A COLUMN MATERIAL AND A METHOD FOR ADSORBING MO-99 IN A 99Mo/99mTc GENERATOR

Abstract: A column material and a method for adsorbing Mo-99 in a 99Mo/99mTc generator. The invention relates to a column material for adsorbing Mo-99 in a 99 Mo/99m Tc generator, said column material (4) comprising a mesoporous MSU- X Al₂O₃ and/or TUD1-Al material. Preferably, a pore size of the mesoporous material is in the range of 1.5 – 50 nm, more preferably the pore size is in the range of 2 – 30 nm. The invention further relates to a method for adsorbing Mo-99 in a 99Mo/99mTc generator, a column (10) and use of a mesoporous material. Figure

Fig. 1
Title: A column material and a method for adsorbing Mo-99 in a 
\(^{99m}\text{Mo}/^{99\text{m}}\text{Tc}\) generator

FIELD OF THE INVENTION

The invention relates to a column material for adsorbing Mo-99 in a 
\(^{99}\text{Mo}/^{99\text{m}}\text{Tc}\) generator.

The invention still further relates to a column for adsorbing Mo-99 in a 
\(^{99}\text{Mo}/^{99\text{m}}\text{Tc}\) generator.

The invention further relates to a method for adsorbing Mo-99 in a 
\(^{99}\text{Mo}/^{99\text{m}}\text{Tc}\) generator.

The invention still further relates to use of a mesoporous material.

BACKGROUND OF THE INVENTION

An embodiment of a method as is set forth in the opening paragraph
is known from US 5, 910, 971. In the known method a molybdenum-99 isotope
is generated in the uranyl sulphate nuclear fuel of a homogeneous solution
nuclear reactor. The 99-molybdenum isotope is extracted from the fuel by a
solid polymer sorbent. The sorbent is composed of a composite ether of a maleic
anhydride copolymer and \(\alpha\)-benzoin-oxime.

In the known method use is made of the following nuclear reaction
for producing the molybdenum-99 isotope: \(^{235}\text{U} \rightarrow ^{99}\text{Mo} \rightarrow ^{99\text{m}}\text{Tc}\). It is
appreciated that \(^{99\text{m}}\text{Tc}\) is the isotope which has relevant clinical value for
diagnostic purposes. However, \(^{99\text{m}}\text{Tc}\) has a half-life time of about 6 hours which
induces logistic problems associated with generation and delivery of \(^{99}\text{Mo}\)
obtained in the nuclear generator.

An embodiment of a column for production of Molybdenum-99 is
known from RU 2 296 712. The known column is used in the nuclear aqueous
solution reactor wherein molybdenum-99 is being produced. The resulting
molybdenum-99 is being sorbed in a column, washed off the sorbent material and subsequently desorbed and cleaned from radio-nuclides and chemical admixtures.

It is a disadvantage of the known column that complicated post-processing steps are required after the molybdenum-99 isotope has been adsorbed in the column.

A still further embodiment of a process and a device for producing molybdenum-99 is known from WO 2011/081576. In the known method and the device use is made of a solution reactor wherein fuel comprising uranyl sulfate is used. After the nuclear reactor is brought into power the production of molybdenum-99 commences after which the produced molybdenum-99 is sorbed. For purposes of sorbing, the solution containing molybdenum-99 is being pumped through a column comprising a suitable sorbent after which the nuclear fuel may be conditioned and reused.

It is a disadvantage of the known method that sorbing capacity of molybdenum-99 isotope in the known column is sub-optimal.

A still further method of generating $^{98}\text{Mo}^{99m}\text{Tc}$ isotopes is known from US 4, 782, 231. In the know method use is made of a column comprising a molybdenum target which is subjected to a medium flux neutron irradiation.

The resulting isotopes are produced by the following reaction: $^{98}\text{Mo}(n, \gamma) \rightarrow ^{99}\text{Mo}^{99m}\text{Tc}$. The resulting $^{99}\text{Mo}^{99m}\text{Tc}$ is eluted from the column using an elution solution of 0.9% solution of NaCl by weight.

