was loaded in the same manner with quantities of mercury-195m (including mercury-195) varying between approximately 200 and 1,000 mCi.

The elution of the column was carried out at room temperature as described in Example II.

The results shown in Figure 6 were obtained: line 2 represents the average elution yields plotted against the loading which yields were found with the gradient-packed column, line 1 those obtained with the normally, hence homogeneously, packed column. From this Figure it is clear that the elution yield decreases with higher loading, but that the elution yields are higher when a gradient-packed column is used than when a homogeneously packed column is used.

CLAIMS FOR EP:

1. A method of preparing a radioactive isotope--containing liquid by allowing a solution of a radioactive parent isotope to pass through an adsorption agent in a column, the parent isotope being adsorbed on the adsorption agent and producing there a radioactive daughter isotope by decay, and by then eluting the daughter isotope from the adsorption agent with an eluent, characterized in that the elution is carried out at elevated temperature, preferably between 30 and 100°C.

2. A method as claimed in Claim 1, characterized in that during the elution either the column comprising the adsorbed parent isotope or both the eluent and the column comprising the adsorbed parent isotope is/are maintained at elevated temperature.

3. A method as claimed in Claim 1 or 2, characterized in that a gold-195m containing liquid is prepared by elution of an adsorption agent on which mercury-195m is adsorbed.

4. A method as claimed in Claim 3, characterized in that an adsorption agent for the parent isotope mercury--195m is used which comprises at least two layers having different adsorption capacities for the parent isotope, and that the solution of the parent isotope is passed through the adsorption agent in such manner that the layers are passed by the liquid in a sequence of increasing adsorption capacities.

5. A method of preparing a gold-195m-containing liquid by allowing a solution of mercury-195m as parent isotope to pass through an adsorption agent in a column, the parent isotope being adsorbed on the adsorption agent and producing there a radioactive daughter isotope by decay, and by then eluting the daughter isotope from the adsorption agent by means of an eluent, characterized in that an adsorption agent for the parent isotope mercury-195m is used which comprises at least two layers of different adsorption capacities for the parent isotope, and that the solution of the parent isotope is passed through the adsorption agent in such manner that the layers are passed by the liquid in a sequence of increasing adsorption capacities.

6. A method as claimed inClaim 4 or 5 in which a zinc sulphide-containing adsorption agent on the basis of silica gel, aluminium oxide, natural or synthetic aluminium silicate, active carbon or glass is used as an adsorption agent for the parent isotope, and an aqueous solution of thiosulphate is used as an eluent for the daughter isotope, characterized in that an adsorption agent is used which comprises at least two layers of different contents of zinc sulphide.

7. A device for generating a radioactive isotope -containing liquid, comprising a column having inlet and outlet apertures in which is present an adsorption agent with a radioactive parent isotope adsorbed hereon, and a reservoir connected to the inlet aperture of the column, characterized in that either the column with the adsorption agent or both the reservoir for the eluent and the column with the adsorption agent comprise(s) external heating means, or is/are placed in a room or rooms having heating means.

8. A device as claimed in Claim 7, characterized in that the heating means comprise one or more jackets in which a heatable liquid may be present or through which a heatable liquid can be passed, one or more electric heating jackets or heating coils, one or more heating plates or immersion heaters, and/or one or more layers of a semiconducting material to be connected to a voltage source.

9. A device as claimed in Claim 8, characterized in that the column with the adsorption agent externally comprises a layer of a semiconducting material which can be connected to a voltage source, which material preferably consists entirely or substantially of stannic oxide or indium trioxide, to which a small quantity of antimony trioxide has been added, if desired.

10. A device as claimed in Claim 8, characterized in that between inlet aperture and adsorption agent the column comprises a space which is not filled with adsorption agent and which may comprise a quantity of eluent sufficient for at least one elution, and that the column including the said space has external heating means.

11. A device as claimed in Claim 8, characterized

in that the column with the adsorption agent is surrounded partly or entirely by a jacket having inlet and outlet apertures through which the eluent can flow, the outlet aperture of the jacket communicating with the inlet aperture of the column, the jacket having external heating means.

12. A device as claimed in any of the Claims 7-11 for generating a gold-195m-containing liquid, characterized in that an adsorption agent having adsorbed hereon parent isotope mercury-195m is present in the column which comprises at least two layers of different adsorption capacities for the parent isotope, the layers being arranged between the two apertures of the column in a sequence of increasing adsorption capacities.