It is a disadvantage of the known method that at least there is a specific maximum to the Mo loading capacity. In addition, it is a disadvantage of the known method that the release efficiency of $^{99}\text{Mo}^{99m}\text{Tc}$ may be relatively low.
SUMMARY OF THE INVENTION

It is an object of the invention to provide an improved method of $^{99m}$Tc generation. In particular, it is an object of the invention to provide an improved method of $^{99m}$Tc generation wherein Mo adsorbing processes in a column are optimized followed by an efficient release of produced $^{99m}$Tc.

To this end in the column material for adsorbing Mo-99 in a $^{99m}$Tc generator, according to the invention, said column material comprises a mesoporous material, having a pore size in the range of 1.5 – 50 nm, wherein for the said mesoporous material either MSU-X Al$_2$O$_3$ and/or TUD1-Al is selected.

It is found that when using a mesoporous material, such as MSU-X Al$_2$O$_3$ and/or TUD1-Al in the column, due to a large surface area of such material, it has a substantially increased capacity than the conventional materials based on Aluminum oxide. It will be appreciated that the MSU-X Al$_2$O$_3$ material, may be adequately referred to as MSU-X, or MSU-X Al$_2$O$_3$.

Accordingly, much higher amounts of Mo can be loaded (adsorbed) in $^{99m}$Tc generators without increasing the volume of the generator. Higher capacity of the generator column allows for the use of $^{99m}$Mo with much lower specific activity (SA) than compared to the devices known from the art. Accordingly, relaxed constrained on SA means that the production of $^{99}$Mo from natural molybdenum rather than from the enriched $^{98}$Mo using a high neutron flux reactor can successfully replace $^{99}$Mo obtained by fission of $^{235}$U. Accordingly, not only the costs of the $^{99}$Mo production may be decreased, but also a substantial contribution to the protection of the environment can be made.

The technical measure of the invention is based on the following insights. According to the practice as is known from the art, a specific quantity of $^{99}$Mo radioactivity and a specific associated Mo mass is loaded onto a specific mass of column material, under specific conditions and procedural approaches,
for purposes of increasing loading efficiency. In addition, specific and complicated measures are undertaken in the prior art methods to avoid Mo breakthrough, and to achieve an efficient release of produced \(^{99m}\)Tc.

Accordingly, the known columns used for adsorption of molybdenum isotopes have to be tuned at least for meeting the following desirable criteria:

i) a specific maximum to the Mo loading capacity;

ii) a specific optimum to the Mo column affinity

iii) a minimum to the \(^{99}\)Mo specific radioactivity (SA) to be applied;

iv) a minimum to the column material mass to be used;

v) a limited number of routes to produce \(^{99}\)Mo of the required high SA;

vi) a limited set of applicable conditions, dictated, for example by column solubility in an elution solution.

It has been found that the limited column Mo capacity (i) requires for a high \(^{99}\)Mo SA (iii), the limited column Mo affinity (ii) may lead to Mo breakthrough incidences, and the overall need of large column mass (iv) implies the necessary large mass of radiation shielding to be implemented into the eventual generator lay-outs. Furthermore, the needed high \(^{99}\)Mo SA (iii) limits the available possibilities for production of \(^{99}\)Mo (v), and experimental approaches and material choices should prevent any column solubility (vi).

Research has indicated that column materials of higher Mo capacity and affinity may permit more Mo to be loaded (i, ii), as well as may permit less column material to be used (iv) with smaller amount of necessary shielding. In addition such column materials may permit \(^{99}\)Mo to be used of lower SA (iii), thereby increasing the production-possibilities for \(^{99}\)Mo in \(^{99}\)Mo-\(^{99m}\)Tc generators. However, an additional feature of the column material should be that it has limited solubility under the conditions of Mo loading and Tc unloading (vi).

It has been found that a material composed of or comprising a mesoporous MSU-X \(\text{Al}_2\text{O}_3\) and/or TUD1-Al materials meets all above criteria and is particularly suitable to be used as a column material for generation
\(^{99}\)Mo\(^{99m}\)Tc as is set forth in the foregoing. The pore size may be in the range of 1.5 – 50 nm, or, preferably in the range of 2 – 30 nm.

It is further found that a material described in US 2006/0052234 is particularly suitable for embodying the column material.

Experimental verification of said column properties is done both in batch approaches, in which column solids and Mo-solutions are mixed for specific mixing time, and in column set-ups, in which \(^{99}\)Mo is loaded and capacity assessment is performed by subsequent elution of 0.9 \% NaCl pH 7 solutions.

Tracking of column (material) properties towards Mo is done by data interpretation routines on Langmuir, Freundlich and other conventional saturation isotherms, thereby specifically giving insight in column Mo capacity and affinity. Basic equations used are the generalized Langmuir isotherm (Rill et al. Langmuir 25 (4),2294 (2009)):

\[
q_e = q_{max} \left[ \frac{(K_c.\mathcal{C}_e)^n}{1 + (K_c.\mathcal{C}_e)^n} \right]^{m/n}
\]

with \(q_e\) as the adsorbed amount of Mo, \(c_e\) as the Mo concentration in solution, \(q_{max}\) as the saturation (maximum) column Mo loading, \(K\) as a constant, to be regarded as the affinity constant, and with \(m\) and \(n\) as surface heterogeneity parameters. For the Langmuir model, \(m\) and \(n\) are both equal to 1, thereby giving

\[
q_e = q_{max} \frac{(K_L.\mathcal{C}_e)}{1 + (K_L.\mathcal{C}_e)}
\]

With \(K_L\) as the Langmuir (adsorption equilibrium) constant. The Langmuir-Freundlich (LF) and Tóth models (T) assume that adsorption energy is not
equal for all sites, as expressed by deviations of \( m \) and \( n \) from unit value. The Langmuir-Freundlich model assumes \( m=n \) (eq 3), the Tóth model assumes \( m=1 \), eq 4)

\[
q_e = q_{\text{max}} \frac{(K_{LF} \cdot c_e)^n}{1 + (K_{LF} \cdot c_e)^n} \tag{3}
\]

or

\[
q_e = q_{\text{max}} \left[ \frac{(K_T \cdot c_e)^n}{1 + (K_T \cdot c_e)^n} \right]^{1/n} \tag{4}
\]

The Freundlich isotherm (F) is a further (empirical) model, with \( K_F \) as the Freundlich affinity constant (see eq 5), which does not limit the adsorption to a monolayer and is often applicable to adsorption on heterogeneous surfaces

\[
q_e = K_F c_e^{1/n} \tag{5}
\]

In addition, an adapted form of the extended Langmuir equation is used (Zhang P., Wang, L. Separation and Purification Technol. 70, 367-371, 2010), as

\[
q_e = q_{\text{max}} \left[ \frac{K_L c_e}{1 + K_L c_e} \right]^{n c_e} e^{c_{\text{max}}} \tag{6}
\]

with \( c_0 \leq c_{\text{max}} \) (\( c_{\text{max}} \) representing e.g. c solubility, for Molybdates reported as ca 65 mg/L at 20 °C), and eq (6) reducing to eq (2) for \( n=0 \).

In experimental verification, mostly eqs 5 and 6 were used.
Column materials, in mixed or un-mixed forms were taken into batch experiments, in which various Mo compounds (e.g. such as dissolved (NH$_4$)$_2$MoO$_4$, Na$_2$MoO$_4$ or MoO$_3$) and were loaded (adsorbed) onto said materials, under variable conditions viz. acidity (e.g. pH 2-8, see Table 2 for various Mo forms depending on acidity), counter ions (e.g. Na$^+$, NH$_4^+$), sorption duration, column pre-conditioning approaches (e.g. washing), and set ionic strength (by adding NaCl). Where considered necessary, all further experiments were performed in Na-acetate (0.15 M) buffered solutions.

Results on sorption time indicate that 10 min is enough to largely reach equilibrium in batches: accordingly all further batch tests were carried out with the 30 min duration to ensure full steady state. Results on Mo sorption for various sorber materials with varying NaCl concentrations show that Langmuir constants decrease with increasing ionic strength. Accordingly, it is found preferably to select the ionic strengths to about 0.15 M.