13. A device for generating a gold-195m-containing liquid comprising a column having inlet and outlet apertures, in which column an adsorption agent having adsorbed hereon parent isotope mercury-195m is present, and a reservoir for an eluent connected to the inlet aperture of the column, characterized in that the column comprises an adsorption agent which has at least two layers of different adsorption capacities for the parent isotope, the layers being arranged between the two apertures of the column in a sequence of increasing adsorption capacities.

14. A device as claimed in Claim 12 or 13, in which the column comprises a zinc sulphide-containing adsorption agent on the basis of silica gel, aluminium oxide, natural or synthetic aluminium silicate, active carbon or glass, characterized in that the adsorption agent comprises at least two layers of different contents of zinc sulphide.

15. A generator column for a device as claimed in any of the Claim 11-13 consisting of an entirely or substantially cylindrical body which is open at each end and the apertures of which are sealed by means of rubber stoppers which comprise or may be provided with connection means from the interior of the body to a reservoir for the eluent and to a receptacle for the radioactive duaghter isotope-containing liquid, respectively, which stoppers are connected in or to the open ends of the body so as to seal circumferentially in

which body an adsorption agent for the parent isotope is or can be enclosed between filters which may be present on the upper side and lower side, respectively, of the adsorption agent inside the body, characterized in that the entirely or substantially cylindrical body has external heating means.

16. A generator column for a device as claimed in any of the Claims 12-14 comprising an entirely or substantially cylindrical body which is open at each end and the apertures of which are sealed by means of rubber stoppers which comprise or may be provided with connection means from the interior of the body to a reservoir for the eluent and to a receptacle for the radioactive daughter isotope-containing liquid, respectively, which stoppers are connected so as to be circumferentially sealing in or to the open ends of the body, in which body an adsorption agent for the parent isotope mercury-195m is enclosed between filters which are present on the upper and lower sides of the adsorption agent, respectively, inside the body, characterized in that the adsorption agent for the parent isotope comprises at least two layers of different adsorption capacities for the parent isotope, the layers being arranged between the filters in a sequence of increasing adsorption capacities.

17. A method of preparing a generator column as claimed in Claim 16 by providing an adsorption agent for the parent isotope mercury-195m on a first filter which is present in an entirely or substantially cylindrical body which is open at each end and the circurmference of which adjoins the inner wall of the body, then providing a second filter on the upper side of the adsorption agent in the body the circumference of which also adjoins the inner wall of the body, and finally sealing the two ends of the body by means of rubber stoppers which comprise or may be provided with connection means from the interior of the body to a reservoir for the eluent and to a receptacle for the radioactive daughter isotope-containing liquid, by connecting said stoppers in or to the open ends of the body so as to seal circumferentially, characterized in that at least two compositions of different adsorption capacities for the parent isotope are used as

adsorption agents, and that the compositions, arranged in layers in a sequence of increasing or decreasing adsorption capacities, are provided on the first filter.

18. A method as claimed in Claim 17, characterized in that after closing the column the adsorption agent in the column is loaded with parent isotope mercury-195m by allowing, through the connection means in the rubber stoppers, a solution of the parent isotope to pass through the adsorption agent in such manner that the layers of the adsorption agent are passed by the liquid in a sequence of increasing adsorption capacities.

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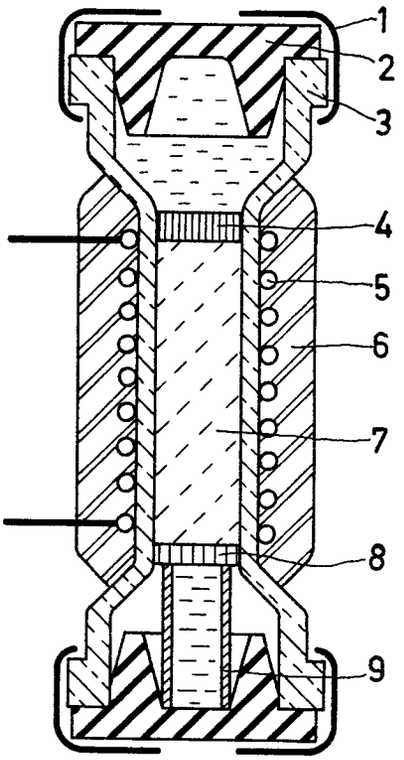