In addition, a number of experiments are presented for pH 2-3, one using a large range of Mo concentrations (remaining far below Mo solubility values), to derive the column capacity $q_m$ and formation constant K$_L$ (eq 6), and the other one using a Mo range, limited to small Mo concentrations, to derive an expression of affinity K$_F$ (eq 5). The results indicate best performance (regarding both $q_m$ and K$_L$) for MSU-X and TUD1-Al materials, with high Freundlich outcomes relative to conventional sorbers.

It will be appreciated that MSU-X (wormhole) is a commercially available mesoporous material (SIGMA-Aldrich 517747), with $S_{\text{BET}}$=364 m$^2$/g, pore size = 3.8 nm average, particle size 5.65 µm on average.

The TUD1-Al material has $S_{\text{BET}}$=428 m$^2$/g, pore volume = 0.832 cm$^3$/g, and pore diameter 6.3 nm. It will be appreciated that the TUD1-Al material is developed and patented by the Applicant, see US 2006/0052234. For the sake of conciseness the disclosure of US 2006/0052234 is not recited here. However, in particular, the paragraphs [0038] – [0061] are herein incorporated by reference.
In addition to batch experiments, also column experiments were performed, in which $^{95}\text{Mo}$ was preloaded (pH 2) into a 2 g sorber column (column total volume 8 cm height by 0.8 cm Φ), after which extended elutions (up to 100 ml, pH 2, 0.9 % NaCl) were used to monitor column capacity. Results indicate 52.6 mg Mo/g column capacity for (acid γ)-Al$_2$O$_3$ and 101.5 mg Mo/g column capacity for mesoporous Al$_2$O$_3$ (MSU-X), thereby fully substantiating the earlier obtained batch results.

Accordingly, it has been demonstrated that a column material composed of or comprising a mesoporous material as is set forth in the foregoing substantially improved adsorption properties of a column used for $^{99}$Mo/$^{99m}$Tc generation.

The invention further relates to a column comprising the column material as is set forth in the foregoing. Preferably, the column is adapted to form part of an elution system. This embodiment will be discussed in more detail with reference to Figure 1.

The method of the invention of adsorbing Mo from a solution into a sorber material, wherein for the sorber material a mesoporous MSU-X Al$_2$O$_3$ and/or TUD1-Al materials are used, having the pore size of 1.5 – 50 nm. Preferably, the pore size is in the range of 2 – 30 nm.

In a further embodiment according to a further aspect of the invention the solution is acidic having pH in the range of 2 – 3.

In a still further embodiment of the method according to the invention an ionic strength of the solution is about 0.15 mol/L.

Use of a mesoporous material according to the invention is effectuated in a column arranged for adsorbing Mo-99 in a $^{99}$Mo/$^{99m}$Tc generator, wherein for the column material mesoporous MSU-X Al$_2$O$_3$ and/or TUD1-Al materials are used, having the pore size of 1.5 – 50 nm. Preferably, the pore size is in the range of 2 – 30 nm is used.

These and other aspects of the invention will be discussed with reference to drawings wherein like reference signs correspond to like elements.
It will be appreciated that the drawings are presented for illustrative purposes only and may not be used for limiting the scope of the appended claims.

BRIEF DESCRIPTION OF THE DRAWINGS

Figure 1 presents in a schematic way an embodiment of a column provided with a mesoporous material, forming part of an elution system.

DETAILED DESCRIPTION OF THE DRAWINGS

Figure 1 presents in a schematic way an embodiment of a column 4 provided with a mesoporous material, forming part of an elution system 10. The column 4 is provided with a mesoporous material used for adsorbing $^{99}$Mo isotopes. In accordance with the invention, the mesoporous materials are MSU-X Al$_2$O$_3$ and/or TUD1-Al. It will be appreciated that MSU-X Al$_2$O$_3$ (wormhole pores) is a commercially available mesoporous material (SIGMA-Aldrich 517747), with $S_{\text{BET}} = 364 \text{ m}^2/\text{g}$, pore size = 3.8 nm average, particle size 5.65 $\mu$m average. However, it will be appreciated that the MSU-X Al$_2$O$_3$ mesoporous material may have pores which are shaped differently than the wormhole pores.

The TUD1-Al material has $S_{\text{BET}} = 428 \text{ m}^2/\text{g}$, pore volume = 0.832 cm$^3$/g, and pore diameter 6.3 nm. It will be appreciated that the TUD1-Al material is developed and patented by the Applicant, see US 2006/0052234. For the sake of conciseness the disclosure of US 2006/0052234 incorporated herein by reference is not recited. In particular, paragraphs [0038] – [0061] are incorporated herewith by reference.

In accordance with the present embodiment, $^{99}$Mo may be loaded in an alumina sorber and provided in the column 4. The elution vial 2 may be used for supplying a suitable elution liquid via the conduit 2a into the
column 4. Preferably, the column 4 is suitably shielded against emanating radiation, for example using a lead shield 3.

The elution solution may comprise 0.9% NaCl, which may be fed into the column with a flow rate of 1 ml/min. The volume of the column 4 may be as large as 100 ml. The extracted solution may be collected in an extraction vessel 7 using an exit conduit 4a. Preferably, prior to the extraction vessel 7 a suitable filet 6 is arranged.

It will be appreciated that the above eluting scheme is exemplary, not limiting. Any other suitable elution scheme as known from the may be used. For example, the elution scheme known from US2011/0250107 may be used.

While specific embodiments have been described above, it will be appreciated that the invention may be practiced otherwise than as described. Moreover, specific items discussed with reference to any of the isolated drawings may freely be inter-changed supplementing each other in any particular way. The descriptions above are intended to be illustrative, not limiting. Thus, it will be apparent to one skilled in the art that modifications may be made to the invention as described in the foregoing without departing from the scope of the claims set out below.
Claims

1. A column material for adsorbing Mo-99 in a $^{99m}$Tc generator, said column material comprising a mesoporous material, having a pore size in the range of 1.5 – 50 nm, wherein for the said mesoporous material either MSU-X Al$_2$O$_3$ and/or TUD1-Al is selected.

2. The column according to claim 1, wherein the pore size of the mesoporous material is in the range of 2 – 30 nm.

3. A column for a radionuclide generator comprising the column materials according to claim 1 or 2.

4. The column according to claim 3, adapted to form part of an elution system.

5. A method of adsorbing Mo from a solution into a sorber material, wherein for the sorber material mesoporous MSU-X Al$_2$O$_3$ and/or TUD1-Al materials are used having a pore size in the range of 1.5 – 50 nm.

6. The method according to claim 5, wherein the solution is acidic having pH in the range of 2 – 3.

7. The method according to claim 5 or 6, wherein an ionic strength of the solution is about 0.15 mol/L.

8. Use of a mesoporous MSU-X Al$_2$O$_3$ and/or TUD1-Al materials in a column for adsorbing Mo-99 in a $^{99m}$Tc generator.
9. Use according to claim 8, wherein a pore size of the mesoporous MSU-X Al₂O₃ and/or TUD1-Al materials is in the range of 1.5 – 50 nm, preferably in the range of 2 – 30 nm.
**INTERNATIONAL SEARCH REPORT**

**A. CLASSIFICATION OF SUBJECT MATTER**

INV. B01J20/06 B01J20/10 B01J20/18 G21G4/08 G21G1/00

B01J20/08

ADD.

According to International Patent Classification (IPC) or to both national classification and IPC

**B. FIELDS SEARCHED**

Minimum documentation searched (classification system followed by classification symbols)

B01J G21G

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

**Electronio data base consulted during the international search (name of data base and, where practicable, search terms used)**

EPO-Internal, WPI Data

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

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X Further documents are listed in the continuation of Box C.

X See patent family annex.

* Special categories of cited documents:

**A** document defining the general state of the art which is not considered to be of particular relevance.

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<td>WO 2011/106847 A1 (AUSTRALIAN NUCLEAR SCIENCE TEC [AU]; LE VAN SO [AU]) 9 September 2011 (2011-09-09) claims 1-5, 23, 26-32 page 13, line 1 - line 20 page 11, line 32 - line 34</td>
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<td>US 6 129 904 A (VON THIENEN NORBERT [DE] ET AL) 10 October 2000 (2000-10-10) claims 1,2 column 1, line 3 - line 5</td>
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