FIG.1a

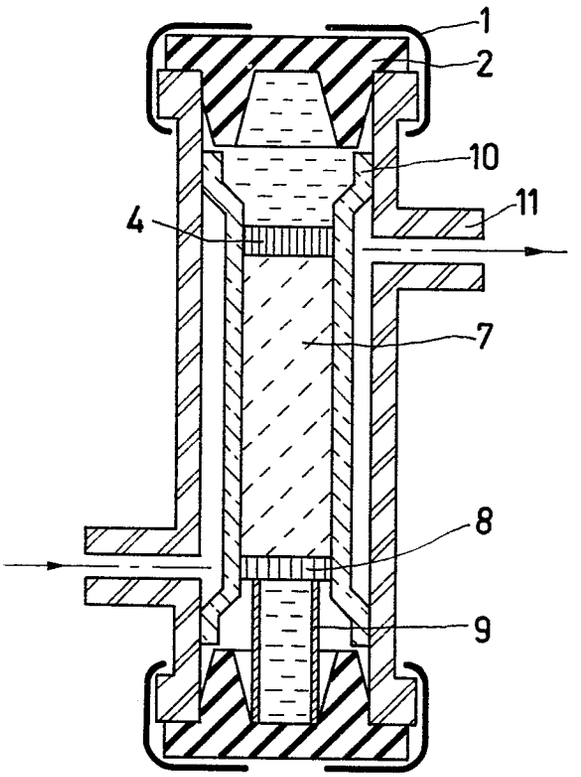

FIG.1b

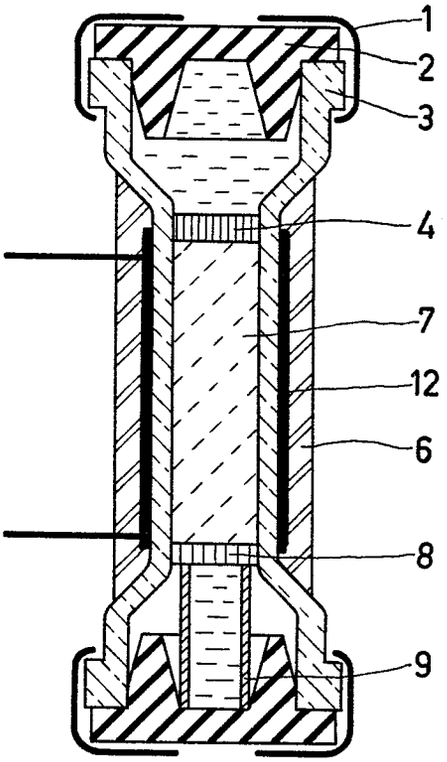

FIG.1c

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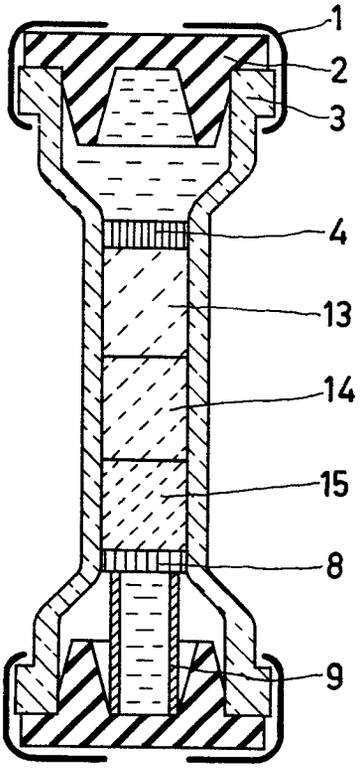

FIG.2

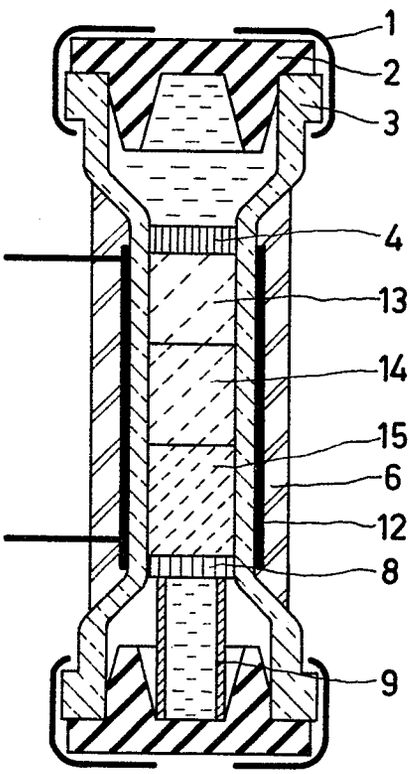

FIG.3

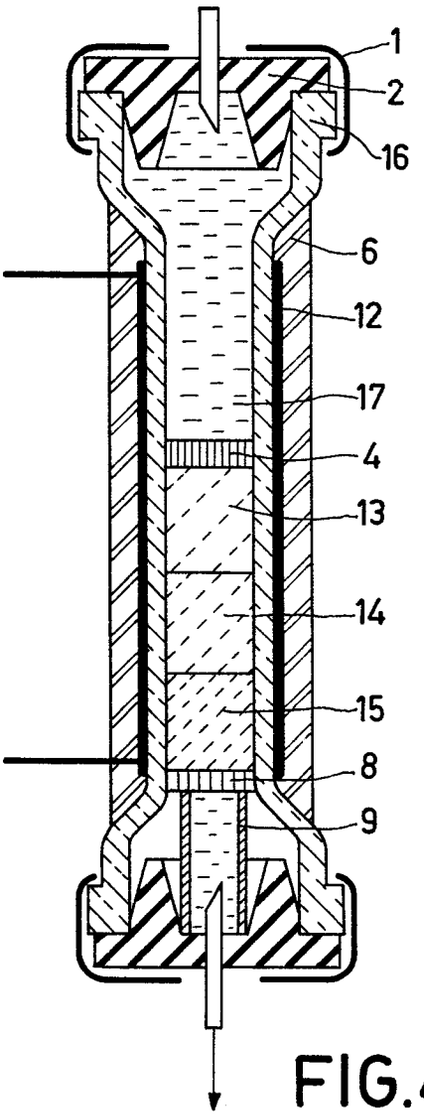

FIG.4a

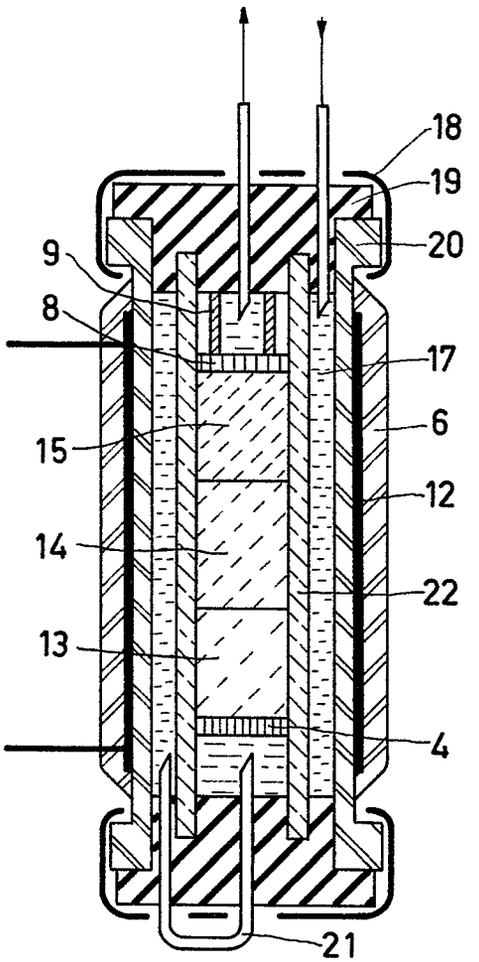

FIG.4b

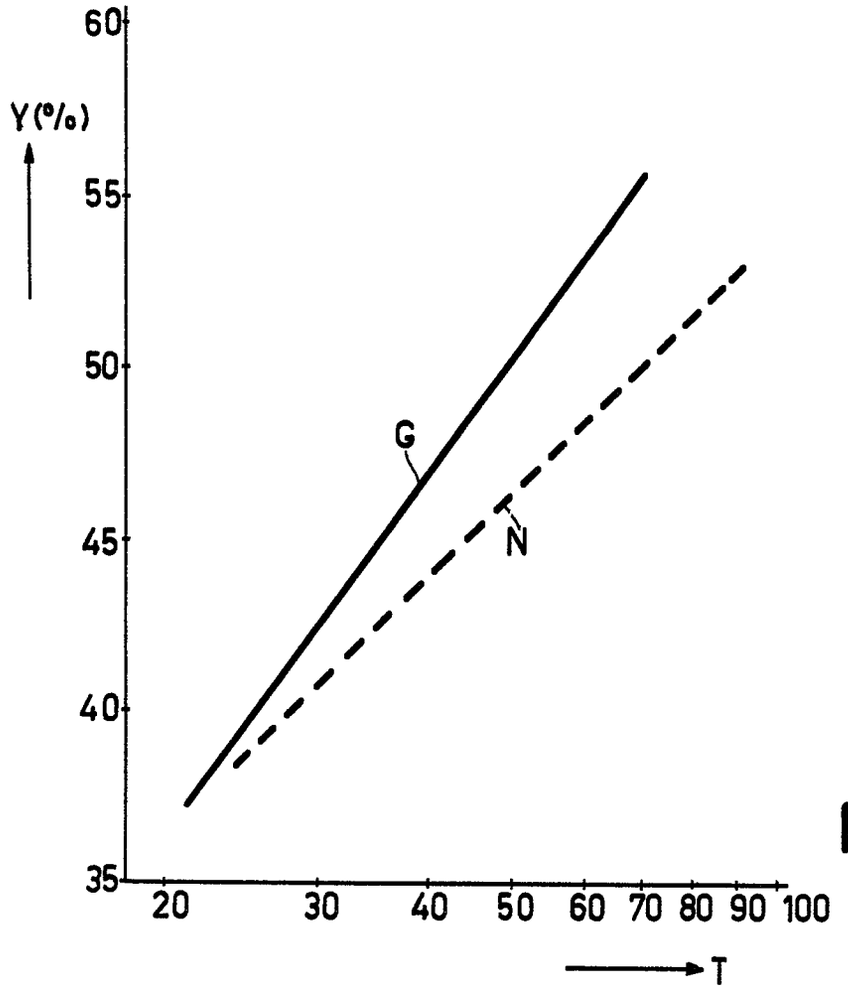
60
Y(%)
55
50
45
40
35
G
N
20
30
40
50
60
70
80
90
100
T

FIG.5

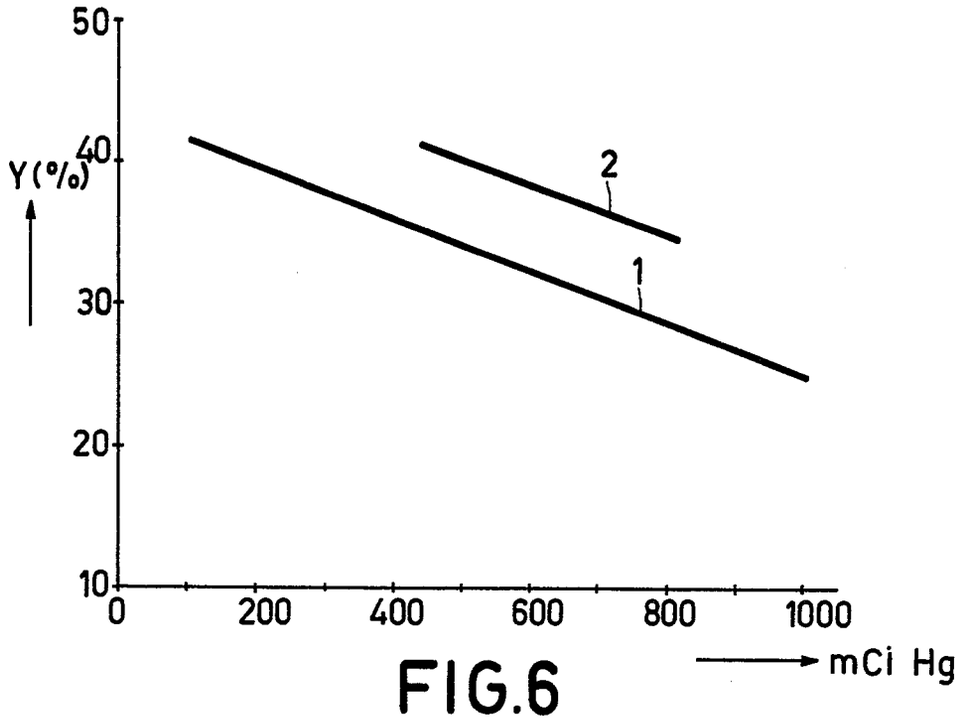
50
Y(%)
40
30
20
10
2
1
0
200
400
600
800
1000
mCi Hg

FIG.6

European Patent Office

EUROPEAN SEARCH REPORT

0096918
Application number

EP 83 20 0774

DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (Int. Cl. ³)
A,D	GB-A-2 047 672 (BYK-MALLINCKRODT) * Claims 1,3-5 *	1,3,6	G 21 F 9/00
A	FR-A-2 110 108 (SMITH) * Claims 1,6-8; figure 1 *	7	
A	GB-A-2 087 633 (UKAEA) * Abstract *		TECHNICAL FIELDS SEARCHED (Int. Cl. ³)
			G 21 G A 61 K

The present search report has been drawn up for all claims

Place of search	Date of completion of the search	Examiner
THE HAGUE	26-09-1983	NICOLAS H.J.F.

CATEGORY OF CITED DOCUMENTS

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